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## Aloe Vera Mediated Emulgel for Topical Delivery of Desoximetasone

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### Abstract:

**Background:** Desoximetasone (DMS), is a recommended drug against plaque psoriasis for topical cure. However, low water solubility and short half-life present the major obstacles in development of effective topical formulation. This demand for the development of effective topical system to deliver the hydrophobic DMS.

**Objective:** The present investigation aimed at developing the aloe vera based emulgel formulation was to enhanced skin deposition of DMS to effectively treat plaque psoriasis.

**Methods:** The different batches (DE1-DE4) of aloe vera emulgel was prepared using dispersion technique using varying concentration of propylene glycol (6 to 14 % w/w) and carbopol 934 (0.5 to 1.0% w/w).

**Result:** The globule size evaluated by zetasizer was found in the range of 10.34  $\pm$  0.9 to 14.60  $\pm$  1.4 ( $n=50$ ). Extrudability analysis revealed 5.6  $\pm$  0.11g/cm<sup>2</sup> and 5.8  $\pm$  0.13 g/cm<sup>2</sup> extrudability with DE3 and DE2 formulations. . The pH were found in the range of 5.8 to 6.8 and formulation DE3 showed maximum drug content 94.64  $\pm$  0.29 ( $n=3$ ) as compared to other formulations and therefore used further in in vitro evaluation. The optimized DE3 formulation was found to be firmer and with optimal spreadability (**'firmness'** 833.37 g mean max. force and **'work of shear'** 324.230 g.sec. mean area) as compared to formulation DE2 as analysed using texture analyzer. Formulation DE3 exhibited 95.40 $\pm$ 1.6 %DMS permeation within 7 h as determined using in house fabricated franz diffusion cell. The release mechanism of DMS was found to fit in korsmeyer Peppas model as revealed in in-vitro release kinetic investigation.

**Conclusion:** The physicochemical characterizations and enhanced in vitro permeation of DMS suggest that aloe vera emulgel could be efficiently employed for the topical treatment of skin ailments.

**Keywords:** Desoximetasone, Plaque psoriasis; Emulgel; Skin penetration; Skin diseases; Kinetic models.

## 1.0 Introduction

Plaque psoriasis, is highly prevalent form of psoriasis and basically an autoimmune disease which is challenging to treat. Being the skin disorder plaque is visible mostly on the skin (Stark, H. J., et. al. 2006), which causes red and white plaque of dead skin cell on elbow, knees, scalp, and lower back of body (Grubauer, G., et. al. 1987). They are usually unquiet, painful, and can crack and bleed (Kuchekar et al. 2011).

Desoximetasone, (11 $\beta$ ,16 $\alpha$ )-9-fluoro-11,21-dihydroxy-16-methylpregna-1,4-diene-3,20-dione (DMS) is a synthetic fluorinated corticosteroid known to exert anti pruritic and anti inflammatory activity and most frequent medication for the treatment of plaque psoriasis (Laws and Young 2010). Despite its use in topical skin formulations (Imran, K., et. al. 2011), DMS's low water solubility and short half-life are the major obstacles impeding its therapeutic efficacy. Emulgel are novel approach for effectively delivery of drug, depend on combined approaches. When gels and emulsions both are together in same dosage form that formulation is called as emulgel (Kumar and Mahant et. al. 2015). Emulgel formulation were prepared for several classes of drug such as anti inflammatory drugs, anti fungal agent, anti-viral drugs, anti bacterial drugs, local anesthetic and plaque psoriasis (Khunt, Mishra et al. 2012). Therefore, emulgel were currently used as a carrier for delivery of various drugs to the skin. (Susmitha and Gudas 2019). The major components of emulgel are emulsifying agent, gelling agent and oil phase (Berdey and Voyt 2016). Their concentration significantly affects the bioavailability of drug release from the formulation (Kumari, Singh et al. 2015). The merit of emulgel include easily entrapment of water insoluble drugs into gel base with the help of oil in water emulsion system (Khullar, Kumar et al. 2012). Which enhance cargo loading capacity, stability, and release of drug at controlled manner (Vyas and Khar (2002).

Emulgel contained favorable properties for treatment of plaque psoriasis such as bio-friendly, thixotropic, easily spreadable, greaseless, easily removable, water soluble, skin softness, transparent, non-staining, pleasant appearance and stable (Singla, Saini et al. 2012). The ability of aloe vera to enhance the penetration power of drug and produce excellent emulsion into an emulgel (H.R. Dhanushree 2017).

Several conventional drug delivery systems like cream, lotion, and gel of DMS are available in market, but use of these formulations for treatment of plaque psoriasis is limited because contact time of the drug and localized bioavailability from these formulations is very low (Prajapati, M. N., 2013). Their property of staying in contact with skin was explored to develop a emulgel formulation using aloe vera which would retained long period of time onto the skin and releases drug (Kasliwal, 2008).

The emulgel formulation of DMS was prepared by incorporation method (Panwar, A. S., et. al. 2011); Aloe vera was selected as gel base for the development of emulgel formulation (Prasanna, R., et. al. 2015). The designed formulations were prepared and evaluated for, showed that superior spreadability and consistency (Joshi, V., et. al. 2012). In conclusion, a physicochemical stable

DMS emulgel was prepared, which can be significantly reached rate and extent of DMS across the cell membrane in controlled manner with help of aloe vera for prolong period of time in the treatment of plaque psoriasis (AlginYapra, 2013).

