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Original Article

# Design and Characterization of Dapsone Nanoemulgel for Treatment of Acne Vulgaris

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## ABSTRACT

**Background:** Acne vulgaris is a disorder related to the skin (pilosebaceous), which is mainly caused by the formation of seborrhea, comedones, etc. It mainly affects the face, back, head and oil glands. In spite of the potent antimicrobial, anti-inflammatory and antibacterial potential of Dapsone (DPS), it has hurdles like poor water solubility and bioavailability. The objective of current research is to design, optimize and characterize Dapsone Emulgel (DPSE) for the treatment of acne vulgaris. **Materials and Methods:** DPSE was prepared by an oil-in-water emulsion-based method and optimized using a central composite design and the effects of carbapol-934 and liquid paraffin concentrations on drug release, viscosity and spread ability were assessed. The optimized DPSE formulation was evaluated for pH, viscosity, extrudability, spread ability, globule size, zeta potential, drug content, *in vitro* antibacterial assay, time-kill and film bio-adhesion assay. **Results:** Results revealed that the optimized DPSE exhibited a mean globule size of 382.3±4.17 nm with a PDI of 0.230.010 and a zeta potential of -21.8±3.21 mV with a drug content of 96.95±1.71% of dapsone. Optimized DPSE showed good viscosity (39481±2.645 cps), spread ability (14.68±0.02 g/cm/sec) and excellent extrudability. Optimized DPSE displayed MICs (Minimum Inhibitory Concentrations) and MBCs (Minimum Bactericidal Concentrations) of 10±1.5 µg/mL and 21±2 µg/mL, respectively, against *P. acne* when compared to *S. aureus*. (MIC-54±2.5 µg/mL MBC-98±4 µg/mL). Furthermore, DPSE inhibited biofilm formation and bacterial adhesion in a dose-dependent manner, with 100% inhibition obtained in 48 hr at MBC. The percentage of live bacteria in the biofilm treated with MBC and the MIC concentration of DPSE was 31.54±1.32% and 62.91±3.12%, respectively, in comparison to the control's 100%. **Conclusion:** From the results, we conclude that optimized DPSE can be used as a competent alternative to a current treatment for effective management of acne vulgaris. However, further *in vivo* studies are required to establish its efficacy in the treatment of acne vulgaris.

**Keywords:** Acne vulgaris, Dapsone, Emulgel, Zeta Potential, Antibacterial assay, *P. acne* etc.

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## INTRODUCTION

Acne vulgaris is a common skin condition that primarily affects the skin and oil glands, including the face. It is typically distinguished by the appearance of seborrhea, comedones (blackheads or whiteheads) and inflammatory lesions on the skin. *Propioni bacterium acnes* and *Staphylococcus epidermidis* are pus-generating bacteria that trigger inflammation in acne on the body.[1,2] It is anticipated that over 23 million Indians will be affected by acne by the end of 2026.

Dapsone (DPS) is used in the treatment of leprosy and has a wide range of pharmacological potential, including antibacterial and anti-inflammatory properties.[3] Oral applicability of dapsone in the treatment of acne vulgaris is restricted mainly due to its low water solubility and abundance of adverse effects such as methemoglobinemia, agranulocytosis, hypersensitivity syndrome, psychosis and neuropathy.[4,5] Therefore, it is a necessity to deliver DPS through a suitable route and delivery approach to overcome the above shortcomings.

Emulgel is a emulsion in gel formulation produced by mixing gel and emulsion.[6] This drug delivery method has several advantages

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compared to others, including the potential to incorporate hydrophobic medicines, higher loading capacity and stability, ease of production, reduced preparation costs, regulated release, avoidance of first-pass metabolism and enhanced patient compliance.[7,8] Furthermore, emulgel has the potential benefit of precisely targeting the medicine to the specific site of action for a prolonged duration.[9] Furthermore, it mitigates the hazards and difficulties associated with intravenous therapy.[10,11] Several commonly used topical treatments, such as ointments, creams and lotions, have numerous drawbacks, including stickiness, which reduces their capacity to spread, friction, which can result in dermatitis and stability issues. Transparent gels have been utilized in both the cosmetic and pharmaceutical industries, however, they suffer from the disadvantage of accommodating hydrophobic medicines. To circumvent this restriction, a technique based on emulsion is employed.[12] Emulgel has several benefits, such as thixotropic properties, absence of grease, effortless spread ability, easy removal, emollient qualities, non-staining nature, water solubility, extended shelf life, eco-friendliness, transparency and aesthetic appeal.[13]

This dermatological emulgel has many beneficial properties, including a good appearance, being transparent, removable, emollient, water-soluble and having a longer shelf life. This can be used to improve DPS topical drug delivery over the conventional drugs currently on the market. Therefore, the objective of the present research was to design and characterize an emulgel of DPS for the effective treatment of acne.

