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# RECENT TRENDS OF INNOVATIONS IN CHEMICAL AND BIOLOGICAL SCIENCES VOLUME I

EDITOR

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## VOLUME - I

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# *PREFACE*

*Chemical sciences and Biological science play an important role in the evolutionary concept of the living world. This book Recent Trends Innovation Chemical and Biological Science: An Approach towards Qualitative and Quantitative Studies and Applications is a considerable effort taken by different authors in the discipline to provide new methodologies of research, its applications, and practical inducements of chemical sciences and Biological Science. The various themes in the book such as application of biological organisms, ethnomedicinal used in different human disorder, biological activity of Indian medicinal plants, Ethnobotanical study ,Ecofriendly energy, Transplastomic plants, Role of Sacred Groves in Biodiversity Conservation, Medicinal property rich plants comphora and Different traditional parts in India its application. It covers topic from environment science like effect of toxic chemical on environment. Also covered point from pharmacognosy like as the pharmacological property of Euphorbiaceae. It cover topic like phytochemistry biochemistry and active ingredients Indian medicinal plants .From chemical science subject like organic and inorganic and as well as applied chemistry included such as the Inorganic Metal Oxide-Polymer Nanocomposites For Near Infra-Red, Qsar: A Useful Tool of Computational Chemistry For Designing New Drug And Predicting Their Biological Activities It also cover there under medicinal and computational chemistry This book acts as an intermediary manual between Chemical sciences with other disciplines paving a way for ideas to new research in the respective arena. The experiments described in the boom chapters are such as should be performed by everyone beginning the study of chemistry, and would also serve as an excellent introduction to a course of qualitative and quantitative analysis. All scientists, academicians, researchers, and students working in the fields of chemistry, biology, physics, materials science, and engineering, among other fields, will find this book quite valuable.*

*This book with valuable book chapters from eminent scientists, academicians, and researchers will surely be a part of almost information for the coming new research taken by the researchers in the field of chemical sciences and other disciplines in the future.*

***Dr. Bassa Satyannarayana***

***Mr. Mukul Machhindra Barwant***

## CONTENT

**Chapter 1**

# ETHNOMEDICINAL PLANTS USED FOR RESPIRATORY DISORDERS IN REASI DISTRICT, JAMMU AND KASHMIR (INDIA)

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**ABSTRACT**

The present enumerated data was directly collected by traditional tribal healers of the Reasi district, Jammu and Kashmir with the aim to identify the ethnic usage of plants used for respiratory disorders during the survey many local, professional, herbalists, occasional practitioners, and traditional healers were brought into confidence to share their ethnic knowledge of their pedigree. After selecting the people discussion was made with the informants in their local language for their ease and was interviewed with a questionnaire the usage of different plant parts and their different processes before taken as medicine were recorded. 22 plant species belonging to 14 families were collected and identification was done by their local and scientific names. The Mimosaceae, Caesalpinaceae, Solanaceae were the most represented family with three species each, followed by Menispermaceae, Asteraceae with two species each. All the remaining 9 families were represented by one species each. The plant part most commonly used to take care of respiratory diseases in the study was reported as Leaf followed by Whole Plant, Root, Stem, Fruit followed by Bark and Flower. Moreover various other plant parts together with Gum and Latex were bring into being in use in a variety of formulations for respiratory diseases treatment.

**KEYWORDS:** Ethnomedicinal, Respiratory Treatment, Reasi, Jammu and Kashmir

## INTRODUCTION

The association of humans and animals to plants originated with the beginning of life on earth (Namdev, 2012). With the progress and need of humans, they recognize and categorize plant material as their importance and necessities of life by which they separated the plants where they can be used (Lichterman, 2004). In India, traditional system of medicine is serving a large portion of the population particularly in rural areas. In India medicinal plants have been used since ancient time. Indian citizens are using spices in their food daily for better health (Jain *et al.,* 2010; Patel & Mahajan 2004). J&K has a rich heritage of over 300 medicinal plants (Kaul, 1997). Other Ethnomedicinal studies (Sarin and Kapur, 1984; Virjee *et al.,* 1984; Kaul *et al.,* 1990; Siddique *et al.,* 1995; Kirn *et al.,* 1999; Kant and Sharma, 2001; Kumar *et al.,* 2009; Sharma *et al.,* 2012) in the State have also listed the medicinal plants of various local areas of Jammu and Kashmir. District Reasi is a hilly area and many sites have no transport facility till date. Due to

less interference of growing population and modernization in these areas or villages, there is a culture, still in existence to use herbs and plants for different ailments in day to day activities for better health. Most of the locals use different recipes and formulations for preparing different medicinal solutions. This knowledge is not documented and is just passed from one generation to another generation through oral transmission and this knowledge hub is gradually deteriorating because the modern young generation has access and interest to the modern technological era and is thus least interested to gather the valuable information from their forefathers. Many new health hazards like Respiratory disorders, Cancer, AIDS, high percentage of Hypertension, Diabetic patients are increasing day by day, challenging the allopathic system and threatening the mankind. This research work is undertaken to document and reveal the Ethnomedicinal properties of the plants used locally in the Reasi District. The aim of this research work is to identify and enlist the number of Ethnomedicinal plants used for respiratory disorders in the district surveyed.

**MATERIALS AND METHODS**

Reasi is one of the Eight, recently created Districts in the UT of Jammu and Kashmir, which came in to being from Ist of April 2007. It is largely a hill District, which enjoys changeable climatic environment, ranging from sub-tropical to the temperate. The District is bordering by District Udhampur on the eastern, District Ramban on northern eastern periphery, District Rajouri on its western & north western split ends, District Jammu on its southern ends and a division of the District also touch District Shopping on Northern periphery. Climatically, a large amount of the area falls in the sub-tropical and the remnant in the temperate. Summers are normally warm and winters are freezing with snowfall on the higher reaches. Reasi is located at 33° 4' 58.1016'' N and 74° 49' 59.9268'' E and the terrain is most mountains. The concerned area of study has very less work done, as one or two research papers and reports (Khan and Dubey, 2015 and Sarver, 2009). Although, the area has rich repository of ethno botanically important plants which are used widely by the tribal communities for fulfill their daily need of life. The data for present research were collected from the locals, tribal, herb sellers. This research work was conducted inReasi district. The ethical approvals were taken from the informants in the form of affirmation with questionnaire. The interviewed and questionnaire studies were recurred a number of times among and between the informants to authenticate and validate the genuineness of their plant based knowledge. Most of the plants, herbarium specimen was significantly examined and acknowledged with the aid of the related literature like Flora of British India, Flora of India, Flora of Jammu, Flora of Udhampur, Flora of Pir Panjal and from the publications.

**RESULTS**

This study anticipated the ethnomedicinal value of 22 plants belonging to 14 diverse families used by the people of Reasi and are enumerated with their Scientific names, Local name, Family and Ethnomedicinal usage as below Table 1.

**Table 1: Ethnomedicinal values of 22 plants**

| Sr. No. | Scientific Name | Local name | Family | Ethnomedicinal usage |
|---|---|---|---|---|
| 1. | *Acacia modesta* Wall | Phulai | Mimosaceae | Bark is used as decoction for throat infection |
| 2. | *Acorus calamus* Linn | Mimosaceae/ Acoraceae | Baria | Rhizome used in preparation of medicine for bronchial disorders and Asthma |
| 3. | *Albizia odoratissima* (L.f.) Benth | Mimosaceae/ Fabaceae | Janaglisiri | Flowers and root are used for lung disorders, bronchitis. Decoction of bark helps in cough. |
| 4. | *Bauhinia variegata* Linn | Caesalpinaceae | Karar | Gargles with bark boiled water helps in throat infections, toothache and Strengthens gum. Flowers decoction helps in cough. |
| 5. | *Butea monosperma* (lam) kuntze | Fabaceae | Palash | Fresh gum is applied to ulcers and sore throat |
| 6. | *Capsella busra pastoris* Medik | Brassicaceae | Chirihalian | A tea made from the plant is used for lung disorders |
| 7. | *Cassia fistula* Linn | Caesalpinaceae | Karangal | Leaves are useful against skin diseases, dry cough and fever. |
| 8. | *Cissampelos pareira* Linn | Menispermaceae | Battalbel/ Thangugli | The plant has been used in cough, asthma and bronchitis Root decoction is used in Pneumonia |
| 9. | *Datura stramonium* Linn | Solanaceae | Datura | Fruit, branch and leaves crushed and dried, if smoked helps in bronchitis and lungs disorder. |
| 10. | *Dioscorea belophylla* (Prain) Haines | Dioscoreaceae | Talad | Its root extract is used to treat asthma |
| 11. | *Grewia optiva* J. R. Drumm. ex. Burret | Tiliaceae | Dhaman | Leaves cure throat infections Powdered plant leaves are taken with honey can stop nose bleeding. |

| | | | | |
|---|---|---|---|---|
| 12. | *Jurinea dolomiaea* Boiss | Asteraceae | Dhup /Gugul | Plant is used in the treatment of Asthma |
| 13. | *Morus alba* Linn | Moraceae | Toot | Extract of leaves and dried fruits used in cough |
| 14. | *Phanera vahlii* Benth | Caesalpinaceae | Maloongarh | Leaves are used in decoction for cough and lung disorders. Meal on leaf plates are believed to cure throat infections. |
| 15. | *Plantago lanceolata* Linn | Plantaginaceae | Goba | Young leaves are used for throat infections. Leaves and roots are helpful in lung diseases. |
| 16. | *Plumbago zeylanicum* Linn | Plumbaginaceae | Chitra | Root is used for treatment of lung disorders |
| 17. | *Rubus ellipticus* Smith | Rosaceae | Aakhey | The juice of fruit is used in the treatment of coughs and sore throat |
| 18. | *Solanum nigrum* Linn | Solanaceae | Khayakhothi | Fruit is useful for high cough, Root bark is useful in burning sensation of throat. |
| 19. | *Solanum surattense* Burm.f | Solanaceae | Neeli Kandiari | Whole herb is useful in asthma |
| 20. | *Sonchus oleraceous* Linn | Asteraceae | Phuldudli | Latex is used for ascites and hydrothorax |
| 21. | *Tinospora cordifolia* (Thunb.) Miers | Menispermaceae | Gloe | Plant is effective for the treatment of tuberculosis. Leaf and stem extract is useful in asthma and cough |
| 22. | *Vitex negundo* Linn | Verbenaceae | Bana | The whole plant is effective in treatment of asthma, cough, bronchitis |

**DISCUSSIONS**

In this research work, number of explorations and investigatory studies were conducted to know the extent of conventional knowledge amid tribal people, such explorations have resulted

in a record of medicinal plant species for the treatment of different respiratory disorder. The tribals do not adore contributing their ancient knowledge with more persons and their wisdom ends with the culmination of their life. However, once evolving understanding with some well-informed and talented medicine men and more customary healers, some details on medicinal service of the plant species have been observed earlier. Although a brief account on ethno-medicinal application of indexed plant species have been confirmed by verifying with the medicine men, well-informed persons, healers and specialized informants of the area, even then further surveys on medicines, healing as well as safety aspects are very much anticipated for human welfare The investigation collected information on 22 plant species noted by the informants for their medicinal use. The Mimosaceae, Caesalpinaceae, Solanaceae were the most represented family with three species each, followed by Menispermaceae, Asteraceae with two species each. All the remaining 9 families were represented by one species each. The plant part most commonly used to take care of respiratory diseases in the study was reported as Leaf followed by Whole Plant, Root, Stem, Fruit followed by Bark and Flower. Moreover various other plant parts together with Gum and Latex were bring into being in use in a variety of formulations for Respiratory diseases treatment. This ethnomedicinal survey of Reasi district have revealed the maximum percentage of plant part used by the locals of the district Reasi for respiratory disorders as Leaves with 21.22% followed by the Whole Plant with 18.18% then the Root usage with 15.15%. The Stem/Rhizome and Fruit with 12.12%, Bark with 9.09%, Flower with 6.06%, and Gum with 3.03% and Latex with 3.03% .The usage of Latex and Gum with 3.03% have also been reported. Leaves, Whole Plant and Roots are the foremost employed plant parts for respiratory ailments, and share of other parts like Stem and Fruits is a bit higher than Bark and Flower that is comparatively low. Latex and Gum are used in very low percentage.

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Chapter
2

# INORGANIC METAL OXIDE-POLYMER NANOCOMPOSITES FOR NEAR INFRA-RED (NIR) REFLECTIVE COATING APPLICATIONS

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**ABSTRACT**

Near infra-red reflective polymer nanocomposites, consisting of nanoparticles dispersed in polymer matrix, have gained interest due to the attractive properties of nanostructured fillers, as inorganic metal oxides, carbon nanotubes and layered silicates. Low volume additions (1-5%) of nanoparticles provide properties enhancements comparable to those achieved by conventional loadings (15- 40%) of traditional fillers. Polymers are considered to be good hosting matrices for composite materials because they can easily be tailored to yield a variety of bulk physical properties. The potential applications of the resultant nanocomposites are various, e.g. automotive, aerospace, opto-electronics. Rising energy costs, pronounced urban heat-island effect and global warming increased the need for intelligent solar heat management solutions like cool coatings. Infrared radiation is responsible for about 50% of the energy coming from the sun. Because of the ultra-high reflectance of solar radiation, the cool coating borne out to reduce the interior temperature effectively. Much interest has attended to roofing materials with high solar reflectance and high thermal emittance, so that interiors stay cool, thereby reducing the demand for air-conditioned buildings. To reduce the heat transmission and save energy NIR reflecting materials can be used as coatings made of polymer composites. Inorganic metal oxide have interesting NIR absorption properties and might be used as a filler in a polymer matrix for NIR reflective applications.

In this chapter, the ability of inorganic metal oxide based NIR reflecting nanoparticles to serve as inorganic-polymer nanocomposites will be exploited.

**KEYWORDS:** Polymer matrix, Nanocomposite, Nano fillers, Cool coatings

## INTRODUCTION

Nanocomposites, nano-scaled particles dispersed or embedded in a host matrix; possess some unique properties of particles and the matrix. Moreover, a strong interfacial interaction between the inorganic nanoparticles and the polymer matrix sometimes led to unexpected new properties in these materials (Chai *et al.*, 2009). In that respect, the metal-polymer nanocomposites have recently gained a wide range of industrial applications such as they are

used in cosmetics, automobile coatings and plastics due to their optical properties (Maile *et al.,* 2005). It has been reported that metal nanoparticles – fillers- have important roles in modifying the properties of various polymers. The effect of fillers on properties of the composite depends on their concentration and their particle size and shape as well as on the interaction with the matrix. The ceramic materials with particle size in the nano-scale have a massive potential market, because of their high surface area, which assures higher surface coverage, higher number of reflectance points and hence improved scattering. In paint formulations, the small particle size allows uniform dispersion by homogenous mixing with binders, which enhances the mechanical strength of the paint after drying (Biswas *et al.,* 2008 and Cavalcante *et al.,* 2009). If we use NIR reflective pigments in the paints, which reflects the NIR range light and pronounce the exterior finishes of the paints. Apart from that dropping the surface temperatures of roofs and walls, which, in turn, reduce the cooling-energy demand of the building in some extent (Levinson *et al.,* 2007). The inorganic NIR reflective pigments are mainly metal oxides and are primarily useful in two major applications: (i) visual camouflage and (ii) reducing heat buildup (Jeevanathan *et al.,* 2007). However, many of these NIR reflective inorganic pigments currently employed on an industrial scale generally comprise toxic metal ions like cadmium, lead, chromium and cobalt and there is a need to develop novel colored, NIR reflecting inorganic nano-pigments that are less hazardous to the environment as nanofillers on nanocomposites.

In general, the IR reflective coatings were made with the matrix acrylic, melamine alkyd, epoxy and polyurethane etc. These synthetic matrices were harmful to environment already, if we loaded the inorganic pigments with this matrix it leads to more toxic. So those, in such case we decide to go with PMMA polymer to reduce toxicity and to reduce the harmfulness to the environment. The IR reflectance and UV resistance coatings are much essential needed in current trends. Due to the global warming unwanted UV and IR radiations are entering our world and affecting the package products. In order to reduce the IR and resist UV radiation we were developed inorganic pigment-based PMMA film for industrially useful coating applications (Stefano Rossi *et al.,* 2020). Aliphatic polyesters such as polylactic acid (PLA), Polycaprolactone (PCL), poly (3- hydroxybutyrate) (PHB) and Polyglycolic acid (PGA) represent important biodegradable polymers, which are now finding commercial applications in combination with bio-based material. Out of all polymers, PMMA is a great 100% recyclable and biocompatible polymer that has been used extensively in environmental and biological systems. Poly (methyl methacrylate) (PMMA) is thermoplastic polyester with excellent properties such as lightweight, low price, biocompatibility, and so on. PMMA or acrylic is a widely used transparent plastic material known for its applications in various markets from car windows, smartphone screens to aquariums. It is a tough plastic, easy to shape and a great alternative to the high cost and less resilient glass.

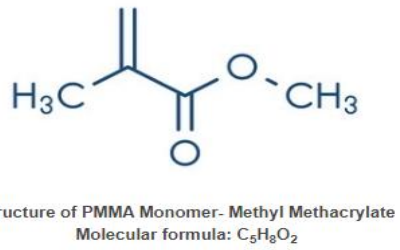


**Fig 1: Structure of PMMA monomer**

These plastic materials can easily be thermoformed without any loss in optical clarity. As compared to polystyrene and polyethylene, PMMA is recommended for **most outdoor application** thanks to its environmental stability. PMMA is a tough, durable and lightweight thermoplastic.

**NIR REFLECTIVE COATING**

Much interest has been tried in the inorganic material/ pigment with high solar reflectance and thermal resistance. Solar radiation consists of 5% UV radiation 43% visible radiation and 52% near- infra red radiation (NIR; 780-2500 nm). The heat producing region of the infrared radiation ranges from 700 to 1100 nm. Color coating with conventional pigments tend to the absorb NIR radiation that bears >50% of the power in sunlight resulting in heat built-up. Complex inorganic materials based on mixed metal oxides (e.g., chromium green, cobalt blue, cadmium stannate, lead chromate, cadmium yellow and chrome titanate yellow), which have been used in camouflage absorb visible light but reflect the NIR portion of incident radiation. However, many of these oxides are toxic and there is a need to develop novel color, NIR reflecting inorganic pigments that are less hazardous to the environment. Recently, the industrial utilization of lanthanides has increased rapidly because of their low toxicity; consequently, a large number of rare earth based NIR reflective pigments have been proposed as alternatives to traditional pigments.

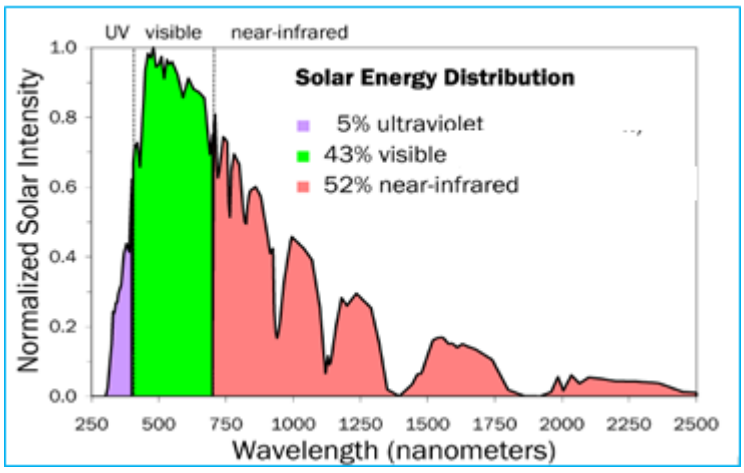


**Fig 2: Solar Energy Distribution**

## SYNTHESIS OF NANOCOMPOSITES

Many methods have been reported for the preparation of polymer-based inorganic particles composites. Historically, the filler incorporation into the polymer matrix takes place through three main methods, *i.e.* (i) the *in situ* polymerization, (ii) the solution casting or (iii) the melt processing**.**

### *1. IN SITU* POLYMERIZATION

This process involves the polymerization of monomer species in the presence of the layered materials. In this process, the nanoclays are first swollen within the liquid monomer or monomer solution, which is followed by its polymerization in between the intercalated sheets (Fig.3a). Polymerization can be initiated either by heat or radiation, by the diffusion of a suitable initiator or by an organic initiator or catalyst fixed through cationic exchange inside the interlayer and before the engorgement step when required. One of the main drawbacks of this method lies in the tendency of inorganic particles to phase separate and sediment quickly from the organic polymer. To enhance the interaction at the solvent/filler interface, specific groups have to be linked onto their surface to stabilize the nanoparticle dispersions. Another relevant aspect concerns the unsuitableness of this method for biomacromolecules such as proteins and polysaccharides (that are already extracted as 'polymerized' entities), which indeed represent target polymers for the generation of bionanocomposites.

### 2. MELT PROCESSING

In the melt processing technique, the nanoparticles are mixed with the polymer in the molten state (Fig. 3b). More specifically, the process involves mixing the particles with the polymer and heating the mixture above the softening point of the polymer, statically or under shear interlayers. The main advantages of the melt processing method are the absence of any solvent throughout the process and its compatibility with current industrial processes, such as extrusion and injection molding. Several factors may affect the extent of exfoliation/intercalation by melt processing, such as the thermodynamic interaction between the polymer and the nanoparticle and the transport/diffusion of polymer chains from the bulk melt into the silicate interlayers. To increase the compatibility between polymer and nanoparticles to ensure proper dispersion, two main factors have to be taken into consideration, namely the favorable enthalpic interaction between the polymer and the nanoparticle (which can be manipulated by chemical modification of the filler and/or the polymer) and proper processing conditions.

### 3. SOLUTION CASTING

The solution casting method is based on a solvent system in which the polymer (or pre-polymer, in case of insoluble polymers) and any other component of the mixture (*e.g.*, surfactants) is soluble. The polymer is usually dissolved in a suitable solvent while the nano-fillers are dispersed in the same or a different solvent before the two are mixed together to generate a homogeneous dispersion (Fig. 3c). The main advantage of this method is the

relatively rapid exfoliation of the stacked layers by the use of an appropriate solvent. The successive addition of polymer solution to the dispersion of the complete delaminated nanoparticles (*e.g.*, platelets) leads to the strong interaction between macromolecules and individual layers. The driving force for the intercalation of the biopolymer into the clay galleries from solution is the entropy gained from the desorption of the solvent molecules, which compensates for the decreased entropy of the confined, intercalated chains. When the solvent is evaporated, the intercalated structure remains which results in the final nanocomposites. Due to the large amount of the solvent required, this method is perceived as unsafe and non-environmentally benign when organic solvents are required (*e.g.*, for non-polar or highly hydrophobic polymers). Conversely, this method has gained increasing attention for water-soluble polymers such as PVOH, especially in the form of thin coatings, which reduces the amount of water used throughout the process. More recently, the solution casting method has been adopted for the generation of bio-nanocomposites, for which both *in situ* polymerization and melt intercalation are often unsuitable due to the inherent characteristics of most biopolymers, as discussed before. From a practical point of view, the fabrication of (bio) nanocomposite films and coatings through the solution casting method requires special attention during the removal of the solvent (evaporation) step. Indeed, if a small amount of solvent remains entrapped in the final product, a lower interfacial interaction between the polymer and the filler can arise. For this reason, coupling infra-red lamps with high performance air ovens is the best strategy to prevent this potential drawback.

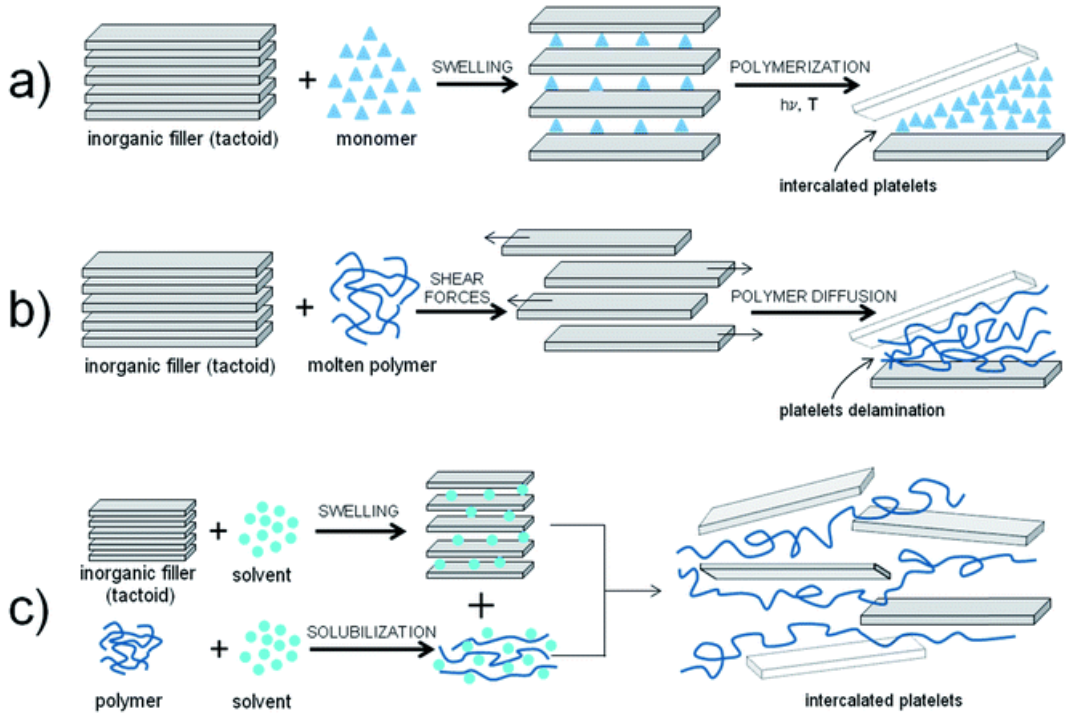


**Fig 3: Schematic representation of (a) *in situ* polymerization, (b) melt processing, and (c) solution casting**

**PROPERTIES OF INORGANIC METAL-POLYMER COMPOSITES**

Polymer-based metal composites were prepared via various processes and showed improved mechanical, thermal and electrical properties. However, the aforementioned properties of resultant metal-composites were not always improved. For example, if one property changed for the better, another property changed for the worse. When metal-composites are designed, one needs to take this tendency into account and find the optimum properties for specific applications.

The choice of the polymer and the dispersed phase is determined by the properties required for the end product. Polymethyl methacrylate (PMMA) has been the primary choice for the preparation of polymeric nanocomposites due to its superior properties such as high strength, compatibility with ceramics, dimensional stability and optical clarity. Moreover, since PMMA is nontoxic, it could be also useful in dentures, medicine dispensers, food handling equipment's, and lenses. It has been found that film of PMMA embedded with inorganic or organically modified inorganic particles show enhanced functional properties such as electrical conductivity, photoconductivity, photo induced charge transfer, nonlinear optical properties, photoluminescence and magnetic properties.

**APPLICATIONS OF INORGANIC METAL-POLYMER NANOCOMPOSITES**

Application of polymer-inorganic nanocomposite are given below

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| Polycaprolactone/$SiO_2$ | Bone-bio erodible for skeletal tissue repair. |
| Polyimide/$SiO_2$ | Microelectronics, electronic |
| PMMA/$SiO_2$ | Dental application, optical devices. |
| Polyethylacrylate/$SiO_2$ | Catalysis support, stationary phase for chromatography. |
| Poly(p-phenylene vinylene)/$SiO_2$ | Non-linear optical material for optical waveguides. |
| Poly(amide-imide)/$TiO_2$ | Composite membranes for gas separation. |
| Polycarbonate/$SiO_2$ | Abrasion resistant coating. |
| Shape memory polymers/SiC | Medical devices for gripping or releasing therapeutics within blood vessels. |
| Nylon-6/LS | Automotive timing-belt-TOYOTA. |
| Nylon-6/clay | Barrier films – Bayer AG |
| Nylon-6/clay | Films and bottles - Honeywell |
| Nylon-6, 12, 66/clay | Auto fuel systems - Ube |
| Nylon-6/PP/clay | Electrically conductive |

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Chapter 3

# BIOLOGICAL ACTIVITY OF TRADITIONAL INDIAN MEDICINAL PLANTS

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**ABSTRACT**

Herbal medicines and phytomedicine have been employed in healthcare systems, since ancient times. Various nations, ethnic groups, and cultures from throughout the world have traditionally employed medicinal herbs. Plants are a potential source of therapeutic compounds with great pharmacological value and significant application in the advancement of healthcare. In both developing and developed countries, the use of herbal medicines to treat many human ailments has enormous potential. Numerous indigenous medicinal plant varieties offer protection against a variety of serious ailments. Secondary metabolites from plants are also becoming quite important in the pharmaceutical and nutraceutical sectors. Products made from traditional system of medicinal plants are reasonably priced, have few adverse effects, and pose little danger. In reality, plants deploy secondary metabolites as defense mechanisms. It strengthens human immunity while also providing defense against bacteria, viruses, parasites, and other serious disorders. It recognizes dangerous compounds entering human body from external environment and destroys them. The plants that are historically utilized for illness prevention and treatment are the subject of the current research. In India, there is a large supply of these medicinal plants with a variety of claimed pharmacological effects. This chapter focuses on those indigenous medicinal plants that can provide defense against a range of human illnesses. A sizable portion of the world's population may find this chapter useful in gaining insight about naturally occurring preventative and therapeutic substances in the traditional medicinal plants of India.

**KEYWORDS:** Medicinal plants, Phytochemicals, Herbal medicine, Pharmacological properties.

## INTRODUCTION

Plant-derived therapeutic items are the most popular, accepted, and acknowledged type of medicine in today's human society worldwide. The basic sources of herbal, pharmacological, and nutraceutical formulations are phytocompounds, which are created by plants in a variety of ways from primary metabolites. These plant's therapeutic and nutritional needs are met by a variety of phytomolecules that have specific biological effects on the human organ system. Different plant components are used by people to create phytomedicine, which serves as a

remedy for contemporary cultures, civilizations and society. Different traditional medicinal plants would be the finest alternative source to acquire high-quality and essential herbal formulations for the treatment and prevention of many ailments [1, 3]. Indian medicinal plants have long been considered a viable source for the treatment of several ailments [4]. Ethno botanicals, natural materials, and their derivatives have demonstrated potential efficacy in the treatment of variety of disorders [5]. Consuming fruits, vegetables, ethno medicinal plants, or their products, in a very efficient manner, generates the defenses against many diseases, since medicinal plants are an incredible source of various phytochemicals, including flavonoids, tannins, terpenoids, polyphenols, steroids, alkaloids, glycosides, chlorophyll, carotenoids, proteins, minerals, and vitamins, which have potent antioxidant properties as well as other biological activities [6, 7]. Around the world, more than 80,000 different species of plants are utilized as medicines, and the majority of them are passed down orally from generation to generation. It implies that the foundation of traditional or folklore remedies is the use of medicinal herbs. Traditional medicinal herbs are currently receiving major attention from the mainstream medical community or healthcare delivery system. Many people in underdeveloped or developing nations continue to use traditional medicines as their main source of treatment for a variety of maladies. These indigenous medicinal herbs are widely utilized as a strong source of alternative medicines to treat a variety of medical conditions. The mainstays of the primary healthcare system for humans are the medicinal plants, due to their accessibility, acceptance, compatibility and cost [8, 9]. In order to create safe and effective herbal formulations, medicinal and aromatic plants are important and significant sources of primary and secondary metabolites that are utilized as templates for lead optimization procedures [10].

Numerous medical professionals and researchers frequently suggest using numerous medicinal plant species or their derivatives to gain protection from a variety of health issues due to their curing potential, ease of availability and cost-effectiveness. The plants examined in this chapter have a long history of use as medicines and are abundant in a variety of bioactive compounds. These herbs are extremely effective against a number of life threatening illnesses, including bacterial and viral infections, diabetes, renal and lung cancer [11, 12]. Hundred species of Indian traditional medicinal plants (herbs, shrubs and trees) are being compiled through this chapter and are shown in the accompanying table. These are incredibly powerful for both preventing and curing a variety of illnesses. By using contemporary pharmacological technology and procedures, these medicinal plants can be exploited to create herbal medicines and efficient nutraceuticals.

**Table 1: Some Important Indian Traditional Medicinal Plants and Their Healing Properties against Various Human Diseases**

| Sr. No. | Botanical Name | Family | Common Name | Phytochemical compounds | Ethnomedicinal Uses | Pharmacological Activities |
|---|---|---|---|---|---|---|
| 1 | *Ocimum sanctum* | Lamiaceae | Holy basil | Phenolics, flavonoids, phenyl propanoids, terpenoids, fatty acid, ursolic acid, apigenin, luteolin, steroids, eugenol, and carvacrol. | It is used for nausea, cold and flu, fever, indigestion, stress, anxiety, earache, bronchitis, malaria, diabetes, asthma, heart disease, snakebite antidote, hepatitis, tuberculosis, genitourinary disorders, migraine, acne, Anti-aging purposes. | Antimicrobial<br>Antioxidant<br>Anti-tussive<br>Anti-inflammatory<br>Anti-diabetic<br>Anti-pyretic<br>Anti-arthritic [13 14] |
| 2 | *Azadirachta indica* | Meliaceae | Neem | Phenolic compounds, alkaloids, glycosides, terpenoids, flavonoids, azadirachtin, nimbin, azharon, nimbidol, azadirone, melianol, steroids, and tannins. | This plant parts are used for the treatment of rheumatism, asthma, fever, worm infestations, bacterial infection, tuberculosis, diarrhea, jaundice, dysentery, to promote healing, measles, smallpox, inflamed gums, urinary Diseases. | Antimicrobial<br>Anti-cancer<br>Anti-fertility<br>Anti-inflammatory<br>Anti-malarial<br>Antioxidant<br>Neuro-protective<br>Insect repellent [15] |
| 3 | *Mentha piperita* | Lamiaceae | Mint | Flavonoids, carbohydrates, alkaloids, phenols, coumarin, saponin, steroids, essential oils (menthol, menthone, pulegone, Menthofuran) azulenes, cholene, carotenes and tannins. | It is used in indigestion, diarrhea, hyperacidity, anemia, morning sickness, bad breath and gum problem, Irritable bowel syndrome, tuberculosis, bronchitis, eczema, acne, anxiety, Crohn's disease, colitis, gallbladder, liver Complaints. | Antibacterial<br>Antioxidant<br>Anti-inflammatory<br>Anti-pyretic<br>Anti-cancer<br>Anti-parasitic<br>Anti-diarrheal<br>Anti-tussive [16] |

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|---|---|---|---|---|---|---|
| 4 | *Zingiber officinale* | Zingiberaceae | Ginger | Phenolic compounds, flavonoids, steroids, triterpenoids, glycosides, tannins, saponins, proteins, carbohydrates, amino acids and proteins,volatile oil. | This plant is used to treat stomach upset, nausea, vomiting, nose bleeds, rheumatism, coughs, chest congestion, cholera, cold, diarrhea, dropsy, stomachache, and baldness,snakebite and toothache. | Analgesic<br>Anthelmintic<br>Anti-arthritic<br>Anti-cancer<br>Anti-diabetic<br>Anti-hypertensive<br>Antimicrobial<br>Antioxidant [15] |
| 5 | *Allium sativum* | Amaryllidaceae | Garlic | Alkaloids, glycosides, saponins, flavonoids, steroids, proteins, carbohydrates, oils, reducing sugars and acidiccompounds. | It is used as natural immunity booster, reduces high blood pressure, diabetes, cardiovascular diseases, and reduces stress, cure nerve problems, skin darkening, and blisteringpurposes. | Antioxidant<br>Anti-cancer<br>Anti-inflammatory<br>Antimicrobial<br>Anti-diabetic<br>Atherosclerosis<br>Anti-hypertensive [13] |
| 6 | *Curcuma longa* | Zingiberaceae | Turmeric | Carbohydrates, protein, curcumin, tannins, alkaloids, saponins, flavonoids, terpenoids and cardiac glycosides, coumarins, and steroids. | It is used to cure burns, cuts, improves digestion, dissolves gallstone, relieves arthritis, prevents cancer, helps in Alzheimer, and inhibits bacteria, virus, fungi, and parasites, cures acne, pimples, allergy, andpores. | Antioxidant<br>Antimicrobial<br>Antiseptic<br>Anti-inflammatory<br>Anti-carcinogenic<br>Anti-allergic<br>Anti-diabetic [13] |
| 7 | *Allium cepa* | Amaryllidaceae | Onion | Flavonoids, carbohydrates, glycosides, proteins, alkaloids, saponins, acid compounds, reducing sugars, oils and tannins. | It is mainly used for common cold, normalizes blood pressure, prevent diarrhea, inhibits microbial infection, increases appetite, treats diabetes, inhibits cancer cell growth, stimulates respiratory tract,helpful in swollen feet, hair growth | Anti-diabetic, Anti-cancer<br>Antimicrobial<br>Antioxidant<br>Anti-platelet<br>Anti-inflammatory<br>Anti-thrombotic<br>Anti-hypertensive [13] |

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|---|---|---|---|---|---|---|
| 8 | *Spinacia oleracea* | Amaranthaceae | Spinach | Flavonoids, carotenoids, β-carotene, apocyanin, ascorbic acid, proteins, amino acids, steroids, tannins, carbohydrates, anthroquinones, coumarin, and saponins. | It is used in digestion, liver and kidney diseases, diuretic, laxative, inflammation of the lungs, bowels, sore throat, ring worm scabies, constipation, anemia, diabetes, fever, brain and heart disease, urinary infection, gallstones. | Anti-diabetic, Antioxidant Anti-inflammatory Anti-carcinogenic Antimicrobial Protection against Gamma Radiation Hepato-protective [17] |
| 9 | *Carica papaya* | Caricaceae | Papaya | Flavonoids, papain, tannins, saponins, alkaloids, phenolic compounds and phytosterols, alkaloids, saponins, and glycosides. | It prevents dengue fever, cancer cell growth, facilitates digestion, menstrual pain, anti- malarial, and helps in IBS, used in skin problems, arthritis, dressing wounds, and cure dyspepsia. | Wound healing Nephro-protective Anti-inflammatory Anthelmintic Antimicrobial Anti-diabetic Analgesic [13] |
| 10 | *Actinidia deliciosa* | Actinidiaceae | Kiwi | Flavonoids, polyphenols, anthocyanin, carotenoids, alkaloids, tannin, proteins, triterpenoids, carbohydrate, and minerals. | Kiwi is used for good digestive health, hair growth, and strong bone, in eye disease, pregnancy period, stress, high blood pressure, cancer, to reduce stone in kidney, lower blood Sugar level, and better sleep. | Anti-diabetic Hepato-protective Dermatological Activity Antioxidant Anti-inflammatory Cardio-protective ACE Inhibitor [18] |
| 11 | *Camellia sinensis* | Theaceae | Green tea | Flavonoids, tannins, caffeine, polyphenols, boheic acid, theophylline, theobromine, anthocyanins, and gallic acid. | Green tea helps in weight loss and metabolism, lowers blood sugar level, used in heart disease, esophageal cancer, high cholesterol, Alzheimer's and Parkinson's disease, helps in depression, good sleep, tooth decay, to reduce wrinkles and signs of aging. | Antioxidant Anti-carcinogenic Anti-arteriosclerotic Antimicrobial Anti-cancer Anti-diabetic Weight control Anti-hypertensive Cardio-protective [19,20] |

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|---|---|---|---|---|---|---|
| 12 | *Prunus dulcis* | Rosaceae | Almonds | Flavonoids, carotenoid, phenolics, tannins, lignans, anthocyanins, phytosterols, polyphenols, and fatty acids. | Almond has memory improving activities, used for insomnia, headache, respiratory troubles, colic pain and peptic ulcer disease, constipation, enhances glow and fairness of skin, cures hair fall, itching, used in kidney stone, ladder, and strengthening of tooth. | Antioxidant<br>Anti-aging<br>Hepato-protective<br>Memory Improving<br>Anxiolytic Activity<br>Hypoglycemic<br>Anti-inflammatory<br>Immuno-stimulant [21] |
| 13 | *Cuminum cyminum* | Apiaceae | Cumin | Alkaloid, coumarin, anthraquinone, flavonoid, glycoside, protein, resin, saponin, tannin and steroid. | It is used against jaundice, lung diseases, nosebleeds, menstrual pains, remedy for colic or diarrhea, digestive problems, stimulates saliva production, excretion of bile, increase production of breast milk, used in menstrual cramp, inhibit formation of tumors, lowers blood sugar, to treat insomnia, fever. | Antimicrobial<br>Anti-inflammatory<br>Antioxidant<br>Anti-diabetic<br>Anti-platelet<br>Anti-cancer<br>Hypotensive<br>Bronchodilatory<br>Anti-amyloidogenic<br>Anti-osteoporotic [13] |
| 14 | *Marsilea quadrifolia* | Marsileaceae | Marsilea | Polyphenols, tannins, saponins, flavonoids, steroids, terpenoids, alkaloids, carbohydrates, and proteins. | It is used to treat cold, respiratory troubles, hypertension, insomnia, anemia, in migraine, epilepsy, diarrhea, bronchitis, hepatitis, to treat snake bite, skin diseases, and inflammation, enhances memory, lowers blood sugar. | Anti-tussive<br>Analgesic<br>Anti-diabetic<br>Anti-pyretic<br>Antimicrobial<br>Anti-tumor<br>Anti-inflammatory<br>Hepato-protective<br>Antioxidant [22] |

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| 15 | *Nigella sativa* | Ranunculaceae | Black cumin | Alkaloids, carboxylic acid, coumarins, phenol, resin, saponin, and steroid, protein, fat, and carbohydrates. | It has been used for the treatment of respiratory problems, digestive tract, and kidney, liver function, cardiovascular system, asthma, inflammatory diseases, externally its oil is used as antiseptic, anesthetic, to stop vomiting, in dropsy, and in treatments of worm and skin eruptions. | Antimicrobial<br>Anti-inflammatory<br>Anti-hyperlipidemic<br>Anti-cancer<br>Anti-diabetic<br>Anti-hypertensive<br>Wound healingactivity<br>Gastro-protective<br>Antioxidant<br>Analgesic [13] |
| 16 | *Lactuca sativa* | Asteraceae | Lettuce | Phenols, flavonoids, triterpenoid, saponins, anthocyanin, β-carotene, ascorbic acid, riboflavin, niacin, carotine, iodine, andfluorine. | The milky leaves of the plant contain 'lactucarium' is used in medicine for its anodyne, digestive, diuretic, hypnotic, narcotic, sedative, to treat insomnia, anxiety, neuroses, dry cough, pain, drowsiness, preventsmicrobial attacks. | Hypoglycaemicactivity<br>Anxiolytic effect<br>Sedative Effect<br>Anti-inflammatory<br>Antioxidant<br>Anti-aging<br>Antimicrobial [23] |
| 17 | *Citrus limon* | Rutaceae | Lemon | Alkaloids, flavonoids, limonoids, steroids, terpenoids, carotenoids, tannic acids and phenolic compound. | Lemon is active against bacteria, reduces inflammation, against fever, prevents scurvy, ulcer, urinary diseases, an antidote against poison, prevents bad breath, body odor, lowers blood pressure, vomiting, liver disorder, enhances immunity, for glowing skin. | Antioxidant<br>Anti-scorbutic<br>Anti-migraine<br>Diuretic<br>Anti-inflammatory<br>Antimicrobial<br>Anti-carcinogenic<br>Anti-pyretic<br>Hypertension<br>Antidote<br>Anti-ulcer [24] |

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| 18 | *Piper nigrum* | Piperaceae | Black pepper | Alkaloids, flavonoid, cardiac glycosides, piperine, piperatine, piperidine, protein, carbohydrats, essential oils, and tannins. | It prevents asthma, arthritis, bronchitis, used in infection that causes diarrhea, headache, stuffy nose, sinus infection, weight loss, menstrual pain, cancer, nerve pain, itchy skin, and people inhale pepper oil to prevent falls, to help quit smoking. | Antioxidant<br>Antimicrobial<br>Anti-inflammatory<br>Anti-thyroid<br>Anti-tumor<br>Anti-asthmatics<br>Anti-diarrheal<br>Anti-depressants [13,15] |
| 19 | *Mangifera indica* | Anacardiaceae | Mango | Alkaloids, flavonoids, saponins, tannins, phenols, ascorbic acid, carotenoids, glycosides and phytosterols. | The leaves are used in the burns and scalds; chewed to strengthen the gums, used for skin ailments, asthma and cough, bark is used for the treatment of fever cholera, rheumatism, to treat ulcerated tongue. | Analgesic<br>Antimicrobial<br>Anti-convulsant<br>Anti-inflammatory<br>Anti-cancer<br>Gastro-protective<br>Hepato-protective [13,15] |
| 20 | *Malus domestica* | Rosaceae | Apple | Phenolics, flavonoids and carotenoid, saponin, glycosides and steroid, carbohydrates, and proteins. | Used in kidney stones, constipation, blood formation, diarrhea, high blood pressure, cardiac problems, useful in sore eyes, inflammation, Alzheimer's, cancer, diabetes, gallstone, obesityloss. | Antioxidant<br>Antimicrobial<br>Anti-inflammatory<br>Anti-diabetic<br>Anti-depressant<br>Anti-asthmatic<br>Anti-cancer [13] |
| 21 | *Musa paradisiaca* | Musaceae | Banana | Alkaloids, flavonoids, tannins, phenolic compounds, carotenoids, anthocyanins, and cardiacglycosides. | It cures depression, treats emotional sickness, increase blood and cures anemia, reduces risk of blood pressure, menstrual cramp, helps to reduce morning sickness, constipation, ulcers, mosquito bites. | Anti-diabetic<br>Anti-hypertensive<br>Antioxidant<br>Anti-diarrheal<br>Antimicrobial<br>Anti-cancer<br>Anti-ulcer [13] |

