Research Article

# Formulation, Optimization And Evalution Of Desonide Loaded Emulgel For Atopic Dermitis By Using 2 Factor 3 Level Full Factoreial Design

Kiran Kaithwar, Vaishali Patidar, Sapna Saini,Dr.Aakash Singh Panwar

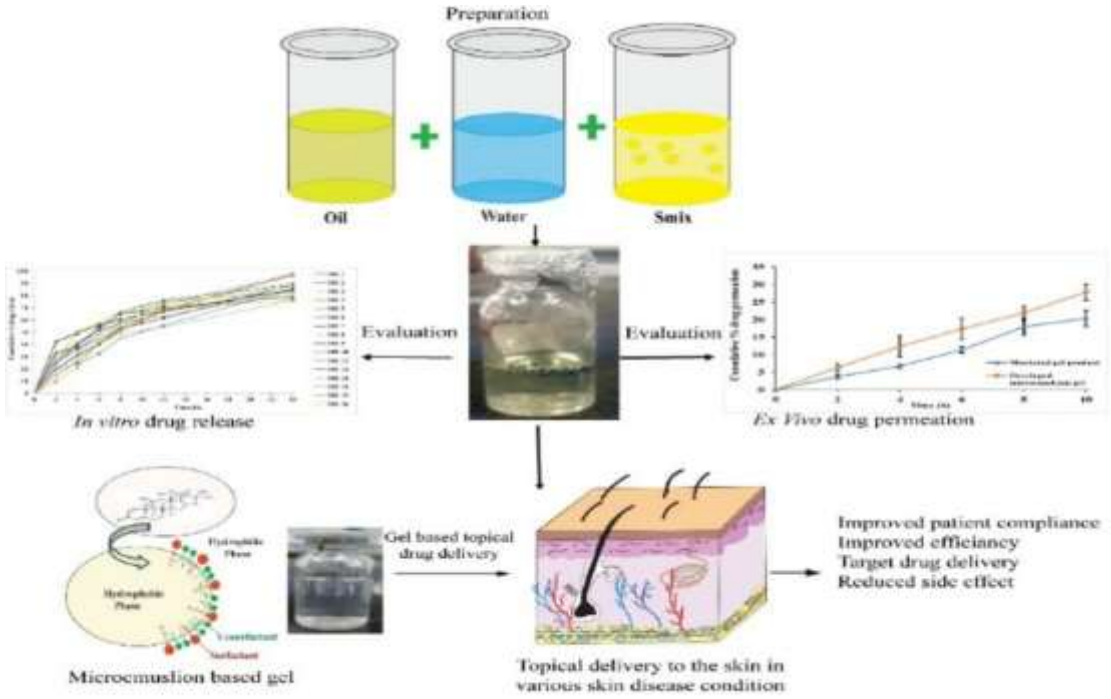
Department of Pharmaceutics, Institute of Pharmaceutical Sciences
Sage University, Indore
kiran.kaithwar@sageuniversity.in

**ABSTRACT**

**Objective:** This research specifically targets the development of a microemulsion formulation with critical quality attributes, i.e., optimal particle size distribution, drug content, and controlled release characteristics. The aim is to enhance the topical delivery of desonide.
**Method:** Oil selection was carried out using the phase titration method for determining the appropriate $S_{mix}$ ratio, followed by the construction of ternary phase diagrams. A Factorial design was employed, considering oil, $S_{mix}$ as independent variables, while particle size, polydispersity index (PDI), zeta potential, % transmittance, and cumulative % drug release (CDR %) as response variables.
**Results:**The optimized microemulsion was clear and transparent with aPS 18nm, PDI 0.42, zeta potential 13.00mV, and transmittance of 92.25%. This microemulsion was incorporated into a 2% Carbopol 971P gel base. The resulting gel was clear, pH 6.02, with a spreadability of 23.379g.cm/sec, CDR (%) of 94.03% in 24 h. followed Higuchi drug release kinetics. Ex vivo drug permeation through porcine skin was 27.83 % in 10 h., showingenhanced permeation when compared with the marketed product.
**Conclusion:** The developed gel possessed all desired quality attributes. The data obtained from in vitro and ex vivo studies validated its efficacy as an improved option over conventional products for the treatment of skin diseases.