## MATERIALS AND METHODS

### Materials

Dapsone was procured from Arati Pharma Pvt. Ltd., Mumbai. Carbopol-934, tween 20, span 20, methanol was procured from Analab Fine Chemicals Pvt. Ltd., Mumbai. Triethanolamine was obtained from Pure Chem. Laboratory Pune. All chemicals and reagents used in current investigation were of analytical grade.

### Formulation and optimization of Dapsone Emulgel (DPSE)

The $3^2$ Central Composite Design (CCD) was utilized for the preparation and optimization of DPSE. 09 different batches of DPSE were deliberated at three different coded levels (-1, 0 and +1) of carbopol-934, liquid paraffin and X2 (Table 1). The different compositions of DPSE in all the batches are depicted in Table 2.

Emulgel is prepared by formulating the emulsion (O/W) and gel basis separately and then incorporating the emulsion into the gel base while continuously stirring. In summary, the gel phase was initiated by distributing carbopol-934 in filtered water, while continuously stirring at a moderate speed using a mechanical stirrer and allowing it to soak overnight. Subsequently, the pH of the gel was modified to a range of 6-6.5 using TEA. The oil phase of the emulsion was created by dissolving 5% weight/weight (w/w) DPS in ethanol. Subsequently, light liquid paraffin oil and span 20 were introduced into the mixture while maintaining continuous stirring on a magnetic stirrer at a speed of 400-500 revolutions per minute. The aqueous phase was created by dissolving a 2% concentration of tween-80 in distilled water. The propyl and methyl parabens were dissolved in propylene glycol and subsequently combined with water. Subsequently, the aqueous and oil phases were individually subjected to heating at temperatures ranging from 70 to 80°C. Ultimately, the oil phase was introduced into the aqueous phase while stirring continuously and then allowed to cool down to the ambient temperature. Ultimately, the oil phase was introduced into the aqueous phase while maintaining a constant stirring motion and subsequently cooled down to the ambient temperature. The emulsion that was obtained was subsequently combined with gel in a 1:1 ratio, while gently swirling, in order to produce an emulgel.[14-16]

### Characterization of DPSE

#### *Viscosity study*

All batches' flow resistance was measured using a Brookfield viscometer (LVDV-II+) with a spindle number of 64 at 10 rpm (Brookfield Engineering). Briefly, 100 g of DPSE was kept in a beaker and allowed to set, the spindle groove was dipped, and the rpm was set. Finally, the dial reading was measured (in triplicate) after 3 min and the mean was calculated.[17,18]

### Spread ability

Briefly, about 1 g of DPSE was positioned between two glass slides and a weight of 500 g was kept on the top glass slide to sandwich the DPSE in between the glass slides and spread at a definite distance. The duration required for gel to travel a distance was recorded at its origin.[19,20]

S=ML/T Where are M-weight tide on top, L-distance traveled and T-time.

### *In vitro* drug release study

All DPSE formulations were tested for *in vitro* drug release using a dialysis membrane and a Franz diffusion cell. Briefly, the DPSE (500 mg) was poured on the surface of the dialysis membrane evenly at 37°C. The receptor chamber was filled with phosphate buffer pH 5.5 and the acceptor compartment was stirred (at 50 rpm) with the help of a magnetic stirrer at 37°C. Samples (3 mL) at specific time intervals for 8 hr and substituted with an equivalent amount of dissolution medium. The samples were duly diluted and analyzed by a UV-visible spectrophotometer (Shimadzu UV-1900) at 293 nm.[21-24]

### Physical examination

The optimized batch of DPSE was visually inspected in terms of color, homogeneity and consistency.[25]

## Determination of pH

The pH of the optimized DPSE was monitored via a digital pH meter (Equip-Tronic's EQ-614). In brief, 1 g of DPSE was dissolved in 100mL of distilled water and pH was measured in triplicate.[26]

## Extrudability

The extrudability of the optimized DPSE was crammed into collapsible tubes and evaluated for extrudability. The amount (g/cm$^2$) of emulgel extruded as a collapsible tube on the appliance of weight (in gram) required extruding at least 0.5 cm of emulgel ribbon in 10 sec was determined.[27-30]

