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ORIGINAL ARTICLE

Development of an *Aloe vera*-based Emulgel for the Topical Delivery of Desoximetasone

Dezoksimetazonun Topikal Uygulaması İçin *Aloe vera* Bazlı Bir Emüljelin Geliştirilmesi

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ABSTRACT

Objectives: Desoximetasone (DMS) is a widely recommended drug for the topical treatment of plaque psoriasis. However, low water solubility and short half life of DMS present major obstacles in the development of an effective topical formulation. Thus, there is a demand for the development of a safe and effective topical system to deliver hydrophobic DMS. The present study aimed to develop an *Aloe vera*-based emulgel formulation to ensure enhanced skin deposition of DMS for effective treatment of plaque psoriasis.

Materials and Methods: Different formulations (DE1-DE4) of *Aloe vera* emulgel were prepared using dispersion technique, wherein varying concentrations of propylene glycol (6-14% w/w) and carbopol 934 (0.5-1.0% w/w) were used.

Results: Zetasizer measurements revealed that the globule size of the formulations ranged from 10.34 µm±0.9 to 14.60 µm±1.4 (n=50). Extrudability analysis for the DE3 and DE2 formulations revealed an extrudability of 5.6±0.11 g/cm^2 and 5.8±0.13 g/cm^2, respectively. The pH of the formulations was recorded in the range of 5.8-6.8. Among these formulations, DE3 showed a maximum drug content of 94.64%±0.29 (n=3), and thus was used for further *in vitro* evalutions. A texture analyzer showed that an optimized DE3 formulation was firmer and exhibited optimal spreadability in comparison with the DE2 formulation. For DE3, the mean max force that represented "firmness" was recorded to be 833.37 g, where as the mean area, denoting "work of shear", was 324.230 g.sec. The DE3 formulation exhibited DMS permeation of 95.40±1.6% over a period of 7 h, as detrmined using an in house fabricated Franze diffusion cell. Evaluation of *in vitro* release kinetics revealed that the release of DMS fitted into the Korsmeyer-Peppas model.

Conclusion: Physicochemical characteristics and enhanced *in vitro* permeation of DMS from *Aloe vera* emulgel highlight its suitability to be efficiently employed for the topical treatment of skin ailments.

Key words: *Aloe vera*, desoximetasone, plaque psoriasis, emulgel, skin diseases, kinetic models

ÖZ

Amaç: Desoximetazon (DMS), plak psöriasisin topikal tedavisi için yaygın olarak önerilen bir ilaçtır. Ancak, DMS'nin düşük suda çözünürlüğü ve kısa yarı ömrü, etkili bir topikal formülasyonun geliştirilmesinde büyük engeller oluşturmaktadır. Bu nedenle, hidrofobik DMS vermek için güvenli ve etkili bir topikal sistemin geliştirilmesine yönelik bir talep vardır. Bu çalışma, plak psöriasisin etkili tedavisi için DMS'nin deride daha fazla birikmesini sağlamak için *Aloe vera* bazlı bir emüljel formülasyonu geliştirmeyi amaçlamıştır.

Gereç ve Yöntemler: *Aloe vera* emüljelinin farklı formülasyonları (DE1-DE4), değişen konsantrasyonlarda propilen glikol (%6-14 w/w) ve karbopol 934 (%0,5-%1,0 w/w) içeren dispersiyon tekniği kullanılarak hazırlanmıştır.

Bulgular: Zetasizer ölçümleri, formülasyonların globül boyutunun 10,34 µm±0,9 ila 14,60 µm±1,4 (n=50) arasında değiştiğini ortaya koymuştur. DE3 ve DE2 formülasyonları için ekstrüde edilebilirlik analizi, sırasıyla 5,6±0,11 g/cm^2 ve 5,8±0,13 g/cm^2'lik bir ekstrüde edilebilirlik ortaya koymuştur. Bu formülasyonlar arasında DE3, %94,64±0,29 (n=3) maksimum ilaç içeriği göstermiş ve bu nedenle daha ileri *in vitro* değerlendirmeler için kullanılmıştır. Bir doku analiz cihazı, optimize edilmiş bir DE3 formülasyonunun DE2 formülasyonu ile karşılaştırıldığında daha sıkı olduğunu ve optimal yayılabilirlik sergilediğini göstermiştir. DE3 için, "sertliği" temsil eden ortalama maksimum kuvvet 833,37 g olarak kaydedilirken, "kesme işini" ifade eden ortalama alan 324,230 g sn bulunmuştur. DE3 formülasyonu tarafımızdan üretilmiş bir Franze difüzyon hücresi kullanılarak belirlendiği üzere, 7 saatlik bir süre boyunca %95,40±1,6 DMS geçirgenliği sergilemiştir. *İn vitro* salım kinetiğinin değerlendirilmesi, DMS salımının Korsmeyer-Peppas modeline uyduğunu ortaya çıkarmıştır.

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Sonuç: Fizikokimyasal özellikler ve *Aloe vera* emüljelindeki DMS'nin gelişmiş *in vitro* permeasyonu, deri rahatsızlıklarının topikal tedavisi için verimli bir şekilde kullanılmaya uygunluğunu vurgulamaktadır.

Anahtar kelimeler: *Aloe vera*, desoksimetazon, plak psöriasis, emüljel, deri hastalıkları, kinetik modeller

INTRODUCTION

Plaque psoriasisis the most common form of psoriasis, and it is basically an autoimmune inflammatory skin disease that is challenging to treat. Being ask in disorder, plaques are visible mostly on the skin Stark et al.[1] In particular, plaque psoriasis leads to the formation of red and white plaques of dead skin cell on elbow, knees, scalp, and lower back of the body Grubauer et al.[2] These plaquesare usually irritating and painful, and these can also crack and bleed Kuchekar et al.[3]

Desoximetasone, (11β,16α) 9 fluoro 11,21 dihydroxy 16 methylpregna 1,4 diene 3,20 dione (DMS), is a synthetic fluorinated corticosteroid that is known to exert antipruritic and antiinflammatory effects. In fact, it is one of the most commonly used medication for the treatment of plaque psoriasis Laws and Young.[4] Despite its use in topical skin formulations Imran et al.,[5] low water solubility and short half life of DMS limit its therapeutic efficacy.