**Keywords:** Desonide, microemulsion,Factorial design, topical gel.

**GRAPHICAL ABSTRACT**




**Formulation design and optiization of microemulsion based gel of desonide**

## INTRODUCTION

Skin conditions affect millions of individuals globally, accounting for a large proportion of the global total of disease(1). Atopic dermatitis, eczema, is a widespread chronic inflammatory skin disorder affecting children and adolescents(2, 3), with 20% of cases affecting this age group. Symptoms often emerge in infancy, with 70% of

cases manifesting before the age of 5(4). Atopic dermatitis is often the initial stage of the "allergic march," a sequential progression of allergic conditions. Psoriasis is an inflammatory immune-mediated illness affecting the skin and joints, with autoimmune pathologic characteristics(5). Acne is an enduring disorder affecting oil glands and hair sacs, with emerging evidence indicating that acne development involves an interplay of genetic predisposition(6), environmental factors, and saprophytic gram-positive bacteria. Vitiligo is a prevalent skin syndrome characterized by the impairment of complexion, with non-scaly chalky-white patches on the skin(7).
The skin is the most commonly used route due to its accessibility and large surface area. These systems offer advantages like non-invasiveness, ease of use, and reduced systemic side effects compared to oral or injectable methods(8). Gels are widely used due to their safety, effectiveness, and patient-friendly nature(9). An effective formulation must be stable, aesthetically acceptable, capable of drug release at the target site, and manufacturable at a commercial scale(10).
Topical corticosteroids are now essential for treating a variety of dermatoses(11). Desonide is a topical corticosteroid used to minimize redness, swelling, and itching caused by skin conditions that respond to steroids. It is a synthetic non-fluorinated corticosteroid used to treat various skin conditions(12). Desonide's pharmacodynamics include anti-inflammatory, anti-itching, and blood vessel constricting action(13).
Microemulsions, introduced by Hoar and Schulman in 1940, are clear mixtures containing oil, aqueous, and emulsifying agents for pharmaceutical administration(14). They enhance absorption and therapeutic efficiency, and have long-term physical stability(15).Microemulsions are classified into water-in-oil and oil-in-water types. In W/O emulsions, water droplets are dispersed in an oil continuous phase, while in O/W emulsions, oil droplets are dispersed in a water continuous phase. The continuous phase defines the emulsion type, with the other acting as the dispersed phase(16). Microemulsions can be made using two main techniques(17, 18).
The present research aims to develop a microemulsion based topical gel of desonide using factorial design assisted formulation optimization with an objective to increase skin retention, sustained drug release, enhanced drug permeation and effective topical drug delivery.

## MATERIALS AND METHOD

### Materials

Desonide was obtained as a gift sample from Farambios. Peppermint oil was purchased from local market, Tween 80 was purchased from Merck Life Science Pvt Ltd., India. Cremophor RH 40 was received from BASF (India) and Carbopol 971P from Lubrizol (India). Marketed desonide gel (0.05% w/w) was obtained from a local pharmacy. All others chemicals used in the study were of standard grade.

## Methods

### Formulation and designing of desonide based microemulsion

To select the appropriate oil, desonide solubility was determined via a saturation method, where the drug was incrementally added to 1 mL of each oil until no further dissolution occurred, and the undissolved residue was weighed. For surfactant selection, each candidate was prepared as a 10% solution in deionized water, followed by gradual oil addition with vertexing after every 10 µL until a milky appearance indicated the oil-loading capacity limit. Similarly, cosurfactants were evaluated by gradually adding oil to a 1:1 mixture of the selected surfactant and each cosurfactant in aqueous solution, with vertexing after each 10 µL oil addition until turbidity developed.

### Construction of pseudo ternary phase diagram for the formulation of desonide microemulsion

Purified water, peppermint oil, and different $S_{mix}$ ratios (surfactant + cosurfactant) were mixed in various proportions. The Smix ratios tested were 1:1, 1:2, 1:3, 2:1, and 3:1, each mixed with oil in nine different ratios. Water was added drop by drop until the mixture turned cloudy or milky, which helped create a pseudo-ternary phase diagram.