Topical delivery has increased in the early decennial of the 21st century. The key benefit of transdermal delivery is to first bypass metabolism (Patel, C. J., et. al. 2013). The significant advantage of topical formulation to minimize the off target effect such as pH variation, empty stomach time, presence of enzyme so that topical formulation was exclude the difficulty and discomfort of endovenous treatment therapy (Sah, Badola et al. 2018). The present research work was to prepare DMS loaded emulgel for effective permeation using aloe vera.

## **2.0 Materials and Methods:**

### **2.1 Materials**

Desoximetasone (Lupin limited pithampur Madhya Pradesh India), Carbapol 934, Tween 20, Span 20, Light liquid paraffin, Triethanolamine, Potassium dihydrogen phosphate and Sodium hydroxide (Loba chemie Pvt. Ltd., ujudhouse road, johangir villa, Mumbai, India), Propyl Paraben, Propylene glycol (Molychem, babu genu road Mumbai, India) Methyl paraben (Merk specialities Pvt. Ltd. shiv sagar estate Mumbai India), Ethanol, (Chang shuhong sheng fine chemical co. ltd. (Changshu city).

### **2.2 Methods:**

#### **2.2.1 Preparation of gel from aloe juice:-**

Central parenchymatous pulp of aloe vera from the fresh leaf of aloe was taken out using spatula (Roy, C. S., et. al. 2012), and then it was washed with distilled water many times. After wards, aloe vera pulp was treated with 0.1N sodium hydroxide to neutralize the acidity. (Shivhare, D. U., et. al. 2009). Then the treated pulp was blended for 20 min using mechanical blender (Secor India research testing instrument, (Mumbai), India) at 10000 rpm to acquire juice, and then the obtained juice was filtered three times using cotton bed to stripping out any adhered peel (Bharadwaj, S., et. al. 2012). The pre-filtered juice was then subjected to vacuum Buchner funnel vacuum suction filtration apparatus (Zheng zhokeda machinery and instrument equipment Co., Ltd. Zhengzhou city, Henan Province) to get the clear fluid (Bhanja, S., et. al. 2013). The 1% w/w carbapol 934 was then mixed with the help of dual shaft mechanical stirrer at 2000 rpm (Secor India research testing instrument, (Mumbai), India) for 30 minutes (khullar, et. al. 2012). Aloe vera gel was prepared via dispersion technique and was ensured for no lumps formation. During the dispersion of juice, carbapol 934 was assorted with propyl paraben and methyl paraben (Dheeraj, T. B., et. al. 2013), and then gel formation was carried out by gradual addition of 1N sodium hydroxide solution (Tambe, R., et. al.2009).

#### **2.2.2 Formulation of different batches containing 0.25% DMSemulgel:**

The 0.25%DMS oil in water (o/w) emulgel was prepared using dispersion method as described earlier. Various batches (DE1-DE4) were prepared using the varying concentration of carbapol 934 as presented in Table 1. Briefly, the oil phase was prepared using 1% w/w span 20 added in liquid paraffin and then 0.25% DMS dissolved in oil Phase (Patwardhan, N., et. al. 2017).

Aqueous phase was prepared via dissolving 0.5% w/w tween 20 in 10 mL distilled water. Similarly, propyl paraben and methyl parabane was mixed in propylene glycol and finally

combined with aqueous phase. The aqueous phase and oil phase were individually heated at 80 °C on water bath (Omkar instruments, Bhiwandi (Maharashtra), India) (Pakhare, S., et. al. 2017). Finally emulsion was formulated using oil phase was mixed with the aqueous phase by continuous mixing using mechanical stirrer at 1500 rpm for 20 min and left aside to cooled at room temperature (Martin, 1994). Above 0.25% DMS emulsion was added to the prepared aloe vera gel with continuously stirring using mechanical stirrer at 1000 rpm for 60 minutes and maintain pH 6.4 of prepared 0.25% DMS emulgel with the help of triethanolamine (Premjeet, S., et. al. 2012).

**2.2.3 Globule size analysis:** The prepared aloe vera emulgel of DMS was studied using zetasizer (Malvern instrument 3000HSA, UK) to determine the globule size. The experiment was performed at 25 °C temperature and the samples were diluted before analysis. The experiments were replicated for 3 times. (Khullar et. al., 2011).

**2.2.4 Determination of extrudability:**

The extrudability was determined by applied required loading grams to remove 0.5 cm of strip of emulgel within ten second, the amount of prepared emulgel (g/cm<sup>2</sup>) squeeze out from the collapsible tube of lacquered aluminum (Vijaya et al 2011). The scalability of optimized preparation was noted down in thrice form. Following equation (I) was used to measure extrudability.

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

**2.2.5 pH studies of DMS emulgel:**

The digital pH meter (Mettler-Toledo India Pvt. Ltd. amar hill Mumbai (Maharashtra), India) was used to measure pH of emulgel formulations (Moghbel and Faghiri, 2006). The pH values of prepared emulgel were noted in triplicates form.