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| 22 | *Coriandrum sativum* | Apiaceae | Coriander | Flavanoids, alkaloids, tannins, saponin, terpenoids, sterol, carbohydrate, protein, and fat. | It treats indigestion, worm infections, rheumatism, convulsion, insomnia, anxiety, pain in the joints, used as a diuretic plant, in skin disease, effective in constipation, irritable bowel syndrome, diarrhea, measles, toothaches, nausea, hernia. | Antioxidant<br>Diuretic<br>Anti-diabetic<br>Sedative<br>Antimicrobial<br>Anti-convulsant<br>Anthelmintic<br>Anti-mutagenic [13] |
| 23 | *Crinum asiaticum* | Amaryllidaceae | Spider Lily | Alkaloids, flavonoids, tannins, phenols, cardiac glycosides, triterpenes, steroids, saponins, hamayne, palmilycorine, lycoriside, ambelline, crinine, powelline, and ungeremine. | It is used to treat injury and inflamed joints, carbuncles and cancer, to treat wounds by poisoned arrows, bites and stings, swellings, fever, inflammation, piles, to stop bleeding and to treat gonorrhea, induces vomiting, toothache, ulcers. | Analgesic<br>Antimicrobial<br>Anti-inflammatory<br>Antiviral<br>Anti-cancer<br>Anti-tumor<br>Anti-mitotic membrane stabilizing [13, 15] |
| 24 | *Cicer arietinum* | Fabaceae | Chick Peas | Alkaloids, carbohydrates, proteins, amino acids, fixed oils, phytosterols, phenolic compounds and tannins, flavonoids, glycosides, saponins, and amino acids. | Used for insufficient milk or sperm, kidney stones, urine problems, menstruation, treats bronchitis, sunstroke, snake bites, diabetes, hypertension, itchy skin, tumor, increases bone health, controls blood pressure, prevent cancer, develops memory and thinking power. | Antioxidant<br>Anti-hypertensive<br>Anti-cancer<br>Anti-inflammatory<br>Antimicrobial<br>Anti-diabetic<br>Anti-pyretic<br>Anti-cancer<br>Estrogenic [13] |

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| 25 | *Ipomoea aquatica* | Amaranthaceae | Water spinach | Flavonoids, amino acids, alkaloids, lipids, steroids, saponins, phenols, reducing sugars, tannins, β-carotene, glycosides, and minerals. | It helps to reduce cholesterol, treats jaundice and liver damages, anemia, useful for indigestion, constipation, diabetes, prevents heart attack, lowers blood pressure, boosts immunity and treats ulcer, menstruation pain, fever, rejuvenates skin. | Antioxidant<br>Anti-inflammatory<br>Antimicrobial<br>Anti-diabetic<br>Anti-diarrheal<br>Antiseptic<br>Anti-cancer [13] |
| 26 | *Citrus aurantiifolia* | Rutaceae | Lime | Alkaloid, glycoside, saponin, tannin, flavonoids, steroids, terpenoids, limonene, pinene, sabinene, protein, ascorbic acid and polyphenols. | It is used in headaches, cold, fever, insomnia, indigestion, to treat diarrhea, chest pain, snake bite, cancer, itching, dandruff, skin diseases, to glow skin, boiled root with alcohol is drunk to abort foetus, It prevents from microbial attack, allergy. | Antimicrobial<br>Anti-cancer<br>Antioxidant<br>Immuno-modulatory<br>Anti-obesity, Anti-fertility<br>Anthelmintic<br>Anti-pyretic<br>Hepato-protective<br>Cardio-protective [24] |
| 27 | *Citrus sinensis* | Rutaceae | Orange | Phenolics, flavonoids, carbohydrates, alkaloids, tannins, fixed oils and lipids, sugars, proteins, terpenoids, steroids, and amino acids, ascorbic acid and carotenoids. | The fruit is appetizer and blood purifier, used to treats bilious diarrhea, acne, skin disease, itching, obesity, enlarged spleen, constipation, coughs, dyspepsia, prevents digestive tract ailments, nerve disorder, blood pressure, it relieves headache and cures rheumatism. | Antimicrobial<br>Anti-parasitic<br>Anti-proliferative<br>Insecticidal<br>Relaxant, Sedative<br>Anxiolytic<br>Protective of UV<br>Anti-osteoporotic<br>Anti-obesity<br>Hypo- cholesterolemic<br>Antioxidant [24] |

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| 28 | *Aegle marmelos* | Rutaceae | Stone apple | Phenols, flavonoids, alkaloids, cardiac glycosides, saponins, terpenoids, steroids, carbohydrate, tannins, and proteins. | Fruits and leaves are used for wound healing, curing digestive disorders, ulcers, headache, hypertension, diabetes, promotes digestion, fight against cholera, diarrhea, to cure constipation, scurvy, skin disorders, liver, heart, kidney problems. | Antimicrobial<br>Anti-cancer<br>Anti-inflammatory<br>Laxative,<br>Hepato-protective<br>Insecticidal<br>Anti-diabetic<br>Anti-diarrheal<br>Anti-ulcer<br>Antioxidant [25] |
| 29 | *Petroselinum crispum* | Apiaceae | Parsley | Flavonoids, volatile oils, proteins, minerals, carotenes, carotenoids, ascorbic acid, coumarins, tocopherol, myristicin, essentials oils and phenolic compounds, Vitamin-A, B and C. | Used to treat asthma, bladder infections, bruises, cough, cracked or chapped skin, digestive problems, swelling, insect bites, Prevents tumor, liver disorder, kidney stones, high blood pressure, diabetes, obesity, anemia, osteoarthritis. | Antioxidant<br>Anti-diabetic<br>Anti-platelet<br>Antimicrobial<br>Hypotensive<br>Anti-pyretic<br>Gastro-protective<br>Cyto-protective<br>Laxative<br>Analgesic [26] |
| 30 | *Cymbopogon citratus* | Gramineae | Lemon Grass | Alkaloids, glucosides, phenols, saponins, flavonoids, tannins, terpenoids, resins, citral, citronellal, cymbogonol, $\alpha$-terpineol, citronellic acid, $\alpha$-camphorene, geranial, isoscoparin. | Used to treat digestive problems, cramping pains, coughs, fever, to reduce swelling, improve blood circulation, bladder problems and leprosy, oil is used as an insect repellent, detergent, carminative for cholera. | Analgesic<br>Anthelmintic<br>Antimicrobial<br>Anti-neoplastic<br>Anti-malarial<br>Antioxidant<br>Hepato-protective<br>Hypoglycaemic<br>Radio-protective [13, 15] |

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| 31 | *Aloe barbadensis* | Asphodelaceae | Aloe vera | Flavonoids, alkaloids, aloin, carbohydrate, tannin, steroid, triterpenoids, glycosides, saponins, salicylic acids, amino acids, and beta- carotene. | Treatment of pimples, acne and mouth ulcers, laxative, wash for piles, burns, edema, pain, swellings and wounds, Juice used to increase menstrual flow and for eye disease, used in case of any type of skin problem. | Angiogenic<br>Anti-inflammatory<br>Anti-cancer<br>Antimicrobial<br>Antioxidant<br>Dermatitis<br>Gastric mucosal<br>Wound healing [15] |
| 32 | *Capsicum annuum* | Solanaceae | Chili | Flavonoids, carotenoids, phenolics, capsaicin, solasdine, scopoletin, capsaicinoids, and ascorbic acid. | It is used to cure toothache, also used to increase blood circulation and stimulate gastric activities, used to treat arthritis, neuralgia, lumbago and chilblains. | Antimicrobial<br>Anti-cancer, Antioxidant<br>Anti-protozoal<br>Immuno-modulatory<br>Pesticidal [15] |
| 33 | *Ananas comosus* | Bromeliaceae | Pineapple | Flavonoids, saponins, tannins, alkaloids, terpenoids, anthraquinones, carbohydrate, steroids, phenols and glycoside. | Pineapples are rich in nutrients, low in calories, fights with oxidative stress, to treat indigestion, reduce cancer, boosts immunity, suppress inflammation, to recover surgery, kill parasites, gout, bronchitis, ulcer, cystic fibrosis. | Anti-inflammatory<br>Hypolipidemic<br>Laxative, Diuretic<br>Antimicrobial<br>Anti-obesity,<br>Anti-diarrheal<br>Antioxidant [13] |
| 34 | *Centella asiatica* | Apiaceae | Pennywort | Flavonoids, tannins, alkaloids, carbohydrate asiaticoside, asiatic acid, brahmic acid, brahmoside, asiaticin, centellicin, terpenoids, sterols, triterpenoids and saponins. | Used to cure diarrhea, diuretic, gravel, leprosy treatment, stones, wound healing the plant is used in cooling drinks when boiled, treatment of nervous system, skin, and blood diseases, treatment for cancer, circulatory stimulant, headache, urinary discharges, peptic ulcer and sore throat. | Antimicrobial<br>Anti-depressant<br>Antioxidant<br>Anti-thrombotic<br>Anxiolytic<br>Gastro-protective<br>Immuno-modulatory<br>Nerve-regenerative<br>Wound healing [13, 15] |

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| 35 | *Agaricus bisporus* | Agaricaceae | Mushrooms | Alkaloids, flavonoids, phenols, tannins, saponins, terpenoids, cardiac glycosides, proteins, carbohydrates, fibers, and ascorbic acid. | It is effective in diabetes, cancer, hardening of arteries, to cure digestive problems, ulcer, hepatitis B, colitis, high cholesterol, osteoporosis, asthma. | Anti-cancer<br>Anti-diabetic<br>Antimicrobial<br>Antioxidant<br>Anti-ulcer<br>Anti-hepatitis<br>Hepato-protective [27] |
| 36 | *Trigonella foenum-graecum* | Fabaceae | Fenugreek | Flavonoids, alkaloids, terpenoids, steroids, saponins, anthocyanins, tannins, volatile oils, phenol, carbohydrates, fat, amino acids and quinones. | It is used to lower blood sugar, reduce menstrual cramps, sexual problems, used as antacid, treats dysentery, stomach disturbances, respiratory infections, fever, and hormonal disorders, induce labor pain, and inducelactation, hair growth. | Carminative<br>Gastric stimulant<br>Anti-diabetic<br>Hypolipidemic<br>Anti-ulcer<br>Antimicrobial<br>Antioxidant<br>Anti-inflammatory<br>Antacid [28] |
| 37 | *Chrysanthemum morifolium* | Asteraceae | Chrysanthemum | Alkaloids, phenols, flavonoids, caffeoylquinic acids, terpenoids, aardiac glycosides, steroids, tannins and saponins. | It is used to cure chest pain, diabetes, and fever, cold, swelling, cancer, to treat headache, inflamed eyes, and pain in the throat, boil syndrome, vertigo, tonic, urinary stones, and swelling feet. | Antimicrobial<br>Antioxidant<br>Anti-cancer<br>Anti-inflammatory<br>Anti-tussive<br>Anti-ulcer<br>Anti-diabetic<br>Gastro-protective [29] |

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| 38 | *Phyllanthus emblica* | Phyllanthaceae | Indian Gooseberry | Falvonoids, saponins, tannins, cardiac glycosides, alkaloids, anthraquinones, phlobotanins steroids, andcarbohydrates. | This plant is used for the treatment of jaundice, inflammation, diabetes, cough, asthma, bronchitis, dyspepsia, anemia, cures colic, peptic ulcer, skin diseases, cardiac disorders, dizziness, snake bite, vomiting, and gonorrhea. | Antimicrobial<br>Laxative<br>Anti-diabetic<br>Anti-diarrheal<br>Analgesic<br>Anti-pyretic<br>Hepato-protective<br>Cardio-protective<br>Anti-cancer[13] |
| 39 | *Boerhaavia diffusa* | Nyctaginaceae | Punarnava | Phenols, flavonoids, terpenoids, reducing sugar, ligans, organic acids, boeravinones, flavone, isoflavone, flavonol, xanthone, lignin, purine nucleoside, and sterols. | It is beneficial in treating obesity, dropsy, liver diseases, bacterial, fungal infections, intestinal worms,and bronchial tubes, treats asthma, ulcers, skin diseases, swelling, anemia, nervous weakness, paralysis, constipation, cough, mild laxative, and improves appetite, cure jaundice. | Laxative<br>Cardio tonic<br>Stomachic<br>Anthelmintic<br>Anti-inflammatory<br>Antimicrobial<br>Anti-metastatic<br>Immuno-modulatory<br>Anti-proliferative<br>Anti-estrogenic<br>Gastro-protective [30] |
| 40 | *Coccinia grandis* | Cucurbitaceae | Ivy Gourd | Alkaloids, glycosides, saponin, amyrine, lupeol, cucubbitacin, cephalandrol, cephalandrine, flavonoids, saponin and polyphenols. | It is useful treatment for diabetes, cancer, eye problems, skin eruptions, it is laxative, treats headache, rheumatism, high blood pressure, endocrine system disorder, stimulate weight loss, malaria, helps in constipation, hypertension, skin wounds, infections. | Anti-pyretic<br>Anti-ulcer<br>Antioxidant<br>Hepato-protective<br>Anti-cancer<br>Anti-malarial<br>Anti-diabetic<br>Analgesic<br>Anti-dyslipidemic [15] |

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| 41 | *Nyctanthes arbor-tristis* | Oleaceae | Night-flowering Jasmine | Flavonoids, terpenoids, saponins, steroids, carbohydrates, cardiac glycosides, alkaloids, proteins and tannins. | It is used in various ailments like fever, enlargement of spleen, malaria, blood dysentery, gastritis, anemia, also used to treat infection of scalp, piles, skin disease, and stem bark cures rheumatic joint pain, eye disease, internal injury, diarrhea, other infections. | Anti-allergy<br>Anti-inflammatory<br>Anti-filarial<br>Antimicrobial<br>Antioxidant<br>Anti-cancer<br>Anti-diabetic<br>Anti-malarial<br>Anti-leishmanial [31] |
| 42 | *Euphorbia hirta* | Euphorbiaceae | Asthma Weed | Alkaloid, flavonoids, saponins, terpenoids, tannin, polyphenols, sugar, amino acids, euphorbon, and euphosterol. | It is used to cure asthma, calculus, cough, eruptions, headache, hypertension, measles, nausea, stomachache, warts and wounds, athlete's foot, dysentery, enteritis, fever, gas, itch, skin conditions. | Analgesic<br>Antimicrobial<br>Anti-diarrheal<br>Anti-inflammatory<br>Anti-platelet<br>Anxiolytic<br>Gastro-protective<br>Molluscicidal [32] |
| 43 | *Moringa olifera* | Moringaceae | Drumstick | Alkaloids, flavonoids, steroids, tannins, saponins, glycosides, carotenoids, ascorbates, tocopherols, beta-sitosterol, moringine, and kaempferol. | It is used to treat ear infection, eye infection, toothache, cold, HIV, male impotency, blood sugar, it helps to treat high blood pressure, fever, typhoid, malaria, indigestion, diarrhea, boost immunity, cure skin diseases, treats snake bite, improves lactation in mother. | Oxidative DNA damage<br>Cardio-protective<br>Anti-proliferation<br>Hepato-protective<br>Hypolipidaemic<br>Hypercholesterolemic<br>Antioxidant<br>Anti-inflammatory<br>Antinociceptive<br>Antimicrobial [33] |

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| 44 | *Hygrophila spinosa* | Acanthaceae | Swamp Weeds | Alkaloids, flavonoids, tannins, saponins, steroids, terpenoids, phytosterol, minerals, polyphenols, proanthocyanins, mucilages, ascorbic acid, amino acids, and glycosides. | It is used to treat biliousness, blood disorders, gonorrhea, diarrhea and fever, urinary affections, rheumatism, hepatic obstruction, urinary calculi, inflammations, eye diseases, cough, joint pains, anemia, abdominal disorders. | Anti-inflammatory<br>Anti-tumor<br>Anti-pyretic<br>Hepato-protective<br>Diuretic<br>Antioxidant<br>Antimicrobial<br>Analgesic [34] |
| 45 | *Bacopa monnieri* | Plantaginaceae | Waterhyssop | Flavonoid, tannin, phlobatannin, saponin, steroid, cardiac glycoside, polyphenol, carbohydrateand alkaloids. | It contains antioxidants, protects against cell damage, prevents Alzheimer's, Parkinson's disorders, reduces inflammation, cure diabetes, heart & kidney disease, boosts brain function, prevent anxiety, stress, lower blood pressure,<br>Inhibit tumor cells, epilepsy. | Anti-depressant<br>Anti-anxiety<br>Anti-cancer<br>Anti-inflammatory<br>Antioxidant<br>Anti-ulcer<br>Analgesic<br>Hypertensive<br>Anti-diarrheal [13] |
| 46 | *Justicia adhatoda* | Acanthaceae | Malabar Nut | Alkaloids, anthraquinoes, flavonoids, carbohydrate, proteins, saponins, phytosterols, triterpenoids,and polyphenols. | Different parts of the plants have been used in cough, cold, asthma, bronchitis, tuberculosis, allergy, wound healing, it prevents intestinal parasites, dysentery, helps in skin disease, scabies etc. chest congestion, breathing problems, spasms. | Anti-tussive<br>Hepato-protective<br>Antimicrobial<br>Anti-ulcer<br>Anti-inflammatory<br>Abortifacient<br>Cardio-protective<br>Thrombolytic [35] |

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| 47 | *Bryonia alba* | Cucurbitaceae | Bryony | Alkaloids, saponins, steroids, triterpenoids, cucurbitane, triterpene, glycosides, carbohydratesand proteins. | It gives relief to constipation, upset stomach, fluid retention, arthritis, inflammation, headache, migraine, prevents cancer, lung disorder, vomiting, wounds, ulcer, edema, rheumatism, epilepsy, snakebite, gout pain. | Analgesic<br>Anti-inflammatory<br>Anti-pyretic<br>Antimicrobial<br>Anti-viral<br>Anti-tumor<br>Antidote<br>Anti-arthritic [36] |
| 48 | *Cinnamomum zeylanicum* | Lauraceae | Cinnamon | Alkaloids, flavonoids, saponins, terpenoids, cinnzeylanin, cinnzeylanol cinnamic acid, phenolic acids, tannins, and essential oils. | It is useful in upset stomach, gastrointestinal problems, diarrhea, morning sickness, cold, vomiting, urinary tract infections, vaginal infections, diabetes, and nose bleeds, colic, prevents head lice, pain-killer, mouth freshener, and cures skin problems. | Antimicrobial<br>Anti-inflammatory<br>Anti-cancer<br>Antioxidant<br>Anti-diarrheal<br>Anti-diabetic<br>Cardio-protective<br>Gastro-protective [37] |
| 49 | *Vitis vinifera* | Vitaceae | Grapes | Phenolic acids, flavonols, flavon-3-ols, myricetin, peonidin, flavonoids, quercetin, tannin, anthocyanin, cyanidin, ellagic acid, and proanthocyanidins. | Leaves are used in diarrhea, unripe fruit astringent, used in throat affections, laxative, stomachic, consumption, uterine tumors, and hardness of the liver, fresh fruits, eaten or processed into wine, juice. | Antioxidant<br>Hepato-protective<br>Anti-carcinogenic<br>Anti-bacterial<br>Anti-viral<br>Anti-diabetic<br>Cardio-protective [38] |
| 50 | *Thymus vulgaris* | Lamiaceae | Thyme | Flavonoids, phenols, terpenoids, protein, fat, essential oils, saponins, steroids and cardiac glycosides. | Thyme is effective in anxiety, arthritis, bad breath, bronchitis, colds, sore throat, colic, diarrhea, dermatitis, gingivitis, earache, hair loss, menstrual cramps, oral thrush, reduce inflammation, swelling oftonsils. | Anti-inflammatory<br>Anti-anxiolytic<br>Antimicrobial<br>Anti-tussive, Antioxidant<br>Anti-spasmodic<br>Insecticidal activity[39] |

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| 51 | *Laurus nobilis* | Lauraceae | Bay Leaves | Alkaloids, flavonoids, tannins, limonien, cineol, linalool, terpinol, essential oil, phenols, coumarins, steroids, triterpenes and saponins. | It has been used to treat indigestion, bronchitis, influenza, upper respiratory tract disorder, arthritic, used to improve appetite, prevent cancer, urinary ailments, rheumatic pain, renal disease, migraine, skin irritation, stimulate hairgrowth. | Anti-cancer<br>Antimicrobial<br>Antioxidant<br>Anti-tussive<br>Cardio-protective<br>Gastro-protective<br>Nematicidal<br>Insecticidal [13] |
| 52 | *Elettaria cardamomum* | Zingiberaceae | Cardamom | Flavonoids, carbohydrates, proteins, minerals, lipids, essential oils, terpenoids and carotenoids. | It is used to treat indigestion, vomiting, congestion of lungs, to prevent stomach pain, gripping, colic, heart burn, stomach disorder, stones, arthritis, sore muscle, scanty urination, cystitis, fight against skin disorders. | Antioxidant<br>Anti-inflammatory<br>Antimicrobial<br>Anti-cancer<br>Insecticidal<br>Gastro-protective<br>Anti-ulcer<br>Anti-asthmatic [13] |
| 53 | *Diospyros virginiana* | Ebenaceae | Persimmon | Alkaloids, proanthocyanidins, flavonoids, tannins, β- carotene, zeaxanthin, phenolics, carotenoids, and dietaryfiber. | It is used to treat bloody stools, cancer, dysentery, diarrhea, for making spirits and beer; fruits are used in treatment of diarrhea, cancers, in the treatment of thrust and sore throats. | Antipyretic effect<br>Anti-inflammatory<br>Anti-diarrheal<br>Gastro-protective<br>Anti-cancer<br>Antimicrobial [40] |
| 54 | *Withania somnifera* | Solanaceae | Ashwagandha | Flavonoids, phenolics, alkaloids, steroidal lactones, tannins, terpenoids, carbohydrates, and saponins. | It is useful in curing the bronchial asthma, chronic fever, dysentery, arthritis, emetic syndrome, insect bites, gastric, cardiovascular, hepatic disorders, nervous exhaustion, insomnia, loose teeth, diabetes, male infertility, fibromyalgia, Parkinson disease. | Anti-stress<br>Anti-arthritic<br>Neuro-protective<br>Analgesic, Anti-tumor<br>Anti-ulcer, Antioxidant<br>Antimicrobial<br>Abortifacient [41] |

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| 55 | *Tinospora cordifolia* | Menisper maceae | Gilory | Alkaloids, flavonoids, glycosides, steroids, phenolics, aliphatic compounds, polysaccharides, protein, terpenoid, lignans, and steroids. | It is used to boost immunity, to treats heart related issues, infertility, swine flu, dengue, constipation, reduces stress, anxiety, tonsils, boosts memory, rheumatoid arthritis, improves the vision, reduces sign of aging, dark spots, pimples, fin lines. | Neuro-protective<br>Anti-ulcer, Anti-diarrheal<br>Analgesic, Aphrodisiac<br>Immuno-modulatory<br>Anti-inflammatory<br>Gastro-protective [42] |
| 56 | *Artemisia vulgaris* | Asteraceae | Artemisia | Flavonoids, coumarins, sesquiterpene, lactones, volatile oils, insulin, alkaloids, volatile oils (camphor, camphene, caryophyllene) and essential oils. | It is used as an immunity booster, itching, burns, colic, diarrhea, constipation, irregular menstrual periods, to treat headache, fatigue, sleeping disorders, depression, asthma, improves digestion, metabolism. | Antimicrobial<br>Anthelmintic<br>Anti-inflammatory<br>Anti-hypertensive<br>Hepato-protective<br>Antiseptic<br>Anti-spasmodic [13] |
| 57 | *Vitex negundo* | Lamiaceae | Lagundi | Flavonoids, carbohydrates, proteins, amino acids, saponins anthraquinones, tannins, triterpenes, lignin and polyphenolics. | It is used to treat oozing from ear, obesity, diabetes, muscular pain, skin disease, cold, diarrhea, swelling of gums, arthritis, joint pain, colon cancer, effective in chronic bronchitis, scrofulous sores, used in burns, and angina. | Anti-inflammatory<br>Antispasmodic<br>Antimicrobial<br>Anti-pyretic<br>Anthelminthic<br>Rejuvenative<br>Tranquilizer<br>Anti-arthritic [13] |
| 58 | *Glycyrrhiza glabra* | Fabaceae | Liquorice | Flavonoids, saponin, isoflavonoids, stilbenoids, coumarins, glycosides, carbohydrates, starches, phenolics, alkaloids, proteins, pectin, lipids, tannins, and steroids. | It improves the symptoms of eczema, sore throats, bad breath, dental plaque, indigestion, ulcer, hepatitis, kidney problems, liver injury, obesity, Parkinson disease, stomach ulcer, and enlarged ovary with cysts, infections, cancer, tuberculosis, chronic fatigue. | Anti-tumor<br>Antimicrobial<br>Anti-inflammatory<br>Anti-diabetic<br>Anti-ulcer, Anti-cancer<br>Antioxidant<br>Hepato-protective<br>Anti-allergic [13 ] |

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| 59 | *Hibiscus rosa-sinensis* | Malvaceae | China Rose | Flavanoides, tannins, anthraquinones, quinines, phenols, alkaloids, terpenoids, saponins, cardiac glycosides, mucilages, anthocyanin, myristic acid, and campesterol. | The plant is used to treat headaches respiratory and digestive tracts, skin problems, mumps, to relieve from fever, astringent for excessive menstruation, used to treat gonorrhea, diarrhea. | Anti-anxiety, Anti-cancer Anti-fertility Antioxidant Hepato-protective Hypolipidaemic Anti-diarrheal Wound healing [15] |
| 60 | *Murraya koenigii* | Rutaceae | Curry Plant | Alkaloids, flavonoids, phenols, saponins, tannins, reducing sugars, terpenoids carbohydrates, and steroids. | It treats diabetes, anemia, eye related problems, improves vision, fights against infection and germs, burns excess fat, It is useful in digestion, constipation, diarrhea, dysentery, piles, nausea, bloating, It prevents cancer, toothache, improves memory, skin, hair, respiratory problems. | Antioxidant Anti-diabetic Anti-inflammatory Anti-tumor Neuro-protective Anti-cancer, Antimicrobial Anti-diarrheal Blood purifying Gastro-protective Anti-depressant [13] |
| 61 | *Punica granatum* | Punicaceae | Pomegranate | Phenolics, flavonoids gallotannins, lipid, ellagic acid, gallic acid, punicalins, punicalagins, tannins Punicafolin, punicalagin, friedelin, andbetulic acids. | It is used for diarrhea, dysentery, vomiting, eye pain, gastrointestinal disturbances, used to relieve itch, used to treat diarrhea, colitis, dysentery, leucorrhoea, paralysis, to treat piles, yellowish discharge from the vagina,nose bleed. | Anthelmintic Antimicrobial, Anti-cancer Hypoglycemic Anti-diarrheal Anti-fertility, Antioxidant Anti-convulsant Gastro-protective Hepato-protective [15] |

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| 62 | *Averrhoa carambol* | Oxalidaceae | Carambola | Alkaloids, phenols, flavonoids, protein, tannins, steroids, carbohydrates and glycosides. | It is used for skin disorder, fevers, high blood pressure, diabetes, coughs, rheumatism, asthma, colic, used to treat chicken pox, ringworm infection, to relieve gastritis, angina, malaria, intestinal worms, diarrhea, and hemorrhoids. | Antioxidant<br>Anti-inflammatory<br>Anti-tumor<br>Antimicrobial<br>Anti-diabetic<br>Anti-diarrheal<br>Hypertensive<br>Hypoglycemic<br>Anti-ulcer [43] |
| 63 | *Syzygium aromaticum* | Myrtaceae | Clove | Alkaloids, glycoside, steroids, carbohydrates, terpenoids, saponins, tannins and phenolic compound. | It reduces plaque on the teeth, excessive sweating of the palms, pain, blood sugar, bacterial infections, it helps in hangovers, diarrhea, gas, dyspepsia, nausea, vomiting, swelling, cholera, earache, mosquito repellent, bone stronger. | Antimicrobial<br>Antioxidant<br>Anti-carcinogenic<br>Analgesic<br>Anti-inflammatory<br>Anti-thrombotic<br>Anesthetic<br>Anti-pyretic<br>Anti-diabetic [13] |
| 64 | *Zea mays* | Poaceae | Corn | Polyphenols, flavonoids, anthocyanins, glycosides, carotenoids, maizenic acid, maysin, rutin, and polysaccharides. | It is used to cure diabetes, cystitis, gout, prevents nose bleeding, menorrhagia, ulcer, swellings, rheumatic pain, cancer, warts, bladder infections, kidney stones, heart failure, high blood pressure, high cholesterol. | Antioxidant<br>Antimicrobial<br>Anti-obesity<br>Anti-diabetic<br>Anti-proliferative<br>Hepato-protective<br>Renal protective<br>Anti-inflammatory<br>Anti-cancer [15] |

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| 65 | *Nelumbo nucifera* | Nelumbo naceae | Sacred lotus | Alkaloids, flavonoids, phenols, tannins, steroids carbohydrate, protein, fatsand glycosides. | The leaves are used to treat sunstroke, dysentery, fever, dizziness and vomiting of blood. It is also used as an antidote for mushroom poisoning and for small pox;it is used to treat cholera, worm infestation, vomiting, and exhaustion. | Anti-anxiety<br>Antimicrobial<br>Anti-diarrheal<br>Anti-inflammatory<br>Hepato-protective<br>Antioxidant<br>Anti-proliferative<br>Anti-pyretic [15] |
| 66 | *Ricinus communis* | Euphorbia ceae | Castor Bean | Flavonoids, glycosides, alkaloids, steroids, terpenoids, ricinoleic acid, ricinine, ferulic acid, syringic acid, cinnamic acids, and stigmasterol. | It is used for anal prolapsed, arthritis, constipation, facial palsy, strabismus, to treat deafness, abscesses, headache, skin problems, bleeding, constipation, boils,piles warts, dandruff, and hair loss. | Anti-fertility<br>Antioxidant<br>Antipsychotic<br>Anti-inflammatory<br>Hepato-protective<br>Haemaglutination<br>Insecticidal [15] |
| 67 | *Bryophyllum pinnatum* | Crassulac eae | Goethe plant | Alkaloids, saponins, flavonoids, carbohydrate, sterols, fatty acids, monoarylphenolics and tannins. | The paste of the leaves are externally used for the treatment of boils, insect bites, burns, to treat dysentery, bleeding piles, fresh wounds, blood mixed diarrhea, to reduce swelling,asthma, cold, ulcer, earache, kidney stones. | Antioxidant<br>Anti-pyretic<br>Anti-allergic<br>Antimicrobial<br>Sedative, Analgesic<br>Anti-diarrheal<br>Anti-ulcer [44] |
| 68 | *Oxalis corniculata* | Oxalidaceae | Creeping Woodsorr el | Flavonoids, alkaloids, tannins, phenols, carbohydrates, reducing sugar, proteins, sterols, cardiac glycosides and ascorbic acid. | It is used for liver and digestive problems, headache, cures digestive problems, to stop bleeding from cuts, used as good appetizer, piles, dyspepsia, swelling, helps in insomnia, an antidote for snake bite, mercury, arsenic poisoning. | Anti-diarrheal<br>Anti-diabetic<br>Antimicrobial<br>Anti-inflammatory<br>Anti-ulcer, Anti-epileptic<br>Wound healing<br>Anti-scorbutic [45] |

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| 69 | *Trianthema portulacastrum* | Aizoaceae | Horse purslane | Phenols, flavonoids, alkaloids, cardiac glycosides, tannins, steroids, saponins, triterpenes, lipids, carbohydrates, and proteins. | This plant has analgesic, laxative, stomachic, used in cardiac diseases, bronchitis, inflammations, piles, cancer, obstruction of the liver asthma, amenorrhea, dropsy, edema, rheumatism, anemia, ulcer, night blindness. | Antioxidant<br>Anti-inflammatory<br>Anti-carcinogenic<br>Hepato-protective<br>Anti-hyperglycemic<br>Antinociceptive<br>Antimicrobial [46] |
| 70 | *Scoparia dulcis* | Scrophulariaceae | Sweet Broom | Flavonoids, alkaloids, tannins, triterpenes, hexacosonal, β-sitosterol, ketone-dulcitone, amellin, carbohydrates, protein, saponins, and steroids. | It is used to treat cough, diarrhea, bronchitis, jaundice, menstrual disorder, and malaria, skin infections, used to cure headache, liver disorders, burns, anemia, urinary tract disorders, ulcer, snake bite, migraine, hepatitis, and hypertension. | Antimicrobial<br>Anti-inflammatory<br>Anti-malarial<br>Anti-diabetic<br>Anti-diarrheal<br>Antioxidant, Anti-cancer<br>Anti-hypertensive [47] |
| 71 | *Psidium guajava* | Myrtaceae | Guava | Flavonoids, alkaloids, anthocyanins, carotenoids, essential oils, fatty acids, lectins, phenols, saponins, tannins, triterpenes and Vitamin C. | It cures diarrhea, reduce fever, gastroenteritis, diabetes, wounds, prevents cancer, skin aging, high blood pressure, colitis, vomiting, obesity, used to treat nail, and enhances hair growth, cure heart disease, and high cholesterol. | Anti-diabetic<br>Anti-diarrheal<br>Antimicrobial<br>Antioxidant, Hepato-protective, Anti-cancer<br>Anti-inflammatory<br>Cardio-protective [13] |
| 72 | *Artocarpus heterophyllus* | Moraceae | Jackfruit | Phenolic compounds, flavonoids, stilbenoids, arylbenzofurons, carotenoids, volatile acid, sterols, vitamins, protein and tannins. | The decoction from its seed, root and bark is used to treat digestion, diarrhea, and dysentery. Root extract used as a remedy of skin disease, asthma, fever, used to cure wounds. It heals abscesses, ear problems, ulcer, gall stones, diabetes, reduce pain, builds muscle. | Anti-inflammatory<br>Antioxidant<br>Hepato-protective<br>Wound healing<br>Anti-carcinogenic<br>Anti-ulcer, Anti-diabetic<br>Anti-diarrheal<br>Antimicrobial [48] |

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| 73 | *Catharanthus roseus* | Apocynaceae | Periwinkle | Alkaloids, flavonoids, terpenoids, saponins, steroids, carbohydrates, anthaquinone, glycosides, carbohydrates and protein. | It is used to treat leukemia, Hodgkin's lymphoma, and increases blood flow in brain, cures hypertension, dizziness, cranial traumas, menstrual irregularities, chronic constipation, dyspepsia, malaria, dengue, skin diseases, wasp stings, toothache, and diabetes. | Anti-carcinogenic<br>Anti-diabetic<br>Antioxidant<br>Antimicrobial<br>Anthelmintic<br>Anti-sterility<br>Anti-diarrheal<br>Hypertensive<br>Wound healing [15] |
| 74 | *Tagetes erecta* | Asteraceae | Marigold | Flavonoids, cadinol, carotenoids, isorhamnetin, saponins, triterpenes, quercetin, kaempferol, quercetagetin, phenolics and syringic acid. | It detoxifies the digestive system, heals viral inflammations, treats urinary, liver, gallbladder ailments, cure sore throats, toothaches, measles, mumps, heals cuts, scrapes, treats sunburn, diaper rash, insomnia. | Antiseptic<br>Wound healing<br>Analgesic<br>Antispasmodic<br>Anti-inflammatory<br>Antimicrobial<br>Stomachic<br>Anti-ulcer [13] |
| 75 | *Heliotropium indicum* | Boraginaceae | Indian Heliotrope | Flavonoids, steroids, tannins, alkaloids, saponins, glycosides, terpenoids, phenols, and carbohydrates, and phytosterols. | Heliotrope is used to heal skin infections, stomach problems, poisonous animal bites, nervous disorders, Prevents dandruff, treats eye diseases, cure wounds, inflammation, tumor, malaria, vein disease, kidney stones, gum infection, ring worm infection. | Anti-inflammatory<br>Antioxidant<br>Anti-cataract<br>Anti-tumor<br>Anti-ulcer<br>Anti-fertility<br>Diuretic<br>Antimicrobial<br>Analgesic [49] |

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| 76 | *Tectona grandis* | Verbenaceae | Teak | Alkaloids, triterpenoids, steroids, lignans, fatty esters, phenolic compounds, tannin, carbohydrate, flavonoids, and physterols. | It is useful in bronchitis, dysentery, hyperacidity, diabetes, leprosy, nerve and skin disease, to treat headache, ringworm, promote hair growth. | Anti-inflammatory<br>Antimicrobial<br>Antioxidant<br>Analgesic<br>Diuretic<br>Laxative [10] |
| 77 | *Leucas aspera* | Lamiaceae | Thumba | Alkaloids, phytosterols, flavonoids, saponins, phenols, glycosides, oleanolic acid, ursolic acid, triterpenoids and beta-sitosterol. | Used orally as stimulant, anthelmintic, laxative, and diaphoretic, to treat inflammation, dyspepsia, and jaundice, diarrhea, used orally for gastroenteritis, cholera, malaria, syphilis, leprosy, and dysentery. | Anti-inflammatory<br>Antimicrobial<br>Antioxidant<br>Hepato-protective<br>Anti-diabetic<br>Anti-diarrheal [50] |
| 78 | *Lantana camara* | Verbenaceae | Indian Lantana | Flavonoids, phenols, saponins, alkaloids, tannin, anthocyanins, flavones, isoflavones, coumarins, lignans, catechins, carotenoids, carbohydrates, proteins, glycosides, and steroids. | Used to treat cuts, rheumatisms, catarrhal infection, tetanus, abdominal viscera, sores, measles, malaria, chicken pox, asthma, ulcer, swelling, bilious fever, used in the treatment of skin, itches. | Anti-cancer<br>Anti-inflammatory<br>Anti-diabetic<br>Anthelmintic<br>Antimicrobial<br>Hepato-protective<br>Antioxidant, Larvicidal [15] |
| 79 | *Oldenlandia corymbosa* | Rubiaceae | Diamond Flower | Alkaloids, sterols, terpenes, flavonoids, saponin, glycosides, cyanogenics, tannins, resins, lactones, quinines, phenolic acids, anthocyanidins, and volatile oils. | To treat skin sores, ulcers, sore throat, bronchitis, gynecologic infections, pelvic inflammatory diseases, fever, jaundice, diarrhea, heat eruption, hepatitis, pneumonia, urinary infection, colic, constipation. | Anti-diabetic<br>Anti-malarial<br>Anti-inflammatory<br>Abortifacient<br>Antimicrobial<br>Antioxidant<br>Hepato-protective [51] |

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| 80 | *Centipeda minima* | Asteraceae | Spreading Sneezeweed | Alkaloids, flavonoids, tannins, phenolic compounds, glycosides, fats, terpenes and carbohydrates. | It is used to prevent pain in joints, used against hepatitis, diabetes mellitus, malaria, opium poisoning, and bronchitis, in night blindness, ring worm, and fever. | Anti-angiogenic<br>Anti-proliferative<br>Anti-arthritic,<br>Anti-diabetic<br>Antioxidant<br>Anti-inflammatory [13] |
| 81 | *Canna indica* | Cannaceae | Canna | Alkaloids, steroids, carbohydrates, proteins, flavonoids, terpenoids, cardiac glycosides, β– carotene, essential oil, lignin, diterpenes, steroids and saponins. | Used as diuretic, diaphoretic, demulcent and stimulant, flowers are used to cure eye disease, to treat dropsy, tonsillitis, malaria, diarrhea and dysentery, fever, diabetics, cancer, bruises. | Antimicrobial<br>Anti-inflammatory<br>Analgesic<br>Immuno-modulatory<br>Anti-diarrheal<br>Anti -pyretic<br>Anti-cancer [52] |
| 82 | *Acalypha indica* | Euphorbiaceae | Acalypha | Alkaloids, catachols, flavonoids, phenolics, tannin, saponins, triterpenoids, steroids, glycosides, anthraquinone, proteins, and amino acids. | Used in curing diabetes, leprosy, jaundice and heart disease, Used to treat asthma, ulcers, bronchitis, headache, cough dysmenorrheal, and skin disease, Also used for constipation, tummy ache, gastrointestinal irritant. | Anti-inflammatory<br>Antimicrobial<br>Anti-cancer<br>Anti-diabetes<br>Anti-obesity<br>Anti-venom<br>Hepato-protective [53] |
| 83 | *Sida cordifolia* | Malvaceae | Country Mallow | Flavonoids, lignin, glycosides, alkaloids, saponins, phytosterols, fixed oils, reducing sugar, and fatty acids. | Used as astringent, diuretic, tonic, cystitis, hematuria, fever, leucorrhoea, and disease of nervous system, paralysis, to treat piles, throat disease, phthisis, and sciatica. | Analgesic<br>Anti-inflammatory<br>Antimicrobial<br>Hepato-protective<br>Anthelmintic<br>Anti-diabetic [13] |

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| 84 | *Sesbania sesban* | Fabaceae | Sesban | Alkaloids, anthocyanins, polyphenols, flavonoids, phytosterol, triterpenoids, Vitamins, tannins, saponins, and glycosides. | It is used to treat diabetics, inflammation, pains, diarrhea, scorpion sting, emmenagogue astringent, skin disease, leucoderma, menorrhagia, and for spleen enlargement. | Anti-inflammatory<br>Antioxidant<br>Anthelminthic<br>Anti-diabetic<br>Antimicrobial<br>Dermatitis<br>Anti-pyretic<br>Antimicrobial [54] |
| 85 | *Daucus carota* | Apiaceae | Carrot | Phenolics, carotenoids, alkaloids, flavonoids, terpenoids, polyacetylenes, ascorbic acid, uccinic acid, $\alpha$- ketoglutaric acid, lactic acid, and glycolic acid. | It is used as a diuretic and treats many urinary problem kidney stone, It also used in digestive disorders such as indigestion, gas formation, also used to treat skin disease, and cancer. | Anti-inflammatory<br>Anti-oxidant<br>Anti-cancer<br>Antimicrobial<br>Anti-flu<br>Anti-anxiety<br>Antispasmodic [13] |
| 86 | *Cocos nucifera* | Arecaceae | Coconut | Phenols, tannins, leucoanthocyanidins, flavonoids, triterpenes, steroids, alkaloids, lpids,phytates and saponins. | Used for the treatment of diarrhea, arthritis, uterine diseases, bronchitis, liver complaints, diuretic, laxative, to treat diseased skin, teeth. | Analgesic<br>Anti-inflammatory<br>Antimicrobial<br>Laxative<br>Diuretic<br>Hepato-protective<br>Anti-diabetic [15] |
| 87 | *Andrographi spaniculata* | Acanthaceae | Green Chiretta | Alkaloids, steroids, flavonoids, tannins, triterpenoids, quinones, protein, and sugars. | It is used to treat diabetes, high blood pressure, ulcer, leprosy, bronchitis, colic, influenza, malaria, blood purifier, cold, constipation, fever, liver disorders, loss of appetite, urinary tract and lung infections, low sperm count. | Anti-inflammatory<br>Anti-hyperglycemic<br>Hepato-protective<br>Antimicrobial<br>Anti-cancer, Anti-viral<br>Gastro-protective<br>Cardio-protective [8] |

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| 88 | *Phoenix dactylifera* | Arecaceae | Date Palm | Carotenoids, flavonoids, polyphenols, isoflavons, lignans, alkaloids, saponins, terpenoids, tannins, cardiac glycosides, and sterols. | Used for the treatment of memory disturbances, paralysis, loss of consciousness, inflammation, nervous disorders, diuretic, sore throat, colds, bronchial asthma, to relieve fever, cystitis, gonorrhea, liver and abdominal troubles. | Anti-ulcer, Anti-cancer Anti-diarrheal Hepato-protective Antioxidant, Anti-inflammatory, Antimicrobial Anti-hyperlipidemic [55] |
| 89 | *Morinda citrifolia* | Rubiaceae | Indian Mulberry | Alkaloids, octanoic acid, terpenoids, anthraquinones, sitosterol, carotene, Vitamin-A, flavones glycosides, amino acids, caproic acid, ursolic acid, rutin and proxeronine. | It is used in diabetes, anxiety, and high blood pressure, also used to treat in colds, flu, asthma, bronchitis, piles, depression, mental disorder, improved high frequency hearing, cure heart disease, leprosy, kidney problems and urinary discharges. | Antimicrobial, Antitumor Hypertensive activity, Mental health and improved high frequency hearing, Anti-convulsant Anti-fertility [15] |
| 90 | *Saraca asoca* | Fabaceae | Ashoka | Glycoside, flavonoids, tannins, saponins, carbohydrates, phenols, steroids, lignins, catechol, leucopetargonidin and leucocyanidin. | Used in treating hemorrhagic, uterine pain, tumors, worm infestations, bacterial infections, skin problems, leucorrhoea, internal, menstrual cycle and uterine disorders, diabetes, diseases of the blood, enlargement of abdomen. | Antimicrobial Anti-implantation Anti-tumor Anti-progestational Anti-inflammatory Antioxidant, Anti-cancer [13] |
| 91 | *Ficus benghalensis* | Moraceae | Banyan | Steroids, flavonoids, tannins, phenolics, leucocyanidin, glycosides, proteins, carbohydrates, fatty acid, amino acid, terpenoids, Vitamin C, and anthraquinones. | It is used to treat diabetes, seminal weakness, leucorrhoea, nervous disorders, burning sensation, ulcers, vomiting, vaginal complains, fever, inflammations, leprosy, syphilis, dysentery, inflammation of liver, applied for reducing pimples. | Analgesic, Anti-pyretic Anti-ulcerogenic Anti-inflammatory Antimicrobial Anti-diabetic Anti-convulsant Anti-diarrheal Hepato-protective Larvicidal [56] |