## Formulation optimization by factorial design

Design expert 13 software was used for the experimental design in this study. A factorial design is an experimental approach, commonly used in statistics and scientific research, to examine the impact of two or more independent variables (called factors) at the same time. Two different independent variables were administered at maximum and minimum levels: A (oil), B ($S_{mix}$) shown in table no.5 and their observed response in table no.6

**Table 1:Independent and response variables of factorial design**

| **Independent variable** | **Unit** | **Limit** | |
|---|---|---|---|
| | | Lower limit | Higher limit |
| Oil | ml | 2 | 4 |
| Smix | ml | 5 | 10 |
| **Response Variable** | **Unit** | **Desired constraints** | |
| Particle size | Nm | Target | |
| Polydispersity index | - | Minimum | |
| Zeta potential | mV | Maximum | |
| Transmittance | % | Maximum | |
| Cumulative % drug release | % | Maximum | |

**Table: 6 Full Factorial design based microemulsion formulations and their observed response**

| **S.No.** | **Factors** | | **Response variable** | | | | |
|---|---|---|---|---|---|---|---|
| | **Oil (ml)** | **$S_{mix}$ (ml)** | **Globule size (nm)** | **Zeta Potential(mV)** | **PDI** | **Transmittance %** | **CDR % at 24 h** |
| DS/ME/01 | 10 | 4 | 18 | 1.67 | -23 | 89 | 84 |
| DS/ME/02 | 5 | 2 | 39 | 1.23 | 12 | 98 | 80 |
| DS/ME/03 | 10 | 2 | 89 | 1.02 | -19 | 87 | 96.57 |
| DS/ME/04 | 5 | 2 | 18.5 | 0.82 | 21 | 90 | 94 |
| DS/ME/05 | 10 | 2 | 55.3 | 1.45 | 10 | 88 | 91 |
| DS/ME/06 | 5 | 4 | 88 | 1.06 | 36 | 85 | 87.34 |
| DS/ME/07 | 5 | 4 | 55.3 | 0.43 | 26 | 87 | 83.87 |
| DS/ME/08 | 10 | 4 | 23 | 1.09 | 15 | 89 | 85.1 |

**Development of a topical gel formulation of desonide**

For enhanced topical utility, the optimized microemulsion was incorporated into a gel formulation. Gelling agents are employed to enhance the viscosity of microemulsion systems, thereby improving their adherence to the skin and prolonging their residence time. In the formulation of the gel base, several polymers were utilized including Carbopol 934,Carbopol 940,Carbopol 971P at concentrations of 2,2.5 and 3% as well as xanthan gum 1% and polycarbophil 2%. These polymers were hydrated in water for a period of 12 hours to ensure full swelling.A microemulsion-based gel was prepared by combining the optimized desonide microemulsion with the gel base.

## RESULTS AND DISCUSSION

**Selection of microemulsion components**

Based on solubility screening, peppermint oil showed the highest desonide solubility (35 mg/mL) and was chosen as the oil phase. Among surfactants with HLB >10 suitable for O/W microemulsions, Cremophor RH 40 provided superior emulsification and the greatest peppermint oil solubilization capacity. For the co-surfactant, various candidates were combined with Cremophor RH 40 at a 1:1 ratio, the Cremophor RH 40/Tween 80 mixture enabled the highest oil incorporation, leading to the selection of Tween 80 as the co-surfactant for the optimized formulation.

**Selection of optimum $S_{mix}$ ratio by the pseudo-ternary phase diagram**

Pseudo-ternary phase diagrams were constructed using peppermint oil, water, and various $S_{mix}$ ratios (1:1 to 3:1) of Cremophor RH 40:Tween 80. The 2:1 $S_{mix}$ ratio produced the largest clear (microemulsion) zone, occupying 61.66% of the diagram, and was therefore selected as the optimal composition.

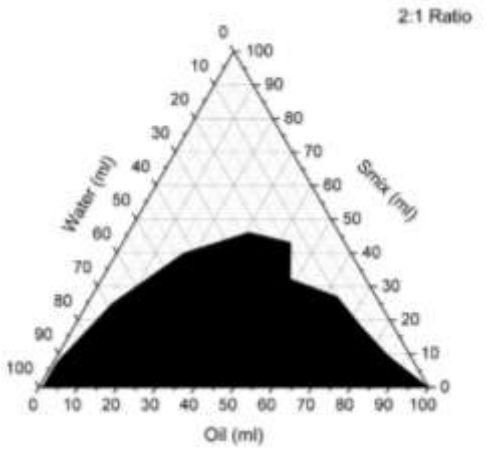



**Fig. 1: Pseudo-ternaryphasediagram ofmicroemulsionusing 2:1 $S_{mix}$ratio**

**Optimization of desonide based microemulsion formulation**

Desonide microemulsions were formulated using a factorial design and phase titration method with varying oil, Smix, and water ratios. Optimization constraints included target particle size (R1), minimized PDI (R2), maximized zeta potential (R3), % transmittance (R4), and drug release, with 3D response surface plots illustrating the effects of independent variables on each response.