In recent years, emulgel has emerged asa promising strategy for effective delivery of drugs, which is usally dependent on the combination of different approaches. In general, emulgel refers to a formulation that contains both gels and emulsions together in the same dosage form Kumar et al.[6] Emulgel formulations have been prepared for several classes of drugs, including antiinflammatory drugs, antifungal agents, antiviral drugs, antibacterial drugs, local anesthetics, and drugs for plaque psoriasis Khunt et al.[7] Currenlty, emulgels are used as a carrier for delivery of various drugs to the skin Susmitha and Gudas.[8] The major components of an emulgel are emulsifying agent, gelling agent, and oil phase Berdey and Voyt.[9] The concentration of these components significantly affects the release of a drug from the formulation, and thereby determines the bioavailability of the drug Kumari et al.[10] One of the advantages of an emulgel is that it easily entraps water-insoluble drugs into a gel base with the help of an oil in water emulsion system Khullar et al.[11] This further enhances the cargo loading capacity, stability, and release of drugsin a controlled manner Vyas and Khar.[12]

The properties of an emulgel that make it a promising option for the treatment of plaque psoriasis include biocompatibility, thixotropic nature, easy spreadability, greaselessness, easy to remove, water solublility, transparency, non staining impact, pleasant appearance, and stability. In addition, the topical application of an emulgel provides softness to the skin Singla et al.[13] The ability of *aloe vera* to enhance the penetration power of drugs and produce an excellent emulsion makes its suitable to be used in the development of an emulgel Thanushree et al.[14]

Several conventional drug delivery systems, including cream, lotion, and gel, have been commercially used for the delivery of DMS. However, the use of these formulations for the treatment of plaque psoriasis is limited, owing to the low contact time and limited localized bioavailability of the drug from these formulations Prajapati.[15] In a previous study, the property of *aloe vera* to stay in contact with skin was explored to develop an emulgel formulation that could be retained for a longer period onto the skin and provide effective and controlled release of drugs Kasliwal et al.[16]

Several previous studies reported the development and evaluation of emulgel formulations for the topical delivery of various drugs. Panwar et al.[17] developed an emulgel formulation of DMS using the incorporation method. Raju et al.[18] utilized *aloe vera* as a gel base for the development of emulgel formulations. Joshi et al.[19] reported that the emulgel formulations they prepared exhibited superior spreadability and consistency. In another study, a physicochemically stable DMS emulgel was prepared, which could significantly release DMS across the cell membrane in a controlled manner with the help of *aloe vera* for a prolong period in the treatment of plaque psoriasis Yapar et al.[20]

Since early decennial of the 21st century, topical delivery of drug has gained immense attention. One of the key benefits of transdermal delivery is that it bypasses metabolism Patel et al.[21] In addition, topical formulations minimize off target effects, such as pH variation, empty stomach time, and presence of enzymes. Thus, topical formulations bypass the difficulty and discomfort associated with an endovenous treatment therapy Sah et al.[22] The present study aimed to developa DMS-loaded emulgel for effective permeation using *aloe vera*.

MATERIALS AND METHODS

Materials

DMS was purchased from Lupin Ltd., Pithampur, Madhya Pradesh, India. Carbapol 934, Tween 20, Span 20, light liquid paraffin, triethanolamine, potassium dihydrogen phosphate, and sodium hydroxide were procurred from Lobachemie Pvt. Ltd., Mumbai, India. Propyl paraben and propylene glycol were obtained from Molychem, Mumbai, India. Methyl paraben was procurred from Merk specialities Pvt. Ltd., Mumbai, India and ethanol from Changshu hongsheng fine chemical Co. Ltd., Changshu city, China.

Methods

Preparation of a gel from aloe vera juice

Central parenchymatous pulp of *aloe vera* was taken out from a fresh leaf using spatula Roy et al.,[23] and it was washed with distilled water several times. Then, the aloe vera pulp was treated with 0.1 N sodium hydroxide toneutralize its acidity Shivhare et al.[24] Further, the treated pulp was blended in a mechanical blender (Secor India research testing instrument, Mumbai, India) at 10,000 rpm for 20 min, and the obtained juice was filtered three times using cotton bed to remove any adhering peel Bharadwaj et al.[25] The prefiltered juice was then subjected to vacuum using a Buchner funnel vacuum suction

filtration apparatus (Zhengzhoukeda machinery and instrument equipment Co., *Ltd*., Zhengzhou city, Henan Province) and clear fluid was collected Bhanja et al.[26] Further, 1% w/w carbapol 934 was added and mixed with the help of a dual-shaft mechanical stirrer at 2.000 rpm (Secor India research testing instrument, Mumbai, India) for 30 min Khullar et al.[27] *Aloe vera* gel was prepared via dispersion technique to ensure that no lumps are formed. During the dispersion of the aloe vera juice, carbapol 934 was assorted with propyl paraben and methyl paraben Baviskar et al.,[28] and gel formation was mediated by the gradual addition of 1 N sodium hydroxide solution Tambe et al.[29]