## Drug content

The optimized DPSE (1.0 g) was dissolved in PBS at pH 5.5 (100 mL) with vigorous stirring for 30 min. Then 1 mL of the sample was withdrawn from the above solution and further diluted with 50 mL of PBS (pH 5.5) and filtered through a membrane filter. Finally, the absorbance was measured by a UV spectrophotometer (Shimadzu UV-1900) at 293 nm. Each trial was conducted in triplicate.[31,32]

## Globule size

The globule size of optimized DPSE emulsion was determined using a Malvern Zettaliter (Nano ZS, Malvern, UK). The globule size distributions of each sample were investigated in triplicate and the mean value was calculated.[33-35]

## Zeta Potential

The optimized DPSE emulsion zeta potential was evaluated using the Malvern Zettaliter (Nano ZS, Malvern, UK), which consisted of appropriate software. Three different samples were tested at 25°C using a cell drive that was kept at 150 mV. The dispersion medium's dielectric constant and viscosity were used to translate electrophoretic mobility into zeta potential values.[36,37]

## Surface Morphology

After discarding the excess fluid, "a carbon-coated copper grid having mesh size of 300 was used to deposit 5 µL of optimized DPSE emulsion on the grid and then fix the grid. The grid was then air-dried before being stained with uranyl acetate stain at a conc. of 1% for 3-5 min with a transmission electron microscope (JEOL-JEM 1400 USA).

## Skin Permeation Study

Fluorescence microscopy was utilized to determine the emulgels' capacity to penetrate the skin layers. A homogenous application of plain Rh6G and Rh6G-loaded emulgel was made to the goat ear skin and placed on the Franz diffusion cell assembly. The skin has been removed from cell and properly rinsed with water to eliminate any remaining formulation after the 1h treatment. The treated portion of the skin specimens was removed and fixed within buffered formalin at a 10% concentration. Following fixation, skin specimens were embedded in paraffin wax and sectioned perpendicular to the surface at 4.5 µm thickness with a microtome. The acquired thin tissue ribbons or sections were placed on the glass slides to be detected using a fluorescence microscope (Olympus, Japan) for the existence of fluorescence within the skin layers.[38-40]

## *In vitro* antibacterial activity

### *Minimum Inhibitory Concentration (MIC)*

For MIC, different dilutions of each of the DPS and DPSE were prepared using a BHI. Thus, the serial dilutions were repeated up to 9-10 dilutions for each formulation. 5 µL were obtained from the preserved stock cultures of the necessary *P. acne* and *S. aureus* organisms and mixed with 2 mL of BHI broth. Each serially diluted tube received 200 µL of the above-mentioned culture solution. After 24 hr of incubation, the tubes were checked for turbidity.[41-43]

## Minimum Bactericidal Concentration (MBC)

It is used to determine either DPS or DPSE have a bactericidal or bacteriostatic effect against *P. acne* and *S. aureus*. Three or five tubes from the MIC test (sensitive in MIC) are briefly plated and incubated for 24 hr and then a colony count is performed the following day. The formulations' bactericidal effect is indicated by the absence of growth, but the presence of growth indicates its bacteriostatic potential.[41-43]

## Time kill assay

Using the micro broth dilution technique, a time-kill experiment was carried out. In microcentrifuge tubes containing bacterial suspensions at control, MBC and MIC conc, DPS and DPSE were cultured. Aliquots of the sample from the supplied mixture were taken at distinct time intervals (0 to 48 hr), serially diluted and then plated on a blood agar plate. After 48 hr of incubation, colonies were counted using a colony counter and a time-kill curve was produced by determining the log 10 CFU ("Colony Forming Units") with time.[44]

## Crystal violet assay for biofilm reduction

Each well comprising BHI broth was used to culture 0.5 McFarland standard bacteria aerobically overnight. The plate was then put in an aerobic chamber and incubated for 72 hr at 37°C. To allow the bacteria to grow and create a biofilm on the well bottom. Afterward, culture medium alone, MBC tests material conc. and MIC test material conc. were substituted in each well (control). An additional day was added to the incubation period while maintaining the same settings. The supernatant was collected after 24 hr period and PBS was used to rinse the wells. It was then fixed for 15 min with methanol, stained for 5 min with crystal violet (0.1% w/v) and rinsed with distilled water.