**Effect of the independent variables on Globule size,polydispersity index, zeta Potential, transmittance and drug release**

Globule size =48.2625-1.9375A-2.1875B-23.6375AB

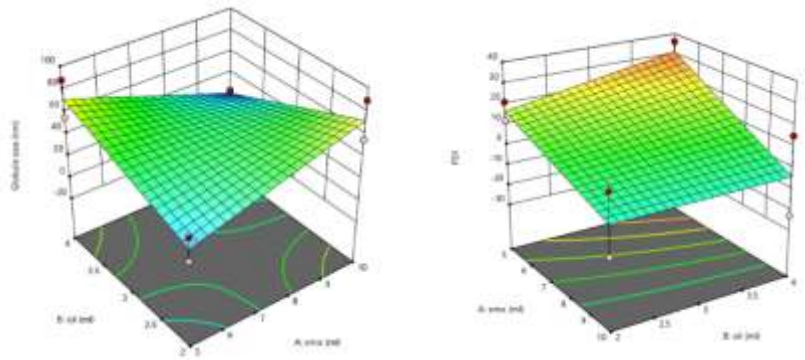
PDI=9.75-14A + 3.75 B-3.5AB

Zeta Potential =1.09625+0.21125A-0.03375B+0.10625AB

Transmittance=89.125-0.875A-1.625B+2.375AB

Drug release =87.7351+ 4325A-2.6575B-1.96AB

The 3D response surface plots reveal that globule size, PDI, zeta potential, transmittance, and drug release are primarily influenced linearly by Smix and oil concentrations, with minimal interaction between the two variables. Globule size increases with both factors, while PDI decreases with Smix but rises with oil. Zeta potential and drug release increase with higher Smix and oil levels, whereas transmittance increases with Smix but decreases with oil. The nearly planar surfaces and parallel contour patterns across all responses confirm predominantly additive, main-effect-driven behaviours with negligible synergistic or antagonistic effects.



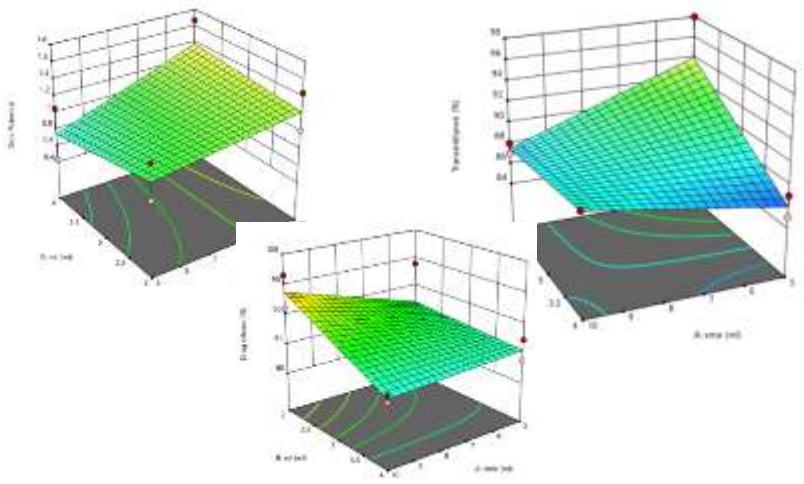


**Fig.2:3D surface plots demonstrating the impact of oil (A), $S_{mix}$(B)on globule size,polydispersity index,zeta potential, transmittance, drug release**