Formulation of different batches of emulgel containing 0.25% DMS

A 0.25% DMS oil-in-water (o/w) emulgel system was prepared using dispersion method, as described earlier. Various formulations of emulgel (DE1-DE4) were prepared using varying concentrations of carbopol 934 as summarized in Table 1. Briefly, 1% w/w Span 20 was added toliquid paraffin in order to prepare an oil phase, and then 0.25% DMS was dissolved in this oil phase Patwardhan et al.[30] An aqueous phase was prepared via dissolving 0.5% w/w Tween 20 in 10 mL distilled water. Similarly, propyl paraben and methyl paraben were mixed in propylene glycol, and these were finally combined with the aqueous phase. The aqueous phase and oil phase were heated separately at 80˚C in a water bath (Omkar instruments, Bhiwandi, Maharashtra, India) Pakhare et al.[31] Lastly, the emulsion was formulated by mixing the oil phase with the aqueous phase using a mechanical stirrer at 1.500 rpm for 20 min. After stirring, the formulation was cooled to room temperature Martin.[32] The prepared 0.25% DMS emulsion was added to the prepared *aloe vera* gel with continuous stirring on a mechanical stirrer at 1.000 rpm for 60 min. Triethanolamine was used to maintain a pH of 6.4 of the prepared 0.25% DMS emulgel Premjeet et al.[33]

Table 1. Formulation of 0.25% DMS emulgel

S. no.	Name of ingredients (% w/w)	DE1	DE2	DE3	DE4
1	Desoximetasone	0.25	0.25	0.25	0.25
2	Span 20	1	1	1	1
3	Tween 20	0.5	0.5	0.5	0.5
4	Propylene glycol	6	10	14	8
5	Methyl paraben	0.03	0.03	0.03	0.03
6	Ethanol	4	4	4	4
7	Liquid paraffin	16	16	16	16
8	*Aloe vera*	10	15	20	10
9	Carbopol 934	1	0.75	0.5	1
10	Propyl paraben	0.02	0.02	0.02	0.02
11	Distilled water	q.s.	q.s.	q.s.	q.s.
12	Triethanolamine	Adjust pH 5.8 to 6.8			

DE formulation denotes desoximetasone emulgel. DE: Different formulation, DMS: Desoximetasone, q.s.:

Globule size analysis

The globule size of the prepared *aloe vera* emulgel of DMS was studied using a zetasizer (Malvern instrument 3.000 HSA, UK). Size measurements were performed at 25˚C. The samples were diluted before analysis. All measurements were performed in triplicates Khullar et al.[34]

Determination of extrudability

The extrudability was determined in terms of the load applied (grams) to extrude a 0.5 cm strip of emugel from the collapsible tube of lacquered aluminium within 10 seconds Vijaya et al.[35] The scalability of optimized preparation was measured in triplicates. The extrudability was measured using the following equation (1):

$$\text{Extrudability} = \frac{\text{Applied load (g) to extruded emulgel from tube}}{\text{Area (in cm}^2\text{)}}$$

equation (1)

pH studies of DMS emulgel

To measure the pH of emulgel formulations, a digital pH meter (Mettler Toledo India Pvt. Ltd., Mumbai, Maharashtra, India) was used Moghbel and Faghiri[36] All measurements were performed in triplicates.

Determination of drug content in DE1-DE4 emulgel formulations

To determine the drug content in the formulations, approximately 200 mg of emulgel was taken in a petri dish and 5 mL of ethanol (65% v/v) was added. Emulgel was dissolved in ethanol by gentle shaking with a glass rod for 15 min. The resulting solution was transferred to a 10-mL volumetric flaskand sonicated for 10 min. The final volume of the solution was made up to 10 mL using ethanol Kumar et al.[37] Further, the solution was filtered using filter paper grade no. 41 (Whatman) and analyzed spectrophotometrically (Shimadzu 1700, Shimadzu analytical Pvt. Ltd., Mumbai, India) at 242 nm Vladimirov et al.[38] The drug content was calculated using the following equation (I2):

$$\text{Drug content (\%)} = \frac{\text{Actual amount of drug determined in 200 mg emulgel}}{\text{Theoretical amount of drug present in 200 mg emulgel}} \times 100$$

equation (2)

An in vitro release study of the optimized DMS emulgel

An *in vitro* release study for the optimized emulgel formulation was performed using a modified dissolution assembly, as previsously described by Bazigha et al.[39] The filter paper grade no. 41 (Whatman®) was cut into desired size and placed at the bottom and inner wall of the stainless steel basket assembly. The modified basket assembly wasplaced in a 50 mL glass beaker containing 30 mL ofphosphate buffer (pH 7.4)as a drug release medium. The dissolution assembly was placed on a magnetic stirrer and ateflon coated magnetic bead was used for stirring the drug release medium ata temperature of 32˚C±0.5˚C.

Emugel equivalent to 2.5 mg of DMS was weighed and applied as a thin layer in the modified basket assembly. At different time intervals, 3 mL of drug release medium was withdrawn and 3 mL of fresh buffer medium was added. The test sample was filtered through the filter paper, and concentration of the test sample was measured in terms of absorbance at 242 nm using a double beam ultraviolet (UV)/visible spectrophotometer (Shimadzu® 1700) Navya et al.[40]

Assessment of DMS permeation using a Franz diffusion cell

To evaluate the permeation of DMS for the optimized emulgel formulation, a Franz diffusion assembly was used, as previously described by Nayak et al.[41] The Franz diffusion cell consists of donor and receptor chambers. In the present study, the donor chamber was kept in contact with the environment and unclosed at the top, with a diffusion area of 1.43 cm^2. Phosphate buffer (pH 7.4) was used as a dissolution medium, and 0.0025% w/v sodium azide solution was added to prevent microbial growth in the receptor chamber. Arice magnetic bead was placed in the receptor chamber. A cellophane membrane was tied to the donor chamber, and the excised diffusion cellwas placed between the chambers of the diffusion cell and clamped into position. The whole assembly was placed on a magnetic stirrer at 37°C±0.5°C Gupta and Gupta.[42] For hydration, the membrane was placed in the cell for 2 h. Then, the emulgel formulation of DMS (5 mL) was spread onto the surface of membrane. At different time intervals, 1 mL of permeated drug sample was withdrawn and 1 mL of fresh release medium was added to the receptor compartment. The test sample was analyzed using a double beam UV/visible spectrophotometer (Shimadzu® 1700 analytical Pvt. Ltd., Mumbai, India) at 242 nm Dhawan et al.[43]