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| 92 | *Tridax procumbens* | Asteraceae | Coatbuttons | Flavonoids, alkaloids, hydroxycinnamates, tannins, phytosterols, lignans, carotenoids saponins, phenols and anthocyanins. | Used to treat diabetes, insect repellent, diarrhea, hemorrhages, hair loss, wounds, inflammation, cough, stomachache, epilepsy, gastrointestinaldisorders. | Anti-diabetic<br>Antimicrobial<br>Antiviral, Anti-oxidant<br>Hypo-lipidaemic<br>Anti-hypertensive [57] |
| 93 | *Solanum nigrum* | Solanaceae | Black Night Shade | Alkaloids, flavonoids, steroids, tannins, phlobatannins, phenols, solanidine, tigogenin, tomatidenol, uttronins and solanigroside. | Used in wounds, cancerous growths, piles, abdominal pain, dysentery, inflammation, asthma, ulcer, neuralgia, heavy female discharge, diarrhea, diuretic, dysentery, febrifuge. | Anti-inflammatory<br>Anti-diabetic<br>Antimicrobial<br>Antinociceptive<br>Anti-cancer<br>Hepato-protective [15] |
| 94 | *Terminalia arjuna* | Combretaceae | Arjuna | Flavonoids, tannins, phenols, phytosterols, saponins, alkaloids, lactones, terpenoids, Carotenoids, stilbenes, lignans, tannins and glycosides. | Used for the treatment of heart diseases, hypertension, to decrease blood pressure, hemorrhages, ulcers, tumors, earaches, dysentery, sexual diseases, urinary tract infection | Antimicrobial<br>Antioxidant<br>Anti-carcinogenic<br>Anti-mutagenic<br>Gastro-protective<br>Anti-hypertensive<br>Anti-atherogenic [58] |
| 95 | *Mimosa pudica* | Mimosaceae | Sensitive Plant | Alkaloids, flavonoids, cardiac glycosides, polyphenols, saponins, tannins, terpenoids, quinines, and coumarin. | Used to treat blood and bile, cure piles, jaundice, leprosy, ulcer and smallpox, dysentery, inflammations, asthma, insomnia, premenstrual syndrome. | Anti-diabetic<br>Antioxidant<br>Anti-hepatotoxin<br>Anti-inflammatory<br>Wound healing<br>Anti-fertility [59] |
| 96 | *Momordica charantia* | Cucurbitaceae | Bitter Gourd | Flavanoids, saponins, terpenoids, coumarins, emodins, alkaloids, proteins, glycosides, anthraquinones, anthocyanins, andsteroids. | Used to treat diabetes, abortifacient, gout, jaundice, abdominal pain, leprosy, laxative, piles, pneumonia, psoriasis, purgative, rheumatism, melanoma, cancer and lymphoma. | Anti-diabetic<br>Antimicrobial<br>Antioxidant, Anti-tumor<br>Anti-inflammatory<br>Hypo-lipidaemic [60] |

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| 97 | *Pterocarpus marsupium* | Fabaceae | Malabar Kino | Alkaloids, glycosides, flavonoids, flavonols, poly, phenols pterostilbene, tannins, lignans, stilbenes, sterols, and terpenoids. | Used in fractures, constipation, hemorrhages, arthritis, sores, boils, stomach pain, cholera, leprosy, toothache, tumors, dysentery, fever. | Anti-diabetic<br>Antimicrobial<br>Antioxidant<br>Anti-cancer<br>Anti-diarrheal [61] |
| 98 | *Gymnema sylvestre* | Apocynaceae | Gurmar | Alkaloids, flavanoids, glycosides, tannins, triterpene, saponins gymnemic acids, phenols, anthraquinones, and phtoseterois. | It is used in the treatment of jaundice, constipation, asthma, bronchitis, conjunctivitis, renal, calculi, laxative, jaundice, piles, colic pain, eye troubles, cardiac, and respiratory diseases. | Anti-diabetic<br>Anti-arthritic<br>Antimicrobial<br>Hepato-protective<br>Anti-cancer<br>Anti-hyperlipidemic[62] |
| 99 | *Enicostemma littorale* | Gentianaceae | Indian Gentian | Flavonoids, steroids, quinones, cardiac glycosides, saponins, quinine, tannins, phenols, and alkaloids. | Used for treating diabetes, stomachic, tonic, reduce fever, tonic for appetite loss, improves kidney function, blood pressure, and malaria. | Anti-diabetic<br>Antimicrobial<br>Antioxidant<br>Anti-inflammatory<br>Anti-tumor [63] |
| 100 | *Clerodendrumphlomidis* | Lamiaceae | Arna | Flavonoids, glycosides, terpenoids, saponins, tannins, lignin, phenols, alkaloids, glycosides, phenylethanoid, steroid, anthraquinones, and cyanogenic acid. | Used to treat inflammation, diabetes, nervous disorder, rheumatism, urinary disorders, asthma, febrifuge, coughs, venereal infections, skin diseases, elephantiasis, tropical burns, and malaria. | Anti-diabetic<br>Antimicrobial<br>Antioxidant<br>Anti-inflammatory<br>Anti-cancer<br>Anti-diarrheal [64] |

## SIGNIFICANCE OF MEDICINAL PLANTS IN PHARMACOLOGY AND PHYTOCHEMISTRY

The current chapter provides research and explanations in a concise manner on a variety of ethno medicinal plants from India that have a variety of pharmacological or therapeutic qualities that can aid to lower the risk of life-threatening disorders in humans. Numerous types of phytochemicals can operate as potent defences against various illnesses or as potent immune boosters. Studying these traditional medicinal plants, aids in developing our understanding of biological processes that will benefit human welfare and healthcare in the future. The careful treatment of these species of medicinal and aromatic plants is required for these innovative objectives. It is also necessary to cultivate and preserve them methodically. The direction of the chapter reveals the pharmacology's future developments as they emerged from observational and experimental therapies for complementary and alternative medicines. Since these plants are a rich source of dietary fibre, minerals, and vitamins, as well as significant primary and secondary metabolites, they are also employed as functional food supplements to support better health. On the basis of pharmacology, phytotherapy and phytochemistry, the plant species shown enormous promise for future usage in the pharmaceutical and nutraceutical industries [1, 5, 65,67].

## CONCLUSION

The current chapter focuses on certain significant Indian traditional medicinal plants and their extensive potential for phytochemicals, pharmacology, therapeutics, and nutritional qualities. These medicinal plants have been utilised as a significant medicinal, pharmacological, therapeutic, pharmaceutical, and nutritional source for many disorders, which can be inferred through this chapter. Comprehensive research studies would provide a detailed understanding of the historically used Indian medicinal herbs, demonstrating their superior value for curing various illnesses or combating other serious, life-threatening conditions.

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**Chapter 4**

# ROLE OF SACRED GROVES IN BIODIVERSITY CONSERVATION WITH SPECIAL REFERENCE TO UTTARAKHAND

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**ABSTRACT**

Nanotechnology deals with manipulating materials at nano scale ($10^{-9}$m). Nanotechnology Indian traditional and indigenous tribes hold the deeply held religious conviction that medicinal plants and trees are sacred parts of the natural world. Patches of trees on forest land known as sacred groves (SGs) are communally preserved with strong religious overtones. Since ancient times, traditional civilizations and indigenous groups have used their socio-cultural and religious rituals to conserve these forest areas. Sacred groves are typically handled with reverence. Except when wood is required for religious activities including the construction and repair of temple buildings, worship, funeral rites, and temple rituals, sacred trees cannot be chopped down or hacked. As a result, SGs possess a direct and enduring pious status and contribute to preserving the social fabric of society.

**KEYWORDS:** Sacred Grove, Biodiversity conservation, Uttarakhand

## INTRODUCTION

Numerous groups around the world, including many regions of India, engage in various types of nature worship. Early people revered nature and only used it to the extent necessary to meet their most basic needs. The fundamental topic of how and where individuals originated, as well as how they should interact with their surroundings, is addressed by many cultural ideas (Elder and Wong, 1994). There is a tonne of myth, tradition, and lore around forests. Societies that have a deep relationship with forests often have a healthy respect for them, are in awe of their beauty and majesty, and occasionally experience dread and fear due to the strong spirits that dwell there. For indigenous and other populations that live in the forest, they have been a lifeline.

People started to exploit the idea of sacred groves to conserve this important resource. The pre-agricultural, hunting and gathering phase of cultures, when human society was in a rudimentary state, has been identified as the origin of fearful groves (Gadgil and Vartak, 1975; Khumbongmayum *et al.*, 2004).

Many human communities had long preserved particular areas of their natural surroundings as sacred groves, including those in Asia, Africa, Europe, America, and Australia (Hughes and

Chandran, 1998). The groves have changed as a result of various socio-ecological and cultural circumstances and now serve a variety of ecological, environmental, and socio-cultural purposes for the community. Early man revered nature and only used its resources to the extent necessary to meet his basic needs. Early humans did not have a tendency to hoard or to overuse their resources due to greed. Native Americans once relied on rivers and woods for their everyday needs and revered a wide range of natural items as sacred.

In the Himalaya, numerous plant species, including *Ficus benghalensis, Ficus religiosa, Ocimum sanctum, Cynodon dactylon, Mangifera indica, Astromonium spp., Azadirachta indica,* and *Sassurea obvallata,* are regarded as sacred and utilised in ceremonies and offerings to gods (Table 1) (Anthwal *et al.,* 2006). Due to their therapeutic potential, several plant species (Table 2) are employed in ayurveda medications to treat illnesses (Anthwal *et al.,* 2006). Tiger, cow, elephant, peacock, bullock, cobra, rat, cat, and birds are some of the revered creatures (like neelkanth, hilas, ababil, and vulture). Through their socio-cultural and religious interactions, Indians, particularly those who live in the hills, have a long heritage of environmental protection. Old Hindu texts like the Puranas make reference of sacred groves in the Garhwal hills. In his incomplete survey of groves in India, Malhotra (1998) counted 5,691 sacred groves. In India, there are believed to be 14,000 sacred groves that serve as repositories for unique fauna and plants. Some researchers estimate that there may be up to 100,000 such sacred groves worldwide (Guha, 2000; Malhotra *et al.,* 2001).

**Table 1: Sacred plant species used in rituals in Garhwal Himalaya (Anthwal *et al.,* 2006)**

| Local Name | Scientific Name | Beliefs/Uses |
|---|---|---|
| Doob | *Cynodon dactylon* | Used in rituals |
| Peepal | *Ficus religiosa* | A sacred tree |
| Tulsi | *Ocimum sanctum* | A sacred herb |
| Dhoop or Kunju | *Artemisia* sp | Used in rituals |
| Bel | *Aegle marmelos* | Sacred plant |
| Banana | *Musa paradisica* | Used in rituals |
| Kush | *Desmostachya bipinnata* | Used in rituals |
| Amla | *Emblica officinalis* | Sacred tree |
| Mango | *Mangifera indica* | Used in rituals |
| Pine | *Pinus* | Used in rituals |
| Paiya | *Prunus cerasoides* | Used in rituals |
| Timroo | *Xanthoxylum achanothopodium* | Sacred tree |
| Deodar | *Cedrus deodara* | Sacred tree |
| Neem | *Azadirachta indica* | Sacred tre |
| Brahmkamal | *Sassurea obvallata* | Sacred flower |

Sacred groves are crucial to both ecology and genetics. They are the homes of rare, endemic, and threatened plant and animal species. Additionally, they maintain the genetic variety of common tree species. The Garhwal Himalayan hill tribe holds a number of different natural features, including rivers, lakes, rivulets, springs, confluences, mountain peaks, flora, animals, and even the entire Himalayas, in high respect.

**Table 2: Medicinal plants used in Ayurvedic medicine (Anthwal *et al., 2006)***

| Local Name | Botanical Name | Parts Used | Used to Cure |
|---|---|---|---|
| Kalonji | *Nigella sativa* | Seeds | Diarrhoea, Dysentery |
| Neem | *Azadirachta indica* | Root,bark, flowers | Arthritis, Bronchitis, Cough, Diabetes |
| Dhatura | *Dhatura stramonium* | Leaves and Fruits | Asthma, Cardiac Pain |
| Tulsi | *Ocimum sanctum* | Leaves | Antiallergic, antidiabetic |
| Anar | *Punica granatum* | Seeds, Flowers | Syphilis, Bronchitis, Stomachic |
| Khajoor | *Phoenix dactylifera* | Fruit | Genitourinary ailments, Diarrhoea |
| Methi | *Trigonella foenumgreacum* | Seeds | Constipation, Diabetes |
| Paiya | *Prunus cerasoides* | Bark, Fruits | Antipyretic, Leprosy |
| Ajwain | *Thymus vulgaris* | Seeds | Antiseptic, Antispasmodic |
| Peepal | *Ficus religiosa* | Bark, Leaves, Fruits, Seeds, Latex | Skin diseases, Neuralgia, Constipation and Gynecological diseases |

**Table 3: Sacred groves and the associated deities (Anthwal *et al.*, 2006 and Bisht and Ghildiyal, 2007)**

| Name of groove | Associated deity | Place | Area (in acres) |
|---|---|---|---|
| Tarkeshwar, Kiunkaleshwar | Lord Shiva | Lansdowne, Pauri Garhwal | 775.9 |
| Binsar | Lord Shiva | Thalisain, Pauri Garhwal | - |
| Kot | Lord Shiva | Kot,Pauri Garhwal | - |
| Nandisain | Local deity | Pauri Garhwal | - |
| Danda Nagraja | Nagdev,Lord Vishnu | Pauri Garhwal | - |
| Paabo | Lord Shiva | Paabo,Pauri Garhwal | - |
| Chapdon,Mundeshwar and Neelkanth Mahadev | Lord Shiva | Pauri Garhwal | - |
| Chandrabadni,Surkunda Devi,Kunjapuri | Goddess Durga | Tehri Garhwal | - |
| Sem Mukhem | Lord Vishnu | Tehri Garhwal | - |
| Tapkeshwar, Hanol (Mahasu Devta) | Lord Shiva | Jaunsar Dehradun | - |

| | | | |
|---|---|---|---|
| Santala Devi | Santala Devi | Dehradun | - |
| Ghanteyal Ki cheevi, Devi Ka Mandir | Local Deity | Badeth,Chamoli | 500 |
| Ghandiyal Devta ka Van | Local Deity | Majyanitalli, Chamoli | 0.50 |
| Laxmivan, Nandaaur Ghantakaran ki Phulwari | Lord Vishnu | Mana,Chamoli | 500 |
| Nanda aur Ghantakaran ki Phulwari | Goddess Durga | Mana,Chamoli | 2.50 |
| Mayawati | Lord Shiva | Deval,Chamoli | - |
| Ansuiya | Local deity | Ansuiya,Chamoli | - |
| Fulana (Chinap sink bugyal), Jaldhara, | Local deity | Thaing,Chamoli | 250 |
| Bugyal,nanda kir phulwari,mandir ke ped | Local deity | Bhunyundar,Chamoli | 2755 |
| Kotgadi ki kokila mata ka sthan | Local deity | Madigaon,Chamoli | 1.00 |
| Pravasi Pavasu Devata | Local deity | Deuti,Chamoli | 500.0 |
| Devrada | Local deity | koti,Chamoli | 250.0 |
| Dronagiri | Lord Hanuman | Dronagiri,Chamoli | - |
| Hariyali Devi | Goddess Durga | Chamoli | - |
| Thal ke Dhar | Local deity | Pithoragarh | - |
| Chiplakedar | Local deity | Tawaghat,Pithorogarh | - |
| Syahi Devi | Goddess Durga | Almora | - |
| Chitai,Gairar, Ghorakhal,Chamarkhan | Local deity | Almora | - |
| Golu Devta, Bineshwar Mahadev | Lord Shiva | Almora | - |
| Kasardevi | Local deity | Almora | - |

Many sceneries in the Garhwal Himalaya (Chiplakedar, Tarkeshwar, Haryali, Binsar, Kuinkaleshwar, Tapovan, Thal ke Dhar, Nagdev, Kalimath, Goldev, Maywati, Kot, Syahi devi, Chandrabadni, Paabo, Dewal, and Chapdon) are examples of the region's vast biological variety and intricate ecosystems. Due to their connection to a deity, these landscapes have been revered and are kept in pristine shape by prohibiting the extraction of any resources from them (Table 3). This tactic is comparable to the modern idea of conserving biodiversity through the defence of sanctuaries, national parks, and biosphere reserves. Below is a brief account of a few of the holy groves in the Garhwal Himalaya:

(1) In the Rudraprayag district of the Garhwal Himalaya, at a height of 2850 metres above mean sea level, is the Haryali Sacred Grove. Since the Epic time, removing fodder and fuel wood, as well as the movement of women and Shudras (scheduled castes), has been rigorously forbidden in this forest (Mahabharata period). In this area of forest is a shrine dedicated to the goddess Hariyali Devi.

(2) In the Dehradun area of the Garhwal Himalaya, at an elevation of 2896 metres above mean sea level, is the sacred Devban grove, which is 16 kilometres from Chakrata. It is surrounded by dense forests.

(3) The Binsar sacred grove is situated at an altitude of 2567m above mean sea level, 20 kilometres north of Thalisain (Pauri Garhwal). Since the post-Vedic era, a strong connection between cultural characteristics and forest preservation has been seen here.

(4) The sacred Surkanda devi grove is located at a height of 3030 metres above mean sea level. The temple, which is on top of a mountain, is very important religiously. On Ganga Dussehra, a fair is conducted every year in May or June.

(5) The Tapkeshwar holy grove is a historic site of worship and is located on the bank of a watercourse in the Dehradun district. Water droplets that originate from a rock fall on the shivling that is housed in the shrine, giving the place the name Tapkeshwar. It has a Lord Shiva shrine.

(6) Sahastradhara, which means literally "the thousand fold spring," is located 11 kilometres from Dehradun. A spectacular view is provided by the Baldi river and caverns. People take baths in a sulphur spring because they think it can treat their skin ailments.

(7) The Gautam Kund, also known as the Chandrabani Sacred Grove, is located 7 kilometres from Dehradun. According to mythology, Maharishi Gautam, his wife, and their daughter Anjani—all of whom are highly revered by the populace—lived at this location. It is thought that Ganga presented herself at the location known as Gautam Kund.

(8) The most sacred Shiva shrine in the Himalayas is Kedarnath. The Skanda Purana compares it to gold among metals, the Brahmin among men, and Jahnavi (Ganga) among rivers. The sacred place is thought to have healing powers that can purify even the most obstinate sinner, and Hindus believe that anyone who dies here becomes one with Shiva. The temple is located near the Mandakini River's head in Kedarnath Peak's shadow. It is devoted to the veneration of Sadasiva, Shiva's ethereal form. The Jyotirlinga or dazzling lingam, one of the twelve dispersed throughout India, is the symbol of the phallus and is also known as the Shankaracharyashiva. The snow-covered area beyond the temple reaches is referred to as the mahapanth, or "highway of heaven." Bhairav-jhanp, also known as Shiva's jump, is a nearby cliff. Prior to the first quarter of the 20th century, some devotees would commit ritual suicide by jumping from a cliff in the hope that Shiva would instantly grant them salvation. The Chorabari Tal, today known as the Gandhi Sarovar, is a nearby location where the Mandakini River begins.

(9)Pithoragarh and the sacred Dhwaj Grove are both close to Totanaula. A mountain called Dhwaj is found at a height of 2134 metres above mean sea level. Goddess Jayanti (or Durga) and Lord Shiva have a home atop the peak. According to a Hindu tale, Devi destroyed the demons "Chanda and Munda" here. Since the dense forests in the mountain are revered, the biome is in great conservation status and is home to many rare flora.

(10) The Tapovan sacred grove is located 17 kilometres from Joshimath in the Chamoli area of the Garhwal Himalaya, at a height of 2744 metres above mean sea level. This region includes a

lot of fauna and a dense canopy of trees. The entire Tapovan region is reverently protected because of its diverse biodiversity.

(11) On a hilltop at a height of 1675 metres, Nilkanth Mahadeo is located above Swarg Ashram. It is one of Rishikesh's most revered temples. According to Hindu legend, the ocean was churned for "amrit" (the immortality potion) during an ancient fight between Devtas and Ashuras, and a pot of poison erupted from the water. At a location that is now known as Nilkanth Mahadeo, Lord Shiva took that poison to preserve the world from its harmful effects. It is 12 miles from Rishikesh and encircled by tranquil, lush trees.

A good example of managing the ethno-environment is sacred groves. Our forefathers understood the need of protecting the natural resources that kept them alive. The groves are deteriorating due to today's rapid increase of infrastructure facilities and farm activities. Many important tree species have been harvested for their timber (e.g., replacing oak forests with pine forests). There is significant ecological harm from this transformation. The cycling of nutrients and soil fertility can be somewhat impacted when the soil gets more acidic. The tourism sector also harms sacred trees because it erodes people's confidence in gods and groves. Such places that are safeguarded by religion offer a wide-ranging and rich ecological niche as genetic diversity reservoirs. Furthermore, it is believed that these groves are under a great deal of pressure, both directly and indirectly, which is endangering their continued existence. These dangers may be linked to growing tourism opportunities (without a built-in conservation effort), increased demand for NTFPs, fuel wood gathering, a decline in religious beliefs, and the current generation's diminished commitment to protecting such natural sacred sites. Finally, one might think about the significant amount of developmental interventions that small governments like Uttarakhand are willing to take on. Groves close to the settlements are disappearing more quickly. In the Garhwal Himalaya, only a select few sacred groves, such as Hariyali, Tapovan, Binsar, and Tarkeshwar, remain in their original, pristine state. As trees are cut down and used to build and renovate god houses, more and more groves are going extinct. Due to inescapable reasons, the majority of temple groves are observed to vanish (e.g., animal grazing and human interference). The sacred groves serve as a visual representation of the dynamic social processes associated with resource access and control. They have a rich gene pool legacy for many forest species with socio-religious significance and therapeutic benefits. Given that they are the home to rare, endemic, and threatened species of both plants and animals, sacred groves are crucial both ecologically and genetically. Querus spp. Oak) is revered and employed in a variety of ways. It plays a significant role in the ecosystem of the mountain forest and is a valuable species for both fuelwood and feed. It increases soil fertility by effectively cycling nutrients. Through the accumulation of humus and partially thanks to a deeply positioned root system with evenly dispersed root biomass throughout the soil profile, it conserves soil moisture. As good suppliers of non-wood forest products, fatty oils, and several other species, sacred groves are of immeasurable importance (like pepper, cinnamon and nutmeg, and medicinal plants). The wildlife in sacred trees is likewise abundant. Future

research should take into account sacred groves because they are crucial for maintaining water supplies and regulating the microclimate in Uttarakhand's mountainous terrain.

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Chapter 5

# QUALITATIVE EVALUATION OF VARIOUS EXTRACTS OF MEDICINALLY RICH PLANT- *COMMIPHORA MUKUL* RESIN

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**ABSTRACT**

Nowadays, people are drawn to medicinal plants because of their enormous therapeutic potential and few negative effects. The aim of this study was to investigate the phytochemicals of a medicinally rich plant Commiphora mukul. Herbalists use it as a significant therapeutic plant. Soxhlet extraction method was used to get successive solvent extracts of Commiphora mukul. The crude chemicals were extracted using methanol, petroleum ether, and ethyl acetate. The presence of alkaloids, flavonoids, phenols, terpenoids, steroids, tannins, carbohydrates, glycosides, and proteins were shown by a qualitative phytochemical analysis of these extracts. This experimental work would substantiate the traditional knowledge scientifically to use the plant for controlling several diseases.

**KEYWORDS:** Commiphora mukul, phytoconstituents, pharmacognostical, phytochemical.

## INTRODUCTION

Around the world, medicinal plants have been crucial in treating and preventing human ailments. Different medicinal plants, including those found in arid zones, herbal plants, and some shrubs, may be used to treat and prevent human ailments. Neutraceuticals are a variety of plants, food ingredients, and other ingestible compounds that have the potential to improve human health and function. It also includes elements obtained from plants and from animal services (Bopana *et al.,* 2007) Antioxidant components are microscopic substances that prevent oxidation of lipids by preventing the start or growth of oxidative chain reactions and also scavenge free radicals (Johnson *et al.,* 2005). Antioxidants have become increasingly used in clinical settings recently for the treatment of chronic degenerative illnesses, ageing, and neurodegenerative disorders (Sohal *et al.,* 2002).

Guggul (oleo gum resin), an extremely valuable herbal remedy that has been used to treat a number of ailments, exudes from the bark plant Commiphora mukul (Burseraceae). It represents a phytochemical reservoir of heuristic medicinal qualities and has a long history in ethnomedicine. It is one among the components in a variety of Ayurvedic formulations, the

most of which have the suffix guggul in their names (Aruoma *et al.,* 1997). Gugulipid, an extract of the Commiphora mukul used to treat a range of human illnesses, contains the major active ingredient guggulsterone. (Sangle *et al.,* 2004). In view of the above, we designed the study to evaluate the phytochemical analysis of Commiphora mukul.

## METHODOLOGY

### PLANT MATERIAL COLLECTION:

### *COMMIPHORA MUKUL*:

Plant material were collected in the month of march in 2021 from the suburban area of Bhopal. The plant that used for research were properly washed in water and then quench in distilled water. Then the subject is allow to dry at room temperature (Hanus *et al.,* 2005). The bark then cut into small pieces and dried for 8-10 days in sheded area without being contaminated. It taken care of that the material must not come in direct sunlight exposure. The shaded dried materials then grind into coarse powder with the help of electronics grinder. The powder of material were dried and stored in an airtight container in some dark place at room tempreture for extraction and phytochemical analysis (Patil *et al.,* 1972).

### DEFATTING OF MATERIAL:

Defating of material is a process of removal of dust, dirt, oil, fat and other foriegn material from plant material so that we can get the appropriate material for process. For defatting we keep plant material i.e. powder in petroleum ether for 24 hours at room temperature. After a period of 1 day the plant material filter with the help of spetula, funnel and filter paper. Spread tme filtered material on paper to dry and then keep tight in a container (Purushothaman *et al.,* 1976)

### CHEMICAL REAGENT:

For phytochemical analysis we used some chemical reagents. They are hydrochloric acid(HCl), Picric acid , Fehling solution A, Fehling solution B, Ferric chloride, Lead acetate, Gelatin solution, Copper acetate.

### EXTRACTION OF PLANT MATERIAL:

The process of separation of active plant materials from inactive plant material by the use of appropriate solvent and standard extraction method is known as extraction of plant material. The active plant materials alkaloids, flavonoids, terpenes, saponins, steroids, and glycosides. The common types of extraction method are maceration, infusion, digestion, soxhilation, percolation, decoctiona. For extraction of plant material here we use soxhilation method with the help of Soxhlet apparatus. In this method we use four solvent. They are chloroform ($CH_3Cl$), ethyl acetate ($C_4H_8O_2$), Ethanol ($C_2H_5OH$), Water ($H_2O$). We select these solvent on the basis of their polarity. The polarity of chloroform is least and the polarity of water is higher than all (Kakrani *et al.,* 1981)

**EXTRACTION OF MATERIAL IN SOXLET APPARATUS WITH SOLVENTS:(13-21)**

Here different solvents like petroleum ether, chloroform, ethyl acetate, ethanol, and water were used. Detailed phytochemical testing was performed to identify the presence or absence of different phytoconstituents.

**1. Test for triterpenoids and steroids:**

**i. Salkowski's test:**

The extract was treated with chloroform and filtered. The filtrate was added with a few drops of concentrated sulphuric acid, shaken and allowed to stand.

If the lower layers turn red, steroids are present.(Kumar *et al.*, 1987)

The presence of a golden yellow layer at the bottom shows the presence of triterpenes.

**2. Test for flavonoids:**

**i. Alkaline reagent test** (Su *et al.*, 2009)

The extract was treated with a few drops of sodium hydroxide separately in a test tube. The formation of intense yellow colour, which becomes colourless with the addition of a few drops of dilute acid, shows the presence of flavonoids.

**ii. Lead Acetate Test:**

The extract was treated with a few drops of lead acetate solution. The formation of yellow precipitate may show the presence of flavonoids (Bose *et al.*, 1966)

**3. Test for Tannin and Phenolic compounds:**

**i. Dilute iodine solution test:**

To 2 ml of extract, a few drops of dilute iodine solution were added—formation of transient red colour shows the presence of phenolic compounds (Ali *et al.*, 1967)

**ii. Lead Acetate Test:**

Some amount of extract was dissolved in distilled water. A few drops of lead acetate solution were added—the formation of a white precipitate shows the presence of phenolic compounds.

**4. Test for Alkaloids:** (Satyavati *et al.*, 1991)

To the extract, dilute hydrochloric acid was added, shaken well and filtered. With the filtrate, the following tests were performed.

**i. Hager's Test:**

To 3 ml of filtrate, a few drops of Hager's reagent were added in a test tube. The formation of a yellow colour precipitate shows the presence of alkaloids.

**ii. Mayer's Test:**

To 1 ml of filtrate, a few drops of Mayer's reagent were added along the sides of the tube. The formation of a white or creamy precipitate shows the presence of alkaloids.

**5. Test for glycosides** (pandey *et al.*, 2004)

**i. Keller-Killiani test:**

To 4 ml of test solution, 4 ml of glacial acetic acid and 1 drop of 5% ferric chloride were added in a test tube. Add carefully 1 ml of concentrated sulphuric acid by the side of the test tube. The formation of blue colour in the acetic acid layer shows the presence of Cardiac glycosides.

**ii. Legal's Test:**

3 ml of test solution was dissolved in pyridine. 3 ml of sodium nitroprusside solution was added and made alkaline using 10% sodium hydroxide solution. The formation of pink to blood-red colour shows the presence of Cardiac glycosides.

**6. Test for saponins (**dev *et al.,* 1987)

**i. Froth test:**

The extract was diluted with distilled water and shaken in a graduated cylinder for 10 minutes. The formation of a layer of foam shows the presence of saponins.

**7. Test for Carbohydrates and Reducing sugar** (Anurekha *et al.,* 2006, Tripathi *et al.,* 2007)

**i. Molish test:**

3 ml of aqueous extract was treated with 3 drops of alcoholic $\alpha$-naphthol solution in a test tube. Then 1.5 ml of concentrated sulphuric acid was added carefully along the sides of the test tube. The formation of a violet ring at the junction shows the presenceof carbohydrates.

**ii. Benedict's test:**

An equal volume of Benedict's reagent and extract were mixed in a test tube and heated in the water bath for 15minutes. The solution appears green or yellow, or red depending on the amount of reducing sugar present in the test solution, which shows reducing sugar.

**8. Test for protein and amino acids** (gujral *et al.,* 1960)

**i. Million's test:**

3 ml of extract was mixed with 5 ml of Million's reagent. A white precipitate formed, which on heating turned to brick red, shows the presence of proteins.

**Ii Biuret's Test:**

The extract was treated with 3 ml of 10% sodium hydroxide solution in a test tube andheated. A drop of 0.7% copper sulphates solution was added to the above mixture. Theformation of violet or pink colour shows the presence of proteins.

**RESULTS:**

**Table 1: Preliminary phyto-profile of extract of Commiphora mukul resins**

| Solvent | Polarity Index | Extraction | Colour | Constituency | Yield |
|---|---|---|---|---|---|
| C | 4.1 | Soxhelation | Green | Dry | 80 gm |
| EA | 4.4 | Soxhelation | Green | Dry | 80.2 gm |
| E | 5.3 | Soxhelation | Brown | Sticky | 78 gm |
| AQ | 9.1 | Soxhelation | Brown | Dry | 91.78 gm |

C- Chloroform extract, EA- Ethyle Acetate extract, E- Ethanolic extract, AQ-Aqueous extract.

**Table 2: Qualitative phytochemical analysis Commiphora mukul resins extract**

| Sr. No. | Experiment | Result | | |
|---|---|---|---|---|
| | | Pet. Ether Extract | Ethyl Acetate Extract | Methanol Extract |
| **1. Test for Triterpenoids and Steroids** | | | | |
| i. | Salkowski Test | Present | Present | Present |
| **2. Test for Flavonoids** | | | | |
| i. | Alkaline Reagent Test | - | Present | Present |
| ii. | Lead Acetate Test | - | Present | Present |
| **3. Test for Tannins and Phenolic Compounds** | | | | |
| i. | Dilute Iodine Solution Test | Absent | Present | Present |
| ii. | Lead Acetate Test | Absent | Present | Present |
| **4. Test for Alkaloids** | | | | |
| i. | Hager's Test | Absent | Present | Present |
| ii. | Mayer's Test | Absent | Present | Present |
| **5. Test for Glycosides** | | | | |
| i. | Keller Killani Test | Absent | Absent | Present |
| ii. | Legal's Test | Absent | Absent | Present |
| **6. Test for Saponins** | | | | |
| i. | Froth Test | Absent | Absent | Absent |
| **7. Test for Carbohydrates and reduce sugar** | | | | |
| i. | Molisch's Test | Absent | Present | Present |
| ii. | Benedict's Test | Absent | Present | Present |
| **8. Test for Protein and Amino acids** | | | | |
| i. | Million's Test | Absent | Present | Present |
| ii. | Biuret's Test | Absent | Present | Present |

Present shows the presence of that phytoconstituents

Absent shows the absence of that phytoconstituents

## CONCLUSION

To increase the sensitivity of plant extract and decrease the side effect of antibiotics, a combination of antibiotics and herbal extract was used. Day by day, bacteria gain strength and regain antibodies against traditional antibiotics. To stop their regenerating power, a combination of antibiotics and plant extracts provides one of the best results in such a direction.

If nontoxic plant extracts have been taken in suitable doses, they may prove the best supplementary remedies to patients. The yield of Commiphora mukul in different extracts are mentioned in Table 1.Yield of selected plant material is highest in aqueous extract.

Qualitative phytochemical analysis of Commiphora mukul extract was performed in Table 2 results is mentioned. Results show that

- In petroleum ether extract, none of the phytoconstituents are present.
- In Ethyl acetate extract Flavonoid, Tanin, Phenolic compound, Alkaloid, carbohydrate, reducing sugar are present.
- In methanol extract, Triterpenoid, Steroid, Flavonoid, Tanin, Phenolic compound, Alkaloid, Glycoside, Carbohydrate, Reducing sugar are present

The obtained phytochemical constituent results demonstrate that the methanol extract of Commiphora mukul resins can be used for curing some diseases. Therefore, further work is necessary to isolate and characterize these constituents.

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**Chapter 6**

# TOXIC EFFECTS OF ENVIRONMENTAL CHEMICAL MIXTURES

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**ABSTRACT**

Bio-synthesis of Nanoparticles through various plant materials is also known as green Ecotoxicology frequently deals with chemical mixtures in the environment, and there is a pressing need for new approaches to be developed in order to lessen the uncertainty surrounding the assessment of their ecological danger. Many different models have traditionally been used to predict the total possible impact of chemicals on organisms. Several combinations, such as concentration, addition and independent action, have been studied using these models. Even though these models typically provide a decent prediction of joint effects, they can have limitations, especially when there are interactions for which they cannot reliably predict joint effects. An experimental study framework is provided to make it simpler to look into the causes of observed interactions, enabling a better mechanistic understanding of interactions in mixture toxicology. The conceptual framework is developed by an extension of the three-stage system that was previously employed to explore chemical bioavailability. According to the concept, chemical interactions in mixers are a result of chemical speciation, binding, and transport processes in the exposure medium, toxico kinetic and toxicodynamic. These approaches come from biochemistry, environmental chemistry, toxicology, and systems biology.

**KEYWORDS:** Ecotoxicology, Chemical mixture, Mixture toxicology, Toxicodynamic

## INTRODUCTION

Historically, owing to the ancient knowledge of toxicology, natural poisons were undoubtedly used for hunting, warfare, medicine, and maybe intentional poisonings. This overview focuses on a more contemporary era of toxicology, even if the origins of toxicology as a scientific subject can be traced back several centuries to practitioners like Paracelsus or Orfila (Borzelleca, 2001). In contrast to the environment, where organisms are exposed to several different chemicals at once, most studies only take into account the toxicity of chemicals in isolation. A mixture's potential danger may be significantly underestimated or overestimated if mixture toxicity is assumed based solely on the data of its individual components. This is especially important when regulatory authorities are tasked with evaluating the use of substances that could

potentially be released into the environment or are already being used in it. The fact that a chemical is present in a mixture and is known to be harmful when used alone is no longer a guarantee of how it will behave when coupled with other agents. Although the emphasis has shifted significantly to considering mixes as a whole, there are still gaps in our understanding and our capacity to evaluate them as such. It may not be possible to predict which chemical combinations will appear in the environment or to test for all of the potential agents and mixtures. Even though environmental mixtures are sometimes extremely complex and diverse in composition, Kortenkamp *et al.* (2007), recently reviewed mixture research and discovered that less than 25% of the tests looked at mixtures with seven or more ingredients.

**ENVIRONMENTAL TOXICOLOGY**

Environmental scientists continue to face significant difficulties in evaluating the possible harmful consequences and quantifying the hazards posed by exposure to chemical mixtures in ecosystems and for specific segments of the human population (Cassese *et al.,* 1998). Even though environmental mixers usually occur at relatively low concentrations, it is frequently unknown what exactly makes them up. As a result, it is likely that other external, non-chemical stressors may also contribute to the overall effects. Although not all mixtures will be ecotoxic, those that are could cause significant harm to species. Numerous different chemical combinations exist, and testing each one for ecotoxic consequences is neither practicable nor always viable. As a result, there is a clear need for reliable methods to determine toxicity. (Cedergreen, 2014). It is a difficult endeavour that necessitates a solid theoretical framework that can be put to the test experimentally to comprehend the potential consequences of a chemical mixture, even for a single species or demographic group. The most popular additivity paradigm, which is based on two core models that take mode of action into account, is used to forecast the combined effects of substances. For chemicals with the same mode of action, the concentration addition model is used, while for chemicals with different mode of actions, the independent action model is used (Eggen *et al.*, 2004).

The Concentration Addition and Independent Action models can both provide a preliminary mathematical basis for the prediction of the mixture effect as quantitative descriptors of the relative toxicities of the individual chemicals in the mixture or as relationships between the probabilities of response under the assumption of completely independent effects (Jonker *et al.,* 2005). Several studies have documented the toxicokinetic and toxicodynamic (TK-TD) models that are now available, specifically formulated as the Concentration Addition and Independent Action models for the TD simulations of various organic compounds, in order to compare and clarify their underlying TD assumptions (Jager *et al.*, 2011; Nyman *et al.*, 2012)

However, when one or more of the mixture's constituents have unknown or unpredictable MoA, it is still uncertain whether such models can be used to forecast effects across the board (Jonker *et al.,* 2005).Using an understanding of the chemical mechanism of action as a foundation, Concentration Addition and Independent Action models are hypothetically

utilised. This approach has drawn criticism and various study support the notion that mixture toxicity effects on an organism level are just too complicated to be predicted only from knowledge of mechanism of action. Secondary modes of action, absorption kinetics, transportation, metabolism, compartmentation, and excretion of the chemicals are some of the activities that could significantly affect the combined effects but were not considered by the models (Borgert, 2004; McCarty and Borgert, 2006). Numerous experiments have been conducted to determine the frequency of interactions in chemical combinations. These have mostly focused on binary or ternary mixes and have highlighted the possibility for frequent and potentially large-scale interactions to occur even in situations where no a prior explanation for the existence of interactions would have been anticipated (Martin, 2009).

**CHEMICAL INTERACTIONS**

Independent Action model is based on the premise that there are no physical, chemical, or biological interactions between the separate elements that make up a combination, similar to Concentration Addition. As a result, they are independent of one another (McCarty and Borgert, 2006). The degree of dilution can be taken into account when calculating the combined effect of chemicals using CA by comparing the concentration of each chemical in the mixture to its single-substance toxicity, adding the concentrations, and determining the effect from the characteristics of the joint dose-response curve. It is believed that the slopes of compounds with the same molecular target site will be identical (Greco *et al.,* 1995; Gennings *et al.,* 2005). A biologically-based framework is suggested to give a foundation for supporting and interpreting the underlying mechanisms that result in chemical interactions that affect mixture toxicity. The framework takes into account the ideas of mixture exposure externally, or bioavailability, as well as exposure in the target species connected with accumulation through toxicokinetics to the expression of toxicity as mediated by receptor contacts within toxicodynamics. When it comes to mixtures, interactions can be divided into following categories:

1. Those that may affect how one or more chemicals are exposed to the outside world i.e. external exposure includes speciation, binding, and transport.
2. Toxicokinetics: encompassing absorption, distribution, metabolism, and excretion. Interactions at the site of uptake and/or elimination of chemicals from the organisms that may modify the detoxification/bioactivation and/or compartmentalization of one or more chemicals.
3. Toxicodynamics: includes interactions with receptor sites. Interactions that might affect the way one or more compounds bind to a receptor, which might (partially) affect toxicity (Jager *et al.,* 2010).

**EXTERNAL EXPOSURE OF CHEMICAL**

The introduction of extra chemicals in a mixture has the potential to modify the environmental availability of chemicals through a number of possible ways. One molecule may have an impact on speciation, binding, and transport in certain situations. The majority of substances that are

released into the environment interact with pertinent abiotic elements, such as soil and sediment particles and dissolved humic substances. As a result of these interactions, the amount of the chemical that may be absorbed and the extent to which organisms are exposed to the chemicals (external exposure) may change (internal exposure). Since these are essential for determining exposure and impact in various environmental media, a lot of research has been done to understand the mechanisms behind the interactions of chemicals with the abiotic environment (Tipping, 1994; Di Toro *et al.,* 2001).

The effect of acidity on the speciation of trace metals is one of the most well-known examples of a pollutant interaction. Pollutant deposition, like that of sulphur dioxide, is known to cause a decreased pH in both freshwater and soil systems. At a given total metal concentration, the concentration of free metal ions in solution is likely to rise under these acidic conditions. Since it is anticipated that the free metal ion will be the main harmful form for many species that live in soil and water (Likens *et al.,* 1996; Di Toro *et al.,* 2001).

When added to pesticide formulations with the goal of enhancing the dispersion of the active ingredient within the product, surfactants and emulsifying agents have a second interaction that might affect external exposure. This improves the chemical's availability to the target organism, increasing its toxicity in the process. Surfactants are also widely utilised in home items, therefore they are frequently found in wastewater and biosolids produced during wastewater treatment (Cirelli *et al.,* 2008).

A few pollutants can directly affect bioavailability in addition to altering ambient circumstances that affect external exposure. These pollutants operate as adsorption surfaces that may hinder or facilitate chemical transit into organisms. Regarding the possible consequences of releasing nanomaterials into the environment, the possibility that one substance could serve as a carrier for another with impacts on overall exposure has recently come to light (Lead and Smith, 2009).

When an influence on half-life is mediated by microbial toxicity, effects on fate pertain to another category of interaction that may change external exposure. In these situations, one chemical functions as a microbial toxicant, which reduces the activity of the guilds or strains of microorganisms that are in charge of the biotransformation of a co-exposed chemical (Principi *et al.,* 2009).

Since lower rates of biotransformation will alter the permanence of the pollutant, changes in the sequences of environmental concentration will ultimately produce effects that are both more severe and/or continue for longer than would be anticipated from single chemical toxicity data alone. When bacterial biocides are employed in conjunction with other pesticides or chemicals and when the pollution of soils and effluents is complicated, as in polluted land, landfill leachate, and wastewater flows from locations with considerable industrial input, these conditions are probably most relevant (Naslund *et al.,* 2008).

**TOXICOKINETICS**

Toxicokinetics is the process of producing kinetic data to measure systemic exposure, either as a crucial step in preclinical toxicity investigations or in particularly constructed supportive studies (Batra, 2015). The basic objective of toxicokinetics is to describe how systemic exposure is achieved in animals, how it relates to dose level and time course of the toxicity study, and how it can be applied to the development of novel medications (EORTC Pharmacokinetics and Metabolism Group., 2015). Toxicokinetics research is primarily necessary to associate the dose or chemical concentration with the mode of action of the chemical and its numerous metabolites. The distribution and creation of numerous chemical entities at the target tissue are caused by the toxicokinetic process, which is also in charge of calculating the dose at the toxicological site (Smyth and Hottendorf, 2015). Before a chemical can have a toxic effect, it typically needs to be absorbed and transported to its intended location.