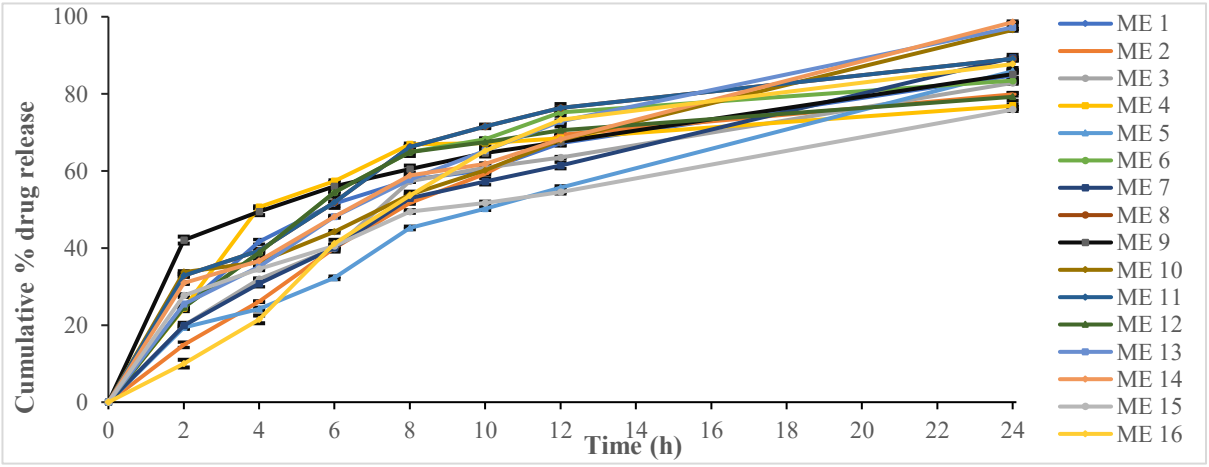



**Fig.11: Invitro drug release studies for Preliminary trail batches**

**Characterization of desonide-based microemulsion**

## Particle size, polydispersity index, and zeta potential

The optimized microemulsion exhibited a droplet size of 18 nm, which remained within the nanometric range even after 100-fold dilution, indicating good compatibility with water. A PDI of 0.42 confirmed a relatively uniform droplet size distribution, while the zeta potential of +13.00 mV suggested acceptable stability and suitability for topical application.

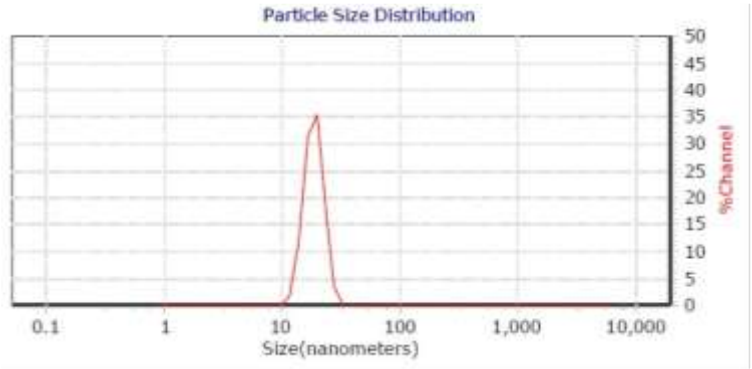


**Fig.3: Globule size distribution of optimized microemulsion formulation**

## Determination of % transmittance

The optimized formulation of desonide had been diluted 10 times with a continuous phase. The % transmittance of the optimized formulation was found to be 92.25%.

## Transmission electron microscope (TEM) analysis

The TEM image spherical droplets with an average diameter of approximately 10-20 nm and doesnot show any aggregation between particles.

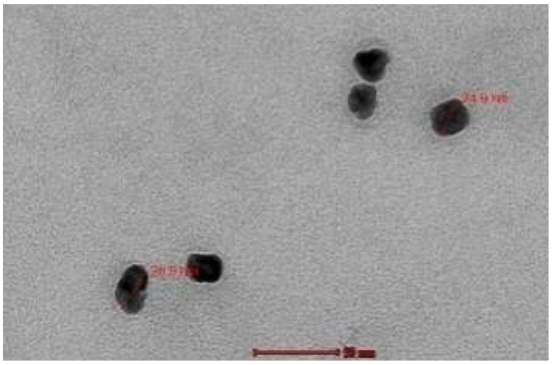


**Fig.4: TEM image of optimized microemulsion**

## DSC study

The DSC thermogram of pure desonide revealed a distinct endothermic peak which corresponds to its melting point, likewise carbopol 971P showed no sharp melting peak, since carbopol is amorphous is nature and the physical mixture (desonide andcarbopol 971P) The Desonide peak is slightly shifted and/or reduced in intensity, which suggests Partial dispersion of Desonide in the polymer matrix and no new peaks appear, indicating no chemical interaction.