Following the addition of ethanol to dissolve the crystal violet, the samples' OD ("Optical Density") at 570 nm was determined with micro microplate reader.[45]

## Stability Study

Optimized DPSE was packed in collapsible aluminium tubes and stored under accelerated conditions of 40°C±2°C and 75%±5% RH. The samples were withdrawn at 1-3 months intervals and evaluated in terms of color, consistency, pH, spreadability and *in vitro* drug release.[46]

# RESULTS

## Optimization of DPSE

### *Effect of formulation variable on viscosity (Response 1; Y1)*

A contour plot (Figure 1A) and a 3D surface response plot (Figure 1B) were used to determine the impact of both carbopol-934 (A) and liquid paraffin (B) on the viscosity of the emulgel. The emulsion's viscosity increased and decreased as a result of both variables. The augment in A caused an increase in the viscosity and in contrast, the augment in B displayed a decrease in the viscosity of emulgel. Furthermore, two variable interactions had a negative influence (increased) on globule size. The carbopol-934 demonstrated a positive effect (an increase in concentration showed an increase in viscosity and vice versa) on the viscosity of the emulgel formulation. [46]

The ANOVA analysis of the results yielded an F-value of 18.21 and a *p*-value of 0.0188, which indicates the implication of the quadratic model. The relevant model for drug content ($R^2$=0.999) was observed to be a quadratic model. All the batches of DPSE were formulated and optimized based on spread ability (Y1), viscosity (Y2) and *in vitro* drug release (Y3) (Table 3). The ANOVA results for the viscosity data are shown in Table 4. The following quadratic equation can describe the effect of the independent variables on viscosity.

Viscosity Y1=+38875.76i+2426.45 A+307.44 B+271.33 AB-1415.14 $A^2$-1934.11 $B^2$

### Effect of formulation variable on spread ability (Response 2; Y2)

A contour plot (Figure 1C) and a 3D surface response plot (Figure 1D) were used to determine the effect of the amounts of both carbopol-934 (A) and liquid paraffin (B) on the spread ability of DPSE. Both variables established increases and decreases in the spread ability of emulgel. The augment in A caused a decrease in the spread ability and in contrast, the augment in B displayed an increase in the spread ability of emulgel. Besides, the negative influence it had on the globule size, two variable interactions were observed. Spread ability is critical for patient compliance and optimized DPSE formulations have excellent spread ability.[47]

ANOVA results yielded an F-value of 18.37 and a *p*-value of 0.0186, which indicates the implication of the quadratic model. The relevant model for drug content (R2=0.999) was observed to be a quadratic model. The ANOVA results for the spread ability data are shown in Table 4. The following quadratic equation can describe the effect of the independent variables on spread ability is:

Spread ability Y2= +13.95 I -2.15 A+1.09 B+0.9258 AB-5.49 $A^2$-1.40 $B^2$

### Effect of formulation variable on drug release (Response 3; Y3)

A contour plot (Figure 1E) and 3D surface response plot (Figure 1F) were used to check the impact of the amounts of both carbopol-934 (A) and liquid paraffin (B) on the *in vitro* drug release from the DPSE. All DPS emulgels (F1 to F9) showed the release of DPS between 57.93 to 93.87% after to 8 hr (Table 3). Batches F1, F5, F7, F8 and F9 had the highest *in vitro* DPS release, which could be attributed to the highest amount of liquid paraffin. In contrast, batches F2, F3, F4 and F6 exhibited

**Table 1: Varying Composition of DPSE Emulgel (%w/w).**

| Ingredient (%w/w) | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
|---|---|---|---|---|---|---|---|---|---|
| Dapsone | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| Carbopol-934 | 1 | 2.5 | 1.75 | 2.5 | 1.75 | 2.5 | 1.75 | 1.0 | 1.0 |
| Liquid paraffin | 5.5 | 8.5 | 5.5 | 7.0 | 8.5 | 5.5 | 7.0 | 7.0 | 8.5 |
| Tween 20 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| Span 20 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Propylene glycol | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Methanol | 2.5 | 2.5 | 2.5 | 2.5 | 2.5 | 2.5 | 2.5 | 2.5 | 2.5 |
| Methyl paraben | 0.03 | 0.03 | 0.03 | 0.03 | 0.03 | 0.03 | 0.03 | 0.03 | 0.03 |
| Propyl paraben | 0.01 | 0.01 | 0.01 | 0.01 | 0.01 | 0.01 | 0.01 | 0.01 | 0.01 |
| Water | q.s | q.s | q.s | q.s | q.s | q.s | q.s | q.s | q.s |
| Triethanolamine (q.s) | Adjusted to pH 6.0-6.5. | | | | | | | | |