Consistency of the optimized DMS emulgel formulation

The consistency of the optimized emulgel formulation was determined using a texture analyzer (TA.XT Plus). Prior to the test, distance calibration of the probe was performed by keeping the return distance fixed at 30 mm. The consistency of the formulated emulgel was measured using a standard-sized container (back extrusion 50 mm diameter). The container was filled with 75% emulgel formulation and a 40 mm extrusion disc was placed at the center, over the test container. Care was taken to hold the container firmly in place to prevent it from lifting when prob returns to start position Shah and Desai.[44] The disk was inserted into the deepest part, where active surface was reported, i.e., the point at which the bottom surface of the disc comes into contact with the product. At this point, the probe moved back to its real position when maximum force was applied. The firmness of the formulation was measured at maximum force or peak value. The area under the curve, at this point, was taken as the measurement of consistency, which showed that higher the area, more dense is the consistency of the formulated emulgel. The gripping effect of the optimized emulgel formulation was measured by back extrusion, where in the negative region of the graph presented consistency. A higher cohesiveness value of the emulgel formulation was indicated by maximum negative force or higher negative value. The negative area region of the curve is called work of cohesion. The consistency of the optimized emulgel formulation showed that more is the area of curve, higher is the resistance to withdraw the emulgel formulation Swamy et al.[45]

Spreadability of the optimized DMS emulgel

The spreadability of the DMS emulgel was determined using a texture analyzer (TA.XT Plus). Spreadability fixity is a group of accurately coinciding male and female cones (febricated with Perspex 90). The test required the use of a heavy duty platform to which the female probe containing the sample was attached. The male cone was positioned centrally over the cone containing the sample. Before starting the experiment, the male cone probe was moved downward such that it was installed into the female cone sample holder. The instrument was calibrated for distance using a void female holder prior to the test. The DMS emulgel was loaded into the female holder using a spatula. Upon starting the test, the male cone probe proceeded toward the female cone and penetrated the sample holder surface (depth of 2 mm). At this point, the maximum penetration depth was attained for the given penetration force, and firmness was measured at a specified depth in terms offorce value. A higher area of firmer sample indicated total quantity of the force required to perform shearing process. The male probe was then allowed to return back to its original position from the female probe. Mean maximum force and mean area were calculated from the curve Gupta and Gaud.[46]

In vitro release kinetics

The release profile for sustained release of DMS from the emulgel formulation could be interpreted in several ways, including diffusion, erosion, or osmosis by using different kinetic models. For *in vitro* release kinetics assesment, zero-order models were used for cumulative % drug released vs. time, Higuchi kinetic model represented cumulative % drug release vs. square root of time, first-order kinetic model as log of cumulative % drug left vs. time, Korsmeyer-Peppas model as log of % drug released vs. log time, and Hixson-Crowell cube root model as cube root of % drug remaining vs. time. The desired model was selected on the basis of excellence of fit test Wesley and Gude.[47]

Zero-order model: In this equation, the release data for emulgel containing DMS showed that DMS was released slowly, which was measured by applying the following equation 3:

$$M_0 - M_t = k_0 t \qquad \text{equation (3)}$$

Where, "M_t" denotes the quantity of DMS dissolved in time t, "M_0" denotes the initial quantity of DMS in the release medium (times, M_0=0), and "k_0" is the kinetic zero-order release constant (concentration/time).

First-order model: This equation was used to explain the absorption and/or elimination of DMS. The DMS release profile following the first-order kinetics model was measured using the equation 4:

$$\ln (M_0/M_t) = k_1 t \qquad \text{equation (4)}$$

Krate constant of first order (time^{-1}).

Higuchi model: This model was used to explain DMS release from the matrix, wherein the obtained data were calculated using equation 5:

$M_t = k\sqrt{t}$ equation (5)

Here, k√t is the Higuchi dissolution constant.

Korsmeyer-Peppas model: The proposed equation was used to explain the release of drugs from a polymer system. To find out the release mechanism of DMS, the obtained data were calculated as per the given equation 6:

$M_t/M_\infty = Kt^n$ equation (6)

Where, "M_t/M_∞" denotes the amount of drug released due to friction at time t, "K" is the rate release constant and "n" denotes the release exponent.

Hixson-Crowell model: According to this model, area of the particle is proportional to the cube root of volume, and the obtained data were calculated as per the given equation 7:

$(W_0)\ 1/3 - (W_t)\ 1/3 = kt$ equation (7)

Where, "W_0"represents the initial quantity of DMS, "W_t" denotes the quantity of remaining DMS at time t, and "k" is a constant incorporating surface volume relation.

Stability study of the DE3 emulgel formulation

The stability of the DE3 emulgel formulation was assessed as per the international conference on harmonization guideline for 6 months. The optimized DE3 emulgel formulation was placed at an accelerated temperature of 40˚C±2˚C/75±5% RH. The drug content of the optimized DMS emulgel formulation was measured at an interval of 0 (beginning), 1, 2, 3, and 6 months Kumar and Verma.[48]

Statistical analysis

All results are presented as mean ± standard deviation (SD). The results were analysed using Duncan's multiple range test, wherein mean values were considered to be well seprated at p≤0.05.

RESULTS AND DISCUSSION

Determination of globule size, extrudability, and pH

The average globule size of the DMS emulgel formulation (DE) was found to bein the range of 10.17-14.60 µm. The extrudability of DMS emulgel formulation correlated with the concentration of emollient. Among different formulations, DE3 and DE2 showed good extrudability. In fact, the extrudatbility of DE3 was recorded to be higher than that of other formulations, which was attributed toa higher concentration of emollient in DE3. To determine the pH of DMS emulgel formulations, a calibrated pH meter (Mettler-Toledo India Pvt. Ltd., Mumbai, India) was used. An ideal topical formulation must be compatible with the skin. Measurements for globule size, extrudability, and pH value were performed in triplicates and expressed as mean ± SD (Table 2).