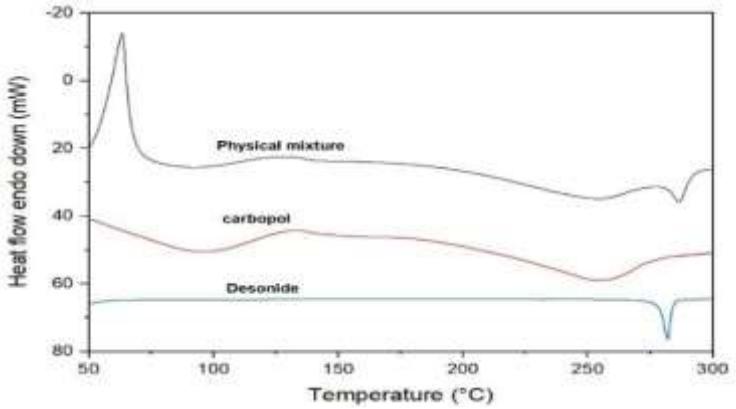



**Fig.5:DSC thermograph of desonide, carbopol 971Pand physical mixture**

## In vitro drug release study

The in vitro drug release of the optimized desonide microemulsion was evaluated using a dialysis membrane method in PBS pH 7.4 containing 1% SLS at 37°C. Samples were withdrawn at predetermined intervals up to 24 hours and analyzed for desonide content using a UV–Visible spectrophotometer at 247 nm, with fresh medium added to maintain sink conditions.

**Development and Formulation of desonide based microemulsion gel**

Various gelling agents were evaluated to convert the optimized desonide microemulsion into a gel and improve its skin retention. Among the tested polymers, only Carbopol 971P successfully formed a clear and transparent microemulsion gel, while Carbopol 934, Carbopol 940, xanthan gum, and polycarbophil failed to produce a suitable gel system.

**Evaluations of a developed microemulsion based gel formulation of desonide**

## Physical appearance

The formulation appeared clear and uniform upon observation, with no presence of lumps or phase separation. These findings confirm the physical homogeneity of the gel, indicating proper formulation and stability.

## pH determination

The pH value recorded for the gel was 6.02, which is within the typical physiological range of the skin. This compatibility suggests that the formulation is unlikely to cause a reactionupon local application making it acceptable for dermal use.

## In vitro drug release and kinetic model fitting

Over a 24-hour in-vitro release study(19), the desonide microemulsion gel exhibited a total drug release of 94.32%, while the marketed gel formulation released 77.32% as shown fig.6.This significant difference in release profiles suggests that the microemulsion-based gel enables more efficient and sustained drug delivery. The in vitro release profile of desonide from the microemulsionformulation was systematically analyzed using five distinct kinetic models to elucidate the mechanism and pattern of drug release. Each offering a different theoretical approach to interpreting drug release behavior from pharmaceutical dosage forms facilitates visual comparison of model fitting. The $R^2$ values for the various kinetic models and were found to be in the range of zero-order (0.875), first order (0.978), Higuchi (0.985), Hixson-Crowell (0.984), Korsmeyer-Peppas (0.935) as shown intable 2.It is clear that the drug release of desonide from the microemulsion based gel properly complies with the Higuchi model because the drug release profile showed the best fit to the regression line, with the highest $R^2$ value($R^2$) of 0.985.

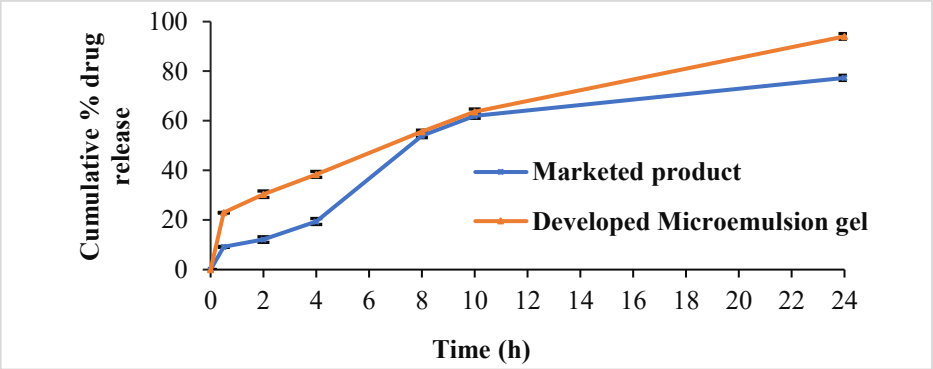



**Fig. 6: Comparative in vitro release of developed microemulsion based gel formulation of desonide with marketed gel product**