The fundamental toxicokinetic parameter is based on *in-vitro* and in silico research, which identify the possibility of chemical accumulation, distribution, or inhibition in tissues and organs (Welling, 2014). The extent to which a substance is exposed externally controls how much of it reaches potential absorption sites.

When combined with the physico-chemical properties of the substance in question, the biology of the organism ultimately determines the rates of absorption and, ultimately, the internal dose/concentration of the chemical within the organism (Randall *et al.,* 1998). Frequently pass through porous membranes like the skin or gills, are ingested, inhaled, or evaporated before entering the body. Depending on the chemical, toxins can flow through a substance passively (by diffusion) or actively (and so mediated by chemical transporters). Charged organic (chemicals and metals, for instance, are usually believed to be assimilated through uptake channels or carrier proteins, whereas neutral organic molecules are typically regarded to be taken mostly through passive absorption. Locations of passive or active chemical absorption across body surfaces provide a definite potential site where substances that are present in combination can interact. Some interactions can be simple, such when one medicine affects the physiological systems that control exposure to another. For instance, chemical exposure may alter ventilation rate, which can affect how much of a different chemical enters the body through the surface of the lungs or gills and how much of that chemical is exposed to the body. (Reynders, 2006).

Numerous toxicokinetic investigations have shown that chemical interactions, which might result in interactions in mixtures, can inhibit or even boost the cytochrome P450s (CYP) system's function. As an illustration, in vitro. Investigations (on antidepressants, anti-inflammatory medications, and lipid regulators) on the CYP enzymes in the carp liver fractions have shown the inhibitory power of specific pharmaceuticals (Xu *et al.,* 2002).

Human toxicology frequently recognises the CYP system as the initial response to exposure to organic compounds. For instance, it is known that members of the CYP3A subfamily, which is expressed in all vertebrates, participate in a number of external organic chemical degradation

processes. One of these is how about 50% of drugs are metabolized in the initial phase. Many key categories of planar organic pollutants, including polycyclic aromatic hydrocarbons, polychlorinated biphenyls, dioxins, and furans, as well as methyl-xanthines like caffeine and theophylline, are metabolised in the first phase by the highly conserved CYP1 family in vertebrates (Boelsterli, 2003; Dorne, 2009).

Simulation models have been created in order to make quantitative predictions about the rates at which organic compounds are metabolised in fish and, more recently, earthworms. The relationship between a species's CYP enzyme complement and the rates at which certain organic compounds are metabolised can be shed light on by combining sequence data with simulation models (Dimitrov, 2005; Weisbrod, 2007).

Therefore, by screening tests for differences in the expression of genes connected to first and second phase metabolic enzymes, the CYP isoform that is active can be identified. As a result, the metabolic potential of the major groups of organic compounds can be determined, as well as the potential interactions between the components of chemical mixtures that share the same CYP-mediated metabolic pathway (Menzel, 2001).

**TOXICODYNAMIC**

The effects at target receptors are a further source of mixture interactions. The concentration addition model makes the assumption that both compounds are present at the target site and are each able to bind freely without the presence of any stimulatory or competing influences. This is true for chemicals acting with the same MoA. The toxicodynamic effects of receptor-binding have been linked in mammalian systems to a variety of endpoints, including neurotoxicity, renal toxicity, cardiovascular toxicity, and the antimicrobial activity of a variety of medicines and biocides. The cholinesterase enzymes and nerve sodium channels are examples of pesticide targets that have been well documented both *in-vitro* and *In vivo* (Dorne *et al.,* 2007a; Bosgra *et al.,* 2009).

The huge variety of species within ecotoxicology makes it more difficult to pinpoint the receptors that control toxicodynamics. Identifying whether pertinent targets are present in the specific species is a difficult first step. This problem can be solved using a creative and simple bioinformatic strategy. The method looked into 16 species' orthologs of 1318 human drug targets, some of which were important for testing ecotoxicity. Only 61 percent of drug targets were discovered to be conserved in Daphnia and 35 percent in algae, but zebrafish were found to express orthologs to 86 percent of drug targets. The expected presence and absence of orthologs matched the available information on the probable toxicity associated with a given pharmacological target quite well (Gunnarsson, 2009).

Proteomics has been widely used in numerous fields of biology as methods for supporting quantitative assessment have evolved. Studies on sentinel species, such as algae (Jamers *et al.,* 2009) and macro-invertebrates that address environmental health and ecotoxicological issues are included in this. LaCourse *et al.* (2009) has been proposed that proteomics may be utilised to

locate and define novel biomarkers connected to specific MoAs expressed within chemical mixtures by characterising the underlying proteome responses of exposure to xenobiotics. Thus, the complex mechanisms behind physiological change in the primary cellular targets of toxicity are well understood (Nesatyy and Suter, 2007).

The availability of appropriate sequence information to assist in the identification of targets is a significant problem for proteome analysis for application in toxicology and ecotoxicology. This does not pose a problem for several extensively used vertebrate species in toxicology (such as rats, mice, and zebra fish), for whom significant genome information is accessible. When it comes to species that are ecotoxicologically important, the situation is frequently more difficult because we don't yet know their genomic sequences. Draft genomes for many species are anticipated to be available soon thanks to the development of huge parallel sequencing and the move toward the $1000 genome. In the meanwhile, peptide identification can be assisted by bioinformatic methods that make use of the sequence data from EST programmes that is now accessible (Wasmuth and Blaxter, 2004).

A Toxicokinetic-Toxicodynamic model can contain a wide variety of toxicodynamic models, from those that describe graded responses to those that describe quantal (the individual either shows the response or it does not) responses (gradual changes in individuals). Additionally, toxicodynamic models can take into account both fatal and sublethal effects. Usually, toxicodynamic models of non-lethal, graded responses to toxicant exposure are used to quantitatively describe changes in the expression of well-chosen biomarkers that are connected to sublethal toxic effects and tissue damage (Ashauer *et al.*, 2011).

## CONCLUSION

Integrating combination toxicity into regulatory systems that, until this point, have only focused on single chemicals is difficult since it is an effectively infinite problem. The long-standing models that are consistent with the principles of concentration addition and independent action have proven useful in accounting for the combined effects of chemical mixtures. These models occasionally fall short of describing combined effects, though. From the viewpoint of economics, public health, and environmental protection, situations of antagonistic relationships, and especially synergistic relationships, have the potential to be harmful. Research on combination toxicity needs to concentrate on locating interactions and comprehending the underlying mechanisms. An analysis and interpretation framework for the interactions in chemical mixtures is provided here. Toxicokinetics of the several chemicals present can be predicted using physiologically based pharmacokinetic models. A greater understanding of not just the frequency of interactions in mixtures but also their mechanistic basis in exposed species, including humans, would seem to await with the instruments at hand and the theoretical framework in place.

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**Chapter 7**

# PHARMACOLOGICAL POTENTIAL OF SELECTED PLANTS OF EUPHORBIACEAE FAMILY

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**ABSTRACT**

Since ancient times, plants have served as the primary source of the basic ingredient of medicine. *Euphorbia Nivulia* Buch. Ham and *Jatropha Curcas* Linn. belongs to the Euphorbiaceae family, two under-utilized plants of many medicinal values. The present article focuses on the various phytoconstituents (secondary metabolites) present in the alcoholic (methanolic and ethanolic) leaf extracts that are actually responsible for the pharmacological potential of drugs derived from these plants.

**KEYWORDS:** Medicinal plant, Euphorbiaceae, *Jatropha Curcas*, *Euphorbia Nivulia* Buch. Ham., Phytoconstituents, Pharmacological activity.

## INTRODUCTION

India has a recorded list of total 45000 plants species, 7500 species among that have estimated as medicinal plant (Hui Tag *et al.*,2007; Shaikh *et al.*, 2011). According to report of (Uwe *et al.*, 2002) India has the widest range of medicinal plant all over the world. In term of percentage about 17% of total plant species found in India are represented as medicinal plants. Plants and plant derived medication occupies a central place (Hui tag *et al.*, 2007; Mamta *et al.*, 2012) due to low toxicity, lesser cost and almost null site effect (Prabhavati *et al.*, 2016). The first step in new herbal drug discovery involve the recognition of medicinal plant composition (Chandrakant *et al.*, 2012). In the present article pharmacological activities of alcoholic leaves extract of two selected plants of Euphorbiaceae family (*Jatropha Curcas* Linn. and *Euphorbia Nivulia* Buch. Ham.) have been studied with the help of phytochemical analysis.

***Euphorbia Nivulia***

***Jatropha Curcas***

**PHYTOCONSTITUENTS**

Active ingredient of plant are classified in two categories i.e. primary metabolites and secondary metabolites. In all plants primary metabolites perform important vital role in nutrition and reproduction. These are related to structure, genetics and physiology. In contrast secondary metabolites are class of compounds derived from primary metabolites. Secondary metabolite (phytoconstituents) are the bioactive compound originated from plants and major source in pharmaceutical drug manufacturing. It constituent the medicinal value of plant and responsible for producing physiological action against several ailments.

**ANALYSIS OF PHYTOCONSTITUENTS**

The chemical tests for the screening of phytochemicals of *Jatropha curcas* and *Euphorbia nivulia* plants were analysed after extracting the leaves with alcohol as solvent (ethanol and methanol) and using the standard procedure as described in (Kokate *et al.*,2005, Anuj Kumar *et al.,* 2017). The tests for the screening of phytochemicals of plants were done in following manner:

**1. TEST FOR ALKALOIDS -**

**Wagner test**: 2 ml of filtrate and few drops of reagent was added, the presence of reddish brown precipitate indicate positive test for alkaloids.

**Dragendorff test**: The filtrate was directly treated with Dragendorff"s reagent appearance of red precipitate observed.

**2. TEST FOR FLAVONOIDS** -

**Shinoda test/Magnesium hydrochloride test:** To the test solution (5 ml) added only few magnesium turning + 1 ml concentrated hydrochloric acid drop wise. Appearance of pink red colour confirm the presence of flavonoid in extract.

**3. TEST FOR PHENOLIC COMPOUND AND TANNIN -**

**Ferric chloride test:** Plant extract in solvent treat with few drops of natural 5% ferric chloride solution intense green colour was formed to indicate the presence of phenolic compound.

**Lead acetate test:** To the test solution added few drops of lead acetate, white precipitate was formed as final product.

**4. TEST FOR CARBOHYDRATE -**

Prepared plant extract were dissolved separately in distilled water and filtered

**Molish test**: Molish reagent (Alcoholic solution of $\alpha$-Naphthol) was added in filtrate, stirred well and poured 1 ml of concentrated sulphuric acid ($H_2SO_4$) slowly along the sides of the test-tube. The violet colour ring appears at the junction, confirm the presence of carbohydrate.

**5. TEST FOR GLYCOSIDES -**

**Keller-Killiani test for cardiac glycosides**: 0.5 ml of glacial acetic acid with trace $FeCl_3$ solution was added to plant extract. Carefully add 0.5 ml of concentrated sulphuric acid along the sides of test tube. A layer of blue colour appears in acetic acid suggest cardiac glycosides presence.

**Borntrager's test for anthraquinone glycosides**: Small amount of plant extract were shaken with benzene and about half of its volume of 10 % ammonia solution added further. The

solution gets divided into organic phase and ammonical phase. Anthraquinone glycosides confirmed with appearance of violet pink colour in ammonical phase (Mamta *et al.,* 2012).

**6. TEST FOR STEROID AND TRITERPENOID -**

**Libermann-burchard test:** Dry extract was dissolved in chloroform, stirred and filtered. Few drops of acetic anhydride mixed to the filtrate, boiled on water bath cooled. $H_2SO_4$ was added slowly along the side of test tube which results in appearance of brown colour ring at the junction of two layers. The green colour in upper layer indicates the presence of steroids and deep red colour obtained with triterpenoid presence (Chaturvedi *et al.,* 2011).

**7. TEST FOR TERPENOIDS -**

To the solution some pieces of tin and thionyl chloride (3 drops) were added. The presence of terpenoids confirmed when violet colour appeared (Anuj Kumar *et al.,* 2017)

On the basis of phytochemical analysis, the result of qualitative test revealed the presence or absence for various bioactive compounds in the dried leaves extract of plants in ethanol. The screening result shown in below table 1

**Table 1: Screening results in ethanolic and methanolic extract**

| **Phytoconstituents** | **Test** | **Screening result in ethanolic extract** | | **Screening result in methanolic extract** | |
|---|---|---|---|---|---|
| | | **JCE*** | **ENE*** | **JCM*** | **ENM*** |
| Alkaloid | Dragendorff test | - | + | + | + |
| | Wagner's test | - | + | + | + |
| Flavonoid | Shinoda test | + | + | + | + |
| Phenolic acid and tannin | Ferric chloride test | + | - | + | + |
| | Lead acetate test | + | - | - | + |
| Carbohydrate | Molish Test | + | + | + | + |
| Glycosides | Cardiac (Keller Killiani test) | + | + | + | - |
| | Anthraquinone (Borntrager's test) | - | - | + | + |
| Steroid | Liebermann Burchard test | + | + | - | - |
| Triterpenoids | Liebermann Burchard test | + | - | - | + |

*JCE and JCM= *Jatropha Curcas* leaves extract with ethanol and methanol respectively

*ENE and ENM = *Euphorbia Nivulia* leaves extract with ethanol and methanol respectively

The qualitative phytochemical analysis shows important indication about the existence of secondary metabolites. It's also plays an important role in term of pharmacological potential biological activity like antioxidant, antimicrobial, anticancer us, antipyretic action. The correlation of secondary metabolite and pharmacological activity shown in table 2 below

**Table 2: Biologically Active Phytochemical in Medicinal Plants**

| **Pharmacological Activity** | **Secondary Metabolites** | **Biological Activity** |
|---|---|---|
| Antifungal and antibacterial | Terpenoids, alkaloids, phenolics | Inhibition of microorganism and fungal infection |
| Antioxidants | Flavonoids, polyphenol, carotenoid, ascorbic acid | Free radical quenching |
| Anticancer | Carotenoid, polyphenol, flavonoid | Inhibition of lung cancer and tumor, antimetastatic activity |
| Detoxifying agent | Tocopherol, phenol, flavones, phytosterol | Inhibition of procarcinogenic activities |
| Other | Alkaloid, terpenoids, volatile compound | Neuropharmacological agents, antioxidant |
| Source : (Mamta *et al.,* 2013) | | |

**ALKALOIDS:** It is one of the important naturally occurring metabolite that has therapeutic properties. These are reported to possess muscle relaxant, analgesic and antioxidant biological properties (Arpita *et al.,* 2017). Alkaloids were found to be present in methanol extract of JC whereas in EN leaves it is found present in extract with both the solvent.

**PHENOLIC COMPOUNDS:** Phenolic compounds are most widely pronounced group of secondary metabolites includes flavonoids, phenolic acid and tannin. These have multi-functional biological activities includes natural antioxidant properties and free radical scavengers (Keline Medeiros *et al.,*2014) cardiovascular diseases inhibitor (Wang *et al.,*2011) anti-inflammatory (Duangjai *et al.,*2018). The presence of phenolic compounds was observed in all the extracts namely methanol, ethanol for both the plants.

**TERPENOIDS:** The term terpenoids covered an range of substances which are based on union of $C_5$ unit, isoprene $CH_2 = C (CH_3) – CH = CH_2$. Terpenoids found present in methanolic and ethanolic extract of leaves of EN as well as JC. Terpenoids found to possess antimicrobial antibiotics, cytotoxic activities (A.K.M.Nasimul *et al.,* 2003). Since because terpenoids are lipid soluble they have been utilized in cosmetics, antibacterial soap and household product (Sam Zwenger, 2008). Antimalarial and anticancerous (Guangyi *et al.,* 2005) are also the therapeutic properties of terpenoids.

**CARBOHYDRATES:** These are most abundant molecules consist of C, H and O also known as saccharides. Therapeutic properties of carbohydrate include anti-inflammatory, anticoagulant

and antithrombotic. These are also useful in treatment of cardiovascular and haematological treatment (Michelle *et al.,* 2007). The presence of carbohydrates was reported in the entire extract sample prepared for both the plants.

**GLYCOSIDES:** Glycosides are natural organic compound derived from sugar part / carbohydrate (glycone) and non – sugar part (aglycone) are used for various therapeutic purposes such as cardiac glycosides used to regulate blood pressure for treating heart failure (Wilhelm *et al.,* 2007). Cardiac glycosides were found to be present in both the extracts of JC however only in ethanolic extract of EN. Anthraquinone glycosides were present in only methanolic extract of both the plant leaves.

**STEROID AND TRITERPENOIDS:** The presence of steroid and triterpenoids in medicinal plant are of great important in new drug discovery because of its pharmacological properties and their relationship with sex hormones (Santhi *et al.,* 2011). Some steroid contains insulin like polypeptide, thus useful in lowering the blood sugar levels and treatment of diabetes (Sathish *et al.,* 2010). In EN leaves steroid found present in ethanolic extract whereas triterpenoid found to be present in methanolic extract only. In JC, steroid and triterpenoid found present in ethanolic extract only.

## CONCLUSION

Phytochemical analysis of all the extract samples revealed the presence of almost all the phytoconstituents namely alkaloid, carbohydrate, steroids, phenolic compound, flavonoids, saponin, glycosides, terpenoids, glycosides etc. There are not much differences notice in result of ethanolic and methanolic extracts in term of phytoconstituents .Therefore from present work it can be concluded that pharmacological result generated will be useful for evidently confirmed the unexplored components in term to establish the folklore claim and botanical identity of the plants. These studies can be utilized significantly as tool to resolve the taxonomic controversies.

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**Chapter 8**

# PHYTOCHEMISTRY AND APPLICATIONS OF ACTIVE INGREDIENTS OF MEDICINAL PLANTS

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**ABSTRACT**

All the medicinal plants have certain active ingredients that help us in treatment of diseases by killing germs and prevention of diseases by increasing the immunity of our body. These active ingredients vary from plant to plant as well as nature of plant part. Some of these active ingredients include *Alkaloids*, *Terpenes*, *Saponins*, *Flavanoids* and *Tannins*. All these active ingredients have profound effect on the physiological activity of human beings. Medicinal plants also show antioxidant activity that helps us in boosting our immunity to great extent. In general, these active ingredients are extracted by the help of different solvents like methanol-water mixture, n-hexane and petroleum ether etc. After extraction and isolation of these bio-active ingredients, their phytotochemistry is studied on the basis of structural elucidation.

**KEYWORDS:** Alkaloids, Terpenes, Saponins, Flavanoids, Tannins

## INTRODUCTION

Plants have been playing a significant role in human life for a very long time. They provide us food, oxygen, fiber for clothing and housing material. Besides this, plants provide us medicines, keeping our body disease free. In present scenario medicinal plants have come up with great demand from disease treatment and prevention as well as employment point of view. As far as livelihood earning is concerned, the medicinal plants can be grown with least labour and cost. Wild animals generally don't destroy the crop of medicinal plants as most of the plants are bitter in taste. Besides this, the medicinal plants don't require much irrigation and insecticides.

The phytochemistry of medicinal plants includes extraction, isolation and structural elucidation of some of the important classes of naturally occurring bio-active chemical compounds found in different parts of plants. These naturally occurring bio active ingredients are the classes of various phytochemical compounds such as Saponins, Alkaloids, Terpenes Flavanoids and Tannins. All these phytochemicals greatly affect the physiological activity of human beings. The phytochemicals are synthesized by plants to save them against insect attack and diseases. In the

same plant various phytochemicals are found, therefore to study the medicinal property of plant these active ingredients of plant must be separated.

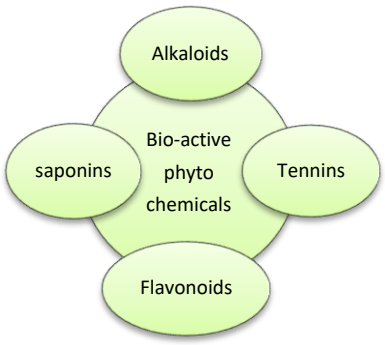


**Fig. 1: Various Bio-active Plant Ingredients**

**SAPONINS**

Saponins are the plant steroids having two different structural subunits an aglycon and a saccharide unit. The structural variability in saponins is seen due to the variations in the aglycon or saccharine subunits. For complete structural estimation of saponins identification of aglycon unit as well as determination of sugar sequence is done. Typically for extraction of Saponins the clean fresh plant material is subjected to exhaustive methanolic extractions and thereafter the crude methanolic extract is further extracted with petroleum ether, 5% aqueous methanol, n-butanol and water. The bulk of the saponins are found in normal butanol fraction.

For structural estimations a complete hydrolysis of the saponins is carried out to know the aglycon subunit as well as the sequencing of sugar units. Multidimensional NMR has been quite useful in structural determination of Saponins.Uses of DEPT or APT analysis gives fruitful clues regarding aglycon subunit and sugar sequencing. The saponins exhibit antimicrobial properties, guarding our body against fungal, bacterial and viruses. At the same time they improve immune system by stimulating the production of T-cells. Saponins act as antioxidants. The saponins are generally found in Soya bean and Peas.

The saponins form foam when mixed with water. Saponins are used in the development of cosmetics and drugs (Lorent *et al., Royal* Society of Chemistry 2014). They show anti-inflammatory and immune-boosting properties as well as antibacterial effects. Their name derived from a latin word 'Sapo' which means soap. The saponins are naturally occurring chemical compounds. They occur in wide range of herbs, seeds and vegetables. In medicine they are used in vaccine formulations (*Sun at al*. 2009) to regulate immune function. Due to their antibacterial and foaming properties, these compounds are added to shampoos, soaps, house cleaners etc. The saponins help in treatment of dyslipidemia (Ejelonu *et al.,* 2017) by reducing cholesterol levels, kill disease causing bacteria and inhibit tumor growth.

The saponins show weak antibacterial activity but strong antifungal activity. The usual mode of action against fungal infection is the pore formation and loss of membrane activity. This mechanism of action is similar to hemolytic activity of saponins. Saponins are widely used as natural detergents. Saponins maintain body weight by reducing abdominal fat, triglycerides

and cholesterol levels. Saponins also inhibit formation of fatty tissues and suppress appetite. Saponins reduce the risk of cancer and inhibit cholesterol absorption by binding with bile salts. Saponins show antidiabetic property as well (Elekofehinti *et al.,* 2015).

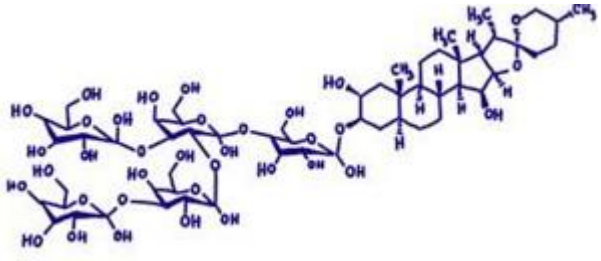

**Fig. 2: Structure of Saponins**

**Table 1: List of plants showing saponin content (*Mir et al.,* 2016)**

| Common Name | Botanical Name | Saponin Content in % |
|---|---|---|
| Green pea | *Pisum sativum* | 0.18-4.2 |
| Soybean | *Glycine max* | 0.22-0.49 |
| Milkwort | *Polygala spp.* | 8-10 |
| Soapwort | *Saponaria officinalis* | 2-5 |
| Quillaja bark | *Quillaja saponaria* | 9-10 |
| Primula | *Primula spp.* | 5-10 |
| Alfalfa | *Medicago sativa* | 0.14-1.71 |

**ALKALOIDS**

Alkaloids are basic substances due to the presence of nitrogen in their structure. Alkaloids are derived from amino acids and the plants can synthesize them too as secondary metabolites. Alkaloids are bitter in taste. They show strong effect on biological activities of plants and animals. Alkaloids show anticancer, anti –inflammatory, analgesic, anesthetic, pain relieving, antimicrobial and antifungal activities. Based on the ring structure, the alkaloids are classified as indole, quinolones (Grundon, 1979), isoquinolines (Bentley, 1965), pyrollidines, pyridines, terpenoids and steroids. On the basis of solubility of alkaloids in water they are classified as quaternary alkaloid salts e.g. quinolone, Alkaloid N-oxide e.g. Indole, Isoquinoline and polyhydroxy alkaloids e.g. pyrollidine and piperidine. Alkaloids can be detected by the help of alkaloid detection reagents for e.g. Dragendroff's reagent (potassium bismuth iodide), Mayer's reagent (potassium mercuric iodide), Sonnenschein's reagent (phosphomolybdic acid), picric acid and picrolinic acid. Plants produce alkaloids and store them in different amount in different parts of plants like leaf, stem, root and fruits. Initially it was believed that alkaloids are plant waste but now researches have proved that they play significant functions in plants.

For extraction of alkaloids, the air dried plant part is ground and passed through fine sieve of 1 mm and extracted by the help of polar solvents like methanol or ethanol in Soxhlet apparatus. The plant part can be pre-extracted with nonpolar solvent Hexane to remove the lipid material. The alcoholic extract is concentrated to dryness under vacuum and the residue is suspended in

dilute mineral acid like HCl. Now the aqueous acid solution is extracted with immiscible organic solvent like chloroform. The aqueous solution is now basified with ammonia solution and is re-extracted with chloroform. The mixture of alkaloids is now separated with the help of thin layer chromatographic techniques.

Alkaloids are essential part of human diet like coffee seeds (Caffein), tomato (tomatine) and potatoes (solaline). Alkaloids are also used as stimulants e.g. Nicotiana tabacum present in tobacco plant, Cocaine (a narcotic drug is obtained from Conium maculatum, an active ingredient of poisonous hemlock) and Morphine (a pain reliever alkaloid). Some alkaloids are poisonous e.g. strychnine obtained from Strychnos species. Besides, alkaloids show antiplasmodial, anticorrosive, antioxidative, antibacterial, anti-HIV and insecticidal activity.

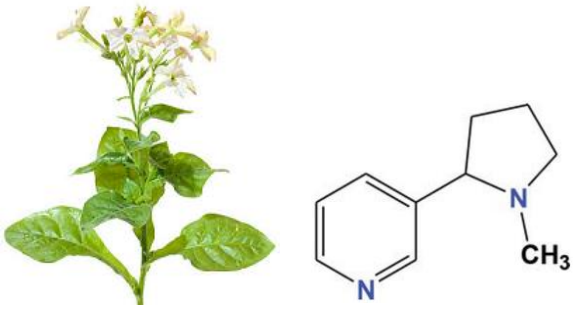


**Fig. 3: Nicotine Alkaloid obtained from Nicotiana tabacum**

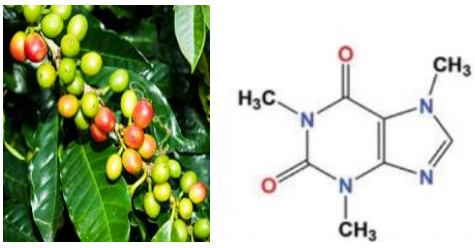


**Fig. 4: Caffeine Alkaloid obtained from Coffea arabica**

**Table 2: Alkaloids found in medicinal plants**

| | | | | |
|---|---|---|---|---|
| Quinine | Codeine | Boldine | Ergosine | Harringtonine |
| Reserpine | Thebaine | Sanguinarine | Ergocrystine | Tetrodotoxin |
| Vincamine | Morphine | Berberine | Ergocryptine | Saxitoxin |
| Vinblastin | Papaverine | Emetine | Caffeine | Lobeline |
| Vincristine | Narcotine | Ajmalicine | Nicotine | Spartine |
| Aconitine | Narceine | Ergocornine | Mescaline | Harmane |
| Serotonin | Taxol | Ergotamine | Ephadrine | Veratrine |
| Cocaine | Colchicine | Ergonovine | Physostigmine | Psilocybine |

**TANNINS**

Tannins (commonly referred as tannic acid, a 3, 4, 5 trihydroxy benzoic acid) are water soluble phenolic compounds found naturally in plants and in some animal species. They have the ability to precipitate proteins and other organic compounds. Tannins are well distributed in various plant species of angiosperms and gymnosperms. Tannins have the property that causes shrink in body tissues, thus they act as astringent. Tannins being a polyphenol compound bind salivary proteins and make them precipitate causing a dry and puckery sensation in mouth. Tannins protect plant from predators as they make plant unpalatable and also regulate their

growth (*Ferrell et al.* Baltimore 2006). The raw fruits have higher tannin content. Tannins are primarily located in the vacuoles or surface wax of plants. Tannins from wood and decaying vegetation undergo leaching into the water bodies making water bitter in taste and smell bad. The leaching of tannin in water turns its color slight brownish and lowers the pH of water.

The extraction procedure of Tannins varies greatly (Hagerman *et al*., The Tannin Handbook 1998). In general acetone is used as solvent to extract tannins from plant. Acetone retards the interaction between tannins and proteins by breaking hydrogen bonds between tannin-protein complexes (*Porter et al*. Condensed tannins 1989). Thus, increase the yield of tannins during extraction. Detection of tannins can be carried out on the basis of precipitation of proteins and reactions of phenolic ring or using ferric chloride solution (5%) to show color reaction. Tannins (as tanbark from oak) are used in tannery to produce leather from hide. Tannins are used as mordant to color the fabrics. Tannins are also used as wood adhesives. Tannins are also used in paints to produce anti-corrosive primer. Tannins play important role in treatment of burns. They show anti-inflammatory, antiseptic, antioxidant and hemostatic activities.

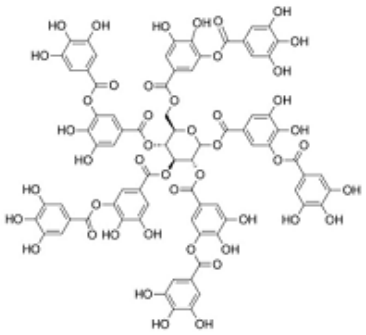

**Fig. 5: Ocimum sanctum (tulsi) having tannins (*Pattanayak et al.* and *Kelm et al.*) and Chemical structure of tannins**

**FLAVONIDS**

Flavonoids are also polyphenolic compounds found in plants. They exhibit remarkable cytotoxic activity and hence used in the preparation of anticancer drugs. A common flavon ring is made up of 15 carbon skeleton having three rings in which two are phenyl rings and the one is heterocyclic ring containing embedded oxygen as hetero atom (*Delage et al.* Flavonoids 2021). The flavonoids are classified as flavonoids, bioflavonoids and isoflavonoids. Flavonoids play many functions in plants. Flavonoids act as pigment and provide color to many flowers. Thus, assist plants in pollination and fruit formation. Flavonoids also assist plant in nitrogen fixation and U.V. filtration. Flavonoids act as physiological regulators, cell cycle inhibitors and chemical messengers. Apart from it some flavonoids display cell inhibitory activity against the organisms that cause plant diseases. From last few decades dietary flavonoids have become core of study of flavonoids due to their health benefits and disease prevention characters.

Flavonoids are not absorbed well by human body and thus quickly excreted. Flavonoids show poor antioxidant activity. Dietary Flavonoids reduce the risk of different types of cancer,

including the prostrate, breast, gastric and colorectal (*Rodriguez-Garcia et al.* 2019). Citrus fruits contain different types of Flavonoids. Blueberries are rich source of dietary fibers (Oomah *et al.*, 1996). Parsley contains flavones (*USDA's Database*). Black tea contains dietary flavan-3-ols. Peanut red skin contains high polyphenol content including flavonoids (De Camargo *et al.*, 2015). The detection of flavonoids can be carried out in plant by adding 10% aqueous sodium hydroxide solution to 4 ml of plant extract, development of yellow color occurs which turns colorless on addition of hydrochloric acid.

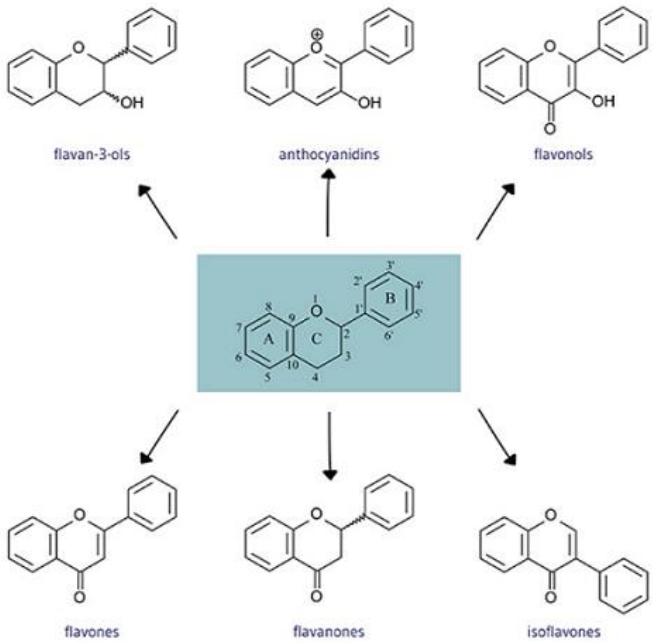


**Fig. 6: Basic skeleton and different subclasses of Flavonoids**

Medicinal Plants like Picrorhiza kurrooa (kutki) have flavonoids apocynin and vanillic acid. Digitalis purpurea (Foxglove) also contains flavonoids

**Fig. 7 Picrorhiza kurrooa (kutki)**

**Fig. 8 Digitalis purpurea (Foxglove)**

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Chapter 9

# INTRODUCTION TO MEDICINAL CHEMISTRY-AN OVERVIEW

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**ABSTRACT**

Medicinal chemistry is important branch of science that deals with discovery and design of new therapeutic agents. This chapter gives brief introduction about the basics of medicinal chemistry viz. drug design and development, pharmaceutical phases. It also deals with the various factors i.e. absorption, distribution, metabolism, excretion (ADME) affecting the drug ability to reach target site. The drug concentration should be optimum enough to maintain a steady concentration at target site. If drug concentration in blood is too low, it would result in inefficient therapeutic activity and if it is too high, it would impart detrimental side effect to the body. This window where drug concentration is optimum enough to impart desirable therapeutic effect on body is known as therapeutic window. The drug release above or below this window would either cause side effects or inefficient pharmaceutical activity respectively. It also deals with important pharmaceutical terms i.e. $LD_{50}$ and $ED_{50}$.

**KEYWORDS:** Medicinal chemistry, pharmacokinetics, pharmacodynamics, pharmaceutical phases.

## INTRODUCTION

Medicinal Chemistry is the branch of science that deals with the design and discovery of biologically active molecules having pharmaceutical properties. The primary objective of medicinal chemistry is the identification, development and synthesis of new therapeutic agents. It also deals with finding their structure activity relationship to elucidate the pharmacological activity of the drug.

According to IUPAC, medicinal chemistry was defined as "it concerns the discovery, the development, the identification and the interpretation of the mode of action of biologically active compounds at the molecular level".[1]

Scientists involved in drug discovery are expected to have in-depth knowledge of not only chemistry but all the other fields incuding biology, mathematics, biochemistry, computing. Thus most medicinal chemist involves participation from team of other scientists such as biochemist, analytical chemist, microbiologists, computational chemists, and toxicologists etc.[2] (**Fig 1**)

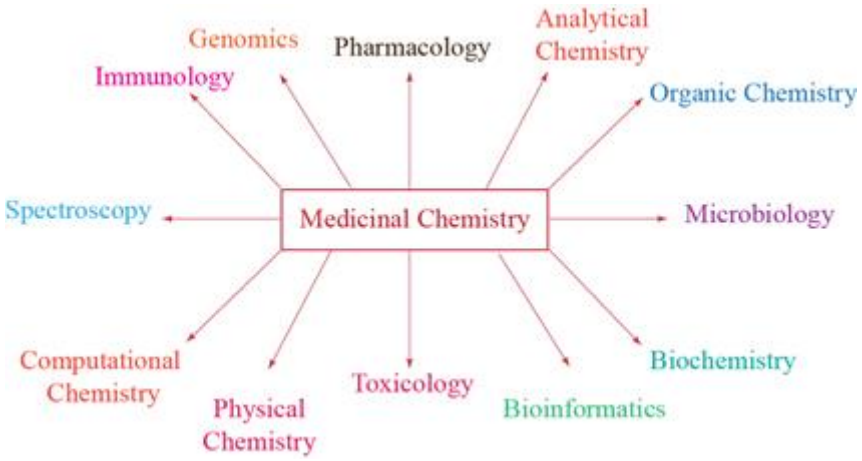



**Fig. 1: Interdisciplinary and modern Medicinal Chemistry**

## DRUG DESIGN AND DEVELOPMENT

Drug can be defined as "any chemical compound (other than food) that can affect living processes in a positive or negative way ". If it affects the body in beneficial manner then drug is called medicine. However, if it affects the body in detrimental manner then drug is called poison. Therefore, any chemical substance that is used in the prevention and/or treatment of disease is known as medicine". But it should be noted that no medicine is fully safe and may result in unwanted, undesirable and harmful effects referred as side effects.

Infact from ancient times, people across the globe have explored various natural products from plants and animals for pharmaceutical uses. However, there was still lack of rational approach in the development of new drugs. With time and increasing knowledge in the field of medicinal chemistry, a wide range of biologically acive molecules derived from natural source would be selected that are likely to possess pharmaceutical properties but need some structural modifications. These compounds are called **lead compounds**. And compounds synthesized by organic chemist based on these lead compounds with optimized pharmaceutical properties are known as **analogues.** For instance, salicyclic acid and acetyl salicyclic acid (aspirin) both are structural analogues but the presence of acetyl group in aspirin enhanced its pharmaceutical property over salicyclic acid.

Paul Ehrlich and Sacachiro Hata synthesized antiprotozoal arsphemamine (**Fig 2**) using rational approach for the first time in 1910.[3]

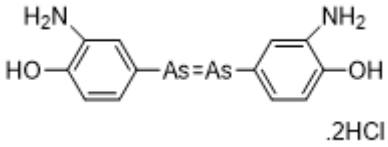



**Fig. 2: Chemical Structure of Arsphemamine**

In fact, Ehrlich at the start of 20th century realized that it was important to evaluate both pharmaceutical and harmful effect of drug and also that effectiveness of drug is directly proportional to its selectivity for disease causing agent when compared to its host. He introduced a term **chemotherapeutic index** to define effectiveness of drug (eq 1).[3]

$$\text{Chemotherapeutic Index} = \frac{\text{minimum curative dose}}{\text{maximum tolerated dose}} \quad ....1$$

But today, chemotherapeutic index has been replaced by more acceptable term therapeutic index (eq 2)

$$\text{Therapeutic Index} = \frac{LD_{50}}{ED_{50}} \quad ....2$$

Where $LD_{50}$ or median lethal dose is amount of substance required to kill 50% of tested population after certain time duration. Lower the value of $LD_{50}$ more would be toxicity of a substance and $ED_{50}$ or median effective dose is amount of substance required to impart desirable therapeutic effect in 50% of tested population after certain time duration. This ratio between $LD_{50}$ and $ED_{50}$ is known as **therapeutic index**. So, one can infer from the above equation that larger the value of therapeutic index, more would be safety margin of the drug. Ehrlich's drug discovery approach is now described by term **Structure Activity Relationship (SAR)** that comprises of synthesizing and screening series of structurally homologues compounds.

Hansch and Fujita introduced a term **Quantitative Structure Activity Relationship (QSAR)** to establish quantitative relationship between structure and activity of the compounds.

**DRUG ACTION AND PHARMACEUTICAL PHASES**

Once a drug is administered in the body and as it enters the blood, it is distributed all over the body. However, a proportion of drug may be lost either by metabolism, excretion or non-differential distribution to the body parts other than target site. The desirable and required dose would be amount of drug that is required to reach and maintain steady concentration of drug at target site. If drug administered is too high when compared to desirable, it would cause undesirable side effects and it is too low, then it would result in inefficient therapeutic activity. Thus, it is very important to deliver the drug at right proportion, at right time and at the right site. The window at which drug would show desirable therapeutic activity is known as **therapeutic window** (Fig 3). The drug release above or below this window would cause either side effects or inefficient therapeutic activity respectively.

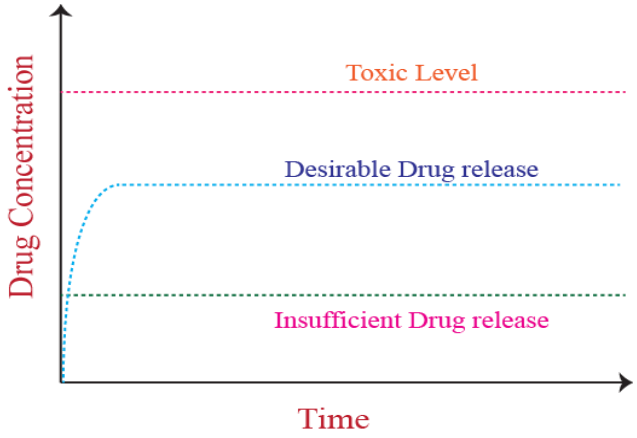



**Fig. 3: Schematic of desirable drug release**

Drug action can be broadly classified into two phases

a. Pharmacokinetics

b. Pharmacodynamics

**PHARMACOKINETICS**

Pharmacokinetic phase deals with parameters that govern the fate of drug from site of administration to its target site. It includes absorption, distribution, metabolism and excretion (ADME).

However, pharmacodynamics phase deals with the effect of drug on human body.

**1. ABSORPTION**

It is first step after drug administration. It can describe as transportation of drug from administration site to general circulation i.e. blood.

In absorption, drug crosses various biological membranes to reach general circulation by two ways:

i) Passive diffusion

ii) Active transport

Passive diffusion occurs from region of higher drug concentration to region of lower drug concentration. Due to difference in drug concentration between absorption site (for instance say gastrointestinal tract) and blood, concentration gradient is developed. So, the rate of absorption would be directly proportional to this concentration gradient (eq 3).

**Rate = KΔC = K (Ca - Cb)**.....3

Where Ca and Cb are concentration of drug at absorption site and blood respectively.

But at the beginning, concentration of drug in blood is negligible. So, rate of absorption would be directly proportional to the concentration of drug at absorption site (eq 4). It follows first order kinetics; larger the concentration of drug, more would be the rate of absorption. And as it is along the concentration gradient, no energy is required in such process.

**Rate = KCa** .....4

Active transport is the process of transportation of drug against the concentration gradient from region of lower drug concentration to region of higher drug concentration. And as it is against the concentration gradient, energy is required in the process. If energy required is utilized in the form of ATP, it is known as primary active transport and if it is utilized in form of electrochemical energy then it is called as secondary active transport.

**2. DISTRIBUTION**

Once drug is absorbed, it is distributed all over the body to various body organs and tissues. Factor affecting drug distribution includes blood flow, capillary permeability, binding of drug to proteins etc. It takes one minute for blood to distribute drug molecule throughout the body.

Human body has around 10 billion capillaries having surface area of approximately 200$m^2$. Pore size between cells in capillary lies in size range of 90 to 150 $A^0$ in diameter that is sufficient for the drug molecules to pass through it. Drug has to cross blood brain barrier in order to deliver any drug into the brain. Blood brain barrier consist of tight fitting cells in the blood capillaries lining the brain. Thick fatty acid coating around the capillaries of blood brain barrier does not allow the polar molecules to enter the brain so easily. Infact, some drugs have tendency to bind to plasma protein present in the blood. And as that proportion of drug remain bound to capillary and cannot reach to its target site.

**3. METABOLISM**

Conversion of a drug molecule into altogether different form, inside the body is known as metabolism. It mostly takes place in liver and less frequently in kidney, skin, lungs and gastrointestinal tract.

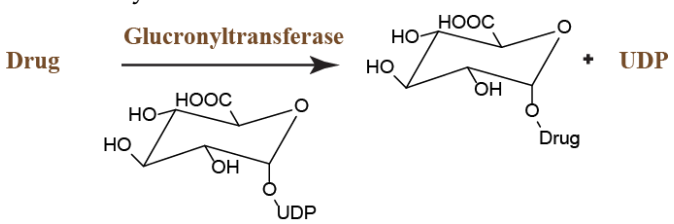
Inside the body, drugs are attacked by various metabolic enzymes. These metabolic enzymes transform drug molecules to different less active form called metabolites so that they can easily be eliminated out of body. Exception being the prodrugs (prontosil) where metabolism convert drug molecule into more active form.

Metabolism is broadly classified into two phases:

1. **Phase I** includes oxidation, reduction and hydrolysis reactions. In oxidation, oxygen molecule is added to drug molecule to make it more polar while in reduction and hydrolysis hydrogen and water molecule are added to drug molecule respectively to enhance its polarity. The main aim of phase I reaction is enhancing the polarity of drug so that it can easily eliminate out of the body. But if even after oxidation, reduction or hydrolysis, drug molecule is not polar enough to excrete out of the body, then it enters phase II. Cytochrome P450 found in liver is the best example of phase I oxidation.


Where D-H is drug containing active hydrogen.

2. **Phase II** includes conjugation reactions. If drug molecule either lack site where oxidation, reduction, hydrolysis could take place or if even after these reactions, drug molecule is not polar enough to throw out of body then phase II reaction take place. In phase II reaction, polar molecule is conjugated to drug molecule or to metabolite from phase I reaction to make it polar enough to excrete out of the body.



**4. EXCRETION**

Biotransformation is collective term for both metabolism and excretion that irreversibly eliminate drug molecule. The process of excretion should be slow enough to maintain required dose to maintain therapeutic effect and at the same time excrete the drug slowly to reduce concentration of drug in the body and reduce its unwanted side effects.