**Table 2: Coding of actual values of variables for DPS Emulgel.**

| Independent variable | F1 | F2 | | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
|---|---|---|---|---|---|---|---|---|---|---|
| X1 | -1 | +1 | | 0 | +1 | 0 | +1 | 0 | -1 | -1 |
| X2 | -1 | +1 | | -1 | 0 | +1 | -1 | 0 | 0 | +1 |

X1: Concentration of carbopol-934: -1=1.0% w/w; 0= 1.75% w/w; +1= 2.5% w/w.X2: Concentration of Liquid paraffin 2: -1= 5.5% w/w; 0=7.0% w/w; +1= 8.5% w/w.

**Table 3: Viscosity, Spreadability and *in vitro* release of DPS from DPSE.**

| | | Factor 1 | Factor 2 | Response 1 | Response 2 | Response 3 |
|---|---|---|---|---|---|---|
| Std | Run | A: Concentration of carbopol-934 | B: Concentration of liquid paraffin | *In vitro* drug release | Viscosity | Spread ability |
| | | %w/w | %w/w | % | cps | gm.cm/sec |
| 5 | 1 | 1 | 7 | 85.46±1.65 | 34849 | 9.98 |
| 7 | 2 | 1.75 | 7 | 93.87±2.85 | 39481 | 14.68 |
| 6 | 3 | 2.5 | 7 | 62.21±3.54 | 39467 | 6.26 |
| 4 | 4 | 2.5 | 8.5 | 68.74±2.96 | 38981 | 7.18 |
| 1 | 5 | 1 | 5.5 | 82.11±1.65 | 32910 | 9.12 |
| 3 | 6 | 1 | 8.5 | 88.98±1.23 | 33468 | 9.89 |
| 9 | 7 | 2.2 | 5.5 | 57.93±3.89 | 37357 | 7.33 |
| 2 | 8 | 1.75 | 5.5 | 79.32±2.32 | 36849 | 11.68 |
| 8 | 9 | 1.75 | 8.5 | 90.16±1.12 | 36468 | 12.88 |