**Table 2:Kinetic behaviour of developed desonide based microemulsion gel**

| S. No. | Drug release kinetic model | Equation | k | R2 |
|---|---|---|---|---|
| 1. | Zero-order | Q0 – Qt = k0t | 0.05 | 0.875 |
| 2. | First order | log Qt = logQ0 – kt/2.303 | 0.01 | 0.978 |
| 3. | Higuchi | Q0 – Qt = kt1/2 | 2.36 | 0.985 |
| 4. | Hixson-Crowell | Q01/3 – Qt1/3 = kt | 0.02 | 0.984 |
| 5. | Korsmeyer-Peppas | Log (Q0 – Qt) = log k + n log t | 0.57 | 0.935 |

k is rate constant; t is time; $Q_0$ is initial drug amount; Qt is drug amount remaining at time

## Exvivo drug permeation of the developed gel formulation

When compared to the commercially available desonide formulation over a 10-hour duration. The cumulative permeation achieved by the marketed product was 20.42 % whereas the microemulsion-based gel reached 27.83 %. A graphical comparison of ex vivo drug permeation between the formulated product and the marketed counterpart is presentedinfig.7and as shown in

table **3**.The apparent permeability (Papp) and permeation flux (Jss) of the developed formulation were found to be 2.017(μg·cm$^{-2}$·h$^{-1}$) and 0.2017(cm·s$^{-1}$) respectively,the developed formulation provides a 4% enhancement in Jss and a 5% enhancement in Papp compared to the marketed product.

**Table 3:Ex-vivo drug permeation data of developed formulation and marketed product**

| S. No. | Sample | Jss (μg·cm$^{-2}$·h$^{-1}$) | Papp (cm·s$^{-1}$) |
|---|---|---|---|
| 1. | Developed formulation | 2.01 | 0.20 |
| 2. | Marketed product | 1.94 | 0.19 |