**2.2.6 Determination of drug content of DE1-DE4 emulgel formulations**

Approximately 200 mg of emulgel was taken in a Petridis and added with 5 mL of ethanol (65% v/v). Emulgel was dissolved in it with a gentle shaking with glass rod for 15 minutes. The solution was then transferred to 10mL volumetric flask and sonicated for 10 min. Final volume was made up using ethanol (Kumar A J et al, 2010). The resulting 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 S et al, 1996). The following equation (II) was used to calculate drug content (II):

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

**2.2.7 Determination of in vitro release study of optimized DMS emulgel**

The release study of optimized emulgel formulation was performed using modified dissolution assembly (Bazigha, K. A. R., et. al. 2010). 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 then hanged in a 50 mL glass beaker containing 30 mL of pH 7.4 phosphate buffers as a drug release medium. Dissolution assembly was placed on magnetic stirrer. The Teflon coated magnetic bead was used for well assorted with drug release medium at 32±0.5 °C. Accurately weighed emulgel equivalent to 2.5 mg of DMS was applied as a thin layer in the modified basket assembly. At different time intervals, withdrawn 3 mL of drug release fluid and 3 mL of fresh buffer medium was added. The test sample was filtered through filter paper and test sample was measured using double beam UV/ visible spectrophotometer (Shimadzu® 1700) at 242 nm (Navya and hemantha, 2011).

**2.2.8 DMS Permeation study by Franz diffusion cell**

Franz diffusion assembly was used to performed DMS permeation study of optimized emulgel formulation (Nayak, A. K., et. al. 2010). The franz diffusion cell consist of donor and receptor chamber. The donor chamber was kept in contact with environment and unclosed at the top with diffusion area 1.43 cm<sup>2</sup>. pH 7.4 buffer solution was used as a dissolution medium and added 0.0025% w/v sodium azide solution to prevent microbial growth filled in the receptor chamber. The rice magnetic bead was assembled in the receptor chamber. The cellophane membrane was tied to donor chamber and excised diffusion cell was placed between the chambers of the diffusion cell and clamped into position. The whole assembly was kept up on the magnetic stirrer at 37±0.5 °C (Gupta, R., et. al. 2017). For the hydration of the membrane, the membrane was placed in the cell for 2 hours. After that, emulgel formulation of DMS (5 mL) was spread out onto the surface of membrane. At the different time interval, withdrawn 1 mL of permeated drug sample and 1 mL of fresh release medium added to receptor compartment. The test sample was analyzed by double beam UV/ visible spectrophotometer (Shimadzu® 1700 analytical Pvt. Ltd., (Mumbai) India) at 242 nm (Dhawan S. et al, 2009).

### **2.2.9 Consistency of optimized DMS emulgel formulation**

The texture analyzer (TA.XT Plus) was used for determination of consistency of optimized emulgel formulation. Before performing the test, distance calibration of the probe was done by keeping the return distance to 30 mm. Consistency of formulated emulgel was performed in standard size container (back extrusion 50 mm diameter). 75% emulgel formulation was filled up in the container and 40 mm extrusion disc was emerged at center over the test container. The holds the container firmly in place to stop it from lift off when probe return to start position (Shah, V. K., et. al. 2012). The disk was inserted into deepest part, when surface active was reported (i.e., the bottom surface of the disc at which point the product comes into contact). The probe backed to its real position at this point when maximum force was applied. The determination of firmness was measured at maximum force or peak value. The area under the curve at this point was taken as determination of consistency that showed higher the area the dense the consistency of formulated emulgel. The gripping effect of optimized emulgel formulation occurred by back extrusion that showed negative region of the graph and that showed consistency. Higher the cohesiveness value of emulgel formulation showed by maximum negative force or higher negative value. The negative area region of curve is called work of cohesion. The consistency of optimized emulgel formulation showed by more area of curve the higher resistant to withdrawn the emulgel formulation (Swamy N.G.N., et. al. 2010).

### **2.2.10 Spreadability of optimized DMS Emulgel**

Spreadability of DMS emulgel was performed by texture analyzer (TA.XT Plus). Spreadability fixity is a group of accurately coincide male and female cones (fabricated of Perspex 90). The test requires the use of heavy duty platform to which the female probe is attached containing the sample. The male cone was positioned centrally over the sample containing cone. Before starting the experiment, male cone probe was moved downwards so it installed into female cone sample holder. Instrument was calibrated for distance using void female holder prior to starting spreadability test. The DMS emulgel was loaded using spatula into female holder. Upon starting test the male cone probe proceeded to female cone and penetrated sample holder surface (depth of 2mm). At that point, enhanced the maximum penetration depth was seen during penetration the force and firmness was measured at specified depth by force value. The higher area of firmer sample was indicated total quantity of force taken to perform shearing process. Male probe was

then allowed to return back to its original position from the sample from female probe. Mean maximum force and mean area was calculated from the curve (Gupta and Gaud, 2005).

### 2.2.11 In vitro release kinetics:

The research scientist interprets release profile of DMS in sustained release formulation with several ways like diffusion, erosion, or osmosis by different kinetic model. The kinetic zero order models were used as cumulative drug percent release Vs. time, Higuchi kinetic model as cumulative drug percent release Vs. square root of time, first order kinetic model as log cumulative percent of drug remaining Vs. time, Korsmeyer-Peppas model as log percent drug released Vs log time and Hixson-Crowell cube root model as percent drug remaining cube root Vs. time. The desired model was selected on basis of excellence of fit test. (Wesley, Z. et. al. 2015).

**Zero-order model:** In this equation the release data of emulgel containing DMS were represent that release of DMS slowly and measured by applying the below equation III.

$$M_0 - M_t = k_0 t \dots\dots\dots (III)$$

$M_t$  quantity of DMS dissolved in time  $t$ ,

$M_0$  Initial quantity of DMS in the release medium (times,  $M_0 \neq 0$ )

$k_0$  kinetic zero order release constant (conc./ time)

**First order model:** This equation was used to explain DMS absorption and/or elimination of DMS. The DMS release profile followed first order kinetics model can be expressed by the equation IV:

$$\ln(M_0/M_t) = k_1 t \dots\dots\dots (IV)$$

$K$  rate constant of first order ( $\text{time}^{-1}$ ).