The principal route for excretion of drug and its metabolites is through kidney viz glomerular filtration and tubular secretion. However, compounds such as amino acid, water, glucose and salts can be reabsorbed by the body via tubular reabsorption.

**PHARMACODYNAMICS**

Pharmacodynamics is study of interaction of drug and body, especially the effects of drug on the body. Medicinal chemist has to design the drug molecule in the way that it would impart maximum therapeutic effect and minimum toxic side effects. This depends on stereo electronic characteristic between drug molecule and receptor site. Stereochemistry of the drug plays an important role since each stereoisomers show different biological effects.

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Chapter 10

# AN OVERVIEW OF ANTIVIRAL LEAD COMPOUNDS DERIVED FROM MARINE SOURCES

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**ABSTRACT**

Infectious disease, a critical public health concern that has garnered attention in recent years, has a considerable impact on human health. Human health can be adversely affected by viral infections, and in some cases, they can be fatal. Colds, influenza, and bronchitis are some of the common viral infections. The identification of novel bioactive natural compounds is a complex process, and the proportion of novel structures discovered each year over the previous decade has remained relatively constant. Antiviral agents must be continuously produced in order to avoid viral outbreaks and the propagation of resistant strains. Antiviral compounds derived from marine sources have been shown to have promising antiviral properties against a variety of viruses. Some of the biologically active marine derived compounds are currently commercially available. Due to the difficulties of isolating these compounds from their marine sources, the majority of them remain unidentified. The search for antiviral compounds in marine sources and their metabolites was undertaken through, among other resources, peer-reviewed publications, an extensive range of electronic resources, and periodicals. This review aims to thoroughly evaluate marine-derived natural compounds with antiviral activities and illustrate their influence on the development of antiviral drugs.

**KEYWORDS:** Infectious disease, Antiviral drugs, Marine sources.

## INTRODUCTION

Many pharmacologically active compounds can be found in marine and higher plants. As an alternative source of new drug candidates, they have attracted considerable interest because they provide a satisfying alternative to conventional sources (Kim & Karadeniz, 2011; Lam, 2007; Srinivasan, 2018). Among the most promising sources of novel chemical entities is the marine environment due to its abundant biodiversity, which includes microorganisms, invertebrates, vertebrates, and plants (Srinivasan *et al.,* 2020). Marine biotechnology has been developed to provide new sources of natural products with individual biological activities from microorganisms inhabiting various environments such as seawater, sediments, mangroves, coral reefs, deep-sea hydrothermal vents, etc. The marine environment is an untapped resource concerning natural product discovery and production. It might be possible to develop new

drugs and lead compounds using the metabolites produced by marine microorganisms. In addition, many of these molecules possess novel structures not found elsewhere. The most important compounds include antibiotics, antivirals, anticancer drugs, immunosuppressants, anti-inflammatory agents, hormones, vitamins, enzymes, etc., which have been the focus of much attention as bioactive substances for disease treatment (Sagar *et al.,* 2010). Current research on antiviral molecules has increased in importance since the emergence of viral diseases such as HIV, hepatitis C, Ebola, and SARS Cov-19 (Yasuhara-Bell & Lu, 2010). There are two classes of antiviral medicines that act against viruses: nucleoside analogues and protease inhibitors. The first class inhibits the viral replication process by preventing it from utilizing the host's DNA-dependent RNA polymerase to transcribe viral RNA into DNA. The second class inhibits viral replication by inhibiting certain enzymes in the viral life cycle. In recent decades, the need to develop a drug to combat viruses has become a public health priority, partly due to the continued rise of potentially deadly viral diseases and drug-resistant strains. The above factors have increased the urgency of developing antiviral drugs. The development of new antiviral is a high priority for many pharmaceutical companies. The most common approach to drug discovery has been based on screening large libraries of compounds against specific targets or biological assays. However, this strategy requires a lot of money, time, and knowledge about the proteins involved in the infection process. In addition, it may be challenging to identify lead compounds that can effectively inhibit multiple viruses with different mechanisms of action. In the late 1950s, scientists discovered that a drug called ziconotide was derived from marine sources. This discovery marked the beginning of modern drug development. A tropical cone snail was found to contain an N- type calcium channel blocker, which is used in the treatment of pain. (Bergmann & Feeney, 1951). In this review, we explore some of the potential antiviral drugs derived from marine sources as well as discuss the challenges in their production and development.

## METHODOLOGY

The different keywords were used to conduct the literature review. The search terms were used including "marine source," "marine-derived chemicals," "marine microorganisms," "marine sponge," "marine peptides," and "seaweed." These terms are usually prefixed with antiviral agents. In search of marine antiviral agents, the above keywords were used in electronic databases, books, and printed journals. This search was conducted using a number of databases, including PubMed, Google Scholar, Research Gate, Web of Science, NOPR, and Science Direct. We reviewed the relevant *In vivo* and *in-vitro* studies published between January 2000 and November 2021 in English. Among the 92 publications initially screened, 53 studies were included in the study. There was no review articles included in the review, only primary literature. In addition, duplicate, non-relevant, and non-English language articles were excluded from the review process. Generally, peer-reviewed scientific literature is considered to be more reliable than other forms of research. We reviewed only peer-reviewed literature

related to marine antiviral agents. Our review focused exclusively on marine-derived antiviral molecules.

## CHALLENGES IN DRUG DISCOVERY FROM NATURAL RESOURCES

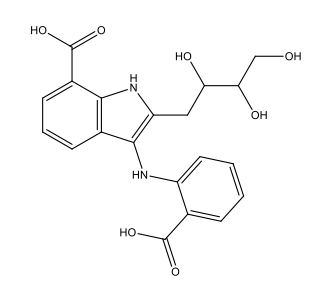
The drug development process is estimated to take ten years or more and cost more than eight billion dollars (Balunas & Kinghorn, 2005; Dickson & Gagnon, 2004). Finding a new lead is a costly and time-consuming process, but the potential outcomes could prove life-changing for people needing specific medicine. While drug tests seem to start directly, there are many phases to follow after receiving a functional prototype. It is critical to establish the cause of the illness during the early stages of drug screening. Biomedical researchers need to carefully examine each compound in the research phase to select a candidate with the appropriate characteristics. Only one in five thousand lead compounds make it through clinical trials and receive approval from the regulatory authorities. The academic department focuses less on research and development involving natural products. The government and non-government organizations control collecting natural resources from wild and sea sources. There is a need for innovative approaches to managing resources, particularly in regard to the legal and political implications associated with benefit-sharing agreements. Isolation of a specific biologically active compound from a complex mixture is problematic because many other compounds interfere with the isolation process. Many novel methods have been developed, including LC-MS, GC-MS, and HPLC-MS, in order to minimize the problems caused by high-resolution separation and mass detection capabilities (Glish & Vachet, 2003). A majority of biologically active molecules are isolated at trace levels which are often inadequate for the optimization of leads during lead development and clinical trials. Medicinal and synthetic chemists must work together to determine whether partial or complete synthesis is feasible (Lombardino & Lowe, 2004). It was difficult to obtain enough rare marine derived chemicals to ensure a sustainable supply. However, even if they were, purification would be a challenging task (Molinski *et al.,* 2009).

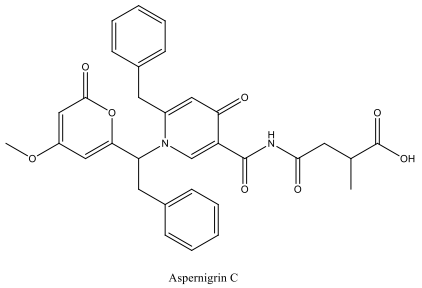
## MARINE MICROBES

In recent years, interest in developing new medicines from marine microbes has increased. Marine microbes in the marine environment produce secondary metabolites that are essential to their survival and adaptation to extreme environmental conditions. They are a great way to get more marine natural products into clinical trials and find new drugs from them. It is often easier to produce active pharmaceutical ingredients through microbial fermentation than by cultivating micro-organisms with a slower growth rate (Waters *et al.,* 2010). One of the most promising applications of marine microbes is their use as antiviral agents. The chemical structure of some of the promising antiviral compounds derived from marine microbes is shown in Fig. I. Marine microbial natural products are effective against various viruses, including HIV, herpes, and influenza (Gerwick & Fenner, 2013). A new actinomycetes, *Streptomyces* sp. CMN-62, was found to produce three new derivatives, anthranosides A−C.

Anthranoside-C showed better inhibitory activity against $H_1N_1$ ($IC_{50}$ = 171 mM) than the other two derivatives (Che *et al.,* 2018). Two distinct metabolites aspernigrins C and D containing 2-benzylpyridin-4-one were produced by *Aspergillus niger* SCSIO Jcsw6F30. Six known compounds were also isolated. TZM-bl cells were treated with aspernigrins C, which had an $IC_{50}$ of 4.7±0.4M and a selectivity index of 7.5 against HIV-1 SF162. (Zhou *et al.,* 2016). Asperterrestide A, a novel alkaloid, was isolated from the fermentation broth of *Aspergillus terreus* SCSGAF0162. Asperterrestide A has been shown to exhibit higher inhibition of $H_1N_1$ and $H_3N_2$ viruses, with $IC_{50}$ values of 15 and 8.1 μM, respectively. This compound contains an unusual 3-OH-N-CH3-Phe residue that contributes to its antiviral properties. As a positive control, ribavirin was effective against $H_1N_1$ and $H_3N_2$, with an $IC_{50}$ value of 20.2 and 0.41 μM, respectively (He *et al.,* 2013). A novel marine sponge-derived fungus, *Aspergillus* sp. SCSIO XWS02F40, has been identified as adding new novel asteltoxins, asteltoxin E and F. A significant anti-$H_3N_2$ effect was observed for both of the compounds, which had $IC_{50}$ values of 6.8±0.08 and 8.9±0.3 μM, respectively. In addition, it was found that asteltoxins E inhibit $H_1N_1$ with an $IC_{50}$ value of 3.5±1.3 μM. An $IC_{50}$ of 18.5 and 16.9 μM was found for oseltamivir, as a positive control. (Tian *et al.,* 2016). Balticolid, a unique 12-membered macrolide, was isolated from the culture broth of the Ascomycota fungus strain 222 that was collected in driftwood gathered from the Baltic Sea. A novel molecule has been identified as having antiviral activity against the HSV-1 virus with an $IC_{50}$ value of 0.45 μM. Balticolid was shown to be more effective than acyclovir ($IC_{50}$ of 0.44 μM), the most frequently used HSV-1 treatment (Shushni *et al.,* 2011). Another investigation using the fungal strain 222 resulted in the identification of six new naphthalenone derivatives designated as balticols A–F. Balticol-E seemed to have the strongest effectiveness, with an $IC_{50}$ value of 0.01 μg/mL against HSV-1 (Shushni *et al.,* 2009). Penicitrinone F is a dimer of citrinin that is derived from *Penicillium chrysogenum* SCSIO41001 hinders EV71 with an $IC_{50}$ value of 14.50 μM (Chen *et al.,* 2017). Five novel phenolic polyketides have been isolated and identified from the fermentation broth of *Streptomyces* sp. OUCMDZ-3434 in association with *Enteromorpha prolifera*. Wailupemycin J, R-wailupemycin K, and 5-deoxyenterocin are three compounds that suppress effectively against $H_1N_1$. At 50 μg/mL, they inhibited 47.8%, 42.5%, and 60% of the virus, respectively. The effectiveness of isolated compounds was compared with Ribavirin, which suppressed the virus in 45.3% (Liu *et al.,* 2017). A total of twenty-three compounds were identified from *Aspergillus* sp. OUCMDZ-1583 fermentation broth. Two compounds, 6-O-demethylmonocerin and (+)-monocerin, have an $IC_{50}$ value of 172.4 and 175.5 μM, respectively, against the $H_1N_1$ virus. The positive control is ribavirin, which has an $IC_{50}$ of 137.3 μm (Kong *et al.,* 2015). Scequinadoline A was isolated from the internal tissue of the soft coral *Lobophytu mcrassum* by the marine fungus *Dichotomo mycescejpii* F31-1. Based on a conventional plaque assay, the molecule demonstrated significant antiviral activity, with 50% inhibition of dengue virus serotype 2 at 50 μM (Wu *et al.,* 2018). Truncateols O-V is isoprenylated cyclohexanols found in the ethyl acetate extract of the sponge-associated fungus *Truncatella angustata*. Furthermore, they were identified in fourteen different

cyclohexanols. The $H_1N_1$ virus was inhibited by Truncateol O with an $IC_{50}$ value of 30.4 μM, whereas the positive control, oseltamivir, had an $IC_{50}$ value of 46.7 μM. They compounds both blocked HIV replication, with $IC_{50}$ values of 39.0 μM for Truncateol O and 16.1 μM for Truncateol P (Zhao *et al.*, 2018). A marine-derived fungus, *Penicillium* sp. IMB17-046, was isolated and three novel compounds were isolated, in addition to five known compounds. In terms of antiviral efficacy against HIV, HCV, and IAV, trypilepyrazinol and 3-hydroxyergosta-8, 14, 24 (28)-trien-7-one had $IC_{50}$ values ranging from 0.5 to 7.7 μM. Inhibition of HIV-1 and HCV was achieved with trypilepyrazinol, a pyrazine derivative with $IC_{50}$ values of 4.6 and 7.7 μM, respectively. (+)-neocitreoviridin, a pyrone polyketide, is more anti-IAV effect ($IC_{50}$=3.6 μM) than the positive control ribavarin ($IC_{50}$=15.4 μM). Another compound, 3-hydroxyergosta-8, 14, 24(28)-trien-7-one, an ergostane analogue, inhibits HIV ($IC_{50}$=3.5 μM) and has the strongest inhibitory effect against IAV ($IC_{50}$=0.5 μM), three hundred times stronger than ribavarin (Li *et al.*, 2019). Trichobotrysins A–F is a series of novel tetramic acid derivatives containing a decalin ring, which have been isolated from a strain of *Trichobotrys effuse* DFFSCS021. Trichobotrysins A, B, and D inhibit HSV-1 with $IC_{50}$ values of 3.08, 9.37, and 3.12 μM, respectively (Sun *et al.*, 2015). A novel class of anthraquinones, aspergilols G-I, has been discovered in the deep-sea fungus *Aspergillus versicolor* SCSIO 41502. Aspergilols-H and aspergilols-I suppress HSV-1 infections with $EC_{50}$ values of 4.68 and 6.25 μM, respectively (Huang *et al.*, 2017).


Anthranoside C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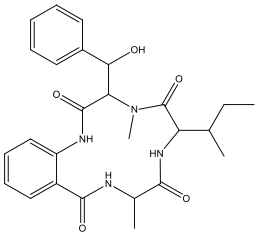
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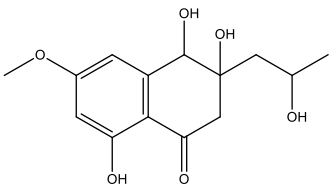
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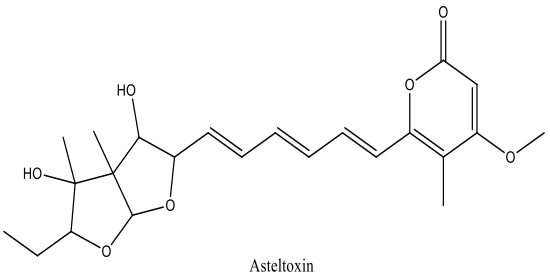
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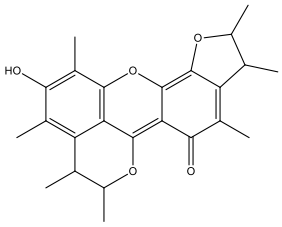
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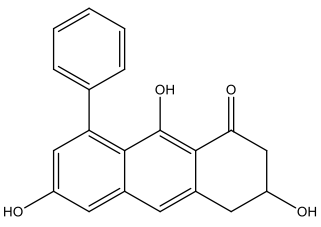
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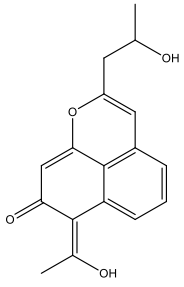

(R)-wailupemycin K

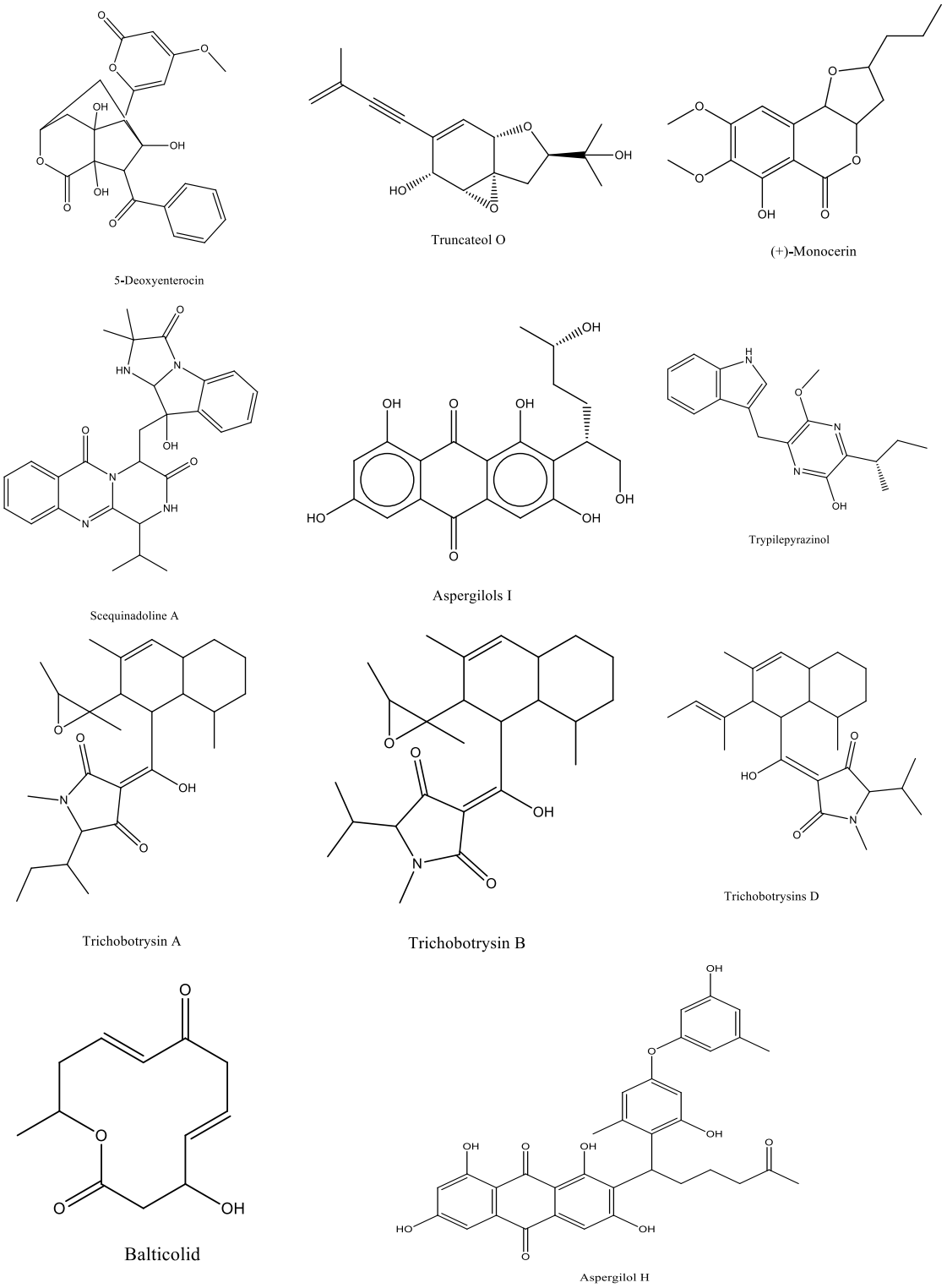
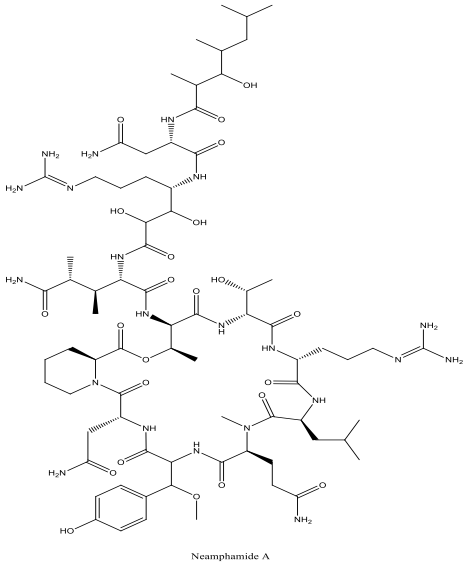



**Fig. 1: Chemical structures of antiviral agents from marine microbes**

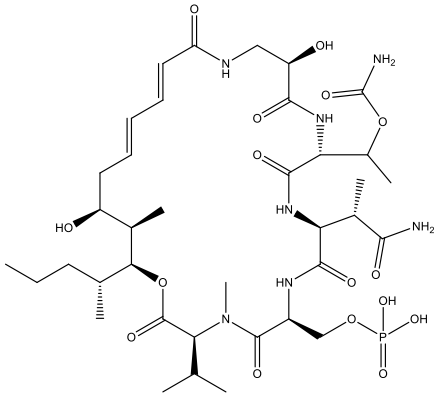
## MARINE PEPTIDES

A variety of biological functions depend on marine peptides, and their molecular mechanisms are unique. Due to their incomparable characteristics and different biological effects, marine bioactive peptides have attracted much attention. Moreover, peptides possess a number of advantages, including selectivity, potency, fewer drug-drug interactions, high activity, and low

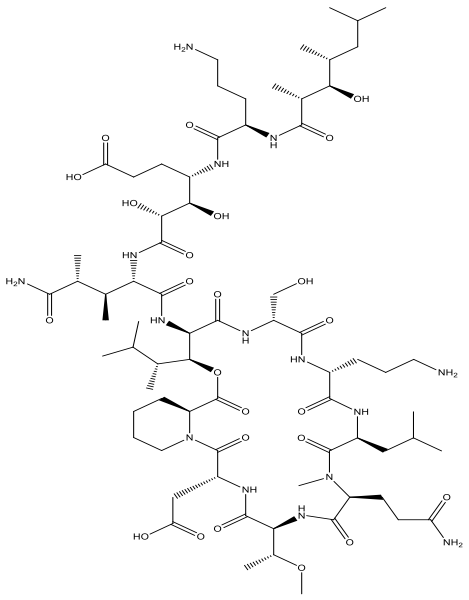
tissue accumulation, which results in minimal toxicity, as well as a great diversity of chemical and biological properties. Marine sources of complex cyclic and linear peptides have provided insights regarding antibacterial agents, cytotoxic mechanisms, and other properties. Consequently, marine peptides have been used for the development of several novel and innovative products (Gogineni & Hamann, 2018). Figure II illustrates the chemical structures of several promising antiviral compounds derived from marine peptides. From marine gorgonians derived *Aspergillus* spp SCSIO 41501, the first cyclic and linear Aspergillipeptides D-G has been found. The aspergillipeptides D and E were effective in inhibiting HSV-1, with $IC_{50}$ values of 9.5 and 19.8 μM against the Vero cell line, respectively. Aspergillipeptide D was also effective against acyclovir-resistant HSV-1 clinical isolates (Ma *et al.,* 2017). The marine sponge *Siliquaspongia mirabilis* has produced six new depsipeptides, designated Celebeside A-C andtheopapuamides B-D. Celebeside-A suppressed HIV-1 in neutralization assay with an $IC_{50}$ of 1.9±0.4 μg/mL, whereas celebeside-C was inactive even at high concentrations (Plaza *et al.,* 2009). Homophymine-A is a potential anti-HIV cyclodepsipeptide found in *Homophymia* spp., a species of New Caledonian coastal sponge. Homophymine A demonstrates a significant cytoprotective effect against HIV-1 infection in cell-based XTT experiments, with an $IC_{50}$ value of 75 nM (Zampella *et al.,* 2008). In addition to the four koshikamides found in deep-water samples, the cyclic koshikamides F and H have also been isolated from *Theonellas winhoei* and *Theonella cupola*. The Koshikamides F and H exhibiting $IC_{50}$ values of 2.3 and 5.5 μM, inhibited HIV-1 entry points. However, their linear equivalents didn't work (Plaza *et al.,* 2010). The depsipeptide microspinosamide is isolated from *Sidonops microspinosa*. This peptide contains several unique amino acids and is the first naturally occurring peptide with a β-hydroxy-ϱ-bromophenylalanine residue. In *in-vitro* experiments based on XTT assay, microspinosamide was found to exhibit significant inhibition against HIV-1 infection with an $EC_{50}$ of 0.02 μg/mL (Rashid *et al.,* 2001). Mirabamides A–D is cyclic depsipeptides that have been isolated from *Siliquariaspongia mirabilis* and have been demonstrated to inhibit HIV-1 invasion in its early stages. Neutralisation and fusion experiments demonstrated that mirabamide A suppressed HIV-1 with $IC_{50}$ values ranging between 40 and 140M (Plaza *et al.,* 2007). Mirabamides E-H, and mirabamide C, are unique depsipeptides derived from the marine sponge Stellettaclavosa. In a neutralization assay, each of the bioactive components significantly reduced HIV-1, with $IC_{50}$ values of 121, 62, 68, and 41M, respectively (Lu *et al.,* 2011). The marine sponge *Neamphius huxleyi* contains a cyclic depsipeptide, known as Neamphamide A. Neamphamide A is made up of eleven amino acid residues, along with an amide-linked 3-hydroxy-2,4,6-trimethylheptanoic acid moiety. Niemphamide A demonstrated effective antiviral activity against HIV-1 infection in the XTT assay and its $EC_{50}$ value was 28 M (Oku *et al.,* 2004).



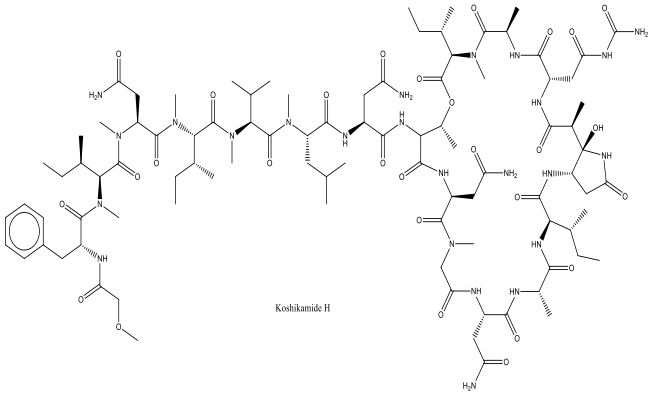
Neamphamide A



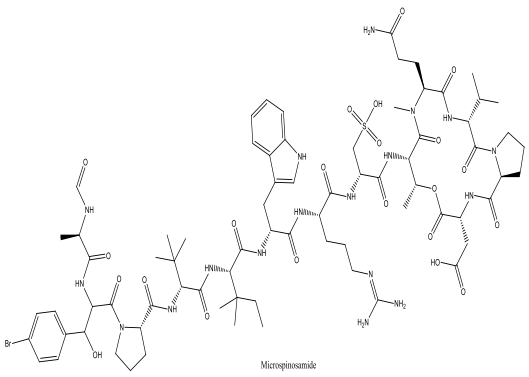
Celebeside A



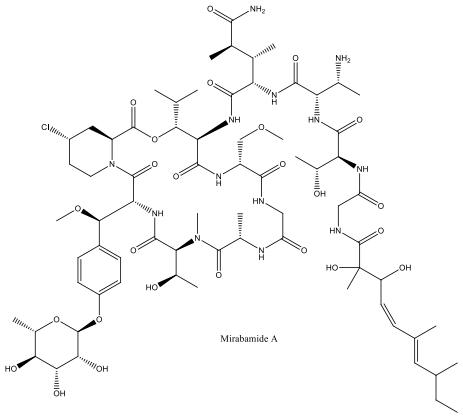
Homophymine B



Koshikamide H



Microspinosamide



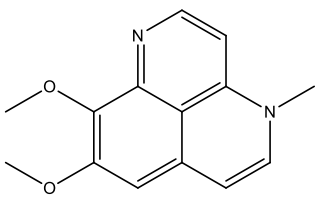
Mirabamide A

**Fig. 2: Chemical structures of antiviral agents from marine peptides**

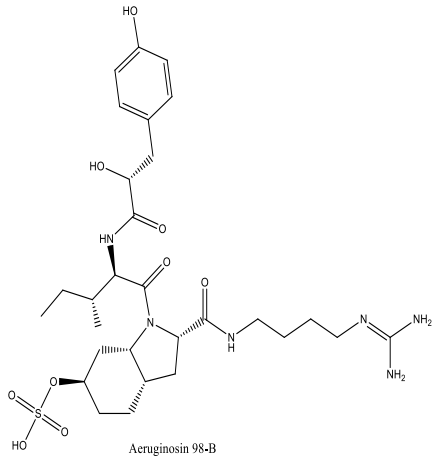
**MARINE SPONGE**

Marine sponges contain a large number of pharmaceutically active compounds. These pharmacologically active compounds serve primarily to facilitate and regulate cellular communication and defence. Marine sponge enzymes and symbiotic microbes are most often responsible for their production. The functions of these enzymes can include degradation of environmental pollutants, biosynthesis of natural products, and metabolism of xenobiotics. Various factors can induce enzyme production, such as ecological changes or exposure to different chemicals. The potential for finding unique and valuable compounds in marine sponges is still largely unexplored, making this a field of great interest for pharmaceutical research. Several compounds produced by marine sponges have been bonded to antiviral activity against viruses such as HIV, hepatitis B, herpes simplex virus, and the common cold. Recently, there has been a growing interest in the potential therapeutic value of compounds that target viruses. This is because viruses are a significant cause of human disease, and many effective antiviral agents are derived from marine sponges. In recent years, a number of these compounds have been developed. Several antiviral drugs have undergone clinical trials and have been approved for use in humans (Sagar *et al.,* 2010). Figure III illustrates the chemical structure of antiviral compounds attain from marine sponges. 4-methylaaptamine is an alkaloidal compound obtained from *Aaptosaaptos* sea sponges. 4-methylaaptamine reduced HSV-1 replication in Vero cells dose-dependently, with an $EC_{50}$ value of 2.4 M thus, 4-methylaaptamine may be able to inhibit the production of an HSV-1 early protein, ICP27, in a number of infection-dependent ways, preventing the virus-induced inhibition of macromolecular synthesis (Souza *et al.,* 2007). TMPRSS2 (human serine protease enzyme) is what the virus uses in order to activate itself and enter cells. Aeruginosin 99B decreased serine protease activity derived from *Microcystis aeruginosa*. Aeruginosin 98B has a guanidino group that resembles its arginine substrate (Buchanan *et al.,* 2008; Ersmark *et al.,* 2008). Avarone and avarol have been separated from the marine sponge *Disideaavara* (Minale *et al.,* 1974). Both the compounds that exhibit a strong cytoprotective effect against H9 cells infected with HTLV-IIIB at doses as low as 0.1 μg/ml. Avarone and avarol inhibit the synthesis of the p24 and p17 gag proteins by HTLV-III in H9 cells upon infection. They also stop the virus from growing, which is shown by the fact that around 80% of reverse transcriptase activity is blocked (Sarin *et al.,* 1987). Dragmacidin F is a new bromoindole alkaloid identified from the genus *Halicortex* marine sponge. A partially oxidized form of dragmacidin D is cyclized to produce dragmacidin F. The purified compound has the ability to inhibit the replication of both viruses, HSV-1 ($EC_{50}$- 95.8 μM) and HIV-1 ($EC_{50}$-0.91 μM) (Cutignano *et al.,* 2000). Ilimaquinone is a metabolite found in the marine sponge *Hippospongia metachromia*. According to the outcome of the computational research, the Ilimaquinone had a strong probability of inhibiting all of the SARS-CoV-2 target proteins, as evidenced by the binding energies (Surti *et al.,* 2020). Manzamines A are β carboline alkaloids found in the marine genus *Haliclona* (Sakai *et al.,* 1986). Manzamine A mono HCl and tartaric acid salts were shown to be extremely water soluble and to have much stronger activity

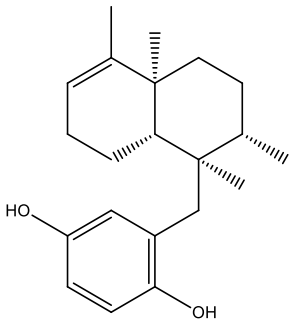
against HSV-1. By increasing the solubility of manzamine A salts, the toxicity against SIRC cells was dramatically reduced. The manzamine A salts cut the effective concentration of manzamine A down from 1 μM to 100 nM, which led to a 10-fold rise in activity (Palem *et al.,* 2017). A novel class of anti-HIV cyclic depsipeptides known as papaamides A, B, C, and D have been isolated from the marine sponge *Theonella mirabilis* and *Theonella swinhoei*. Human T-lymphoblastoid cells were not infected by HIV-$1_{RF}$ after exposure to papuamides A and B at an $EC_{50}$ of 4 g/mL *in-vitro* (Ford *et al.,* 1999). Papauamides A's ability to prevent HIV-1 infection was due to its ability to stop the viral life cycle at an early stage, although it was not specifically targeted against HIV-1 envelope glycoproteins. As with Papuamide A, Papuamide B inhibits virus entry into the body by interacting with phospholipids on the virus membrane (Andjelic *et al.,* 2008). Pseudotheonamides C and D have been found in the marine sponge *Theonellas winhoe I* (Nakao *et al.,* 1999). They have been shown to be good at blocking the serine protease (Gentile *et al.,* 2020). A sesquiterpene quinone, puupehedione, has been isolated from marine sponges, namely *Verongida* sp. and *Hyrtios* sp., and has been found to influence T-cell immunological responses at relatively low doses of 3 μg/ml. Puupehedione has potential as a COVID-19 treatment, especially in the later phases (Hamann *et al.,* 1993). The Caribbean sponge *Tethya crypta* contains spongothymidine and spongouridine (Bergmann & Feeney, 1951). Vidarabine is a novel antiviral agent that is a synthetic analogue of spongouridine. In contrast to the more common ribose sugar, these nucleosides contained arabinose sugar (Sagar *et al.,* 2010). Vidarabine is three to five times more effective than cidofovir in plaque reduction assays against vaccinia and cowpox viruses (Hilfinger, 2006). Vidarabine pro-drugs are 5′-O-D- and L-amino acid derivatives and 5′-O- (d-and-l-amino acid methyl ester phosphoramidate) vidarabine (ara-A) derivatives. The pro-drug has superior antiviral activity against vaccinia and cowpox *in vitro*. It has been demonstrated that substitution at the 5'-OH group can increase the absorption of vidarabine or its pro-drugs, as well as protect them from ADA metabolism. (Shen *et al.,* 2009).



4-Methylaaptamine



Aeruginosin 98-B



Avarol

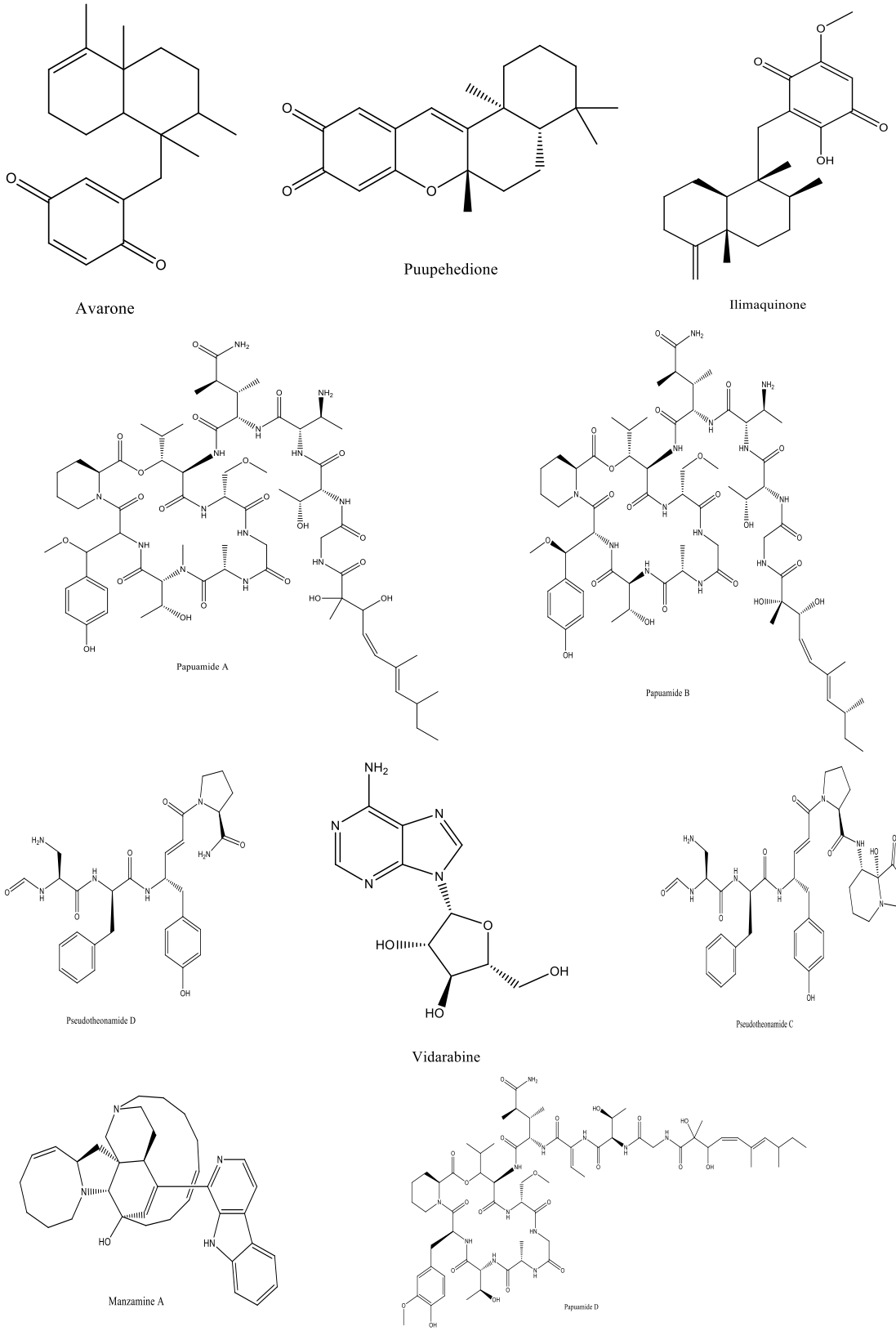



**Fig. 3: Chemical structures of antiviral agents from marine sponge**

## CONCLUSION

Several epidemics have killed millions of people-sometimes within just a few months. Since the first discovery of these diseases, scientists have made significant progress in understanding

them and finding ways to combat them. The potential for new drugs from marine organisms is high, partly because of the great chemical diversity of these organisms. Marine natural products can be used to make new drugs that treat a variety of illnesses, especially viral infections. A reasonable pharmacological screening of marine-derived compounds is likely to yield promising leads for the treatment of viral infection. Antiviral drugs that are powerful and effective may come from these sources in the future because of the development of novel drug discovery technologies. These new agents could potentially be used to treat a variety of viral infections, including HIV, herpes, and influenza. It will take a great deal of research to determine the safety and efficacy of these new agents. Antiviral therapy faces a major challenge due to the fact that drugs become resistant to viruses, which encourages scientists to find better antiviral drugs to treat viruses. In view of the rapidly spreading SARS-CoV-2 virus worldwide, it is essential to investigate new antiviral natural products, particularly those from marine sources. Antiviral compounds derived from marine sources may exhibit distinct mechanisms of action. In order to produce these natural antiviral products in a more sustainable and manageable way, biosynthesis and chemical synthesis strategies are used. Consequently, a more stable supply of these important compounds is assured, which will have a less detrimental effect on the ecosystem. Scientists are now exploring these marine-derived compounds with the goal of developing novel therapeutics for viral infections. There is a possibility that antiviral leads from marine sources will saturate the pharmaceutical market in the next few years.

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Chapter 11

# A BRIEF INTRODUCTION AND CLASSIFICATION OF CARBON-BASED NANOMATERIALS

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**ABSTRACT**

Nanomaterials have evolved as a fascinating class of materials that includes a wide range of samples with at least one dimension in the 1 to 100 nm range. The sensible design of nanoparticles can result in extremely high surface areas. In the name of nanotechnology the term nano means nanometer and Richard Adolf Zsigmondy coined the term "nanometer" in 1914. Richard Feynman, an American physicist and Nobel Laureate, coined the term "nanotechnology" in a lecture to the American Physical Society's annual conference in 1959. This is said to be the first scholarly discussion on nanotechnology.

**KEYWORDS:** Nanoparticle, Fullarenes, Nanotube, Graphene.

## INTRODUCTION

[1]Nanomaterials can be made with magnetic, electrical, optical, mechanical, and catalytic capabilities that are vastly superior to those of their conventional material. Nanotechnology is a wonderful example of a technological innovation since it offers tailored nanoparticles with a lot of potential for generating goods with significantly better performance. [2] Before studying the nanotechnology it's very important to know about the types of nanomaterials. In this chapter we will specially discuss the type of Carbon based nanomaterials.

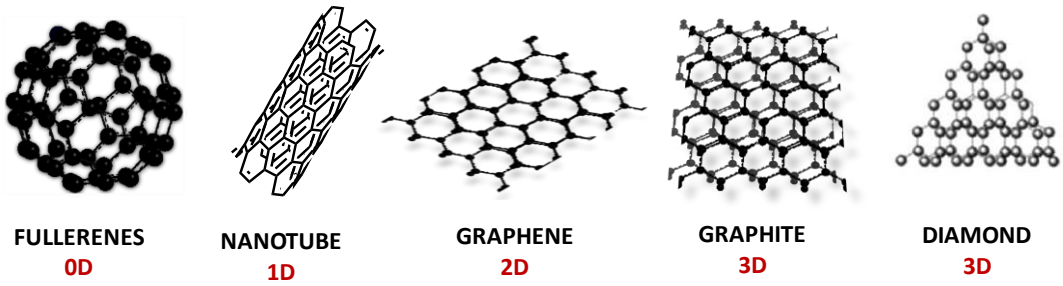


**Fig. 1: The most common carbon materials classified based on their dimension**

**SPECIAL CARBON-BASED NANOMATERIALS**

The carbon-based nanostructured materials family includes nanostructures that have been intensively investigated for a variety of applications unique physical and chemical properties. The amazing capabilities of tunable carbon-based nanomaterials have sparked a lot of attention for their potential applications in new technologies and solving modern problems.[3] CNTs, fullerenes, graphene, carbon nanohorns, carbonbased quantum dots, and a variety of other nanomaterials belong to the carbon family. In this section, the key qualities and relevance of these nanomaterials are briefly reviewed.

**FULLERENES**

Because of its small size, spherical shape, and isotropic nature, fullerene (C60) is regarded an excellent zero-dimensional material. 109 Fullerenes are a fascinating carbon allotrope that was discovered in 1985. Fullerenes are sp2-hybridized carbon atom cages that are very symmetrical. Fullerenes are separate compounds with a specified number of carbon atoms, which distinguishes them from other carbon allotropes. Fullerenes are classified by the number of carbon atoms in their structure, such as C60, C70, C72, C76, C84, and C100.[4] C60 fullerene is the most common and well-known of them. C60 fullerene has icosahedral symmetry and is made up of a hollow structure with 12 pentagons and 20 hexagons made up of 60 carbon atoms joined together by covalent bonds that are sp2 hybridised in nature.[5] Six-membered rings isolate the five-membered rings in fullerenes. The sphere is regarded as one of nature's more stable forms, and fullerene is no exception. Fullerenes have a number of distinguishing characteristics that make them appealing for use in a variety of sectors. Fullerenes have some solubility in a variety of solvents, which distinguishes them from other carbon allotropes.[6] Chemical alteration of fullerenes is a fascinating topic that could improve their utility in a variety of applications. Further Fullerenes can be modified from inner-space and outer-surface. It is used in various fields like Medicine, Catalyst, Electronic devices and lubricants.

**CNTS**

Carbon nanotubes are an integral part of the carbon nanomaterial class, having been discovered by S. Iijima in 1991.[7] Following the discovery of carbon nanotubes, substantial study was conducted to investigate their characteristics for a variety of uses. Later, Toshinari Ichihashi and S. Iijima published single-shell carbon nanotubes with a diameter of 1 nm. Carbon nanotubes are single-layered sp2 hybridised carbon atoms folded into thin sheets. The nanotubes' surfaces are made up of sp2-hybridized carbon atoms organised in hexagons. Carbon nanotubes are further split into single-walled carbon nanotubes, double-walled carbon nanotubes, and multi-walled carbon nanotubes based on the number of rolled graphene sheets.