Determination of the drug content informulated batches of emulgel formulations

The percentage of the drug present in the prepared emulgel formulations was measured in terms of absorbance at 242 nm using a UV spectrophotometer (Shimadzu 1700, Shimadzu analytical Pvt. Ltd., Mumbai). The percentage of DMS in the DE2 and DE3 emulgel formulations were recorded to be 92.30±0.21% and 94.06±0.29%, respectively. Importantly, these drug percentages lied within the pharmacopoeia limits (Table 2). The drug content of the formulated batches are graphically presented in Figure 1.

Thus, based on these results, the DE2 and DE3 formulations were selected for further analysis.

In vitro release study of optimized DMS emulgel

An *in vitro* drug release study revealed that the DE3 emulgel formulation showed better drug release than DE2. The release

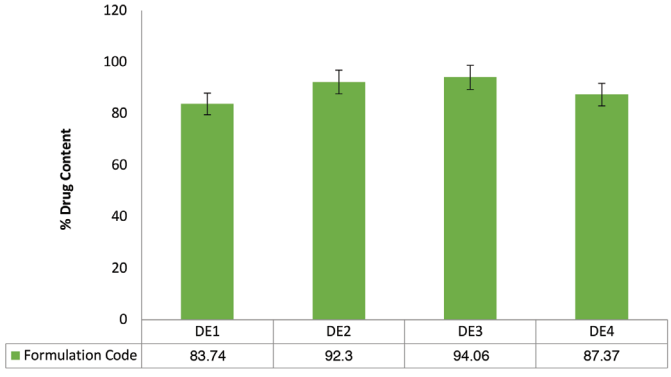

Figure 1. Drug content of the prepared emulgelformulations. DE3 displayed the highest drug content as compared with other formulations, but with non-significant differences (p<0.01)

DE: Different formulation

Table 2. Globule size, extrudability, pH, and drug contents of the developed emulgel formulation

S. no.	Formulation code	Globule size (µm) (n=50)	Extrudability (g/cm^2)	pH	Drug content (%) (n=3)
1	DE1	12.21±1.3	5.4±0.15	5.8	83.74±0.64
2	DE2	10.34±0.9	5.6±0.11	6.4	92.30±0.21
3	DE3	10.17±0.5	5.8±0.13	6.2	94.06±0.29
4	DE4	14.60±1.4	4.4±0.26	6.8	87.37±0.82

Average globule size, extrudability, pH, and drug contents of various formulation codes. The globule size results are presented as mean ± SD (n=50).The extrudability results are presented as mean ± SD (n=3). The recorded pH of all emulgel formulations of DMS was in acceptable range, which is important to avoid the risk of skin irritation. The determination of drug content is important to determine topical dosage form performance. The results are presented as mean ± SD (n=3). DE: Different formulation, DMS: Desoximetasone, SD: Standard deviation

of DMS from emulgel was found to be dependent on the concentrations of *aloe vera* and propylene glycol that were used as gel base and penetration enhancer, respectively. For the DE3 formulation, DMS release of 87.84±2.5% was recorded in 7 h. Thus, the DE3 formulation was selected as an optimized formulation and further used for *in vitro* DMS permeation study. The results for cumulative % DMS released measured using a cellophane membrane are reported in Supplement 1 and graphically presented in Figure 2.

In vitro permeation study usingthe Franz diffusion cell

The DE3 emulgel formulation exhibited higher DMS permeation than the DE2 formulation. For DE3, the drug permeation was found to be 95.40±1.6%, which was consistent over a period of 7 hr. Thus, DE3 was selected as an optimized emulgel formulation for the evaluation of firmness, cohesiveness, consistency, and viscosity. The results of *in vitro* permeation study are summarized in Supplement 2 and graphically presented in Figure 3.

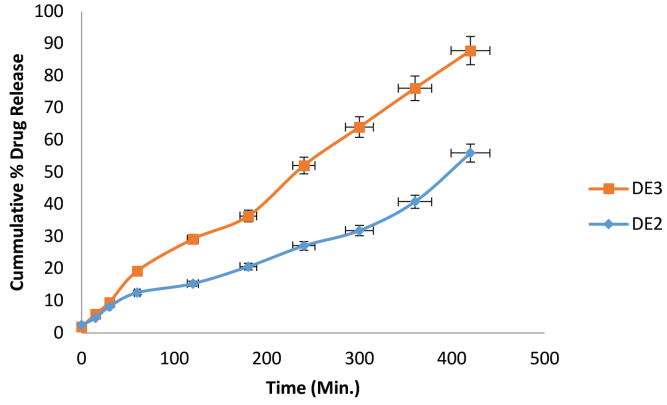

Figure 2. *In vitro* cumulative % drug release evaluated using a modified dissolution assembly. DE3 showed better drug release than DE2. Values are represented as mean ± SD (n=3)

DE: Different formulation, SD: Standard deviation

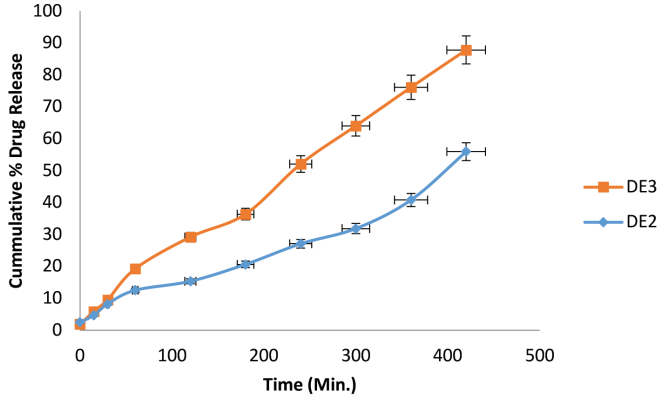

Figure 3. *In vitro* permeation study using a Franz diffusion cell

The permeation rate of DMS for DE3 and DE2 emulgel formulations was assessed using the Franzdiffusion cell. Phosphate buffer (pH 7.4) was selected as a drug diffusion medium. A cellophane membrane was used for permeation study at a temperature of 37°C±0.5°C. The data are presented as mean ± SD (n=3)