**Higuchi model:** This model was used to explain DMS release from the matrix, in which understanding the DMS release from the matrix and obtained data were calculated by given equation V.

$$M_t = k\sqrt{t} \dots\dots\dots (V)$$

Where,  $k\sqrt{t}$  Higuchi dissolution constant.

**Korsmeyer-Peppas model:** The proposed equation explains release of drug from polymer system. To find out release mechanism of DMS and obtained data were calculated by as per the given equation VI.

$$M_t / M_\infty = Kt^n \dots\dots\dots (VI)$$

$M_t / M_\infty$  drug released fraction at time  $t$ ,

$K$  rate release constant

$n$  release exponent.

**Hixson-Crowell model:** This model was accepted that area of the particle is proportional to the volume of cube root and obtained data were calculated by as per the given equation VII:

$$(W_0)^{1/3} - (W_t)^{1/3} = kt \dots\dots\dots (VII)$$

Where,  $W_0$  Initial quantity of DMS and  $W_t$  refer to the quantity of remaining DMS at time  $t$  and  $k$  constant incorporating the surface-volume relation.

### 2.2.12 Stability study of the DE3 emulgel formulation

The stability study of the emulgel (DE3) formulation was carried out as per international conference on harmonization (ICH) guideline for 6 month period. The optimized DE3 emulgel formulation kept at accelerated temperature  $40^\circ\text{C} \pm 2^\circ\text{C} / 75\% \text{RH} \pm 5\% \text{RH}$ . The initially determination of drug content of optimized DMS emulgel formulation and at an interval of the first, second, third and six months. (Kumar, L., et. al. (2011).

### Statistical Analysis

All results interpreted are showed as mean  $\pm$  SD. The means were separated by Duncan's multiple range test (DMRT) at  $p \leq 0.05$ .

### 3.0 Result and Discussion:

#### 3.1 Determination of globule size, extrudability and pH:

The result of average globule size of DMS emulgel formulation (DE) was obtained in the range from 10.17 to 14.60  $\mu\text{m}$ . The DE3 extrudability was more as compared to other formulation because higher concentration of emollient was presence in DE3. The extrudability of DMS emulgel formulation was based on the concentration of emollient. The DE3 and DE2 showed good extrudability. The pH determination of DMS emulgel formulation was performed by calibrated pH meter (Mettler-Toledo India Pvt. Ltd. amar hill Mumbai (Maharashtra), India). The first priority of based topical formulation is compatibility of skin. The result of globule size, extrudability and pH value was noted at average of three samples in **Table 2**.

#### 3.2 Determination of drug content of formulated batches of emulgel formulations

Determination of percentage drug contents of prepared emulgel formulations was done by UV spectrophotometer (Shimadzu 1700, Shimadzu analytical Pvt. Ltd., (Mumbai) India). The observed absorbance data was measured and calculated percentage drug content. It was observed that DMS emulgel formulations DE2 showed 92.30% $\pm$ 0.21, and DE3 showed 94.06% $\pm$ 0.29, which is within the pharmacopoeia limits (**Table 2**). **Hence DE2 and DE3 formulations were selected for % cumulative drug release and drug permeation study.**

#### 3.3 In vitro release study of optimized DMS emulgel:

The emulgel formulation DE3 showed better drug release as instead of formulated DE2. 7h diffusion studies disclosed that the DMS release from emulgel was dependent on the concentration of aloe vera as a gel base and propylene glycol as penetration enhancer. The DE3 formulation showed 87.84 $\pm$ 2.5% release in 7 h. Therefore, DE3 formulation was selected as optimized formulation and further used in vitro DMS permeation study through the cellophane membrane. The percentage cumulative DMS release was analyzed and reported in **Table 1S** and graphically presented in **Fig. 2**.

#### 3.4 In vitro permeation study by franz diffusion cell

The emulgel formulation DE3 exhibited higher DMS permeation instead of DE2 formulation. The result showed that the drug permeation was found to be 95.40 $\pm$ 1.6 consistent for 7 hr. of study period. The DE3 was therefore selected as optimized emulgel formulation for firmness, cohesiveness, consistency and viscosity studies. In vitro permeation data was showed in **Table 2S** and graphically represent in **Figure 3**.

#### 3.5 Evaluation of consistency, cohesiveness, viscosity and firmness of optimized emulgel formulation

Consistency, cohesiveness, viscosity and Firmness of optimized emulgel formulations of DMS (formulation code DE3 & DE2) were measured using texture analyzer. Emulgel formulation DE3 was found firmer, cohesive, and had a superior consistency than formulation DE2. The Firmness showed maximum positive force 67.604 g, maximum negative area showed cohesiveness of DMS emulgel was found to be -49.480 g, the consistency value of DMS emulgel was showed mean positive area of curve 591.697 g.sec and the mean area negative

index of viscosity was found to be 450.153 g.sec of optimized emulgel formulations of DE3 was superior consistency as compared to DE2 formulation were measured using texture analyzer. The results were representing in **Table 3** and graphically represents in **Figure 4 & 5**.

### **3.6 Determination of Spradability:**

Spreadability of optimized emulgel formulations of DMS (formulation code DE3 & DE2) was determined. Emulgel formulation DE3 was found to be firmer and had desired optimal spreadability as compared to formulation DE2 as evident by the very high value of mean maximum force showed '*firmness*' 833.37g and Mean area '*work of shear*' 324.230g.sec. showed in **Table 4**. Spradability graph of optimized formulation of DMS emulgel represents in **figure 6 and 7**.