**GRAPHENE**

Graphene, a part of the carbon nanomaterial family, has arisen as a magical material that has exploded in popularity in just a few years since its isolation from graphite in 2004. Graphene's unique properties have the potential to revolutionise batteries, supercapacitors, solar cells, field-effect transistors, catalysis, sensors, and membrane technology. [8]

**NANODIAMONDS**

Nano diamonds, like other carbon-based materials, have a number of intriguing features that make them appealing nanomaterials for a variety of applications. Monocrystalline diamonds with particle sizes less than 100 nm are referred to as nanodiamonds.[9] Nanodiamonds are carbon nanoparticles that have been sp3 hybridised. Nanodiamonds are carbon-based nanomaterials with remarkable optical, mechanical, and mechanical capabilities, as well as large specific surface areas and complex surface structures.

**CARBON NANOHORNS/NANOCONES**

Carbon nanocones are another name for carbon nanohorns. They appear as sp2 carbon sheets arranged in conical carbon nanostructures. Singlewalled carbon nanohorns are made up of a tubular structure with a conical end and a graphene sheet. They are viewed as a subset of fullerenes because of their closed cage structure, and their elongated shape gives them a structural counterpart to short single-walled carbon nanotubes. Carbon nanohorns are 40–50 nm long and 2–5 nm wide, with a diameter of 2–5 nm.[10] Carbon nanohorns have several clear advantages over carbon nanotubes, including the ability to synthesise without harmful metal catalysts and large-scale manufacturing at ambient temperature.

**NANOPOROUS**

Materials chemists have been attracted by explorations and research into the production of porous materials for decades.[11] Activated charcoal is an example of a porous material that has been utilised for many years. Porous solids' technical and scientific significance stems from their capacity to interact with ions, atoms, and molecules at their outer surface while also allowing access to their interior. When the pore diameter of porous materials is less than 100 nm, they are called nonporous materials.[12] Porous materials can be classified into three groups based on pore size: [13]

**MACROPOROUS** materials. Porous materials are recognized as macroporous when they have pore sizes greater than 50 nm.

**MESOPOROUS MATERIALS** Porous materials are called mesoporous when they have pores in the range of 2 to 50 nm.

**MICROPOROUS MATERIALS**.

Pore diameters in microporous materials are in the 2 nm range. The size distributions, volumes, and forms of pores in nanoporous materials have a direct impact on the performance of porous materials for certain applications. The development of materials with precisely regulated pores and arrangements has been a hot field of research. Recent research has focused on precisely controlling the shapes, sizes, and volumes of pores to generate high-performance nanoporous materials. In the literature, there are several state-of-the-art reviews that focus specifically on the synthesis, characteristics, developments, and uses of nanoporous materials.[14] Nanoporous materials can be split into three classes based on the materials used: inorganic nanoporous materials, carbonaceous nanoporous materials, and organic polymeric nanoporous materials. In zeolites, the micropores are uniform in shape and size, and these pores can effectively discriminate between molecules based on shape and size**.**[15]

**ULTRATHIN TWO-DIMENSIONAL NANOMATERIALS BEYOND GRAPHENE**

Nanomaterials are classed as zero-dimensional, one-dimensional, two-dimensional, or three-dimensional based on their dimensions (0D, 1D, 2D, or 3D, respectively). The relevance of nanoscopic materials in technology cannot be overstated.[16] These materials further can be divide into following categories.

**SILICENE.**

Due to its many superior features, which it shares with graphene, silicone, a 2D silicon (Si) allotrope that is one atomic layer thick and has a distinctive low-buckled structure, has gained a lot of theoretical research in recent years. Takeda and Shiraishi published the initial study on this Si-based graphene-like sheet in 1994.[17] later, in 2007, Guzman-Verri et al. re-examined the structural similarities between this unique Si nanomaterial and graphene, coining the term "silicone." [18] When Si atoms are in silicone sheets, they are not in the same plane as C atoms in graphene, and they are thought to show sp3 /sp2 -like hybridization, resulting in a buckled honeycomb atomic configuration. Furthermore, the typical Si–Si spacing within this honeycomb pattern of resilient silicone is 0.225 nm, according to DFT calculation data provided by Cahangirov *et al.*, [19], with an ambipolar system represented by the electronic density of states. The electrical structure of silicone is equal to that of graphene, displaying semi-metallic properties, according to first-principles calculations.[20]

**MXENES**.

MXenes the graphene-like 2D nanomaterials have received a lot of interest in recent years because of their unique physical and chemical properties. The inclusion of early transition metal carbides, nitrides, and carbonitrides from MAX-phases, known as MXenes, has recently greatly increased the range of 2-D materials.[21] MXenes have a similar lateral scale to graphene, ranging from hundreds of nanometers to several micrometres, with a theoretical thickness of 0.98 nm

(single layer), as well as excellent physical and chemical properties. MXenes are made up of transition metal carbides, nitrides, or carbonitrides with thin layers of a few atoms. Mn+1XnTx (n = 1, 2, or 3) is the traditional form of MXenes, where M stands for a transition metal element and X and Tx stand for carbon and/or nitrogen atoms and additional surface functional groups (–O, –OH, or –F), respectively.[22] In other words, MXenes are created through a controlled etching process from layered MAX-phase precursors (Mn+1Xn) with modified termination groups (i.e., –O, –OH, or –F). Using the practical application of material designability, this etching technique may be further adjusted to yield fine-tuned MXenes with varied physical properties. Naguib, Barsoum, and Gogotsi from Drexel University in the United States published the first research on MXenes (Ti3C2Tx) in 2011, which featured the exfoliation of MAX-phases as a substitute for graphene in supercapacitors. Since then, more than 19 different types of MXenes have been discovered, and various structural predictions for MXenes have been proposed.

**2D MATERIALS FROM GROUP 15**

Arsenene and antimonene are important compounds. Due to their similar behaviour to graphene-related materials and their suitability for forming mono-elemental 2D layered nanomaterials with potential for a variety of applications, such as optoelectronics and electronics,[23] plasmonics, and energy-storage devices, 2D nanomaterials composed of group 15 elements have attracted attention in recent years. Pnictogens are one-atom-thick 2D structures with monolayers that have a wide range of band gaps, such as phosphorene from black phosphorus, and share similar fascinating features with graphene materials, such as electrical and vibrational properties.

**TWO-DIMENSIONAL METAL–ORGANIC FRAMEWORK NANOSHEETS (2D-MOFS)**

Nanosheets made up of two-dimensional metal–organic frameworks have developed as a new type of two-dimensional material with unique properties like ultrathin thicknesses, tuneable molecular porous architectures, and high surface–volume ratios. Due to their remarkable physical and chemical properties, these innovative 2D-MOF nanosheets provide high-performance 2D materials with a wide range of applications, including electrochemical, sensing platform, and membrane-based gas separation, among others. As a result, tremendous progress has been made in the design and fabrication of 2D-MOF nanosheets for a variety of applications in recent years. The most common synthetic strategies for creating pristine 2D-MOF nanosheets are top-down and bottom-up approaches. Top-down procedures, in general, refer to a strategy for single or few-layer exfoliation of MOF nanosheets using a variety of techniques, such as ultrasonic-assisted exfoliation.[24]

Electrochemical applications.

Sensing platforms.

Membrane-based gas separation.

Other applications.

## METAL-BASED NANOSTRUCTURED MATERIALS

The design of nanoscale catalysts has emerged as a powerful research area due to their extraordinarily high catalytic activities, allowing reactions to be achieved more effectively and efficiently.[25] Metal-based nanomaterials are constantly being researched for a broad array of applications due to their promising features. The thermodynamics and kinetics of transportation for heterogeneous reactions are favored by materials at the nanoscale level, which provide rich surface textural features, massive numbers of binding sites, large surface areas, and incredibly small sizes. Metal based nanostructured materials are also being explored for the manufacturing of next-generation artificial enzymes.[26] More attention has been aimed toward designing appropriate nano-architectures to achieve better performance for heterogeneous reactions.

It may be concluded from this discussion that metal-based nanostructured materials offer a lot of potential when compared to their bulk counterparts. To attain great performance and higher selectivity, materials must be converted to the nanoscale. Research is now shifting away from traditional nanoparticles and toward more advanced and intelligently developed nanomaterials. Nanomaterials with better-controlled morphologies and regulated characteristics are being developed in recent research.

## CORE–SHELL NANOPARTICLES

Depending on whether the nanoparticle is made up of a single material or numerous materials, it can be classified as simple, composite, or core–shell instances. Simple nanoparticles are nanoparticles that are made up of only one substance. Nanoparticles made up of two or more materials are known as core–shell and composite nanoparticles. Core–shell nanomaterials are those that have an interior material that forms a core and an exterior material that forms a shell around the core material. Core–shell nanoparticles can be made in a variety of configurations, including organic/organic, inorganic/organic, inorganic/inorganic, and organic/inorganic.[27]

## CONCLUSION

As described throughout this chapter, we discussed the various types of carbon based nanomaterials. Nanomaterials are very tiny, with at least one dimension of 100 nanometers or less. Nanomaterials can be one-dimensional (e.g., surface films), two-dimensional (e.g., strands or fibres), or three-dimensional (e.g., strands or fibres) (eg. particles). They come in spherical, tubular, and irregular shapes and can be solitary, fused, aggregated, or agglomerated. Nanotubes, dendrimers, quantum dots, and fullerenes are examples of common nanomaterials. Nanomaterials are used in nanotechnology and have physical and chemical properties that are distinct from ordinary substances (i.e., silver nano, carbon nanotube, fullerene, photo catalyst, carbon nano, silica).

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Chapter

12

# FACILE SYNTHESIS OF ZN-AL LAYERED DOUBLE HYDROXIDE IMMOBILIZED Ni (II) SCHIFF BASE COMPLEXES AS A NANOCATALYST FOR LIQUID-PHASE OXIDATION OF TOLUENE

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**ABSTRACT**

Catalytic oxidation of toluene was studied over Ni(II) Schiff base complexes supported layered double hydroxide synthesized by the intercalation method and abbreviated as LDH-[NAPABA-Ni(II)]. The Schiff base ligand (E)-4-((2-hydroxy naphthalene-1-yl) methylene amino) benzoic acid have been synthesized from the condensation of 2-hydroxy-1-naphthaldehyde and 4-amino benzoic acid. The synthesized complexes were fully characterized by using ICP-AES, XRD, SEM, EDX, TEM, FTIR, BET and TGA. The catalytic activity of synthesized catalysts was tested for the oxidation of toluene with tert-butyl hydro peroxide under solvent-free conditions. Interestingly, LDH-[NAPABA-Ni(II)] catalyst was exhibited a maximum of 67.39% conversion of toluene with benzaldehyde selectivity of 81.62%, stability, and reusability at least six cycles without significant loss of catalytic activity.

**KEYWORDS:** Layered double hydroxide, Schiff base complex, nanocatalyst, toluene, tert-butyl hydro peroxide.

## INTRODUCTION

The most flexible and significant organic intermediates are benzaldehyde and benzoic acid, which are widely employed in industries for the manufacture of dyes, medicines, foodstuffs, medicine, preservatives, inhibitors, agrochemicals, and perfumes [1, 2]. In the domestic sector, benzaldehyde is mostly manufactured by hydrolysis of benzylidene chloride [3]. This technique is corrosive and ecologically unfavorable due to the production of hydrochloric acids and acidic solvents [4]. Furthermore, homogeneous catalysts have important limitations, such as difficulty in separating them from the reaction mixture for reuse, whereas heterogeneous catalysts may be easily separated and reused after the reaction. As a result, several researchers have focused their efforts on building a suitable heterogeneous catalytic system for the oxidation of toluene [5-7].

On the other hand, layered double hydroxides (LDHs) have received a lot of attention as useful catalyst support because of their appealing properties like expansion, anion exchange, high surface area, and chemical inertness, with various potential applications like intercalation

chemistry [8], a precursor for heterogeneous catalyst [9], adsorbents [10], drug delivery [11], and anion exchangers [12]. $[[M^{II}_{1-x}M^{III}_{x}(OH)_2]^{x+}.(A^{n-}_{x/n}).mH_2O$ is the general formula for LDH. $M^{II}$ and $M^{III}$ are the metallic divalent ($Mg^{2+}$, $Cu^{2+}$, $Co^{2+}$, $Zn^{2+}$) and trivalent ($Al^{3+}$, $Fe^{3+}$) cations, respectively [13]. These trivalent (MIII) cations are found near the heart of the brucite-like layer, octahedrally ($OH^-$). $Cl^-$, $OH^-$, $NO_3^-$, $CO_3^{2-}$, $SO_4^{2-}$ are examples of interlayer anion [14]. The substitution rate between MII and MIII cations determines the value of x and m. The uniform dispersion of the cations M (II) and M (III) into the layers of LDH, as well as the preferred interlayer anion orientation, are beneficial when using LDH as precursors for the synthesis of stably supported catalysts [15].

The current research will concentrate on the solvent-free catalytic oxidation of toluene over LDH-supported heterogeneous catalysts, LDH-[NAPABA- Ni (II)], with tert-butyl hydro peroxide as an oxidant. To optimize the reaction conditions for maximum conversion and selectivity, we investigated the effects of various solvents, oxidants, the molar ratio of toluene to TBHP, the quantity of catalyst, and the effect of temperature. The probable mechanism was also investigated for the oxidation of toluene.

## PREPARATION OF CATALYSTS

### PREPARATION OF SCHIFF BASE LIGAND

By treating 2-Hydroxy-1-napthaldehyde with 4-amino benzoic acid in a 1:1 ratio, the Schiff base ligand (E)-4-((2-hydroxy naphthalene-1-yl) methylene amino) benzoic acid was synthesized. A methanolic solution of 2-hydroxy-1-napthaldehyde was treated with a solution of 4-amino benzoic acid (10 mmol) and NaOH diluted in 50 ml methanol. The reaction mixture was refluxed for 3 hours with steady stirring in a nitrogen environment. Before being treated under vacuum, the yellow material was filtered, washed with acetonitrile, and recrystallized from methanol.

### PREPARATION OF Ni (II) SCHIFF BASE COMPLEXES

Nickel Schiff base complex NAPABA-Ni(II) has been prepared using ligand, and nickel perchlorate hexahydrate in a 2:1 ratio. This step consists of drop wise addition of a methanolic solution of nickel perchlorate hexahydrate (5 mmol) in the methanolic solution of ligand and the resulting mixture is refluxed for 4 h with continuous stirring. The greenish-brown precipitate of nickel complex, NAPABA-Ni (II) was filtered and washed several times with petroleum ether and dried in a vacuum.

### PREPARATION OF HETEROGENEOUS NANOCATALYST

The LDH-[$NH_2$-$C_6H_4$COO] was formed according to a previously reported procedure using the co-precipitation method [16, 17]. A 250 ml solution of zinc (II) nitrate hexahydrate (14.82g) and aluminum (III) nitrate non-hydrate (6.25g) was prepared in decarbonized water having a Zn-Al molar ratio of 3. With constant stirring, a solution of 4-amino benzoic acid (10.86g) and NaOH (7.8g) in decarbonized water is added to this mixture in deionized water, gel-like slurry was

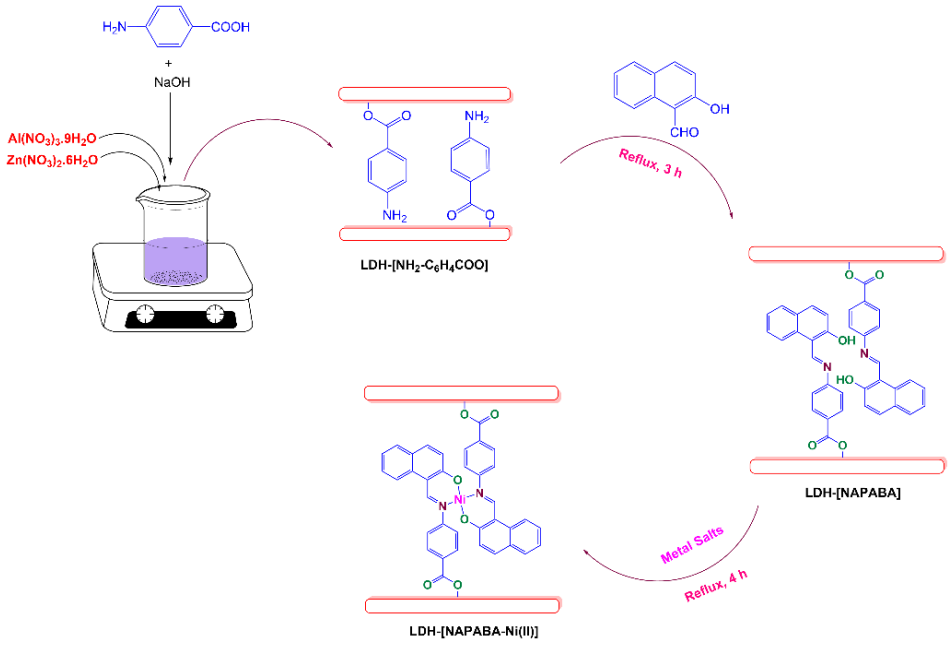
obtained, which was digested at 348 K for 48 hours. The substance was isolated by filtration after cooling, washed with water, then methanol, and dried at 333 K overnight. The nanocatalyst, LDH-[NAPABA-Ni (II)] was prepared in two steps. The first step includes the synthesis of the LDH-NAPABA ligand in which (1.0g) LDH-[$NH_2$-$C_6H_4$COO] was suspended in 50 ml methanol and 2-hydroxy-1-naphthaldehyde (0.48g) added under continuous stirring. The nickel perchlorate hexahydrate (5 mmol) was added to this suspension for 4 h with continuous stirring. The greenish-brown solid was filtered and washed several times with methanol and acetone, and dried overnight at 353 K in the air.

## GENERAL PROCEDURE OF TOLUENE OXIDATION

In a typical experiment, the 100 ml round bottom flask is being loaded with the calculated amount of substrate, TBHP, catalyst, and internal standard dodecane (0.1 ml). The mixture was stirred for appropriateness of time and the progress of the reaction was monitored by GC using the SE-60 ss column at 343 K. As soon as, the reaction is completed, the content present in the flask is being cooled in an ice bath and the solid catalyst is filtered out, to prevent further oxidation which may occur. Finally, the conversion and selectivity values of products were determined by GC. The obtained products are identified by GC-MS. The catalyst was washed twice with ethanol followed by acetone and reused.

## RESULTS AND DISCUSSION

The heterogeneous transition metal Schiff base catalyst, LDH-[NAPABA-Ni (II)] has been synthesized by the immobilization of transition metal Schiff base complexes in the interlayers of LDH-[$NH_2$-$C_6H_4$COO]. The Schiff base ligand has been derived from 2-hydroxy-1-naphthaldehyde and 4-amino benzoic acid. The schematic illustration of the synthesis of heterogeneous catalysts, LDH-[NAPABA-Ni (II)] is given in Scheme 1.




**Scheme 1: Synthesis of heterogeneous catalysts, LDH-[NAPABA-Ni (II)]**

**ICP-AES AND ELEMENTAL ANALYSIS**

The metal content of metal plays a key role in catalytic reactions. The metal content of nickel has been determined by Inductive Coupled Plasma-atomic emission spectroscopy (ICP-AES) analysis which indicates the percentage of metals, present in the catalysts. The ICP-AES results indicate that the 5.48% and 5.41% nickel content present fresh and reused catalyst respectively. The catalyst's chemical composition is confirmed by EDX analysis. The nanocatalyst is comprised of carbon, oxygen, zinc, aluminium, and zinc metal, suggesting that it was effectively synthesized.

**XRD ANALYSIS**

The d-spacing and particle size of support, as well as the catalyst, has been derived from XRD analysis (Fig. 1). The results are given in Table 1. The strong and narrow diffraction lines corresponding to (003) and (006) reflections of a crystalline ZnAl-LDH phase can be seen in the XRD patterns of LDH-[$NH_2$-$C_6H_4COO$] and LDH-[NAPABA-Ni(II)] [18]. LDH-[$NH_2$-$C_6H_4COO$] showed the most intense basal reflection in the (003) plane with a d-spacing of 15.71 Å. The basal spacing of the (003) plane of LDH-[NAPABA-Ni (II)] increases from 15.71 to 22.23 Å, while the LDH structure is unaffected by the metal Schiff base complex during intercalation. The appearance of (003) and (006) reflections indicate the ZnAl-LDH material has a layered structure. There are no other peaks attributed to other phases or impurities, suggesting that ZnAl-LDH is in its pure phase [19]. The characteristic reflections correspond to the (110) plane, which is dependent on the Zn/Al molar ratio, and are similar to the atomic distribution density. Based on the basal spacing d003 the calculated gallery height of LDH-[NAPABA-Ni(II)] is 17.45 Å, which is determined by subtracting the brucite layer thickness (4.78 Å) while the calculated gallery height of LDH is 10.93Å. However, the gallery height of LDH is lower than that of LDH-[NAPABA-Ni (II)], indicating that the NAPABA-Ni (II) complex has been intercalated into the LDHs' interlayer galleries. In addition, the Particle size of support and all the heterogeneous catalysts has been calculated from the Debye-Scherrer equation.

$$D = 0.9\lambda / \beta\cos\theta$$

Where, $\lambda$ = X-ray wavelength, $\beta$ = Full width at half the maximum intensity in radian, $\theta$ = Bragg's angle. The average particle size has been calculated for the most intense peak which is corresponding to the (003) plane. The calculation reveals that particle size of LDH-[$NH_2$-$C_6H_4COO$], and LDH-[NAPABA-Ni (II)] are 9.84 and 14.78 nm respectively.

**FT-IR ANALYSIS**

The Fourier Transform Infra-Red (FT-IR) spectroscopy has been used to obtain the data regarding stretching and bending frequencies. The FT-IR data of LDH-[$NH_2$-$C_6H_4COO$] and homogeneous and heterogeneous catalyst is shown in Fig. 2. The absorption bands at 3118 and 1382 cm–1 in the support, LDH-[$NH_2$-$C_6H_4COO$] are due to the stretching mode of -OH and -$NO_3^-$ group [20]. The lattice vibration modes of the layered double hydroxides sheets are shown

by M–O, and O–M–O vibrations (where M= Zn/Al). The M–O and O–M–O vibrations bands appear in the range 428–784 $cm^{-1}$. In the spectrum of LDH-[NAPABA-Ni (II)], the stretching mode of >C=N, appears at 1610 $cm^{-1}$, while the free ligand shows it on 1605 $cm^{-1}$. The shifting of this stretching mode to higher wavenumber in complex concerning the ligand is attributed to coordination in between the nitrogen of azomethine group with nickel. The existence of water, in the complex, is proved by the broadband at 3360 $cm^{-1}$ and weak bands at 649 and 889 $cm^{-1}$. The weak bands are due to wagging and rocking modes of water. The involvement of oxygen of –OH group and nitrogen of >C=N group of ligands in the coordinate bond formation is confirmed by the presence of two bands at 439 and 641 $cm^{-1}$, which arises due to Ni-N and Ni-O bonds.

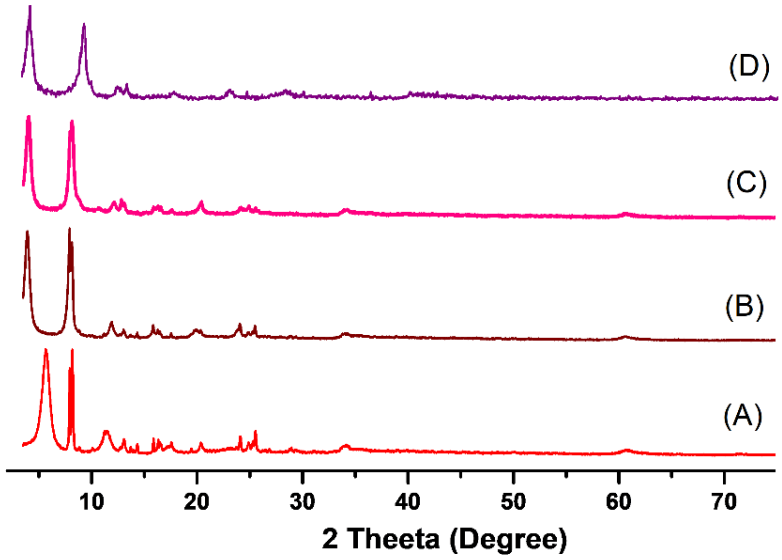



**Fig. 1: XRD pattern of (A) LDH-[$NH_2$-$C_6H_4$COO], (B) NAPABA-Ni (II), (C) LDH-[LDH-NAPABA-Ni (II)] and (D) reused LDH-[LDH-NAPABA-Ni (II)]**

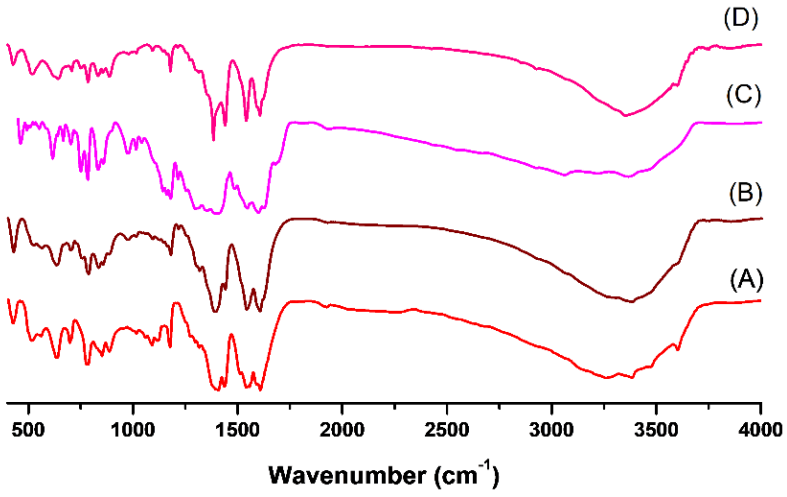



**Fig. 2: FTIR spectra of (A) LDH-[$NH_2$-$C_6H_4$COO], (B) NAPABA-Ni(II), (C) LDH-[LDH-NAPABA-Ni(II)] and (D) reused LDH-[LDH-NAPABA-Ni(II)]**

**Table 1. Chemical composition and textural properties of LDH-[$NH_2$-$C_6H_4$COO] and LDH-[NAPABA-Ni (II)] catalyst**

| Compounds | Elemental analyses (Wt(%)) | | | | | | | d-spacing (Å) | Particle size (nm) |
|---|---|---|---|---|---|---|---|---|---|
| | Ni* | Zn* | Al* | C | H | N | O | | |
| LDH-[$NH_2$-$C_6H_4$COO] | - | 26.39 | 7.73 | 32.49 | 3.2 | 4.27 | 29.12 | 15.71 | 9.84 |
| LDH-[NAPABA-Ni(II)][b] | 5.48 | 20.47 | 6.74 | 47.68 | 3.5 | 3.93 | 15.38 | 22.23 | 14.78 |
| LDH-[NAPABA-Ni(II)][a] | 5.41 | 20.42 | 6.65 | 47.59 | 3.4 | 3.88 | 15.27 | 22.21 | 14.47 |

a: After catalysis, b: Before catalysis. *ICP-AES

## SEM AND TEM ANALYSIS

To examine the morphology of support, LDH-[$NH_2$-$C_6H_4$COO] and the heterogeneous nanocatalyst, Scanning Electron Microscopy (SEM) and Transmission Electron Microscopy (TEM) have been used **(Fig. 3).** The SEM analysis reveals more or fewer morphologies of all the components viz. support and catalysts. All are appearing as compactly agglomerated small irregular lamellar crystals. It is in strong agreement with the fact that morphology of the host layered double hydroxide material is retained even after intercalation of the transition metal Schiff base complex into the layers of LDH-[$NH_2$-$C_6H_4$COO]. The images, obtained from TEM analysis show aggregated flake-like morphology of support as well as the heterogeneous nanocatalyst.

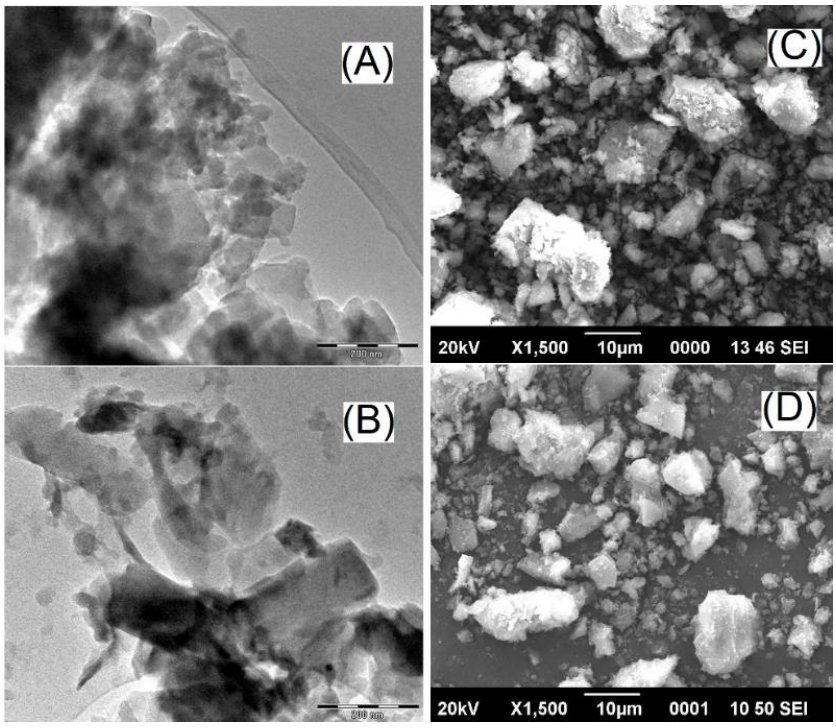



**Fig. 3: TEM images of (A) LDH-[$NH_2$-$C_6H_4$COO] and (B) LDH-[NAPABA-Ni (II)]; SEM images of (C) LDH-[$NH_2$-$C_6H_4$COO] and (D) LDH-[NAPABA-Ni (II)]**

**BET ANALYSIS**

The surface area of heterogeneous catalysts plays a key role in catalysis. Therefore, the support and the heterogeneous catalysts have been characterized by Brunauer Emmett Teller (BET) surface area analysis. The BET surface area analyses have revealed that the surface area of LDH-[$NH_2$-$C_6H_4COO$] is 6.92 $m^2/g$, which is comparable to previously published results [21]. LDH-[NAPABA-Ni(II)] nanocatalyst has a surface area of 17.69 $m^2/g$, which is higher than LDH-[$NH_2$-$C_6H_4COO$] due to the intercalation of a bigger complex molecule into the LDH layers, which leads to layer expansion.

**TGA ANALYSIS**

Thermo-gravimetric analysis was used to determine the thermal stability of the support and the heterogeneous catalyst (TGA) shown in Fig. 4. There are three weight losses in the TGA curves of LDH-[$NH_2$-$C_6H_4COO$] and LDH-[NAPABA-Ni (II)]. At temperatures ranging from 30 to 165 ºC, the first weight loss includes the elimination of interlayer water. The second weight loss observed at 190-510 ºC was attributed to the removal of interlayer benzoate anions and deterioration of the brucite layer. The LDH-[NAPABA-Ni (II)], TGA curve shows the first weight loss caused by the removal of the interlayer water molecule from room temperature to 160 ºC. The second weight loss occurred between 210 and 340 ºC as a result of partial dehydroxylation of the double hydroxide layers. The third observed weight loss at 350-560 ºC is attributed to the complete decomposition of the organic Schiff base ligand and the formation of the oxide.

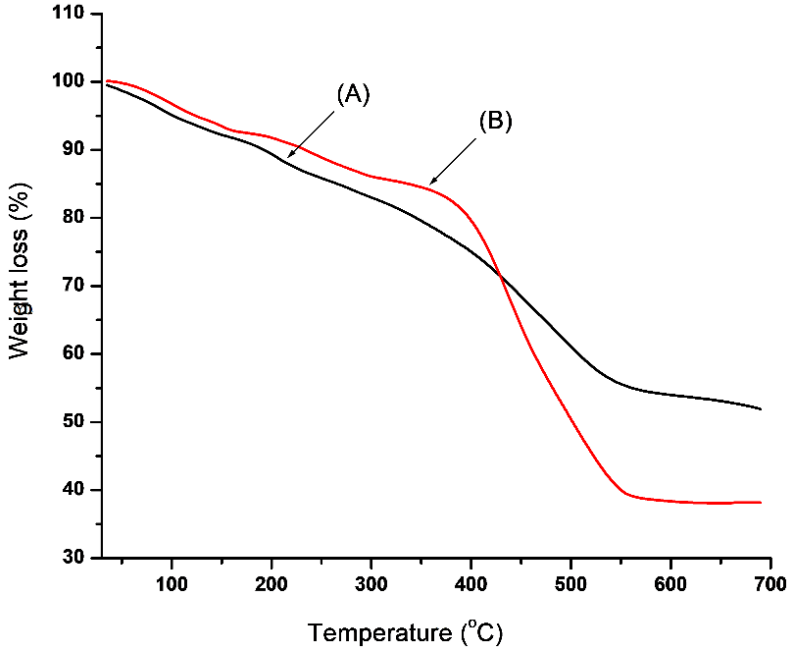



**Fig. 4: TGA curves of (A) LDH-[$NH_2$-$C_6H_4COO$] and (B) LDH-[NAPABA-Ni (II)]**

## CATALYTIC ACTIVITY OF LDH-[NAPABA-NI (II)] FOR TOLUENE OXIDATION

We tried to investigate the scope of the catalytic system after establishing the remarkable catalytic performance of LDH-[NAPABA-Ni (II)] in the aerobic oxidation of toluene, and toluene was used as a substrate under optimal reaction conditions. The obtained results are listed in **Table 2.**

Table 2 depicted the effect of the TBHP molar ratio on conversion and selectivity at 393 K for 7 h. As the initial toluene to TBHP molar ratio increased from 1:1 to 1:2, the conversion of toluene increased rapidly from 32.81 to 45.24%. The conversion (67.39%) increased dramatically when the toluene to TBHP molar ratio was raised to 1:3. Furthermore, the selectivity for benzaldehyde increased from 59.61 to 81.62%, the higher amount of oxygen, further oxidized benzaldehyde to benzoic acid. Therefore, the appropriate molar ratio of toluene to TBHP is 1:3.

**Table 2: Effect of various parameters on the oxidation of toluene over LDH-[NAPABA-Ni (II)]**

| Toluene:TBHP molar ratio | Catalyst Amount (mg) | Temperature (K) | Conversion (%) | Selectivity of products (%) | | TON |
|---|---|---|---|---|---|---|
| | | | | BZ | BA | |
| 1:1 | 100 | 393 | 32.81 | 59.61 | 40.39 | 298 |
| 1:2 | 100 | 393 | 45.24 | 71.24 | 28.76 | 411 |
| 1:3 | 100 | 393 | 67.39 | 81.62 | 18.38 | 612 |
| 1:3 | 75 | 393 | 48.78 | 74.86 | 25.14 | 588 |
| 1:3 | 50 | 393 | 32.67 | 61.24 | 38.76 | 594 |
| 1:3 | 100 | 373 | 40.51 | 71.50 | 28.50 | 368 |
| 1:3 | 100 | 353 | 27.86 | 78.57 | 21.43 | 253 |

BZ: benzaldehyde, BA: benzoic acid; TBHP: 74% TBHP in toluene; Time 7 h.

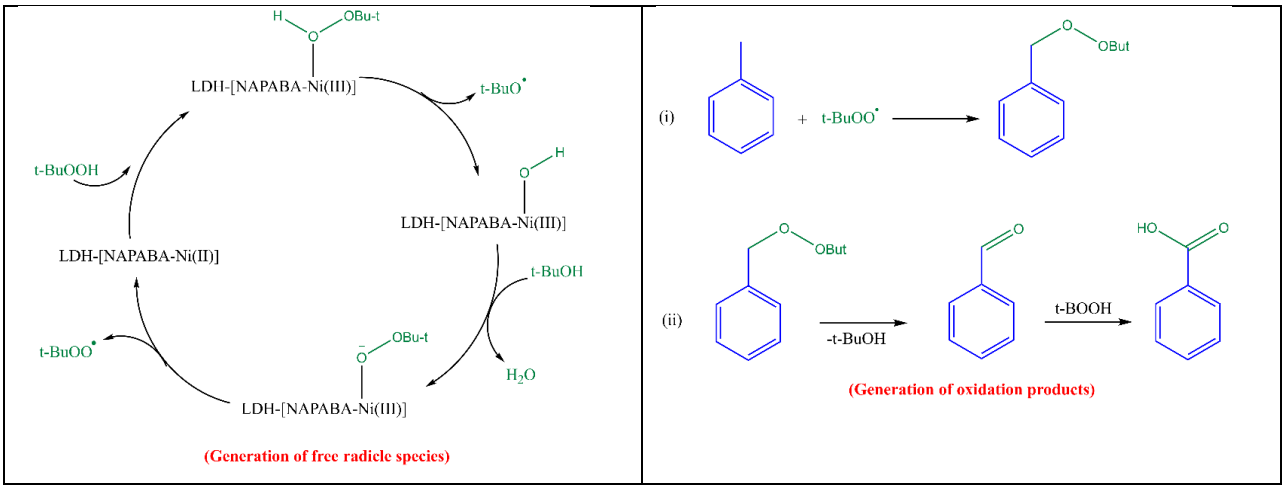
The effects of reaction temperature on toluene conversion and benzaldehyde selectivity at 1:3 for 7 h. Toluene conversion increased rapidly from 27.86 to 67.39%, and benzaldehyde selectivity increased first from 78.57 to 81.62%, as the temperature increased from 353 to 393 K. The nanocatalyst LDH-[NAPABA-Ni(II)] is more easily activated toluene, resulting in a high concentration of tert-butylhydroxytoluene species at the high reaction temperature. Tert-butylperoxytoluene was quickly converted to benzaldehyde. As a result, 393 K was chosen as the appropriate reaction temperature.

## PLAUSIBLE MECHANISM

The experiment was carried out utilizing the Quenching agent 2, 6-di-tertbutyl-4-methyl phenol (BHT), for trapping free radicals to identify a probable mechanism of toluene oxidation which

was catalyzed by the LDH-[NAPABA-Ni (II)]/TBHP system. Two sets of reactions were concurrently carried out under optimum conditions. The first set of reactions is performed in the absence of BHT. The second set of reactions is in BHT, where after 1 hour of reaction BHT is introduced. The constant conversion, obtained in the second set of reactions is due to the trapping of free radicals by BHT thereby stopping the further reaction. The observations favor the free radical mode of the mechanism of toluene oxidation.

The plausible mechanism was based on the above experiment and reported literature [22]. The first step involves the interaction of oxidant molecules (TBHP) on the metal surface which results in coordination between the metal center and TBHP. The steps of the mechanism are illustrated in Scheme 2. It leads to the formation of nickelhydroperoxide and tert-butoxy radical species. When the second molecule of TBHP reacts with nickelhydroperoxide species then it leads to the formation of nickelhydroperoxo species and the elimination of water molecules. In the last step, tert-butylperoxy radical is formed by cleavage of Ni–O bond of nickelhydroperoxo species. The same cycle continues throughout the reaction. The tert-butylperoxy radical reacts with toluene to give tert-butylperoxytoluene. Tert-butylperoxytoluene leads to the formation of benzaldehyde by the elimination of tert-butanol and benzaldehyde on further oxidation gives benzoic acid.




**Scheme 2: The plausible free radical mechanism for the oxidation of toluene with TBHP catalyzed by the LDH-[NAPABA-Ni (II)] nanocatalyst**

## THE RECYCLABILITY OF LDH-[NAPABA-NI(II)]

The LDH-[NAPABA-Ni (II)] catalyst's recyclability was tested under optimal reaction conditions. Even after six cycles, there was no reduction in catalytic activity was observed for the catalyst. The FTIR and XRD pattern of recycled catalyst reveals that the layered structure of the reused catalyst was completely preserved after six cycles. Furthermore, ICP analysis of recycled catalyst indicates the Ni content of the regenerated catalyst almost did not change after the recycling. These findings strongly suggest that the LDH-[NAPABA-Ni (II)] nanocatalyst has excellent structural and catalytic stability during the oxidation of toluene under optimized reaction conditions.

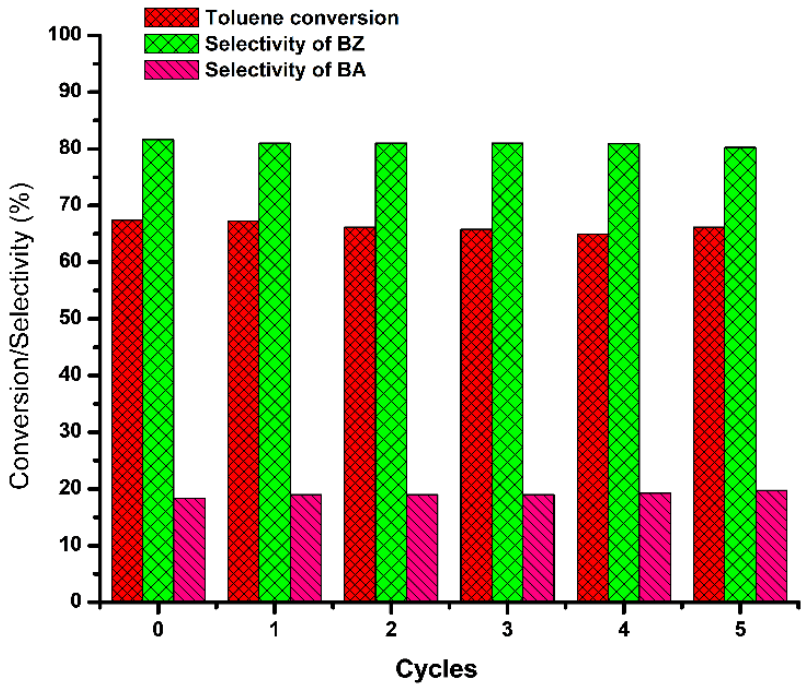



**Fig. 5: Recycling of LDH-[NAPABA-Ni (II)] nanocatalyst**

## CONCLUSIONS

In this paper, we propose LDH-[NAPABA-Ni (II))], a stable, more active, and environmentally friendly heterogeneous nanocatalyst for the oxidation of toluene with tert-butylhydroperoxide as an oxidant in a solvent-free environment. The heterogeneous nanocatalyst, LDH-[NAPABA-Ni (II))] has remarkable catalytic activity, with a maximal 67.39% conversion of toluene and 81.62% selectivity of benzaldehyde. The catalyst was heterogeneous in nature, and it could be recycled up to six times without losing its catalytic activity. Furthermore, a feasible mechanism based on the free radical route was proposed.

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Chapter 13

# FORMULATION DEVELOPMENT, EVALUATION AND TECHNOLOGY TRANSFER FOR LACOSAMIDE ORAL SYRUP

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**ABSTRACT**

The Formulation Development and Technology Transfer of generic Lacosamide oral syrup was the primary goal of this research, by using the reference product of VIMPAT. Lacosamide was used as an adjunctive treatment of refractory partial-onset seizures. The Formulation developmental studies, optimization studies for sweetening agents, viscosity modifier (carmellose sodium and macrogol) and preservative efficacy test were performed. All the parameters were evaluated and found within the limit. The Process developmental studies and Process optimization studies were carried out for large scale manufacturing. Based on the outcome of the Process optimization batch, a similar manufacturing condition is recommended for the future Exhibit batches. From this study, it can be concluded that generic Lacosamide oral syrup can be prepared and able to transfer its technology to large scale manufacturing. Further studies are required to verify the stability and process development optimization studies. Long term pharmacokinetic and pharmacodynamic investigations in humans are needed to evaluate the drug's effectiveness and safety.

**KEYWORDS:** Lacosamide, Partial-onset seizures, Process development studies, Exhibit batch.

## INTRODUCTION

Condensed aqueous formulations of sugar or its substitutes, with or without other flavouring ingredients and therapeutic compounds, are known as syrups. There are several syrups on the market, and they all have the same basic ingredients: purified water, sugar, preservatives and flavourings [1-3]. Lacosamide is a functionalized amino acid that may be used to treat partial-onset seizures and diabetic neuropathic pain. Recent studies show that Lacosamide only affects neurons that are depolarized or active for a long period, which is typical of neurons at the focus of an epileptic seizure, as opposed to other antiepileptic drugs like carbamazepine or lamotrigine, which slow the recovery from inactivation and reduce the ability of neurons to fire action potentials. It is eliminated in the urine in the form of Lacosamide and its metabolites 95% of the time. To yet, the drug's metabolism has remained uncharacteristically unstudied. Lacosamide promotes the delayed inactivation of voltage-gated sodium channels without altering the quick inactivation of voltage-gated sodium channels [4-6]. In this present research

work, formulation development along with technology transfer for the new developed process of Lacosamide oral syrup. As a result, the proposed development study can find to be good and accurate for the target of action associated with Lacosamide oral syrup.

## MATERIALS AND METHODS

### MATERIALS

Drug and other necessary excipients are procured from the selected approved vendor Jigs Chemicals Ltd.

### FORMULATION DEVELOPMENT OF LACOSAMIDE ORAL SYRUP

### EXCIPIENTS SELECTION

The Anti-epileptic medication Syrup's excipients are chosen in accordance with the excipients found in the Reference product and Literature. The generic product was developed using excipient types that were identical to those used in the reference product's formulation and literature study. Literature study and past formulation expertise were utilised to choose the excipient grade and supplier. Knowledge of excipients that have been used effectively in authorized products was also taken into consideration [7-8]. Excipient amounts were explored in following formulation development experiments, as shown in the table below. Based on the excipients utilised in the Reference product & Literature search, Anti-epileptic medication Syrup excipients have been developed.