DE: Different formulation, DMS: Desoximetasone, SD: Standard deviation

Evaluation of the consistency, cohesiveness, viscosity, and firmness of the optimized emulgel formulation

The consistency, cohesiveness, viscosity, and firmness of the optimized DMS emulgel formulations (DE3 and DE2) were measured using a texture analyzer. The DE3 emulgel formulation was found to be firmer, cohesive, and displayed superior consistency than DE2. For firmness, the maximum positive force was recorded to be 67.604 g. The maximum negative area representing cohesiveness of DMS emulgel was found to be -49.480 g, and the consistency value of DMS emulgel, measured in terms of mean positive area of curve, was recorded to be 591.697 g.sec. The mean area for negative index of viscosity was found to be 450.153 g.sec. The DE3 emulgel formulation displayed superior consistency than the DE2 formulation,as measured using a texture analyzer. All these results are summarized in Table 3 and graphically presented in Figure 4, 5.

Determination of spreadability

The spreadability of the optimized emulgel formulations of DMS (DE3 and DE2) was measured, wherein DE3 was found to be firmer and displayed optimal spreadability, which was superior than that exhibited by DE2. For DE3, a very high value of mean maximum force of 833.37 g was recorded, which represented "firmness", and mean area, representing "work of shear", was observed to be 324.230 g.sec. These results are summarized in Table 4. Graphs of spreadability for the optimized formulations of DMS emulgel are shown in Figure 6, 7.

In vitro release kinetics model for the optimized emulgel formulation

The best model for studying the release kinetics of the optimized emulgel formulation was determined as per the regression data. The zero-order model showed a regression value of 0.996 (Figure 8A). The regression value for first-order model was recorded to be 0.926 (Figure 8B), whereas the Higuchi kinetic model showed a regression value of 0.941 (Figure 8C). The Korsmeyer-Pappas model and Hixon-Crowell model displayed regression values of 0.972 (Figure 8D) and 0.967 (Figure 8E), respectively. For the aforementioned models, regression values were recorded to be <1. Intial release data of 60% of DMS fitted into Korsmeyer-Peppas model, indicating that the release mechanism obeyed the Korsmeyer-Peppas model and confirmed that the release of DMS followed a diffusion mechanism. Release data for DMS emulgel are summarized in Supplement 3.

Stability study ofthe emulgel formulation

The stability data indicated that the emulgel formulation was stable for 6 months. The stability results are summarized in Table 5.

Study limitations

The DMS emulgel formulation showed a higher rate of drug release than that showed by traditional DMS ointment and DMS cream. Despite several benefits of the emulgel, the delivery of water-insoluble drugs poses a great challenge. Thus, the aim of this study was to prepare a DMS emulgel using a conventional

method. The present study aimed to formulate a DMS emulgel using *aloe vera*, which is considered to be safe to use, non sensitive, and non irritant, and displays good spreadability and penetrability across the skin. An emulgel is used to deliver DMS deep into the skin in a better manner. In this way the study limitation further relates to methods for making and using such compositions.

CONCLUSION

In the present study, an aloe vera-based topical emulgel of DMS was optimized, formulated, and characterized as an attractive alternative for the local delivery of DMS into the skin. The developed formulation presented an attractive option for better patient compliance, long contact timeat the target site, and ease of use. Among the different formulations, the DE3 formulation

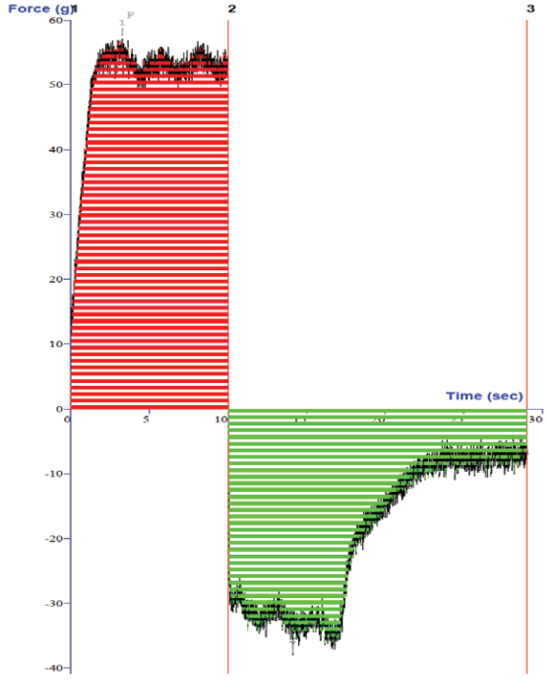

Figure 4. Consistency graph ofa DMS emulgel formulation (formulation code DE3)