### **3.7 In-vitro release kinetics model optimized emulgel formulation**

The best model for release kinetic of optimized emulgel formulation was determined as per the regression data. The zero order model was showed regression value 0.996 (**Figure 8A**). The regression value of first order model exhibited 0.926 (**Figure 8B**). The regression value of Higuchi kinetic model showed 0.941 (**Figure 8C**). The Korsmeyer Peppas model indicates regression value was found to be 0.972 (**Figure 8D**). The regression value of Hixon Crowell model was found to be 0.967 (**Figure 8E**). All above the model having regression was found to be below 1. The first 60% DMS release data were fitted in Korsmeyer Peppas model so that the release mechanism was obeyed Korsmeyer Peppas model and confirmed the release of DMS by diffusion mechanism. Release data of DMS emulgel are tabulated in **Table 3S**.

### **3.8 Stability study of the emulgel formulation**

The stability data indicates that emulgel formulation is stable for six months study period. The results were showed in **Table 5**.

### **4.0 Study Limitation:**

The formulation of DMS gel was shown higher drug release instead with traditional DMS ointment and DMS cream. Instead of several benefit of gels the huge task to delivery of water insoluble drug so that the aim of this study present conventional to prepared DMS emulgel. The present invention is aimed to formulate the DMS emulgel using aloe vera to be safe to use, non-sensitive, non-irritant, good spreadability and penetrability across the skin. So that the present invention of this study to formulate and optimize DMS emulgel using herbal aloe vera gel. Emulgel is used to help better in delivering the DMS drug deep into the skin. In this way, the study limitation further relates to methods for making and using such compositions.

### **5.0 Conclusions**

In the present investigation, aloe vera based topical emulgel of DMS is optimized, formulated and characterized as an attractive option for local delivery of DMS to the skin. The developed formulation presented an attractive option for better patient compliance, long contact time at the site of desire, and ease of use. DE3 formulation was found to adhered to biological membrane for extend period of time and releases drug for effective treatment of plaque psoriasis. As compared to the traditional formulations such as ointment and cream better contact time was achieved using DE3 formulation. Finally, it could be stated that the aloe vera based emulgel formulation of DMS can be developed to overcome the skin barriers to effectively treat the plaque psoriasis. However, further development as commercial formulation warranted in-vivo and clinical studies.

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**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 denoted desoximetasone emulgel*

**TABLE 2:**  
**Globule size, extrudability, pH determination and drug contents of developed emulgel formulation**

S.No.	Formulation Code	Globule Size ( $\mu\text{m}$ ) (n=50)	Extrudability ( $\text{g}/\text{cm}^2$ )	pH	Drug content (%) (n=3)
1.	DE1	12.21 $\pm$ 1.3	5.4 $\pm$ 0.15	5.8	83.74 $\pm$ 0.64
2.	DE2	10.34 $\pm$ 0.9	5.6 $\pm$ 0.11	6.4	92.30 $\pm$ 0.21
3.	DE3	10.17 $\pm$ 0.5	5.8 $\pm$ 0.13	6.2	94.06 $\pm$ 0.29
4.	DE4	14.60 $\pm$ 1.4	4.4 $\pm$ 0.26	6.8	87.37 $\pm$ 0.82

*Average globule size, extrudability, pH determination, drug contents of various formulation codes. The globule size results are showed as Mean  $\pm$  SD (n=50). The extrudability results are presented as Mean  $\pm$  SD (n=3). The pH of All emulgel formulations of DMS were acceptable for avoiding the risk of skin irritation and drug content is important to determine to assess topical dosage form performance. The results are presented as Mean  $\pm$  SD (n=3).*

**TABLE 3 :**  
**Consistency study of optimized emulgel formulations of DMS (formulation code DE2 and DE3)**

S. No	Formulation code	Mean max. +ve force 'firmness' (g)	Mean +ve area 'consistency' (g.sec)	Mean max. -ve force 'cohesiveness' (g)	Mean -ve 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

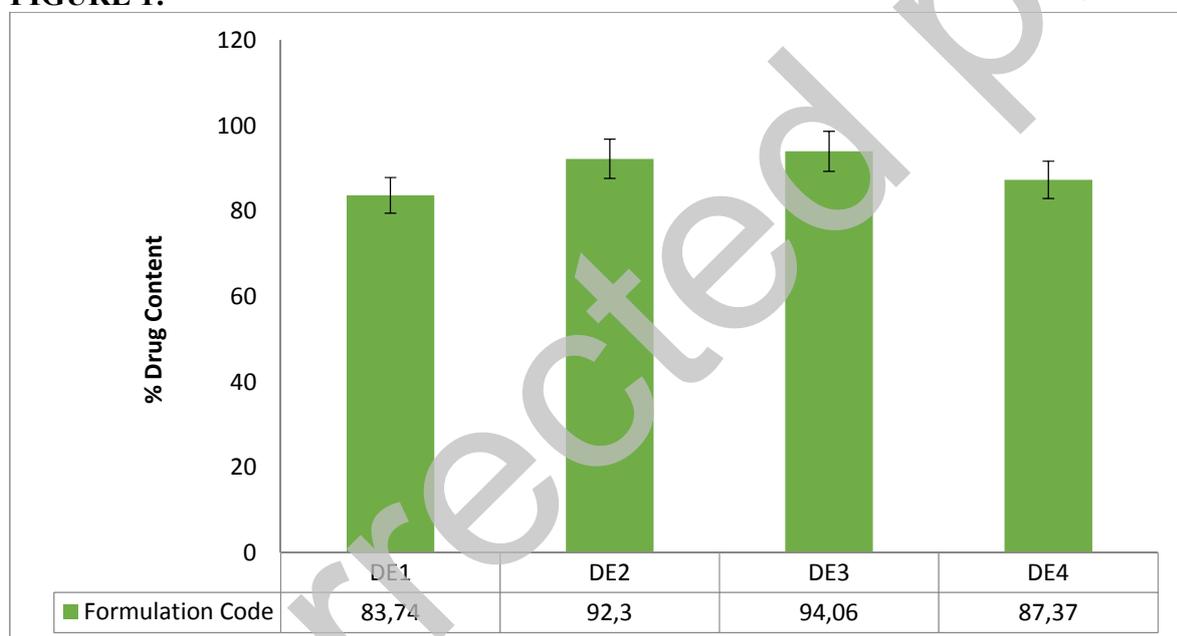
**TABLE 4 :**  
Spradability study of optimized emulgel formulations of DMS (formulation code DE2 and DE3)