### PREFORMULATION STUDIES

It is one of the important prerequisites in the development of any drug delivery system. Pre formulation studies were performed on the drug, which included melting point determination, and compatibility studies.

### DETERMINATION OF MELTING POINT

The melting point of Lacosamide was determined by the capillary method. Introducing a tiny amount of fine powder of Lacosamide into a small capillary tube (previously sealed on one end), attaching this to the stem of a thermometer centered in a heating bath, heating the bath slowly, and observing the temperatures at which melting begins and is complete.

### DRUG EXCIPIENTS COMPATIBILITY STUDY (DEC STUDY)

API-Excipient compatibility of the combination of drug substance to be performed with binary and tertiary mixtures as applicable with selected grades of Excipient including those which are part of final composition at 40°C/75%RH, 25°C/60%RH in Closed Vial (Amber Glass) Condition, for a period of initial and 4 weeks. Samples shall be Analysed for appearance, assay and related substances. Table 1 shows the initial state and ratio of the chemicals before DEC studies.

**Table 1: Initial state and ratio of the DEC study**

| Vial No. | Drug & Drug-Excipient blend | Ratio | Initial |
|---|---|---|---|
| 1 | Lacosamide API | 10mg | White coloured |
| 2 | API: Water | 10mg: 1ml | API dispersion |
| 3 | API: Glycerine | 10mg: 500 mg | Viscous dispersion |
| 4 | API: Sorbitol solution | 10mg: 350 mg | White viscous dispersion |
| 5 | API in Glycerine, Sorbitol Solution and Purified water without pH adjustment | 10mg :1ml | Clear, colourless Solution |
| 6 | API in Glycerine, Sorbitol solution and Purified water with pH adjustment with citric acid | 10mg: 1ml: q.s. | Clear, colourless Solution |
| 7 | API: Base Solution with pH adjustment: Sodium CMC | 10 mg :1ml: 1 mg | Clear, colourless Solution |
| 8 | API: Base Solution with pH adjustment: Acesulfame Potassium | 10mg :1ml: 60 mg | Clear, colourless Solution |
| 9 | API: Base Solution with pH adjustment: PEG 4000 | 10mg :1ml: 500 mg | Clear, colourless Solution |
| 10 | API: Base Solution with pH adjustment: Methylparaben | 10mg :1ml: 6 mg | Clear, colourless Solution |
| 11 | API: Trisodium citrate and citric acid buffer with pH 4 | 10mg :1ml | Clear, colourless Solution |
| 12 | API: Base Solution with pH adjustment: Sodium Chloride | 10mg :1ml: 5 mg | Clear, colourless Solution |
| 13 | API: Base Solution with pH adjustment: Strawberry Flavour | 10mg :1ml: 10 mg | Clear, colourless Solution |
| 14 | API: Base Solution with pH adjustment: Masking Flavour | 10mg :1ml: 10 mg | Clear, colourless Solution |
| 15 | API Composite sample | q. s | Colourless to white Solution |
| 16 | API: Trisodium citrate and citric acid buffer with pH 5 | 50mg :1ml | Clear, colourless Solution |

## FORMULATION DEVELOPMENT

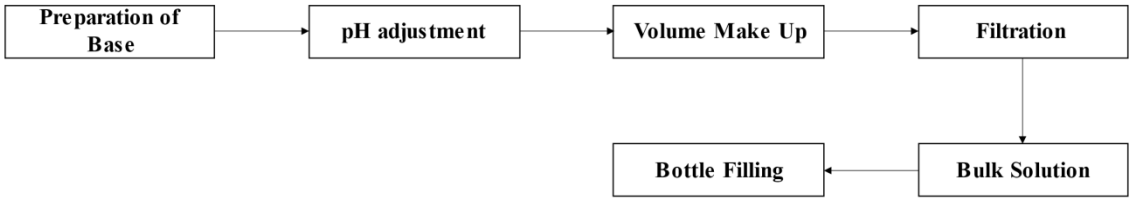


**Fig 1: Schematic representation of Oral Syrup Process**

Formulation Development was started to develop a stable and generic equivalent product of Anti-epileptic drug syrup for the EU market. The selection of excipients was based on RLD excipients and drug excipient compatibility studies. The proposed generic formulation was developed to mimic the reference listed drug, which is an oral solution. Based upon the clinical, pharmacokinetic and physicochemical characterization of the RLD product, the initial formulation strategy was defined. Figure 1. represents the formulation steps involved in the manufacturing of drug products.

## PROCESS SELECTION

Lacosamide belongs to BCS Class I drug and the manufacturing process involves dissolving API in an aqueous phase containing purified water, Glycerol & sorbitol liquid with continuous stirring followed by the addition of a flavouring agent, sweetening agent and pH adjusting agent. Manufacturing process includes Stirring, Mixing, Filtration, and Packaging.

## FORMULATION DEVELOPMENT OPTIMIZATION STUDIES

Optimization is the process of finding the best way of using the existing resources while taking into account all factors that include decisions in any experiment. The term Optimize is defined as making perfect or as functional as possible. The manufacturing process and manufacturing formula are optimized, and the results are discussed. The table 2 describes the unit composition of the dosage form.

## MANUFACTURING PROCESS

**1.0. Dispensing**

1.1. All the materials were weighed accurately using a calibrated weighing balance.

1.2. About 90gm of Water Purified was dispensed in an S.S vessel using a calibrated weighing balance.

**2.0. Preparation of Preservative Solution**

2.1. Dispensed quantity of Purified Water as per step 1.2 was taken in an S.S vessel and heated to 70-80°C.

2.2. Accurately weighed quantity of Methyl Para hydroxy benzoate was added to step 2.1 heated water and stirring continued to form a clear solution.

2.3. Step no. 2.2 methyl para hydroxy benzoate solution was cooled to 55-65°C temperature.

**3.0. Addition of viscosity modifier**

3.1. Dispensed quantity of Carmellose Sodium was added into dispensed quantity of Glycerol and stirred manually with the help of a stainless-steel spatula to form dispersion.

3.2. Step no. 3.1 dispersion of Carmellose Sodium was added to step no 2.3 preservative solution maintained at 55-65°C temperature in manufacturing vessel and stirring continues for 30 minutes at 500rpm speed of stirrer.

**4.0. Addition of viscosity modifier, sweetening agent and taste enhancer**

4.1. Under continuous stirring accurately weighed quantities of Macrogol (Polyethylene Glycol 4000), Acesulfame Potassium, Sodium Chloride and Sorbitol Liquid (Non-Crystallizing) were added to step no. 3.2 solution.

4.2. About 26 gm of Purified Water was added to step no. 4.1 and stirring continued for 20 minutes at 750rpm speed.

**5.0. Addition of Buffering Agents and pH adjustment**

5.1. Accurately weighed quantity of Citric acid anhydrous and Sodium citrate was added to step 4.2 and stirring was continued for 30 minutes at 750 rpm to form a clear solution.

**6.0. Addition of Flavouring Agents**

6.1. Accurately weighed quantity of Strawberry flavour and Masking Flavour were added to step no. 5.1 and stirring was continued for 10 minutes at 750rpm.

**7.0. Addition of Lacosamide API**

7.1. Accurately weighed quantity of Lacosamide API was added in step no. 6.1.

7.2. About 90gm of water purified was added to step no. 7.1 and stirring was continued for 60 minutes at 750rpm to form a clear solution.

**8.0. pH adjustment**

8.1. pH of the bulk solution was recorded; Observed pH: 4.6; Target pH: 4.60 (Range pH 4.5 to pH 4.7). (If the pH of the solution is found to be above 4.7, adjust the pH with 0.1 M citric acid anhydrous solution to the target pH of 4.6 and if the pH of the solution is found to be below 4.5, adjust the pH with 0.1 M Sodium citrate solution to the target pH of 4.6)

8.2. Stirring continued for 10 minutes at 750rpm.

**9.0. Volume adjustment**

9.1. The volume of the bulk solution was checked and volume adjustment was done with the addition of the required quantity of purified water.

9.2. Step no. 9.1 bulk solution was stirred for 30 minutes at 750rpm.

**10.0. Filtration**

10.1 The bulk solution was filtered through a 75µ Stainless Steel screen.

**11.0. Bottle Filling & Capping**

11.1. About 200 mL of bulk solution was filled in an Amber coloured Glass bottle (Type III) and closed the bottle with a polypropylene child-resistant closure.

**Table 2: Ingredients used in the syrup**

| Sr. No. | Name of Ingredients | Function | Composition mg/ml |
|---|---|---|---|
| 1 | Lacosamide | API | 10.000 |
| 2 | Glycerol | Viscosity modifier | 80.000 |
| 3 | Sorbitol, Liquid (Non-Crystallizing) | Sweetening agent | 267.000 |
| 4 | Carmellose Sodium | Viscosity Modifier | 0.200 |
| 5 | Macrogol (Polyethylene Glycol 4000) | Viscosity Modifier | 65.000 |
| 6 | Acesulfame Potassium | Sweetening Agent | 10.000 |
| 7 | Methyl Para hydroxy benzoate | Antimicrobial Preservative | 2.000 |
| 8 | Sodium Chloride | Taste enhancer | 2.750 |
| 9 | Strawberry Flavour | Flavouring Agent | 1.000 |
| 10 | Masking Agent Flavour | | 5.000 |
| 11 | Citric Acid Monohydrate | Buffering agent | 1.800 |
| 12 | Sodium Citrate | | 2.700 |
| 13. | Purified Water | Vehicle | q.s. |
| | | **Total** | **1.00** |

**TECHNOLOGY TRANSFER OF LACOSAMIDE ORAL SYRUP**

**PROCESS DEVELOPMENT STUDY 1#**

**Stirring speed optimization study of Anti-epileptic drug syrup**

To provide a stirring speed range for the manufacturing process, it was decided to manufacture formulation using different stirring speeds (Batch 1-500 RPM, Batch 2-750 RPM, and Batch 3-1000 RPM) and to evaluate the same for physical and chemical parameters. The results of the stirring speed study are provided in the result section.

**PROCESS DEVELOPMENT STUDY 2#**

**Stirring time optimization study of anti-epileptic drug syrup**

To provide a stirring time range for the manufacturing process, it was decided to manufacture formulation using different stirring times (Batch 4-45 min, Batch 5-60 min, and Batch 6-75 min) and to evaluate the same for physical and chemical parameters. The results of the stirring time are provided in the result section.

**STABILITY STUDIES**

Drug substance or drug product 'stability' is described as the ability to stay within parameters specified to maintain its identification, strength, quality and purity throughout the retest or expiry date period's duration. Product failures may be caused by the drug's inability to work as

expected. All pharmacological dosage forms benefit from having an expiry date. If possible, provide information about how long the product will be kept beyond its expiry date.

**ACCELERATED AND LONG-TERM STABILITY**

Batch with finalized composition was kept for accelerated stability i.e.,40°C/75% RH and Long-Term Stability i.e.,25°C/60% RH & 30°C/65% RH. The Analytical results are shown in the result section.

**CONTAINER CLOSURE SYSTEM**

The proposed product Anti-epileptic drug syrup is packaged in an amber glass bottle (Type III) with CRC Closure.

**RESULT AND DISCUSSION**

**PREFORMULATION STUDIES**

Melting Point Determination: The melting point of Lacosamide was found to be 144°C.

**Drug-Excipient Compatibility Study**

**Table 3: Result of DEC Study**

| Vial No. | Drug & Drug-Excipient blend | Ratio | Initial | 25±2°C/60±5 %RH (Closed Condition) (30 days) | 40±2°C/75±5 %RH (Closed Condition) (30 days) |
|---|---|---|---|---|---|
| 1 | Lacosamide | 10mg | White coloured | No change | No change |
| 2 | API: Water | 10mg: 1ml | API dispersion | API dispersion | API dispersion |
| 3 | API: Glycerine | 10mg: 500 mg | Viscous dispersion | Viscous dispersion | Viscous dispersion |
| 4 | API: Sorbitol solution | 10mg: 350 mg | White viscous dispersion | White viscous dispersion | White viscous dispersion |
| 5 | API in Glycerine, Sorbitol Solution and Purified water without pH adjustment | 10mg :1ml | Clear, colourless Solution | Clear, colourless Solution | Clear, colourless Solution |
| 6 | API in Glycerine, Sorbitol solution and Purified water with pH adjustment with citric acid | 10mg: 1ml: q.s. | Clear, colourless Solution | Clear, colourless Solution | Clear, colourless Solution |

| | | | | | |
|---|---|---|---|---|---|
| 7 | API: Base Solution with pH adjustment: Sodium CMC | 10 mg :1ml: 1 mg | Clear, colourless Solution | Clear, colourless Solution | Clear, colourless Solution |
| 8 | API: Base Solution with pH adjustment: Acesulfame Potassium | 10mg :1ml: 60 mg | Clear, colourless Solution | Clear, colourless Solution | Clear, colourless Solution |
| 9 | API: Base Solution with pH adjustment: PEG 4000 | 10mg :1ml: 500 mg | Clear, colourless Solution | Clear, colourless Solution | Clear, colourless Solution |
| 10 | API: Base Solution with pH adjustment: Methylparaben | 10mg :1ml: 6 mg | Clear, colourless Solution | Clear, colourless Solution | Clear, colourless Solution |
| 11 | API: Trisodium citrate and citric acid buffer with pH 4 | 10mg :1ml | Clear, colourless Solution | Clear, colourless Solution | Clear, colourless Solution |
| 12 | API: Base Solution with pH adjustment: Sodium Chloride | 10mg :1ml: 5 mg | Clear, colourless Solution | Clear, colourless Solution | Clear, colourless Solution |
| 13 | API: Base Solution with pH adjustment: Strawberry Flavour | 10mg :1ml: 10 mg | Clear, colourless Solution | Clear, colourless Solution | Clear, colourless Solution |
| 14 | API: Base Solution with pH adjustment: Masking Flavour | 10mg :1ml: 10 mg | Clear, colourless Solution | Clear, colourless Solution | Clear, colourless Solution |
| 15 | API Composite sample | q. s | Colourless to white Solution | Colourless to white Solution | Colourless to white Solution |
| 16 | API: Trisodium citrate and citric acid buffer with pH 5 | 50mg :1ml | Clear, colourless Solution | Clear, colourless Solution | Clear, colourless Solution |

Significant incompatibility of API with flavour was observed; further investigation confirmed that the flavour initially selected for the DEC study was containing Acetic Acid as one of the components. Due to which pH of flavour was strongly acidic i.e., around 2.1. So, based on the above developmental data and DEC study data, it was decided to substitute both the flavours (Firmenich) with another source (FONA) which does not contain either acetic acid or any other strong acid as a part of the flavour composition. All other excipients studied were observed to be compatible with Lacosamide API in solution form. Stability of Lacosamide in Syrup from Observed to be Improved Further Addition of Buffering System to ensure the desired pH of that syrup.

**TECHNOLOGY TRANSFER STUDIES**

**PROCESS DEVELOPMENT STUDY 1# & 2#**

**Stirring speed and time optimization study of Anti-epileptic drug syrup**

Physical And Chemical Characterization of manufactured batches was carried out and data is presented in Table 4.

**Table 4: Stirring speed and time optimization studies**

| Sr. No. | Test | Specification | Speed optimization | | | Stirring time optimization | | |
|---|---|---|---|---|---|---|---|---|
| | | | Batch 1 | Batch 2 | Batch 3 | Batch 4 | Batch 5 | Batch 6 |
| 1. | **Description** | Slightly viscous clear, colourless to yellow-brown liquid. | Complies | | | | | |
| 2. | **Assay** | 95% -105% | 98.5 | 98.6 | 98.4 | 98.4 | 98.6 | 98.6 |
| 3. | **pH** | 4.2 to 5.2 | 5.02 | 4.56 | 4.99 | 5.0 | 4.56 | 5.02 |
| 4. | **Preservative content** | 1.60 to 2.40mg/ml | 1.96mg/ml | 1.98 mg/ml | 1.96 mg/ml | 1.96 mg/ml | 1.98 mg/ml | 1.96 mg/ml |
| 5. | **Sp. Gravity** | 1.100±1 | 1.1092 | 1.1067 | 1.1084 | 1.1089 | 1.1067 | 1.1088 |
| 6. | **Viscosity** | NMT 40 cP. | 5.48 | 5.56 | 5.30 | 5.06 | 5.56 | 4.95 |
| 7. | **Related substances** | | | | | | | |
| | **Total Impurity** | NMT 1.00 % | 0.19 | 0.10 | 0.20 | 0.21 | 0.10 | 0.21 |

**ACCELERATED AND LONG-TERM STABILITY**

The batch with finalized composition was kept for accelerated stability i.e.,40°C/75% RH and Long-Term Stability i.e.,25°C/60% RH & 30°C/65% RH analytical results are given in Table 5.

**Table 5: Accelerated and long-term stability studies**

| Parameters | Specifications | Reference Product | | Generic Anti-epileptic drug Syrup | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Initial | 40°C/75% | Initial | 40°C/75% | | | 25°C/60% | 30°C/65% |
| | | | 3 M | | 1 M | 2 M | 3 M | 3 M | 3 M |
| **Description** | Slightly viscous clear, colourless to yellow-brown liquid. | Complies | | Complies | | | | Complies | |
| **pH** | 4.2 to 5.2 | 4.32 | 4.51 | 4.56 | 4.15 | 4.32 | 4.31 | 4.32 | 4.32 |
| **Assay (%)** | 95% -105% | 93.7 | 96.0 | 98.6 | 97.9 | 98.7 | 99.1 | 98.4 | 99.0 |
| **Preservative Content (mg/ml)** | 1.60 to 2.40 | 2.067 | 2.22 | 1.96 | 1.97 | 1.93 | 1.96 | 1.93 | 1.95 |
| **Viscosity (cP)** | NMT 40 cP | 24.18 | 24.24 | 6.31 | 6.20 | 5.64 | 6.28 | 6.28 | 6.06 |
| **Total Impurity** | NMT 1.00 % | 0.12 | 0.40 | 0.11 | 0.13 | 0.15 | 0.15 | 0.11 | 0.11 |

With reference to 3 months of lab scale stability data, it can be concluded that Anti-epileptic drug syrup is having acceptable stability. Further 6 months study to be conducted.

## EVALUATION STUDY

**Table 6: Evaluation of formulated Lacosamide syrup**

| Sr. No. | Test | Specification Limits |
|---|---|---|
| 1. | **Appearance** | Clear, colourless strawberry-flavoured liquid |
| 2. | **Identification Test** | |
| | **Identification for Lacosamide** | |
| | **By HPLC** | The retention time of the Lacosamide peak in the chromatogram of sample preparation should correspond to that in the chromatogram of the standard preparation, as obtained in the Assay (by HPLC) |
| | **By UV** | The UV spectrum of the Lacosamide peak in the chromatogram obtained with the test solution is similar to the UV spectrum of the principal peak in the chromatogram obtained with a standard solution in the Assay test (by HPLC) |

| | | |
|---|---|---|
| | **Identification of Methyl Parahydroxybenzoate** | |
| | **a. By HPLC** | The retention time of the Methyl Parahydroxybenzoate peak in the chromatogram of sample preparation should correspond to that in the chromatogram of the standard preparation, as obtained in the Assay (by HPLC) |
| 3. | **pH** | 4.0 to 5.2 |
| 4. | **Specific gravity** | 1.12 ± 0.1 |
| 5. | **Viscosity** | NMT 40 cP |
| 6. | **Deliverable volume** | The average volume of liquid obtained from the 10 containers is not less than 100%, and the volume of no container is less than 95 % of the volume declared in the labelling. |
| 7. | **Preservative content** (by HPLC) | |
| | **Methyl Parahydroxy benzoate** | 1.80 to 2.20 mg/mL (90% - 110% w/w) |
| 8. | **Assay** (by HPLC) | NLT 95.0 % and NMT 105.0 % w/w of the labelled amount of Lacosamide |
| 9. | **Related substances** (by HPLC) | |
| | i) Lacosamide Impurity-D | NMT 0.60 % |
| | ii) Any Individual Unspecified Impurity | NMT 0.20 % |
| | iii) Total Impurities | NMT 1.0 % |
| 10. | **Microbial Limit Test** | |
| | a) Total Aerobic microbial count | NMT 100 cfu/g |
| | b) Total combined yeasts/moulds count | NMT 10 cfu/g |
| | c) Specified Micro-organisms: *E. coli* | Should be absent/1 g |

## CONCLUSION

This formulation development and technology transfer studies were carried out to develop and assess the generic Lacosamide oral syrup which possesses the reference product

characterization for the adjunctive treatment of partial-onset seizures in patients with epilepsy. The Formulation developmental studies, optimization studies for sweetening agents, viscosity modifier (carmellose sodium and macrogol) and preservative efficacy test were performed. All the parameters were evaluated and found within the limit. The process developmental studies and process optimization studies were carried out for large scale manufacturing. The Formulation development parameters, process optimization batches observation, manufacturing process and unit composition formula, process parameters and process evaluation study were finalized. Based on the outcome of the Process optimization batch, a similar manufacturing condition is recommended for the future Exhibit batches. From this study, it can be concluded that generic Lacosamide oral syrup was prepared and transferred its technology to large scale manufacturing. Further studies are required to verify the stability and process development optimization studies. Long-term pharmacokinetic and pharmacodynamic investigations in humans are needed to evaluate the drug's effectiveness and safety.

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Chapter
14

# ETHNOBOTANIAL STUDY - OVERVIEW

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**ABSTRACT**

Botany is the science which deals with floras including physiology, morphology, genetics, ecology, distribution, taxonomy, and economic importance. Occasionally, fungi are included in botany. Ethnobotany is the study of how people of a particular culture and region make use of indigenous (native) plants. Plants provide food, medicine, shelter, dyes, fibers, oils, resins, gums, soaps, waxes, latex, tannins, and even contribute to the air we breathe. Since our earliest origins, humans have depended on plants for their primary needs and existence. Over time, people and cultures have tested and continued to use the plants that were beneficial. Our cultures evolved by passing ever more sophisticated knowledge of plants and their usefulness from generation to generation. Examining human life on earth requires understanding the role of plants in historical and current day cultures. Even today, we depend upon plants and their important pollinators for our existence and survival. Let's explore people's use of plants.

**KEYWORDS:** Ethnobotany, Taxonomy, Herbal medicines, Human Life, Plants.

## INTRODUCTION

In aspect of botany which has received recent attention and recognition as an organized discipline in India is ethnobotany, defined as the total direct relationship between humans and plant kingdom.

Jain (1987) elaborated it as the total natural and traditional relationship and interaction between man and his surrounding plant wealth. Recently, Wickens (1990) defined ethno botany as the study of useful plants prior to commercial exploitation and eventful domestication. In fact, ethno botany is the first knowledge on plants which primitive and aboriginal people had acquired by sheer necessity, intuition, observation and experimentation in the forests. It is also not restricted to the study of medicinal plants by indigenous cultures.

The 1990's has seen a growing shift in interest once more; plants are reemerging as a significant source of new pharmaceuticals. Industries are now interested in exploring parts of the world where plant medicine remains the predominant form of dealing with illness.

Ethnobotanists use different methods and materials for their ethnobotanical studies, including ancient writings, surveys, discussions with key informants, and field investigations of the relationship between the plants and human beings. They typically work together with native people or traditional healers who have knowledge about the plants to record the indigenous biodiversity including plants, and also for the identification of botanical diversity, parts used for the treatment of human and livestock diseases, and method of preparations and applications By necessity, ethnobotany is multidisciplinary. This multidisciplinary approach gives ethnobota nists more insight into the management of tropical forest reserves in a period of tremendous environmental stress. Ethnobotany covers various disciplines, including botany, biochemistry, pharmacognosy, toxicology, medicine, nutrition, agriculture, ecology, evolution, comparative religion, sociology, anthropology, linguistics, cognitive studies, history, and archeology, due to the fact that plants have significant purpose in day-to-day activity of human beings. The multidisciplinary habit of ethnobotany permits a widespread range of methods and uses and leads to the investigation of plants in various ways by the researchers.

Around the world, different cultures have developed their own ethnobotany systems, making use of their indigenous plants based on long-term empirical observations. Humans discovered the value of plants as agents for health promotion, disease prevention, and medicinal uses.

The tribal people are the real custodians of the medicinal plants. Out of 45,000 species of wild plants. 7500 species are used for medicinal purposes. The World Health Organization (WHO) has been promoting a movement for saving plants for saving lives.

Ethnobotany has a very long history dating back to the Biblical Old Testament times. It has been established that up to 25% of the drugs prescribed in conventional medicine are related directly or indirectly to naturally occurring substances mostly of plant origin.

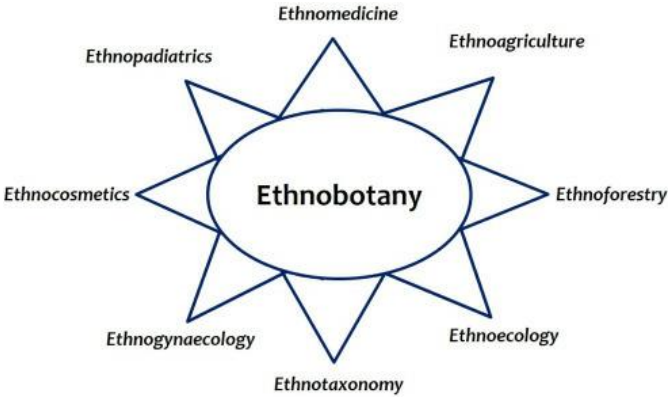


**Fig 1: History of Ethnobotany**

It is interdisciplinary between plant science and ethnology. The botanical knowledge of an ethnic people can be useful in many aspects, so it is called a "multidisciplinary science." In recent years, several disciplines have come to be used in connection with ethnic people and their knowledge, namely ethnomedicine, ethnotaxonomy, ethnotoxicology, ethnoecology, ethnogynaecology, ethnopharmacology, ethnopadiatrics, ethnoforestry, etc. Ethnobotany is a multidisciplinary science involving the traditional use of plants by human beings. Billions of people in the world rely chiefly on herbal medicines. The great majority of medicinal and aromatic plants (MAPs) used locally or entering into trade and herbal industries comes from wild sources and constitutes the source of livelihoods of millions of people. In recent years, the increasing demand for herbal medicines in industrialized countries is being fueled by a growing consumer interest in natural products.

The ancient Egyptians (3000 B.C) were specialists in using remedies for curative and preventive purposes. The crude drugs used for the plant derivation included Aloes, Gum, Myrrh, Poppy, Pomegranate, Colocynth, Linseed, Squill, Coriander, Onion, Anise, Melon, Castor etc. The Ebers papyrus found in Eqypt in the 1870s contains prescriptions written in heirooglyphics for over 700 preparations. This prescription for an asthama remedy is prepared by the cocmbination of herbs heated on a brick so that the victim possibly will inhale their smokes. The Babylonian medicine was known as Laws of Hamorabi (772 B.C).

The first step is collecting detailed knowledge about the local and indigenous people. Researchers prepare a regional study on the epidemiology, traditional medicine, culture and ecology of the people and their environment. Herbarium is a process of collecting dried-out plant samples that used for study purposes. the key roles of a herbarium are to make available reference materials for botanical diversity identification of newly collected specimens, help as a supply for botanists and botany subjects, record the occurrence of a plant types in a specific area, decide taxonomy concerns, and store type and voucher samples. A type specimen is the exact specimen on which the name of a taxon is based.

They are vastly valued and may be stored distinctly or attached on to different colored paper to escape loss or harm. A voucher specimen helps as the root for a specific research. It is a consistent technique to authenticate the exact identity of the plant used for the research. Incase if questions are raised the about the identity the medicinal plants, the only way to answer this questions is by using the voucher numbers given for the specific plants. This shows whether the plants are correctly identified by the experts.

Plants produce economically important organic compounds such as oils, resins, tannins, rubber, gums, waxes, dyes, flavors and fragrances, pharmaceuticals and pesticides. Aspirin, Codeine, Ipeacac, Pilocarpine, Pseudoephedrine, Quinine, Reserpine, Scopolamine, Theophylline and Vinblastine etc., have been derived from medicinal plants based ethnobotanical research program.

People use medicinal plants for ailment treatment according to their cultural traditions and indigenous knowledge. Medicinal plants are natural asset of great significance and play a

crucial role in the primary healthcare system of remote, developing and under-developed regions of the world. For instance, medicinal plants in the Himalayas and adjoining regions are the major source of ethno-medicines based on indigenous knowledge of the elderly persons. Thus, the indigenous knowledge about medicinal plants has been transmitted from generation to generation through oral conversation. This oral conversation although promotes transmission of indigenous knowledge about medicinal plants but also alters with the passage of time while passing from one person to another. Through ethnobotanical surveys, indigenous knowledge of medicinal plants from local elderly persons and professionals is compiled and documented in a manner to describe plants, which can be a source of medicines to cure diseases.

Ethnomedicinal knowledge is very ancient in India and might be among the earliest in the world and all traditional systems of medicine had their roots in ethno botany. During the last two decades, work has started at, National Botanical Research Institute (NBRI), Lucknow, National Bureau of Plant Genetic Resources (NBPGR), Delhi, Central Institute of Medicinal and Aromatic Plants (CIMAP), Central Council for Research in Ayurveda and Siddha (CCRAS), and Central Council for Research in Unani Medicine (CCRUM). Several Botany departments of Universities are also associated with this type of work.

Ethnobotanical studies on various sub-groups of the plant kingdom, like an algae, fungi, bryophytes, pteridophytes, lichens etc. Are linked under the sub heads of ethnoalgology, ethnomycology, ethnobryology, ethnopteridplogy, ethnolichenology etc.

In recent years, the demand of Indian medicinal plants has increased considerably at national and global markets. India is second largest volume exporter of raw herbal drugs to the global market. In the present study, it was noted that the majority of the species used for medicine were collected from the wild. India occupies premier position in the use of herbal drugs utilizing nearly 2,500 plant species in different formulations. Estimated number of medicinal drug manufacturing units in India is over 7800 which consume about 2000 tons of herbs annually.

While the demand for medicinal plants is growing, some of them are increasingly being threatened in their natural habitat. For meeting the future needs cultivation of medicinal plant has to be encouraged. According to an all India ethno biological survey carried out by the Ministry of Environment and Forests, Government of India, there are over 8000 species of plants being used by the people of India.

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Chapter 15

# QSAR: A USEFUL TOOL OF COMPUTATIONAL CHEMISTRY FOR DESIGNING NEW DRUG AND PREDICTING THEIR BIOLOGICAL ACTIVITIES

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**ABSTRACT**

Drug discovery is a very difficult process, and it has been shown that out of hundreds of compounds synthesized in the lab, only one, or none, is marketed as a 'drug'. Traditional methods of synthesizing compounds are based on trial-and-error methods, and random screening of compounds to test their activity is presumed to be very expensive and time-consuming. Recent advances in the fields of pure and applied sciences, analytical chemistry, and informatics have proven to be useful tools for designing new chemicals and predicting their biological activity prior to synthesis. QSARs are quantitative structure-activity relationships that enable chemists to describe and elucidate the effects of various physicochemical properties on drug efficacy and determine the biological activity of new compounds.

**KEYWORDS:** QSAR, new drug, biological activity, physicochemical properties, elucidation.

## INTRODUCTION

**Quantitative structure-activity relationship** (QSAR) is a computational modeling technique for revealing the relationship between structural properties and biological activity of compounds. Although QSAR modeling is essential for drug discovery, it has many limitations. Virtual 2-screening (VS) has emerged as a powerful computational approach in drug discovery to screen large libraries of small molecules to identify molecules with desired properties. New hits can be found and tested, which can be analyzed experimentally. As with other computational approaches, the goal of VS is not to replace *in vitro* or *In vivo* assays, but to speed up the discovery process, reduce the number of candidates to experimentally test, and streamline their selection. Additionally, VS is very popular with pharmaceutical companies and academic institutions due to its time, cost, resource and effort savings. Among the VS approaches, quantitative structure-activity relationship analysis (QSAR) is the most powerful method due to its high throughput, high speed and high hit rate. Various approaches have been attempted for rational drug development and design, including 1. Hantzsch's method, 2. Additive model and 3. Principal component analysis. Molecular orbital method 5. Discriminant analysis 6. Molecular modeling etc. as a first preparatory step for developing a QSAR model collect relevant chemogenomics data

from databases and literature. Chemical descriptors are then computed at different representation levels of the molecular structure from 1D to nD and correlated with biological properties using machine learning techniques. Once developed and validated, QSAR models are applied to predict the biological properties of new compounds. Applications of QSAR Quantitative structure-activity relationship (QSAR) analysis is a ligand-based drug development technique developed by Hansch and Fujita (1964) over 50 years ago. Initially, QSAR modeling was limited to a set of related compounds and simple regression techniques. Quantitative structure-activity relationship analysis (QSAR) is a ligand-based drug design method developed by Hansch and Fujita (1964) over 50 years ago. 3 Since then and to this day, QSAR has been an efficient mathematical modeling technique for analyzing chemical structures and continuous (pIC50, pEC50, Ki, etc.) or categorical/binary (active, inactive, toxic), non- toxicity) using regression/classification techniques (Cherkasov *et al.,* 2014). In the past decades, QSAR has undergone several transformations, ranging from the dimensionality of molecular descriptors (from 1D to nD) to different methods for finding correlations between chemical structures and biological properties. QSAR modeling was limited to sets of related compounds and simple regression techniques. Today, QSAR modeling has grown, diversified and evolved into modeling and virtual screening (VS) of very large datasets containing thousands of different chemical structures using various machine learning techniques (Cherkasov *et al.,* 2014; Mitchell, 2014; Ekins *et al.,* 2015; Goh *et al.,* 2017). QSAR-based virtual screening vs. High-throughput screening High-throughput screening uses automated plate-based experimental assays to rapidly identify a large subset of molecules with desired activity from large screening collections of compounds (105-106 compounds). Identifiable (Mueller *et al.,* 2012). However, the hit rate of HTS is between 0.01% and 0.1%, which a common is finding that most of the compounds screened are routinely reported to be inactive for the desired biological activity. (Thorne *et al.,* 2010). As a result, drug discovery costs increase with the number of compounds tested (Butkiewiczet al. 2013). On the other hand, typical hit rates for validated VS methods (including QSAR-based) are usually between 1% and 40%. Therefore, the VS campaign was found to have a higher proportion of biologically active compounds and a lower cost than HTS. From this point of view, the hit rate of his HTS campaign was estimated using QSAR-based VS. Show that you can improve. For example, Mueller *et al.* (2010) used both HTS and QSAR models to search for novel positive allosteric modulators of mGlu5, a G protein-coupled receptor implicated in diseases such as schizophrenia and Parkinson's disease. A QSAR model (a combination of physicochemical descriptors and neural networks) was then applied to screen a database of approximately 450,000 compounds. Finally, 824 compounds were purchased for biological testing and 232 compounds were confirmed to be active (28.2% hit rate) (Mueller *et al.,* 2010). In another study, Rodriguez et al. (2010) screened approximately 160,000 compounds to identify 624 antagonists of mGlu5. In addition, using this data he developed a QSAR model and applied it to screen approximately 700,000 compounds from the

ChemDiv database. Among them, 88 acquired connections were active with a hit rate of 3.6%, while HTS had a hit rate of 0.2% (Müller *et al.,* 2012). Tuberculosis Mycobacterium tuberculosis, the causative agent of tuberculosis (TB), kills about 1.6 million people each year (WHO, 2018e). Current treatment for this disease lasts approximately 9 months, which typically leads to non-compliance and the emergence of multidrug-resistant strains (AlMatar *et al.,* 2017). Aiming at the design of new anti-tuberculosis drugs, our group used his QSAR model to design a new series of chalcone derivatives (1, 3-diaryl-2-propen-1-ones). First, we identified all chalcone compounds with in vitro inhibition data against M from the literature. Tuberculosis H37Rv strain. After rigorous data management, these chalcones were subjected to structure-activity relationship (SAR) analysis. Based on the SAR rule, we used bioisosteric surrogates to design new chalcone derivatives with optimized anti-tuberculosis activity. In parallel, a binary QSAR model was generated using multiple machine learning techniques and molecular fingerprinting. A 5-fold external cross-validation procedure confirmed the high predictive power of the developed model. Using these models, we prioritized a number of chalcone derivatives for synthesis and biological evaluation (Gomes *et al.,* 2017). As a result, we found that five 5-nitro-substituted heteroaryl chalcone exhibited MICs at nanomolar concentrations against replicating mycobacteria and activity in the low micromolar range against non-replicating bacteria. Furthermore, four of these compounds were more effective than the standard drug isoniazid. This series also showed low cytotoxicity against commensal bacteria and mammalian cells. These results suggest that the engineered heteroaryl chalcone identified using the QSAR model is a promising anti-TB lead candidate (Gomes *et al.,* 2017). Viral Infections Every year, influenza epidemics can severely affect all populations worldwide. These annual epidemics are estimated to result in approximately 5 million cases and 650,000 deaths (WHO, 2018b). Because influenza viruses are constantly mutating and new resistant strains are emerging, the development of new anti-influenza drugs that are effective against these new strains is critical to prevent pandemics (Laborda *et al.,* 2016). With the goal of discovering new anti-influenza a drugs, Lian *et al.* (2015) used SVM and Naive Bayes methods to build a binary QSAR model to predict neuraminidase inhibition, a validated protein target for influenza. Then, applying his four different combinations of machine learning methods and molecular descriptors, from an internal database he screened 15,600 compounds, from which he screened 60 compounds for experimental evaluation of neuraminidase activity. Selected. Nine inhibitors were identified, five of which were oseltamivir derivatives that exhibited potent neuraminidase inhibition at nanomolar concentrations. His other four agents belonged to new scaffolds that showed potent inhibition at low micromolar concentrations (Lian *et al.,* 2015) According to WHO, approximately 35 million people are living with HIV (WHO, 2018a). Treatment of HIV infection requires lifelong antiretroviral therapy that targets different stages of the HIV replication cycle. As a result, the emergence of resistance and lack of tolerance has increased demand for the development of new anti-HIV drugs (Cihlar and Fordyce, 2016; Garbelli *et al.,*

2017). Aiming to discover new anti-HIV-1 drugs, Kurczyk et al. (2015) developed a two-step VS approach to prioritize compounds targeting HIV integrase, a key target of the viral replication cycle. The first step was based on a binary QSAR model and the second step was based on privileged fragments. Subsequently, 1.5 million commercial compounds were screened and 13 compounds were selected and tested in vitro for inhibition of HIV-1 replication. Among them, two new chemo types with moderate anti-HIV-1 potency were identified, thus providing a new starting point for future structural optimization studies. Conclusion In summary, we would like to emphasize that QSAR modeling is a time-, effort- and cost-effective tool for discovering hits and leading candidates early in the drug discovery process. An analysis of examples of QSAR-based VS available in the literature shows that many of them have led to the identification of promising lead candidates. However, in addition to success stories, many QSAR projects fail during the model building stage. This is due to a lack of understanding that QSAR is highly interdisciplinary and application-specific, and a general ignorance of best practices in the field (Tropsha, 2010; Ban *et al.*, 2017). Earlier, I explained this by having an undesirably high number of "button pushers". H. Researchers who model without understanding and analyzing the data and the modeling process itself (Muratov *et al.*, 2012). This was also explained by the elusive ease of obtaining computational models and the ease of even performing advanced computations without understanding the spirit and limitations of the approach (Bajorath, 2012). Moreover, even many experienced researchers aim for a "vicious cycle of statistics" where the main goal is to validate the model on as many metrics as possible. In this case, QSAR modeling boils down to one simple question. While we recognize that the right choice of statistical approach and particularly rigorous external validation is a critical step in computational drug discovery research, QSAR modeling is used to solve formulated problems. I would like to emphasize that it is only useful if it leads to the development of new compounds with desirable properties. As for future directions, I would like to point out that the age of big data has just begun, and we are still in the stage of collecting chemical and biological data. Therefore, to avoid situations where the number of tested compounds available in the literature exceeds modeling capacity, there is an urgent need for the development and implementation of new machine learning algorithms and data curation methods capable of handling millions of compounds. . Finally, the overall success of his QSAR-based VS project will depend on the ability of scientists to think critically and prioritize the most promising hits according to experience. Furthermore, the success rate of collaborative drug discovery projects is one in which the final selection of computational hits is made by both modelers and experts in a particular field, compared to projects driven solely by computational or experimental scientists. Much higher than the success rate.

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Chapter 16

# TRANSPLASTOMIC PLANTS: DEVELOPMENT, INNOVATION AND APPLICATION FOR WAY TOWARDS ECO FRIENDLY AGRICULTURE

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**ABSTRACT**

The green Revolution and improvement of advanced plant breeding tools have led to increase in agricultural production. But, thousands of humans are nonetheless undernourished; total arable land is even lower due to weather trade, urbanization, and pollution. All these issues necessitate a 2nd green revolution, wherein biotechnological engineering of economically and nutritionally critical traits should be significantly taken into consideration. To address global agricultural problems, genetic amendment of crop vegetation is a rapid and promising technique to adapt the surroundings-pleasant and well controlled farming machine. Because the early 1990s, feasible applications of plastid transformation in higher flowers have been continuously developed. The transplastomic plant with excessive accumulation of overseas proteins (as much as 45–46% TSP) and stable transgene expression with gene containment can be a unique choice for the rural innovation of coming centuries. Even though the transplastomic flowers still facing issues, the removal of hardness and obstacles of this era and commercialization can make contributions for the sustainable improvement of future agriculture. In this book chapter, we intend to success of transplastomic plant which include gene switch processes in plastid genomes, regulation of expression of plastid transgene and normal beneficial factors. We trust that the utilization of transplastomic plants will ensure an ecofriendly approach in agriculture with minimized dangers and public concerns.

**KEYWORDS:** Plastids transformation, Biotic & Abiotic stress, Biofortification, Green revolution, Crop quality, Eco friendly environment.

## INTRODUCTION

Climate change creates additional challenge to food security (1). Regional decrease in available soils and their quality represents global concern. Exploitation, improper land use, use of pesticides, in agriculture order to achieve high crop yields often bring about pollution and nutrient imbalance within the soil (2). These perturbances cause nutrient deficiency in fit to be eaten plant parts (3). Therefore, it's far commonplace that an international integration of

progressed crop cultivars with revolutionary and sustainable agricultural methods, i.e., a 2nd inexperienced Revolution. As a way to adapt farming systems that make sure crop productiveness and food protection of vital vegetation and elevating their yields may be carried out in an environment friendly by using simultaneously holding herbal habitats and assets. Similarly to hunger and insufficient macronutrient (protein, carbohydrate, lipid, oil, and fiber) deficiency, frequently termed as hidden starvation, ends in compromised fitness and financial losses. Conventional plant breeding is frequently considered as an enormously time-ingesting and lengthy technique, while genetic amendment of flora is known as a fast and promising solution for several global troubles. Because the commercialization of the primary genetically modified (GM) plants in 1994, agricultural biotechnology has introduced numerous GM plant lives with improved agronomic developments, consisting of meals functionality, resistance to biotic and Abiotic stress factors, decreased allergenicity (5)

On this chapter, we talk over with GM plants obtained through nuclear or plastid transformation as transgenic or transplastomic plants, respectively. This discusses information related to genetic modification of the plastid genome of higher flowers with emphasis on plants.

**BACKGROUND**

Plastids are semi-self-reliant, endosymbiotic organelles of prokaryotic foundation. They include circular dsDNA; have retained their own nucleic acid and protein synthesis equipment. The plastid genome also termed plastom or ptDNA is noticeably polyploid. This effects in 500 to 10,000 plastome copies in a mesophyll mobile (5, 6). The best regarded plastid type is the chloroplast that is characterized through its ability to assimilate carbon, nitrogen, and sulfur. Further to carbohydrates, plastids also are worried inside the synthesis of amino acids, lipids and fatty acids, starch, oil, and a few 20 metabolites along with carotenoids, terpenoids, alkaloids, important nutrients or polyphenolic compounds like condensed tannins.

To modify the plastid genome of higher plants, there are 4 major steps to accomplish:

- To deliver foreign DNA through the cell wall, plasma membrane and then the double envelope membrane of the plastid
- To direct the stable insertion of the foreign DNA into the plastid genome via site-specific recombination
- Selective enrichment of transferred DNA within plastids and of transformed plastids in cells to reach the high-copy homoplasmic state
- Regeneration of homoplasmic cells carrying the transgene into fertile transplastomic plants

In order to obtain new and genetically uniform transplastomic crops, the transformed plastid DNA copies have to be maintained, while the plastids carrying non-transformed DNA have to be gradually eliminated on a selective medium.