DE: Different formulation, DMS: Desoximetasone

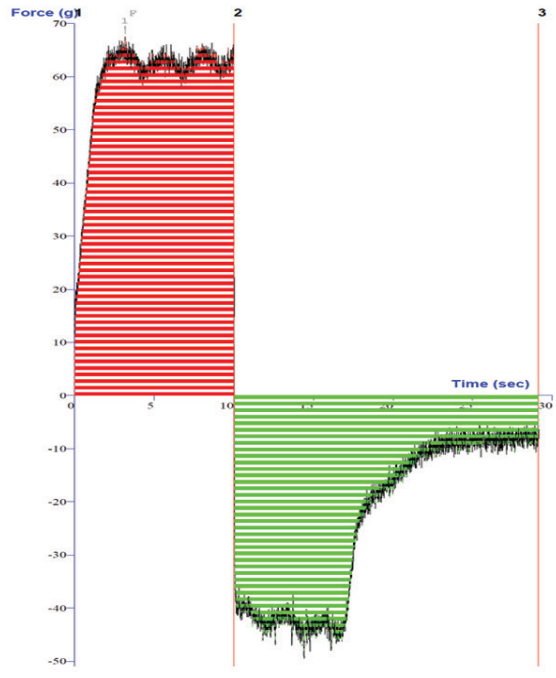

Figure 5. Consistency graph ofan optimized DMS emulgel formulation (formulation code DE2)

DE: Different formulation, DMS: Desoximetasone

Table 3. Results of consistency study ofoptimized emulgel formulations of DMS

S. no.	Formulation code	Mean maximum positive force "firmness" (g)	Mean positive area "consistency" (g.sec)	Mean maximum negative force "cohesiveness" (g)	Mean negative area "index of viscosity" (g.sec)
1	DE2	57.152	504.173	-38.027	-364.294
2	DE3	67.604	591.697	-49.480	-450.153

DMS: Desoximetasone

Table 4. Results of spreadability study ofoptimized emulgel formulations of DMS

S. no.	Formulation code	Mean max force "firmness" (g)	Mean area "work of shear" (g.sec)
1	DE2	734.522	276.821
2	DE3	833.37	324.230

DMS: Desoximetasone, DE: Different formulation, max: Maximum

Table 5. Preliminary results ofstability study ofthe emulgel formulation of DMS (formulation code DE3) (n=3)

Storage condition	Assay (%)				
	0 day	First month	Second month	Third month	Sixth month
40±2°C/75±5% RH	98.86±0.57	97.68±0.37	96.74±1.3	96.03±0.04	94.73±0.5

DMS: Desoximetasone, DE: Different formulation, RH: Relative humidity

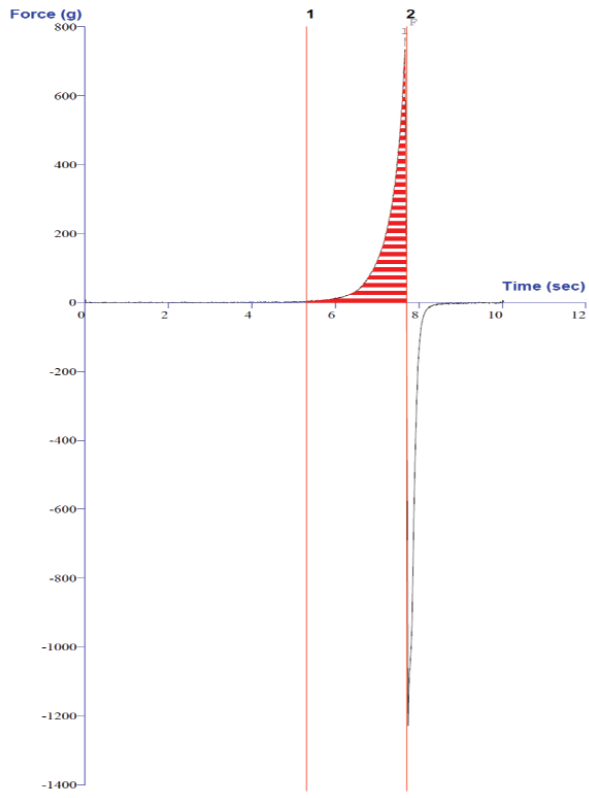

Figure 6. Spreadability graph ofan optimized DMS emulgel formulation (formulation code DE2)

DE: Different formulation, DMS: Desoximetasone

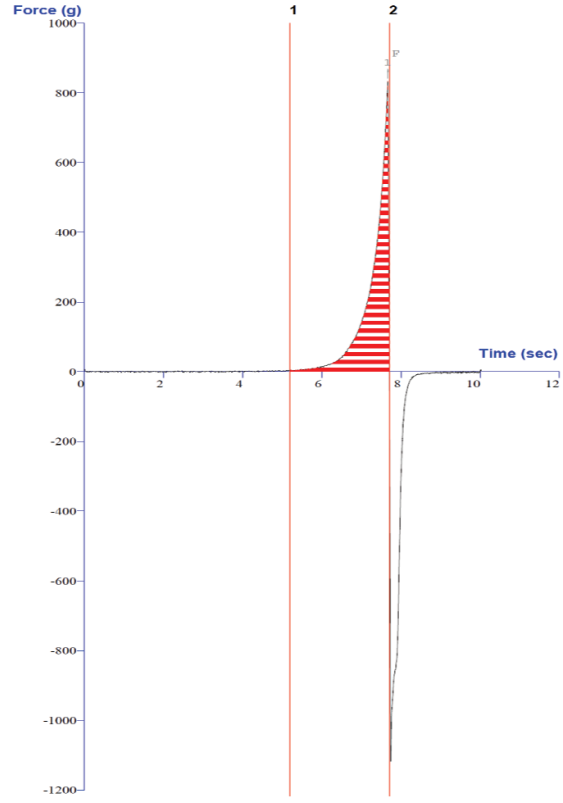

Figure 7. Spreadability graphof an optimized DMS emulgel formulation (formulation code DE3)