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

**TABLE 5:**  
**Preliminary stability study of the emulgel formulation of DMS (formulation code DE3)**  
**(n=3)**

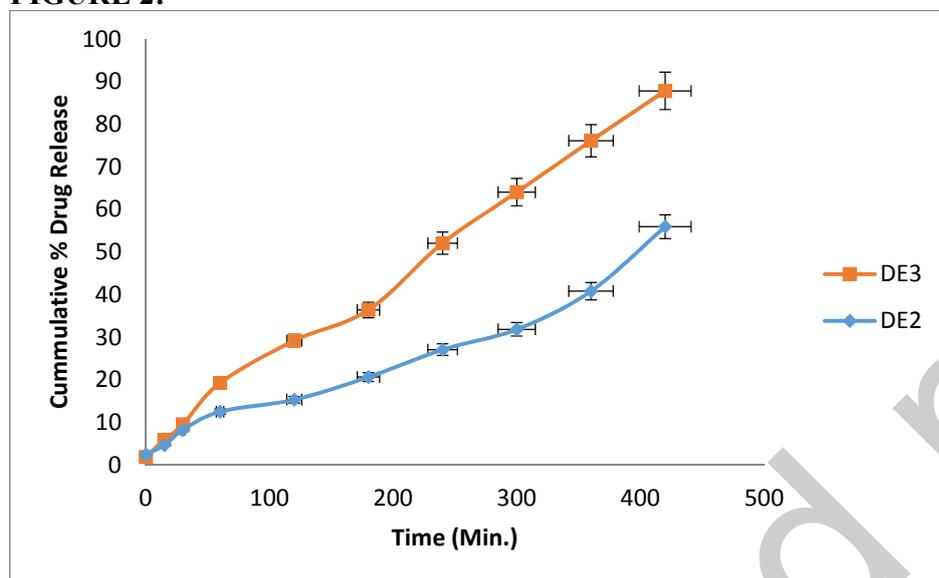
Storage condition	Assay (%)				
	0 day	one month	Second Month	Third Month	Six Month
40°C±2°C/75%RH±5%RH	98.86(±0.57)	97.68(±0.37)	96.74(±1.3)	96.03(±.04)	94.73(±0.5)

**FIGURE 1:**



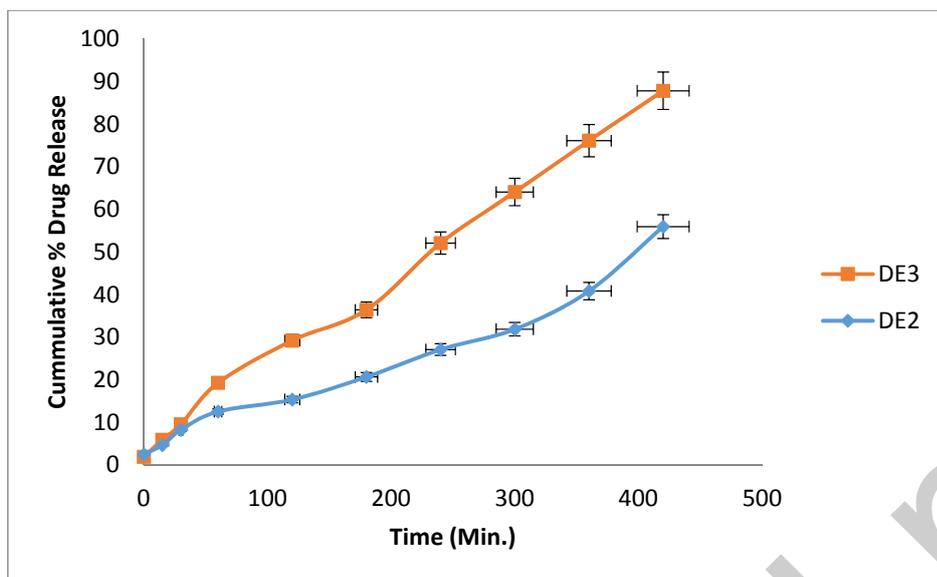
**Figure 1:** Drug Content of prepared emulgel contain DE3 is greater than the other formulation but with non-significant difference ( $P < 0.01$ )

**FIGURE 2:**



**Figure 2:** *In vitro* % Cumulative release study modified dissolution assembly was employed. Developed emulgel formulation DE3 showed better drug release as compared to formulated DE2. Values are represented as mean  $\pm$  SD ( $n = 3$ ).