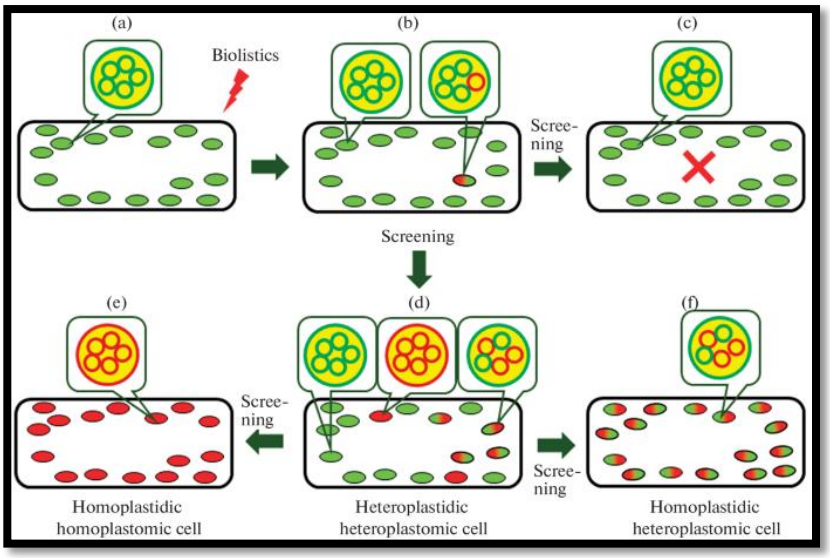


**Fig 1: Reorganization of plastid genome as a result of screening on selective media for attaining homoplastomy and homoplastidity** [7]

## USES OF PLASTID TRANSFORMATION

Plastid engineering is considered as a promising technology for production of recombinant proteins in plants. [8]

## APPLICATION IN AGRICULTURE

Below, it discussed the different potential agricultural applications of transplastomic plants developed so far. For example, transplastomic plants with altered fatty acid un-saturation pattern have increased cold tolerance but could have at the same time an improved nutritional value. So in such cases, resistance engineering and increased crop quality may go hand in hand.

## TRANSPLASTOMIC PLANTS WITH INCREASED INSECT RESISTANCE

The crystal proteins of *Bacillus thuringiensis* (Bt) are considered as safe biological insecticides. However, the potential application of transplastomic plants in this field may contribute to overcoming limitations and problems raised in connection with Cry1Ab in maize and Cry1Ac in cotton Bt proteins [9]. In some nuclear transformants, the insecticidal crystal protein is targeted towards the chloroplast to obtain expression levels of up to 2 % of total soluble proteins [7]. However, in contrast with nuclear transformants, the transplastomic plants are able to synthesize much higher amounts of the Bt protein or also the larger, inactive protoxins (instead of the active mature protein), which further limits the damage to non-target insects. [7, 8]

## TRANSPLASTOMIC PLANTS WITH INCREASED DISEASE/PATHOGEN RESISTANCE

Plastid transformation also represents a potential tool to increase disease resistance to phytopathogenic bacteria and fungi due to high concentrations of the target protein accumulating in a single compartment and released only locally during hypersensitive reaction. To this end, the *msi-99* transgene, which encodes a magainin 2 analog antimicrobial peptide, was first successfully introduced to the plastid genome and was proven to be efficient against different bacteria and fungi [9]

**TRANSPLASTOMIC PLANTS WITH IMPROVED ABIOTIC STRESS TOLARANCE**

Agronomic productivity affects food quantity and quality and is substantially affected by human exploitation. The latter results in unpredictable weather conditions leading to drought, heat, and cold stress in several areas under cultivation. Examples of transplastomic plants with enhanced abiotic stress resistance follow below;

**1. TEMPRETURE (COLD AND HEAT) STRESS**

Increasing fatty acid desaturation results confers tolerance for the membranes towards cold and/or chilling stress. Elevated fatty acid unsaturation levels both in the leaves and the seeds of transplastomic tobacco plants expressing desaturase genes such as Δ9-stearoyl-ACP desaturase from *Solanum commersonii* and Δ9-acyl-lipid desaturase from *Anacystis nidulans*. [11]

2. **DROUGHT AND SALINITY TOLERANCE**

Several osmoprotectants, e.g., the sugar trehalose and betaines, are known to confer resistance towards drought and/or salt stress via ROS detoxification in the cell. Targeting and successfully expressing a yeast trehalose phosphate synthase (*tps1*) in tobacco plastids resulted in a 20-fold increase in trehalose accumulation when compared to non-transformed plants, and conferred drought and osmotic stress tolerance to the transplastomic plants. [12, 13]

**3. ANTHROPOGENIC POLLUTANTS**

Anthropogenic pollutants represent one important segment of abiotic stressors. For instance, several transgenic crops with herbicide resistance encoded in the nucleus are commercialized. Herbicides can also be used as selective agents; therefore, much effort has been devoted to develop transplastomic plants with resistance to different herbicides such as glyphosate, phosphinothricin/ glufosinate ammonium, sulcotrione, isoxaflutole/diketonitrile, chlorophenylthio-triethylamine (CPTA), pyrimidinylcarboxylate, imidazolinone and sulfonylurea, and paraquat (methyl-viologen). **Glyphosate** is a competitive inhibitor of one enzyme of the plastid aromatic amino acid biosynthesis pathway, namely 5-enolpyruvylshikimate-3-phosphate (EPSPS). This enzyme is nuclear-encoded, but plastid targeted. The transplastomic plants overexpressing a mutant EPSPS gene in the chloroplast accumulated 250-fold EPSPS proteins than transgenic plants overexpressing the nuclear gene.[14]

**BIOFORTIFICATION**

Biofortification is the idea to produce and grow edible crops with increased nutritional values. This can be achieved by enhanced agricultural management. These include increased protein levels in potato, increased amino acid (lysine in maize and rice, methionine in alfalfa), choline, folate, flavonoid, anthocyanin, vitamin E, carotenoid, iron, and zinc contents in several crops. **Carotenoids** involved among others in plant photosynthesis [15, 16, and 17]. The link between carotenoid intake and health was first established after the discovery that assimilated β-carotene (also termed provitamin A) serves as precursor of vitamin A, an important molecule for vision, skin protection, and cell growth. [12,17]

**Tryptophan** (Trp) is an essential amino acid in humans. In addition to fatty acid biosynthesis, the synthesis of most essential amino acids is also plastid located. However, nuclear genes encoding mRNAs translated on cytosolic ribosomes and targeted to chloroplasts are responsible for Trp biosynthesis. In addition, Trp synthesis in the plastids is also regulated by the abundance of the mRNA of anthranilate synthase [20, 21]. Therefore, metabolic engineering of Trp biosynthesis by insertion and overexpression of a $\alpha$subunit of anthranilate synthase (ASA2) in tobacco plastids resulted in a 10-fold increase in free Trp in the leaves and slight increase in total Trp in the seeds [22, 23].

## CONCLUSION AND FUTURE PERSPECTIVE

To ensure global food security in the long term, adaptation to extreme climate change is a must. This adaptation includes coping with the changing climate. Genetic engineering of crop plants is one possibility to be considered as solution to these challenges. GM crops have been commercialized and cultivated since 1994. Transgenic plants carrying nuclear modifications that result in herbicide or pesticide tolerance are already predominantly used in several countries and in four major crops i.e. soybean, maize, canola, and cotton. Transgene containment in the plastids represents a significant improvement as compared to the present practice of incorporating transgenes in the nuclear genome, when 100 % of shed pollen carries the transgene and can move to non-transgenic crops or wild relatives. Thus, the use of transplastomic plants could successfully address public concerns related to gene flow. In addition, plastid genetic engineering is a valuable tool to understand plant metabolism, to engineer complex metabolic pathways into the plastids and plastid-derived compounds in an economic and environment-friendly way. It is therefore quite striking that in spite of clear advantages of chloroplast transformation technology, no transplastomic plants have been commercialized almost 25 years after the first report on these plants. Although plastid genetic engineering is promising for plant biotechnology, there is still a long way to go before the technology can reach its full potential. The major problem is that the majority of available protocols for plastid transformation has been performed on tobacco leaf chloroplasts as targets, but is not (yet) directly applicable to other crops.

Much technical progress of plastid transformation (i.e. publicly available vectors, development of highly efficient selection, tissue culture and regeneration protocols for major crops, understanding the biology of non-green plastids, etc.), improved public acceptance, and more field tests with approved and economically viable products are still needed to assess the real impact of transplastomic plants on sustainability of agriculture and on their potential in a second Green Revolution aimed at feeding the world by 2050.

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**Chapter 17**

# BIOLOGICAL APPLICATIONS OF *ALLIUM CEPA L.* EXTRACT

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**ABSTRACT**

One of the most significant vegetables for increasing the flavor and taste of a wide range of cuisines is the onion. In addition, because raw phytochemicals have immediate health advantages when consumed, onions play a significant role when added to salads. The onion stands out as being of tremendous value to the food and pharmaceutical industries due to the significance of phytochemicals in treating a variety of human illnesses. The creation of premium cultivars with high levels of phytochemicals will determine the future of onions in the food business. From the farmer's field to the processing facility, more research is needed at every stage of production. Additionally, appropriate technologies must be created to retain the beneficial phytochemicals for the protection of human health. Onions contain biologically active phytochemicals that provide a wealth of health advantages. Onions show a remarkable difference in the formation of phytochemicals of high biological value according to the kind of variety and the region of cultivation. It is necessary to create an appropriate breeding strategy for the creation of onion types with sufficient levels of phytochemicals. The significance and uses of onion peel in biological studies are discussed in this chapter.

**KEYWORDS:** Onion peel, phytochemical studies, Biological assay.

## INTRODUCTION

Since ancient times, the onion (Allium cepa L.) has been prized as both a food and a healing plant. It is a vegetable bulb crop that is known to most cultures and is consumed globally. Its cultivation is second only to that of the tomato (FAO, 2012). It is a short-lived horticultural crop raised at low latitudes (Brewester, 1990). Due to its highly regarded flavour, scent, and distinctive taste as well as the therapeutic capabilities of its flavour constituent, it is referred to as the "Queen of the Kitchen" (Selvaraj, 1976; Griffiths*et al.*, 2002). Throughout the year, onions are used in a variety of dishes, including curries, as spices, in salads, as a dipping sauce, and when boiled or baked with other vegetables. It is also known for its therapeutic properties and is utilised in a variety of processed foods, such as pickles, powder, paste, and flakes.

**HISTORICAL ASPECTS**

Throughout the world, onions are still used today as they have been since the Neolithic era. Over the course of this long time, there have always been individuals who valued the usage of on utilized and utilised them in significant amounts, but there have also been those who rejected and despised them (Koch and Lawson, 1996). For around 5000 years, onions have been grown all over the world in at least 175 nations. The round bulb was viewed by the ancient Egyptians as a representation of the universe. The name is most likely derived from the Latin unus, which means "one," and the Romans brought the onion to Britain, where it may have travelled to the Americas (Burnie *et al.,* 1999). Onion history is first recorded in writing by the Sumerians between 2600 and 2100 BC. The Papyrus Ebers, which is based on texts and knowledge from ancient Egypt, reveals that leeks played a significant part in the old Egyptian kingdom. Onion was recommended as a diuretic, laxative, and emmenagogue by the famous physician Hippocrates. Additionally, he applied onion externally to mend rotten wounds and treat pneumonia (Koch and Lawson, 1996).

**PRODUCTION STATISTICS**

Onions are a biennial bulb crop that is widely cultivated with a global yield of 74,250,809 tonnes from an area of 4,364,000 hectares. The top two onion-producing nations are China and India, followed by the United States, Egypt, Iran, Turkey, Pakistan, Brazil, the Russian Federation, and the Republic of Korea (FAO, 2012). The Republic of Korea has the highest onion productivity (66.16 t/ha), followed by the USA (56.26 t/ha), Spain (53.31 t/ha), and the Netherlands (51.64 t/ha); the global average is 19.79 t/ha. Economically speaking, 6.77 million tonnes of onions are exported globally. The Netherlands exports the most onions (1.33 million tonnes), followed by India, China, Egypt, Mexico, the United States, Spain, and Argentina. Bangladesh, Malaysia, the United Kingdom, Japan, the Russian Federation

**Fig 1: Onion**

**Fig 2: genus Allium**

**BOTANY**

In the northern hemisphere, the genus Allium is extensively dispersed throughout temperate zones and has a huge number of wild edible species (only a small portion is economically farmed) (Hanelt, 1990; Gautam *et al.,* 1997). It is claimed that central Asia is the origin, with the Mediterranean areas being the secondary origin (CSIR, 2003). More than 780 species of Allium

exist, and their physical characteristics are very varied (Burnie *et al.,* 1999). A typical onion has 16 chromosomes (2n).

It has been classified in hierarchical level as follows:

- Kingdom: Plantae
- Subkingdom: Tracheobionta
- Super division: Spermatophyta
- Division: Liliopodia
- Subclass: Liliales
- Order: Liliaceae
- Genus: *Allium*
- Species: *Allium cepa* L.

**Fig 3: hierarchical level**

The plant is either perennial or biennial depending on the cultivar, and when crushed, onions, which are a member of the Amaryllidaceae family, have a pungent odour (WHO, 1999). According to Ranjitkar (2003), the plant has tubular leaves, a bulb, and shallow adventitious fibrous roots. During the second year of a plant's existence, the stem grows 100–200 cm tall. The plant's outer leaves for storing food are an extension of its green leaves. A ring-shaped apical meristem gives rise to an umbel-shaped inflorescence. The umbel is a group of developing flowers that typically contains 200–600 little individual flowers, although it can contain up to 1000. (Ross, 2001). In the second year of the plant's life, it is made up of tiny white or greenish-white flowers that sprout at the stem's tip. The shape of the onion bulb might be flat, globular, or oblong, and there are often three colours: red, white, and yellow (Fritsch, 2005). The capsule-shaped fruits have black seeds inside. The bulb is made up of larger and fleshy leaf bases. The edible onion bulb, which has numerous overlapping layers on a central core, can get up to 10 cm in diameter. By the time the bulb is harvested, the outer leaf bases are dry and scaly, but the inner leaves get thicker as the bulb grows. Most onion species prefer humid weather and grow best on open, bright, dry ground. On the other hand, the Allium species have been adapted to numerous ecological niches around the globe (Fritsch and Friesen, 2002).

**ROLES IN BIOLOGY**

In addition to flavour, onions contain phytochemicals that are beneficial to health. Natural substances called phytochemicals, which are present in onions, may benefit human health and provide protection against a range of illnesses, including cancer. Organo-sulfur compounds have antibacterial, allergic, inflammatory, and antithrombotic properties (Block *et al.,* 1997). Onions also contain flavonols, such quercetin and kaempferol, which have a variety of important biological functions for maintaining health, including antiviral, antibacterial, anti-

inflammatory, and anticancer action, as well as protection of the heart and brain (Alexander, 2006; Harwood *et al.,* 2007; Utesch *et al.,* 2008; Ansari *et al.,* 2009).

Onions are a very popular and abundant source of dietary flavonoids, and they include flavonoids, fructans, and organosulfur compounds, three different and extremely beneficial phytochemicals, in just the right amounts. It is thought that these substances have advantageous impacts on human health. Strong antioxidants such flavonoids and organosulfur compounds are mostly found in onions.

The (+)-S-alk(en)yl-L-cysteine sulfoxide and -glutamyl peptide found in the entire onion bulb, which together make up more than 70% of the total 4dourle in onions, are good sources of nutrition (Lawson, 1996). Onions contain three major alkyl cysteine sulfoxides that are odourless and non-volatile. These include S-methyl cysteine sulfoxide (methiin), S-trans-prop-1-enyl cysteine sulfoxide (isoalliin), and S-propyl cysteine sulfoxide (propiin). Isoalliin, which comprises almost 80% of the total amount of alk(en)yl cysteine sulfoxides, is the main flavour precursor. While alliin and propiin are only found in very small amounts, methiin is present in higher proportions (Jones *et al.,* 2004).

Alliinase enzymes break down the alk(en)yl-L-cysteine sulfoxides when the tissue is being destroyed. New chemicals are created as a result, including alkyl alkane-thiosulfinates, which affect the alliums' distinctive flavour and aroma. Allicin, dipropyl disulfide, diallyl sulphide, methyl propanyl disulfide, ajoene, propyl-1-propanyl thiosulfinate, and 1-propanethial-S-oxide are some of the other organosulfur compounds that may form from these elements. In addition, -glutamyl cysteine is changed into a variety of organosulfur compounds, such as S-allyl cysteine and S-allyl mercaptocysteine (Block, 1985). Onions contain a variety of organosulfur compounds, primarily four different forms of diallyl sulphides: diallylmonosulfide (DMS), diallyldisulfide (DDS), diallyltrisulfide (DTS), and diallyltetrasulfide (DTTS). Flavonoids, a subset of the polyphenol family, are thought to be abundant in onions. A major and important dietary flavonoid found in onions, quercetin, is a member of the flavonol subclass of flavonoids. Other flavonols, like kaempferol and isorhamnetin, have also been detected in onions in addition to quercetin (Dorsch and Wagner, 1991; Dorant *et al.,* 1994; Goldman *et al.,* 1996; Lanzotti, 2006). In addition to these, onions also contain a number of other sulfoxides, including (+)-S-(1-propenyl)-L-cysteine sulfoxide (PRENCSO), (+)-S-methyl-L-cysteine sulfoxide (MCSO), S-propyl-L-cysteine sulfoxide, S-methyl-L-cysteine sulfoxide, and S-propeny (Mateljan, 2015). Alliin (S-allyl-L-cysteine S-oxide), diallyldisulfide (allyldisulfide), S-methyl-L-cysteine S-oxide (3-methyl sulfinyl alanine), propanethial S-oxide (thiopropanal S-oxide), and 3-mercapto-2-methypentan-1-ol are the additional phytochemicals known to be present in onion extract (Rose *et al.,* 2003). The onion bulb has the greatest ascorbic acid, which has a concentration of 1 mg/g dry weight (Breu, 1996). Steroid saponins found in onions (Carotenuto *et al.,* 1999) limit cholesterol absorption in the intestine. In onions, the main storage carbohydrates are fructans (polysaccharides). In a study of 60 vegetables, onions were shown to contain the most fructans, which may help to reduce the number of germs (Roberford, 2007). Fructooligosaccharides are

the primary component of fructans. Utilizing cutting-edge methods like HPAEC-PAD (high performance anion exchange chromatography with pulsed amperometric detection) and MALDI-MS (matrix-assisted laser desorption/ionization mass spectroscopy) for the separation and identification of fructooligosaccharides, it was discovered that cells' vacuoles contain fructooligosaccharides (Stahl *et al.,* 1997). Numerous fructofuranosyl sucrose subunits, together known as 1- kestose (3a), neokestose (3b), nystose (4a), and so forth, make up the fructooligosaccharides class (Shiomi *et al.,* 2005). Flavonols and anthocyanins, two different forms of flavonoids, are found in onions. Quercetin, kaempferol, and isorhamnetin are the three main flavonols (Slimestad *et al.,* 2007). Onion secondary metabolites called phenolics have antioxidant properties and are made up of hydroxylated aromatic rings (Nuutila *et al.,* 2003)

**HEALTH BENEFITS OF ONION**

Even though all vegetables are vital for good health, several varieties have particular advantages. The flowering plant genus Allium, which also includes garlic, shallots, leeks, and chives, includes onions. These veggies contain a variety of vitamins, minerals, and strong plant chemicals that have been demonstrated to support health in a number of different ways. In fact, onions' therapeutic benefits have been known since the dawn of humanity, when they were utilised to treat conditions including migraines, heart disease, and mouth sores.

Onions are nutrient-dense foods, which mean they have few calories but a lot of vitamins and minerals. Despite providing a significant amount of vitamins, minerals, and fibre, one medium onion only has 44 calories. Vitamin C, a component essential for maintaining immunological function and collagen formation, is particularly abundant in this crop. Eating vegetables of the *Allium* genus like garlic and onions has been linked to a lower risk of certain cancers, including stomach and colorectal. A review of 26 studies showed that people who consumed the highest amount of allium vegetables were 22% less likely to be diagnosed with stomach cancer than those who consumed the least amount. Moreover, a review of 16 studies in 13,333 people demonstrated that participants with the highest onion intake had a 15% reduced risk of colorectal cancer compared to those with the lowest intake. These cancer-fighting properties have been linked to the sulfur compounds and flavonoid antioxidants found in allium vegetables. For example, onions provide onionin A, a sulfur-containing compound that has been shown to decrease tumour development and slow the spread of ovarian and lung cancer in test-tube studies. Onions also contain fisetin and quercetin, flavonoid antioxidants that may inhibit tumour growth.

Those who have diabetes or prediabetes should take particular note of this because eating onions may help regulate blood sugar. After four hours, eating 3.5 ounces (100 grammes) of fresh red onion decreased fasting blood sugar levels by roughly 40 mg/dl, according to a research done on 42 persons with type 2 diabetes. The eating of onions may also help with blood sugar regulation, according to numerous animal studies. According to a study, diabetic rats given diet containing 5% onion extract for 28 days had lower fasting blood sugar and more

significant body fat reduction than the control group. Onion-derived substances with antidiabetic properties include sulphur compounds and quercetin. The small intestine, pancreas, skeletal muscle, and fat cells, for instance, have been demonstrated to interact with quercetin. Onions are a rich source of fiber and prebiotics, which are necessary for optimal gut health. Prebiotics are nondigestible types of fiber that are broken down by beneficial gut bacteria. But bacteria feed on prebiotics and create short-chain fatty acids — including acetate, propionate and butyrate. Research has shown that these short-chain fatty acids strengthen gut health, boost immunity, reduce inflammation and enhance digestion. Additionally, consuming foods rich in prebiotics helps increase probiotics, such as *Lactobacillus and bifidobacteria* strains, which benefit digestive health. A diet rich in prebiotics may help improve the absorption of important minerals like calcium, which may improve bone health. Onions are particularly rich in the prebiotics inulin and fructooligosaccharides. These help increase the number of friendly bacteria in your gut and improve immune function.

A thin, lightweight, durable, and frequently translucent paper known as "onionskin" or "onion skin." It looks like the thin, papery skin of an onion, but it isn't formed from onions. For permanent records when little bulk was necessary or for airmail correspondence, it was typically used with carbon paper for typing duplicates in a typewriter. It normally ranges from 25 to 39 g/m2 (9 pounds of basis weight in US standards) and comes in white or canary hues. The deeply textured cockle finish of onion skin, which was popular during the age of the typewriter and made it simpler to correct typing errors, was also available at the time, though it's possible that alternative glazed and unglazed finishes are more popular now. The high percentage of cotton fibres in onionskin paper makes it both relatively strong and light. Given these characteristics,

Due to its advantages for human health, onions have gained popularity recently. In addition to well-known antioxidant activity, anticancer characteristics were found to lessen the carcinogenic activity of a number of mutagens in cooked meals and to inhibit the enzymatic activities linked to a variety of tumour cell types. The practical way to extract such bioactive chemicals from various plant sources is therefore becoming more and more in demand. We urgently need techniques to separate such chemicals from the parent materials in order to use such valuable bioactive compounds in plants. Because of this, cutting-edge methods including DPPH radical scavenging, total phenol content, and total flavonoid assays are continued.

The onion is one of the most common and plentiful naturally occurring sources of flavonoids. The flavonoids in onions, specifically quercetin and its five hydroxyl groups are present in quercetin (Figure 1.1), and these groups control both the compound's biological function and the number of potential derivatives. Glycosides and ethers are the two main classes of quercetin derivatives that are present in onions. Only trace levels of sulphate and prenyl substituents are present (Harborne, 1994; Williams and Grayer, 2004).

**Fig 4: Onion Skin Paper**

**PREPARATION OF ONION PEEL EXTRACT**

Red onion skins were gathered from a neighbouring motel. The peels were scrubbed, dried at 40 degrees Celsius, and then cut into extremely tiny pieces. To create onion peel extract, dried onion peels weighed around 20g were combined with 200ml of distilled water in a beaker. The mixture was then heated for 15 minutes while being constantly stirred. After cooling the extract to room temperature, Whattman No. 1 filter paper is used to filter the mixture. As a result, more research using the produced onion peel extract was done.

**TOTAL PHENOL CONTENT**

The Folin-Coicalteu test method was used to determine the total phenol content. One millilitre of the extract was combined with two millilitres of the 20% Na2CO3 solution and 0.5 millilitres of the 10% folin-Ciocalteu reagent before being stirred together and incubated at 450°C for 15 minutes. The OD value was determined upon incubation using a spectrophotometer at 765nm (LABTRONICS LT-291). Calculating the mg/g of the phenol content required the use of gallic acid as a reference.

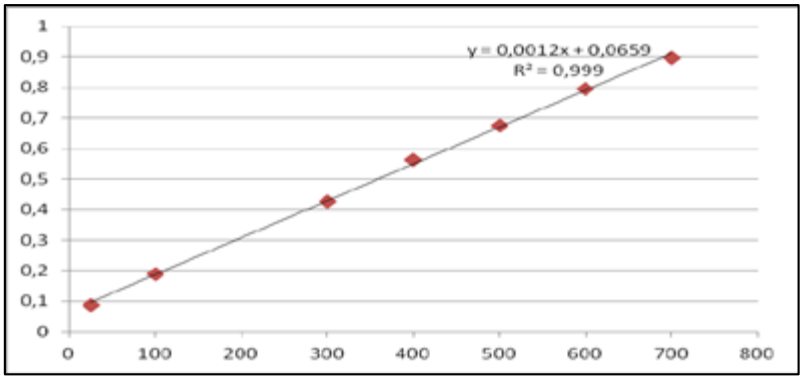
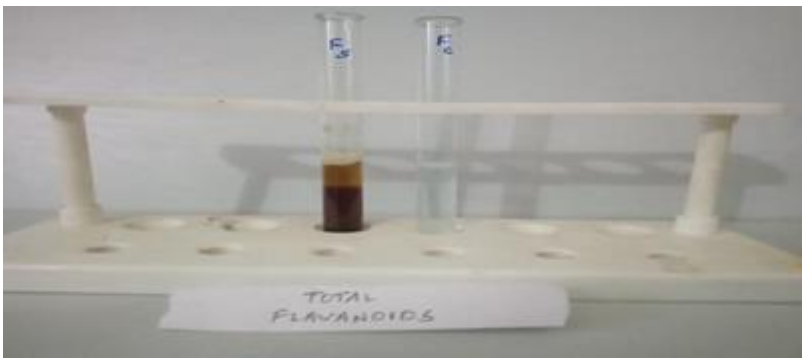




**Fig 6: UV spectrum of Total phenol content**

**FLAVONOIDS CONTENT**

Spectrophotometric analysis utilizing the aluminium chloride test technique was used to calculate the total flavonoids content. One milliliter of the extract was dissolved in 0.1 milliliters of 10% aluminium chloride solution, 0.1 milliliters of sodium potassium tartrate, and 2.8 milliliters of purified water. After reagent addition, the tubes were incubated at room temperature for 30 minutes, and a measurement in the 415nm range was made using a spectrophotometer (LABTRONICS LT-291).Blank was maintained without adding the sample andstandard quercetin was used to calculate the mg/g of the flavonoids content.



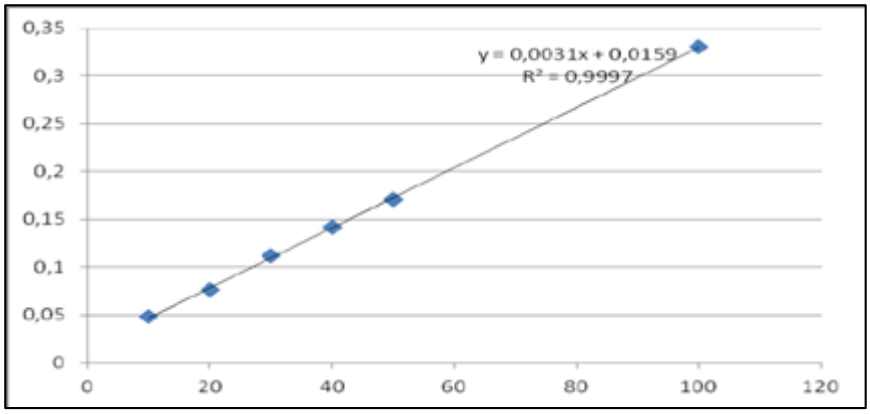




**Fig 7: UV Spectrum of Total Flavanoid content**

**1, 1-diphenyl-2-picryl-hydrazyl (DPPH) ACTIVITY**

DPPH (2, 2-diphenyl-l-picryl hydrazyl) Radical Scavenging Assay The antioxidant activity of the sample was estimated using the DPPH radical scavenging protocol. DPPH solution (0.004% w/v) was prepared in 95% ethanol.

0.1 ml of freshly prepared DPPH solution (0.004% w/v) was added in the test tubes containing different concentration of the sample from 250 µl, 500µl, and 0.4 ml of 50mM tris HCl solution. The reaction mixture was incubated in the dark for 30 min and thereafter the optical density was recorded at517 nm against the blank. For the control, 2 ml of DPPH solution in ethanol and the optical density of the solution were recorded after 30 min. The decrease in optical density of DPPH on addition of test samples in relation to the control was usedto calculate the antioxidant activity. Standard ascorbic acid was prepared in the concentration of 10mg/1ml and mg/g of DPPH was calculated.

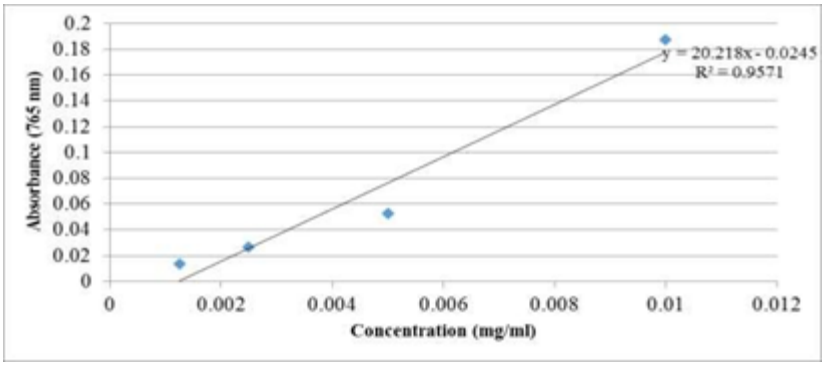




**Fig 8: UV Spectrum of DPPH**

The food industry produces a large amount of onion waste and there is need to search for possible ways of their utilization. This research has found that onion peel has high content of carbohydrate, flavonoid and phenol. It further revealed that onion peel ethanoic extract could delay oxidation in cooked beef as well as the inhibited growth of some pathogenic bacteria. It may be suggested that after proper cleaning, onion peel may be included in food processing instead of discarding it. Also, further studies should be done to investigate the capability of onion peel toserve as a functional ingredient in food formulations.

From the above conducted tests, we can conclude the amount of DPPH, Total phenol and Flavonoids present in the onion peel. The values are given in table 1

**Table 1: Values of total phenol and Flavonoids present in the onion peel**.

| Test | Standard | Value |
|---|---|---|
| Total Phenol | Gallic acid ($C_7H_6O_5$) | 134mg/ml |
| Flavonoid content | Quercetin ($C_{15}H_{10}O_7$) | 540µg/ml |
| DPPH Radical Scavenging | Ascorbic acid ($C_6H_8O_6$) | 46mg/g<br>35mg/g |

## CONCLUSION

Both biotic and abiotic stressors, which inhibit the endogenous production of phytochemicals, must be carefully researched, as well as the effects of preharvest procedures used on the farm. The need of the hour is for the creation of processable onion varieties, as well as standardized

processing techniques and engineering technologies. By maintaining the phytochemicals in a stable state, will promote the development of processed products based on onions. By creating a quality-based system for processing raw onions, the phytochemicals in onions must be retained. The effects of postharvest processing techniques on the phytochemicals present in onions are little understood from a scientific perspective. Additionally, more study is required to fully understand the effect of preharvest procedures on phytochemical development, which has not been fully investigated to date.

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**Chapter**
**18**

# PHYTOCHEMISTRY OF FRUIT PEEL WASTE

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**ABSTRACT**

All the meals reassess include safe to eat and non-safe to eat waste portions. With growing call for meals and feed, the contemporary agriculture is that specialize in agro-processing to make use of the most part of the plant or animal resources. The gift reputation of usage of jackfruit (*Artocarpus heterophyllus Lam*, Moraceae) wastes in meals, feed, and different industry. Artocarpus heterophyllus Lam and Artocarpus integer, commonly known as jackfruit trees, are members of the Morus Alba family and are exotic trees native to the Western Ghats of India. Jackfruit is usually grown in the vegetable gardens of tropical and subtropical countries. Fruits are an important source of carbohydrates, fiber, minerals and vitamins. Bark, roots, leaves and fruits are mainly used in foods, food additives, and medicinal ingredients and in the textile industry. Jackfruit is considered an underutilized fruit, where most fruits are wasted due to ignorance, lack of post-harvest technology, and gaps in the supply chain system. The big gap in marketing Jackfruit and its waste can be processed into value-added products that can be filled for both additional revenue and food security.

**KEYWORDS:** Jack fruit peel, phytochemical composition, extraction application, jack fruit peel waste utilization.

## INTRODUCTION

The various agro-climatic zones of Bangladesh are amenable to develop an extensive kind of culmination like mango, jackfruit and pineapple. Among them, jackfruit (*Artocarpus heterophyllus Lam*.) belonging to the own circle of relatives Moraceae is one of the maximum famous and evergreen timber in tropical regions like Bangladesh. The climatic situation of this us of a may be very appropriate for jackfruit cultivation. It is a main supply of bioactive compounds like diet C and beta-carotene that act as antioxidants to guard the frame in opposition to loose radicals and strengthens the immune system. It is likewise wealthy in numerous phytonutrients including lignans, Flavanoid, and saponins (Swami *et al*., 2012). There are plentiful manufacturing of meals wastes at some stage in processing the uncooked agricultural merchandise to completed merchandise. Some of these wastes turn out to be as

animal feed and a few are lower back to the land as a nutrient. Different industries associated with the rural region generate a number of wastes within side the shape of peels, seeds, waste liquid, molasses, biogases, and so on. The generated waste isn't always best biodegradable but additionally wealthy in nutrient additives including carbohydrate, protein, and nutrients relying upon the sources. Recycling is one of the maximum essential approaches of usage of the rural waste additives to quite a number of latest merchandise including natural fertilizer and as an uncooked fabric within side the paper industry. Recovery of the useful bioactive compounds from end result and vegetable wastes is a more recent studies trend. The extracted valuables from those wastes are obviously contributing to satisfy the dietary necessities for human, animal, and plant in addition to within side the pharmaceutical industry (Sogi *et al.,* 2002). The expanded meals call for via way of means of the hastily developing populace of the sector has posed an excellent assignment to the incumbent sectors including meals researchers and producers to maximize the usage of the present meals or plant resources. About, 70 to 80% of a jackfruit includes waste and via way of means of-merchandise. The outer rind or peel, valuable core, and perianth make up approximately fifty five to 60% of this fruit. Seed is an essential spinoff that is composed round 12-14% of an entire jackfruit.

**JACKFRUIT PEEL**

Jack fruit peel, also called rind or skin, is the outer shielding layer of the fruit which is composed of 57.17, 46.45, and 40.05% in Khaja, Gala, and Durasha ranges respectively (Anonymous, 1996). The unsystematic disposal of peel imposes an extreme burden on the environment. However, the right usage of the by-merchandise now no longer simplest will increase the financial cost however additionally reduces the fee of disposal. Jack fruit peel is reportedly wealthy in cellulose, pectin, protein, and starch comprising approximately 27.75%, 7.52%, 6.27%, and 4%, respectively.

Jackfruit wastes, which include perianths of unfertilized fruits, have been generally process to make syrups and jellies due to its good basis of pectin and cellulose. Rinds along with other waste parts of the fruits are utilize as a beneficial feed for livestock (Feili 2014). To optimize the digestibility has to be provided. Thus, molasses-urea cake is fed along with the jackfruit waste for cattle for a better digestibility (Haq, 2006). Nevertheless, it only composes about 16% of the total fruit width. The fruit matures, the latex amount in the core increase, however, it is compact as the fruit ripens (Moncur, 1985).

The results of activation temperature and impregnation ratio at the pore shape and floor chemistry of activated carbon derived from *Metacarpus heterophyllous* wastes with chemical activation strategies the usage of phosphoric acid as an activator to be pronounced through Ismadji *et al.* (2008b). Selvaraju and Bakar (2017) have studied the manufacture of a brand new industrially possible inexperienced-activated carbon from Artocarpus integer fruit processing wastes and the estimation of its physicochemical properties. Jackfruit waste is plentiful in Indonesia, making it doubtlessly one of the inexperienced refinery feedstock for the

manufacturing of biofuel. As an intermediate of bio fuel, jackfruit peel is processed into bio-oil (Ismadji *et al.,* 2014) Pectin changed into extracted and characterized from Jackfruit (*Artocarpus heterophyllus*) waste the usage of extraordinary extraction situations like ammonium oxalate, dilute sulphuric acid and sodium hexameta phosphate to evaluate its feasible rather useful resource of monetary pectin was pronounced through Begum *et al.* (2014).

Among the various solvents, extraction with sodium hexameta phosphate gave the very best yield, however, it consists of excessive ash and the lowest solubility. Noranizan *et al.* (2014) have studied the Microwave-assisted isolation of pectin from Jackfruit wastes the usage of extraordinary strength stages have been 450, six hundred, and 800 W. water-primarily based extraction approach changed into completed with the extraction duration for traditional isolation. The maximum yield of pectin is received from traditional isolation (14.59%) and microwave isolation (17.63%). Microwave isolation calls for a shorter time than traditional isolation in setting apart the great of pectin from jackfruit wastes. Lokhande *et al.* (2016) have investigated the extraction of pectin from numerous peels of *Mangifera indica* and *Artocarpus heterophyllus* unearths primary marketable use as a gelling agent and stabilizer in numerous meals factories. Moorthy *et al.* (2017) have studied the four elements of three stage face-targeted Central composite Design to optimize the numerous impact of procedure variables together with, liquid-strong ratio (10:1-2:1 ml/g), pH (1-2), sonication time (15 - 30 minutes) and isolation temperature (50 - 70 °C) at the most isolation yield of pectin from *Artocarpus heterophyllus* peel the usage of ultrasound-assisted isolation strategies. Rahman *et al.* (2014) have investigated the isolation of cellulose from numerous agro-wastes, together with the outer pores and skin of jackfruit (*Artocarpus heterophyllus* Lam.), non-fit to be eaten a part of jackfruit, the internal stick of jackfruit, skins of lychee (Litchi chinensis Sonn.) and skins of lotion (Baccaure aramiflora Lour.) Cellulose acetate and carboxymethyl cellulose (CMC) was organized from the ones removed cellulosic materials. The organized cellulose derivatives are characterized through FTIR spectrum analysis, and titrimetric approach analysis, drastically which may be used for numerous business and business purposes.

**PREPARATION OF PLANT EXTRACT**

The Jack fruit peel was dried it in shadow places. The dried plant materials were powdered and stored for further studies. Two grams of each fruit peel material were soaked in 10 ml of Acetone, Benzene, Ethanol, Petroleum ether and Aqueous with intermitted shaking. The fruit peel extract were filtered through Whattman No.1 filter paper. The filtrate was collected and stored at $4^0$C for further use.

**PRELIMINARY PHYTOCHEMICAL SCREENING**

Solvents Acetone, Benzene, Ethanol, Petroleum ether and Aqueous used to extract the phytochemical. The extracts were then subjected to various tests to identify the secondary

metabolites present in them. The preliminary chemical composition of fruit peel were Analysed following the method described by (World Health Organization, 1998)

## MATERIALS AND METHODS

### TEST FOR ALKALOIDS

To a few ml of plant sample extract, two drops of Mayer's reagent are added along the sides of test tube. Appearance of white creamy precipitate indicates the presence of alkaloids.

### TEST FOR AMINO ACIDS

The extract (100 mg) is dissolved in 10 ml of distilled water and filtered through Whattman No. 1 filter paper and the filtrate is subjected to test for Amino acids.

Two drops of ninhydrin solution (10 mg of ninhydrin in 200 ml of acetone) are added to 2 ml of aqueous filtrate. Appearance of purple colour indicates the presence of amino acids.

### TEST FOR CARBOHYDRATES

To 2ml of plant extracts, 1ml of Molisch's reagent and few drops of concentrated sulphuric Acid were added. Purple colour formation indicated the presence of carbohydrates.

### TEST FOR CARDIAC GLYCOSIDES

To 0.5 ml of extract, 2ml of glacial acid and few drops of 5% ferric chloride were added. This was under layered with 1ml of concentrated sulphuric acid. Brown ring formation at the interface indicated the presence of cardiac glycosides

### TESTS FOR FLAVONOIDS

*Shinoda Test*. Pieces of magnesium ribbon and HCL concentrated were mixed with aqueous crude fruit peel extract after few minutes and pink colour showed the presence of Flavanoid.

### TEST FOR REDUCING SUGAR

Few drops of Molisch's reagent were added with dilute extracts and heated for 30 minutes and observed for the formation of brick red colour precipitate.

### TEST FOR SAPONINS

5.0 ml of distilled water was mixed with aqueous crude plant extract in a test tube and it was mixed vigorously. The frothing was mixed with few drops of olive oil and mixed vigorously and the foam appearance showed the presence of Saponins.

### TEST FOR STEROIDS

2 ml of chloroform and concentrated $H_2SO_4$ were added with the 5 ml aqueous plant crude extract. In the lower chloroform layer red colour appeared that indicated the presence of steroids.

### TEST FOR TANNINS

10 ml of bromine water was added to the 0.5 g aqueous extract. Discolouration of bromine water showed the presence of tannins

**TEST FOR TERPENOIDS**

2.0 ml of chloroform was added with the 5 ml aqueous fruit peel extract and evaporated on the water path and then boiled with 3 ml of $H_2SO_4$ concentrated. A grey color formed which showed the entity of terpenoids.

**RESULTS AND DISCUSSION**

**Table 1: Phytochemistry of jack fruit peel**

| Sr. No. | Secondary Metabolites | Acetone | Benzene | Ethanol | Petroleum ether | Aqueous |
|---|---|---|---|---|---|---|
| 1 | Alkaloids | + | - | + | + | - |
| 2 | Amino acids | + | - | - | + | - |
| 3 | Carbohydrate | + | - | + | + | - |
| 4 | Cardiac glycosides | + | + | - | + | - |
| 5 | Flavanoid | + | + | + | - | + |
| 6 | Reducing Sugar | - | - | - | - | - |
| 7 | Saponins | - | - | - | - | - |
| 8 | Steroids | + | + | + | + | + |
| 9 | Tannins | + | - | - | - | - |
| 10 | Terpenoids | - | - | - | + | - |

**PHYTOCHEMICAL OF JACK FRUIT PEEL EXTRACT**

The results of qualitative screening of phytochemical components in Acetone, Benzene, Ethanol, petroleum Ether and Aqueous extract of Jack fruit peel revealed the presence of Alkaloids, Carbohydrates, Steroids, Reducing sugar, Tannins, Saponins, Flavanoid, Terpenoids, Cardiac Glycosides, and Amino acids (Table 1).

The Acetone extracts of jackfruit peel contains all the testes phytochemical like Alkaloids, amino acids, Tannins, Flavanoid, Cardiac Glycosides and Carbohydrates. The benzene extract contains Steroids, Flavanoid, and Glycosides. The Ethanol extract contains alkaloids, steroids, Flavanoid and Carbohydrate. The petroleum Ether extract contains Alkaloids, amino acids, Steroids, Terpenoids, Cardiac Glycosides, and Carbohydrates. The Aqueous extract contains only for Flavanoid and steroid.

The powdered pectin changed into study for the qualitative and quantitative analyses of methoxyl, anhydrouronic acid contents, and diploma of esterification. The mango and jackfruit peels were observed to be an awesome supply of pectin, with a yield of 10.33% for mango and 7.33% for jackfruit wastes. But the result of mostly present the steroids in secondary metabolites. There the jack fruit completely absent in Amino acids, Tannins and Terpenoids. The most common technique used to obtain the extracts with the antioxidant activity is the

extraction using organic solvent. The extraction of the jack fruit peel with acetone and petroleum ether was efficient in extracting the phytochemical compounds petroleum ether is effective than other solvents for extracting jack fruit peel extract. This study was focused on waste minimization in aqua fed processing.

## CONCLUSION

The present study of within side the world, nowadays is to make use of and convert waste into beneficial merchandise and to recycle waste merchandise as approach of accomplishing sustainable improvement. The presence of numerous phyto-constituents makes the peel beneficial for treating special illnesses and has the ability of supplying beneficial tablets for human use. In conclusion, the end result of this *Artocarpus heterophyllus* Lam and *Artocarpus integer*, typically called jackfruit timber, are individuals of the Morus alba own circle of relatives and are distinguished timber local to the Western Ghats of India. Jackfruit is normally grown within side the vegetable gardens of tropical and subtropical countries. Fruits are a crucial supply of carbohydrates, fiber, minerals, and vitamins. Bark, roots, leaves, and culmination are especially utilized in foods, meals additives, medicinal ingredients, and within side the fabric industry. Jackfruit is taken into consideration an underutilized fruit, in which maximum culmination is wasted because of ignorance, loss of post-harvest technology, and gaps within side they deliver chain system. The huge hole in advertising and marketing Jackfruit and its waste may be processed into value-delivered merchandise that may be stuffed for each extra sales and meals security. Numerous carbohydrates like pectin, protein, starch, cellulose, and its derivatives for numerous business applications.

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# RECENT TRENDS OF INNOVATIONS IN CHEMICAL AND BIOLOGICAL SCIENCES

## VOLUME I

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