DE: Different formulation, DMS: Desoximetasone

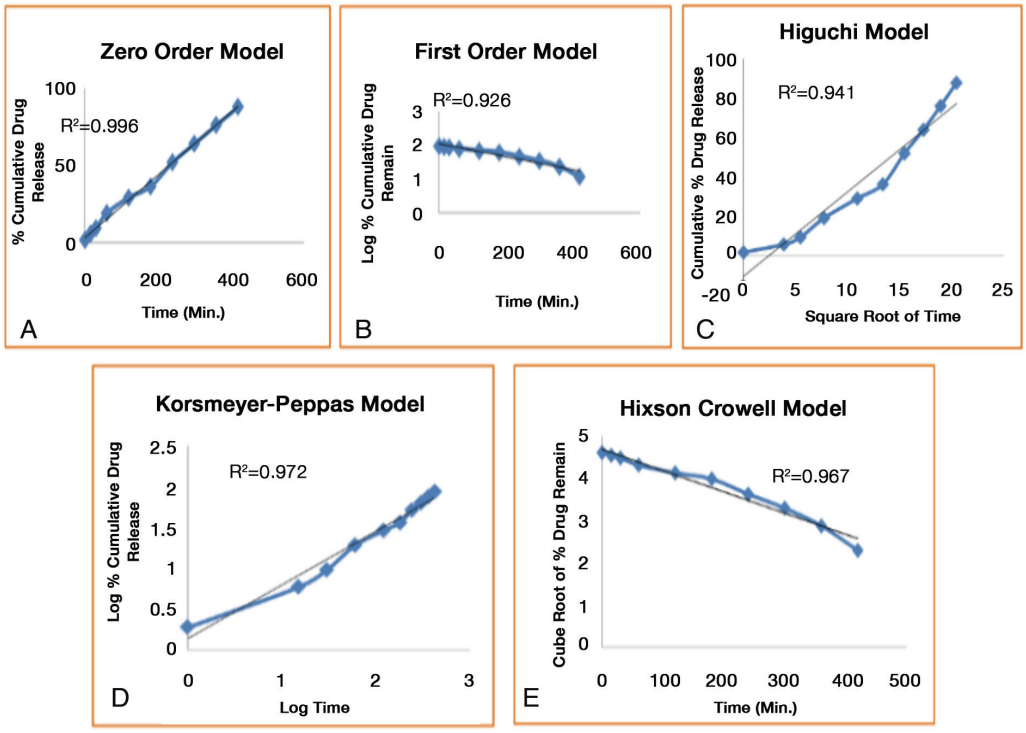

Figure 8. *In vitro* release kinetics model. A) Zero-order model, B) first-order model, C) Higuchi, D) Korsmeyer-Peppas model, and E) Hixson-Crowell model. For *in vitro* release study, a modified dissolution assembly was employed. Values are represented as mean ± SD (n=3)

SD: Standard deviation

was found to adhere to biological membrane for an extended period of time and provided an optimum drug release for the effective treatment of plaque psoriasis. The DE3 formulation displayed a better contact time than traditional formulations, including ointmentand cream. These results highlighted the suitability of an aloe vera-based emulgel formulation of DMS to overcome the skin barriers for the effective treatment of plaque psoriasis. However, *in vivo* and clinical studies are further required to validate its suitability for commercial development.

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Supplement 1. *In vitro* drug release from optimized emulgel formulations of DMS

Time (min)	Cumulative percentage drug release	
	Formulation code	
	DE2	DE3
0	2.496±0.010	1.89±0.5
15	4.68±0.1	5.906±2.1
30	8.237±0.5	9.545±4.8
60	12.532±1.8	19.27±6.3
120	15.347±3.6	29.21±8.1
180	20.647±4.8	36.40±5.8
240	27.094±6.2	52.09±6.7
300	31.866±0.7	64.06±1.1
360	40.82±1.3	76.13±0.7
420	55.96±4.0	87.84±2.5

For *in vitro* drug release of emulgel formulations containing DMS, dissolution of DE2 and DE3 formulations was performed using amodified dissolution assembly at a temperature of 32˚C±0.5˚C. Phosphate buffer (pH 7.4) was used as a release medium. The results are presented as mean ± SD (n=3). DE: Different formulation, DMS: Desoximetasone, SD: Standard deviation

Supplement 2. *In vitro* drug permeation of emulgel formulations of DMS

Time (min)	Cumulative percentage drug release	
	Formulation code	
	DE2	DE3
0	0	0
15	4.68±0.4	8.90±0.9
30	8.23±0.8	16.54±1.3
60	12.53±1.1	32.27±1.1
120	15.34±1.6	46.21±1.6
180	20.64±1.4	58.40±0.9
240	27.09±1.7	64.06±1.4
300	31.86±0.9	76.62±0.8
360	40.82±1.8	88.29±0.7
420	55.96±0.3	95.40±1.6

Values are represented as mean ± SD (n=3). DE: Different formulation, DMS: Desoximetasone, SD: Standard deviation

Supplement 3. Percentage drug release valuescalculated using different kinetic models. Data was fitted in zero-order model, first-order model, Higuchi matrix, and Hixon-Crowell model

Time (min)	√t	Log time	Cumulative % drug release	Log of cumulative % drug released	Cumulative % drug remaining	Cube root of % drug remaining	Log of cumulative % drug remaining
0	0	0	1.89	0.276	98.11	4.612	1.991
15	3.872	1.176	5.906	0.771	94.09	4.548	1.973
30	5.477	1.477	9.545	0.979	90.45	4.488	1.956
60	7.745	1.778	19.27	1.284	80.73	4.321	1.907
120	10.95	2.079	29.21	1.465	70.79	4.136	1.849
180	13.41	2.255	36.40	1.561	63.60	3.991	1.803
240	15.49	2.380	52.09	1.716	47.91	3.631	1.680
300	17.32	2.477	64.06	1.806	35.94	3.300	1.555
360	18.97	2.556	76.13	1.881	23.87	2.879	1.377
420	20.49	2.623	87.84	1.943	12.16	2.299	1.084

The best model for release pattern of DMS was determined as per the regression data. For release study, a modified dissolution assembly was employed. Values are presented as mean ± SD (n=3). DMS: Desoximetasone, SD: Standard deviation