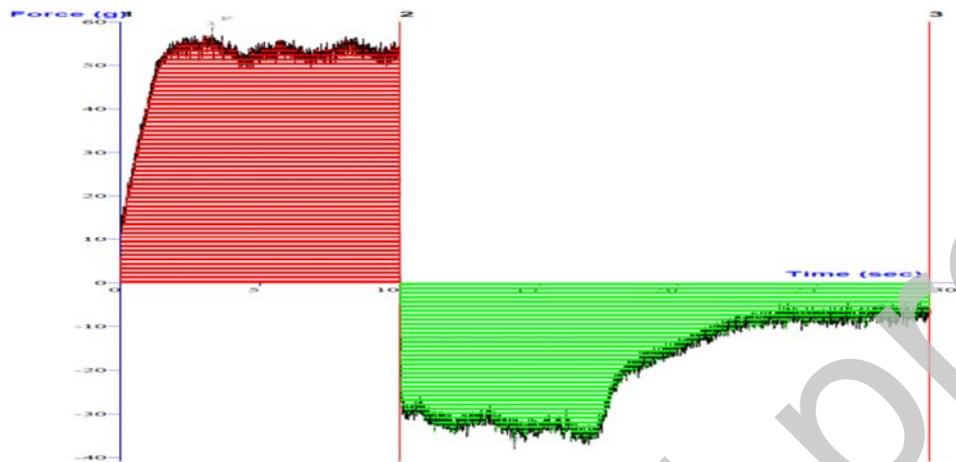
**FIGURE 3:**



**Figure 3: In vitro permeation study by franz diffusion cell**

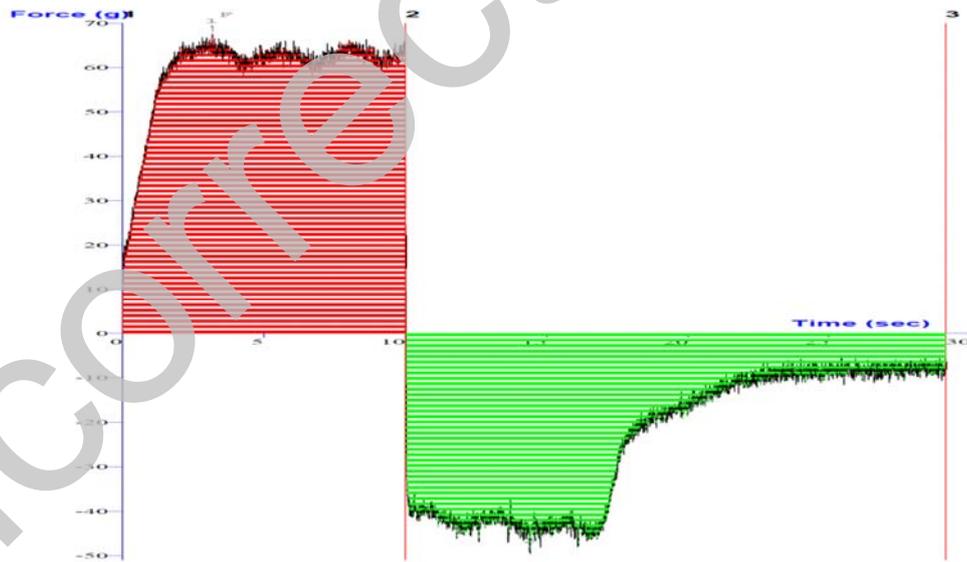
Permeation rate of DMS emulgel for DE3 and DE2 formulation was performed by franz diffusion cell and phosphate buffer pH 7.4 was selected as drug diffusion medium. The cellophane membrane selected for permeation study at temperature  $37 \pm 0.5$  °C and The data are presented as Mean  $\pm$  SD (n=3).