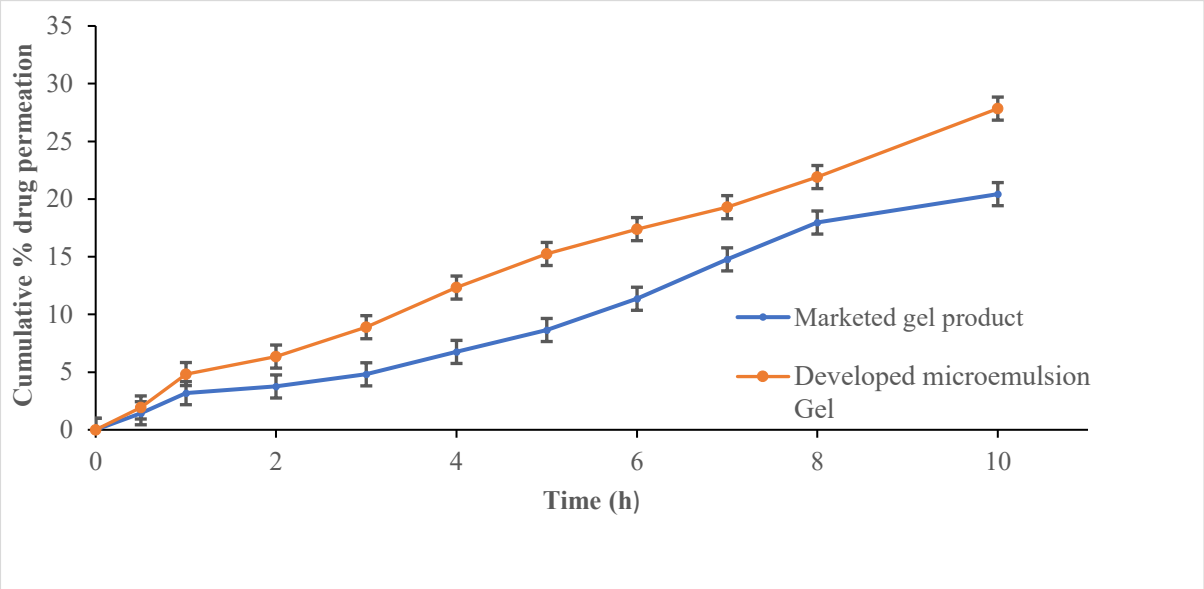



**Fig.7: Ex vivo permeation profile of microemulsion based gel formulation and marketed gel product**

## CONCLUSION

An optimized, sustained-release microemulsion for desonide was developed. The formulation met all quality targets, including particle size and drug release. The release was sustained and followed the Higuchi model, demonstrating its potential for effective topical delivery.Exvivo permeation studies revealed that the optimized gel enhanced drug permeation compared to the marketed formulation, suggesting potential benefits for improved localized therapy, patient compliance, and therapeutic outcomes.Its favourable characteristics, such asphysical stability, ease of use, and better skin retention, contribute to enhanced patient adherence and satisfaction. Moreover, the sustained release profile supports once-daily application, improving treatment outcomes for chronic inflammatory skin disorders.

## REFERENCES

1. Sawada Y, Saito-Sasaki N, Mashima E, Nakamura M. Daily Lifestyle and Inflammatory Skin Diseases. Int J Mol Sci. 2021;22(10):5204.
2. Hebert AA, Group DFPICS. Desonide foam 0.05%: safety in children as young as 3 months. JAAD. 2008;59(2):334-40.
3. Akhtar N, Verma A, Pathak K. Exploring preclinical and clinical effectiveness of nanoformulations in the treatment of atopic dermatitis: Safety aspects and patent reviews. B-FOPCU. 2017;55(1):1-10.
4. Mayba JN, Gooderham MJ. Review of atopic dermatitis and topical therapies. J Cutan Med Surg. 2017;21(3):227-36.
5. Grän F, Kerstan A, Serfling E, Goebeler M, Muhammad K. Current Developments in the Immunology of Psoriasis. Yale J Biol Med. 2020;93(1):97-110.

6. Antiga E, Verdelli A, Bonciani D, Bonciolini V, Caproni M, Fabbri P. Acne: a new model of immune-mediated chronic inflammatory skin disease. G Ital Dermatol Venereol. 2015;150(2):247-54.
7. Bergqvist C, Ezzedine K. Vitiligo: A Review. Dermatology. 2020;236(6):571-92.
8. Bhowmik D. Recent advances in novel topical drug delivery system. Pharm Innov. 2012;1(9):12-31.
9. Kathe K, Kathpalia H. Film forming systems for topical and transdermal drug delivery. Asian J Pharm Sci. 2017;12(6):487-97.
10. Tadwee IK, Gore S, Giradkar P. Advances in topical drug delivery system: A review. Int J Pharm Res and All Sci. 2012;1(1):14-23.
11. Mehta AB, Nadkarni NJ, Patil SP, Godse KV, Gautam M, Agarwal S. Topical corticosteroids in dermatology. Indian J Dermatol Venereol Leprol. 2016;82(4):371-8.
12. Iqbal J, Husain A, Gupta A. Photochemistry of desonide, a non-fluorinated steroidal anti-inflammatory drug. Chem Pharm Bull. 2006;54(6):836-8.
13. PubChem [Internet]. Bethesda (MD): National Library of Medicine (US), National Center for Biotechnology Information; 2004 2024 [Available from: .
14. Zhang X, Song M, Chai J, Cui X, Wang J. Preparation, characterization and application of a surfactant-free microemulsion containing 1-octen-3-ol, ethanol, and water. J Mol Liq. 2020;300:112278.
15. Paul BK, Moulik SP. Microemulsion: An overview J Dispers Sci Technol. 1997;18(4):301-67.
16. Callender SP, Mathews JA, Kobernyk K, Wettig SD. Microemulsion utility in pharmaceuticals: Implications for multi-drug delivery. Int J Pharm. 2017;526(1):425-42.
17. Gallani N, Choudhary R, Dighade S. Novel Ionic Liquid Based Microemulsion Formulation: A Potential Tool for Drug Delivery. Int J Pharm Res Sch. 2022;11:34-43.
18. Sujatha B, Himabindu E, Bttu S, Abbulu K. Microemulsions-A review. J Pharm Sci & Res. 2020;12(6):750-3.
19. Chouhan P, Saini T. D-optimal design and development of microemulsion based transungual drug delivery formulation of ciclopirox olamine for treatment of onychomycosis. Indian J Pharm Sci. 2016;78(4):498-511.