**FIGURE4:**



**Figure4: Consistency graph of emulgel formulation of DMS (formulation code DE3)**

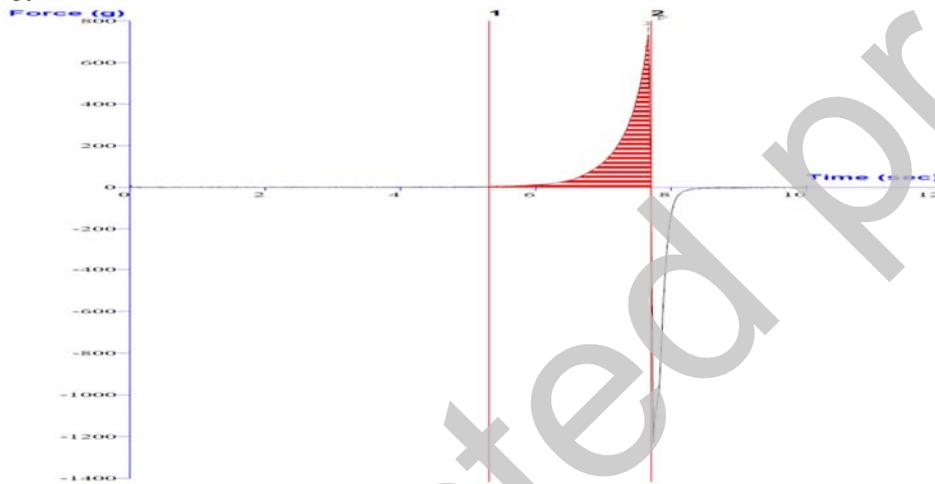
**FIGURE 5:**



**Figure 5:**

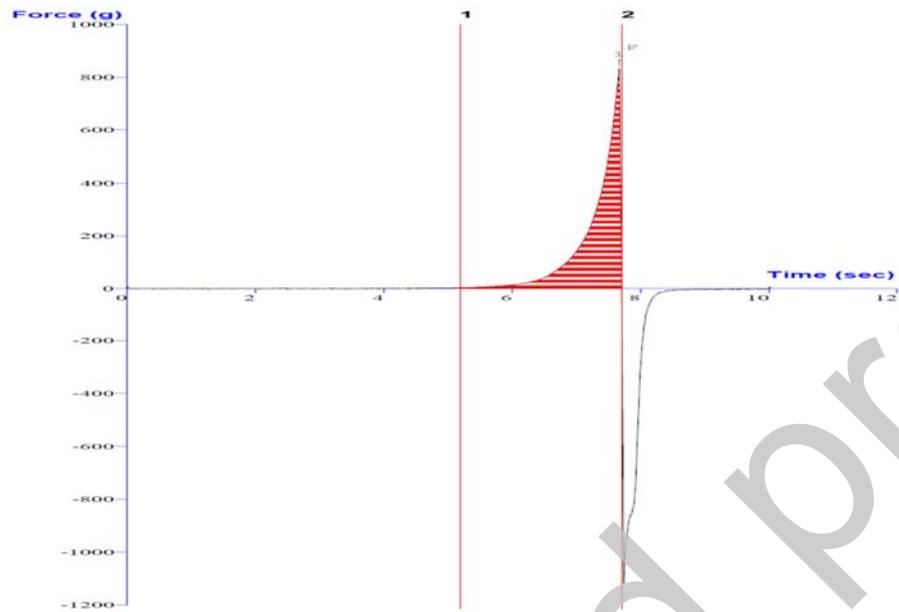
**Consistency graph of optimized emulgel formulation of DMS (formulation code DE2)**

**FIGURE 6:**



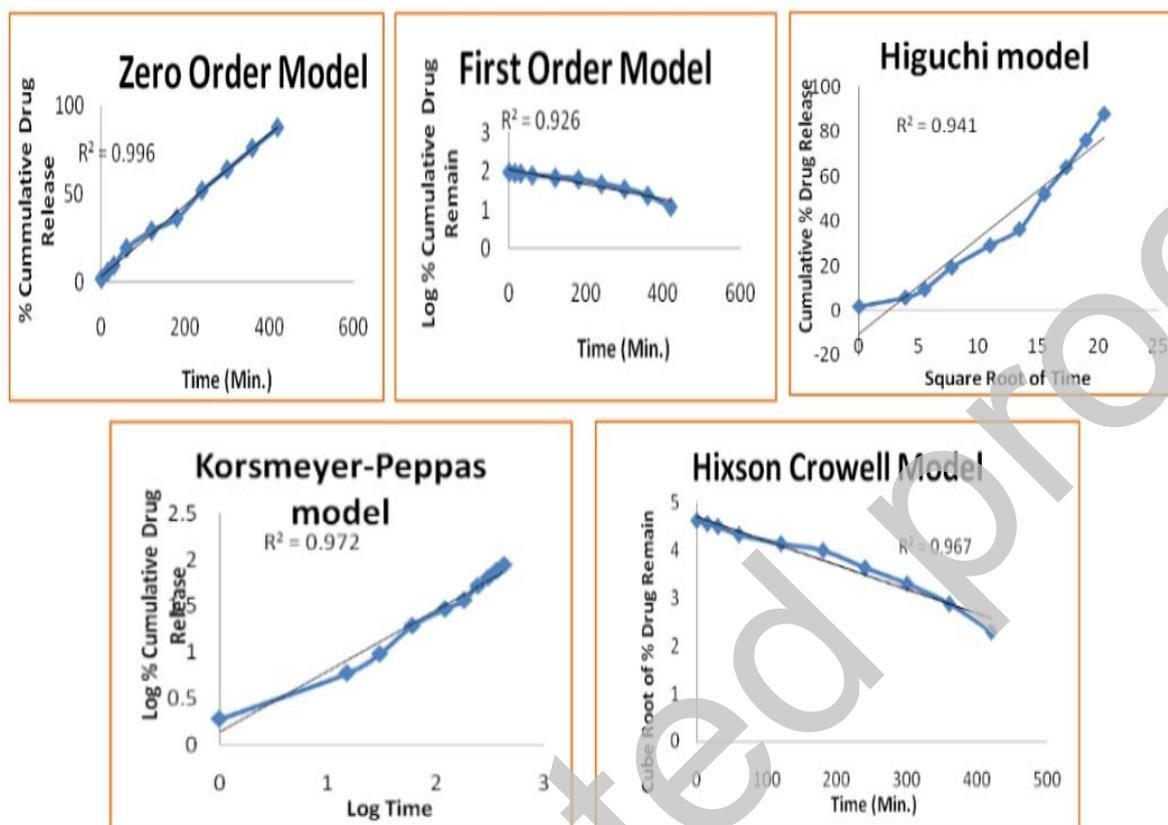
**Figure 6: Spreadability graph of optimized emulgel formulation of DMS (formulation code DE2)**

**FIGURE 7:**



**Figure 7: Spreadability graph of optimized emulgel formulation of DMs (formulation code DE3)**

**FIGURE 8:**



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

Uncorrected proof