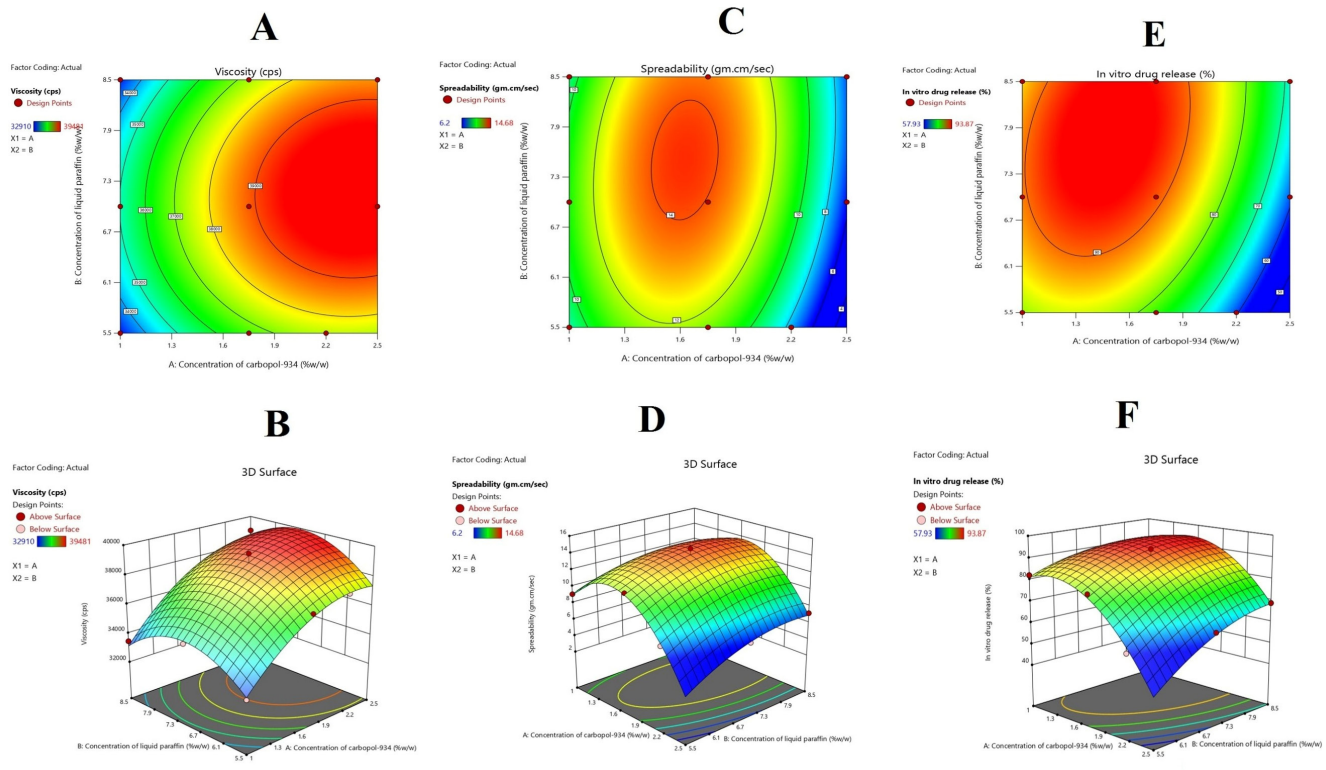


**Figure 1:** A) Drug release Counter plot B) Drug release 3D Graph C) Viscosity Counter plot D) Viscosity 3D Graph E) Spread ability Counter plot F) Spreadability 3D Graph.

the lowest drug release of DPS, possibly owing to the maximum amount of carbopol-934. Both variables established increases and decreases in the drug release of DPS from the emulgel. Thus, the decrease in the release of DPS from emulgel may be owing to the concentration of carbopol-934 (gelling agent) used. As the amount of gelling agent increases, the drug release from emulgel formulations decreases and vice versa.[48]

Comparative DPS release from the DPSE (93.45±0.5) and marketed formulation (78.25±1.2) in phosphate buffer pH 5.5 was shown in Figure 2A. The augment in a caused a decrease in the *in vitro* drug release, while the augment in B displayed an increase in the *in vitro* release of DPS. Furthermore, with variable interactions, a negative influence (increased) on globule size was observed. ANOVA yielded F-value 15.21 and *p*-value 0.0242. The relevant model for drug content ($R^2$=0.999) was observed to be a quadratic model. The slower diffusion of DPS in the F7 batch might be due to higher viscosity, which results in controlled diffusion of DPS through the dialysis membrane. The ANOVA results for the *in vitro* drug release data are shown in Table 4. The following quadratic equation can describe the effect of the independent variables on *in vitro* drug release is:

Drug Release Y3=+90.97i-14.06 A+7.71 B+5.16 AB-15.68 $A^2$-5.59 $B^2$

## Optimization

The DPSE formulation was optimized using a $3^2$ central composite design. The two independent factors chosen were carbopol-934 concentration and liquid paraffin and the three dependent factors (responses) chosen were viscosity, spread ability and *in vitro* drug release. Based on these responses, batch F7 of DPSE was selected as the optimized batch. Results were shown in Table 3.

## pH

pH is a key requirement of every dermal formulation. The compatibility of topical formulations with the skin's pH is of huge importance for better patient compliance. The pH of the optimized DPSE was found to be 6.80±0.21, which is in the range of dermal pH, indicating that DPSE is biocompatible with the skin and, thus nonirritant to skin.[49]

## Extrudability

The optimized DPSE was found to be simply extrudable because of the collapsible tube, revealing its good extrudability. The good extrudability (+++) of DPSE could be due to the use of an optimized quantity of carbopol-934.

## Drug content

The results of drug content showed that as the concentration of amphiphiles and concentration of oil phase is increased there is an increased drug loading. This is due to the high solubility of the drug in the oil phase and the appropriate solubilization effect exerted by amphiphiles. The drug content of optimized DPSE was found to be 96.95±1.71%.

## Surface morphology

The surface morphology analysis of optimized DPSE revealed the presence of sphere-shaped globules with clear surroundings (Figure 2) along with spherical oil globules surrounded by the thick film monolayer. Thus, developed dispersions were found to be stable and the monolayer prohibits coalescence and drug precipitation, thereby offering stability to the developed DPS emulgel formulation.[50]

## Globule size

The efficacy of emulgel is critically measured by globule size, which primarily controls the rate and amount of drug release.

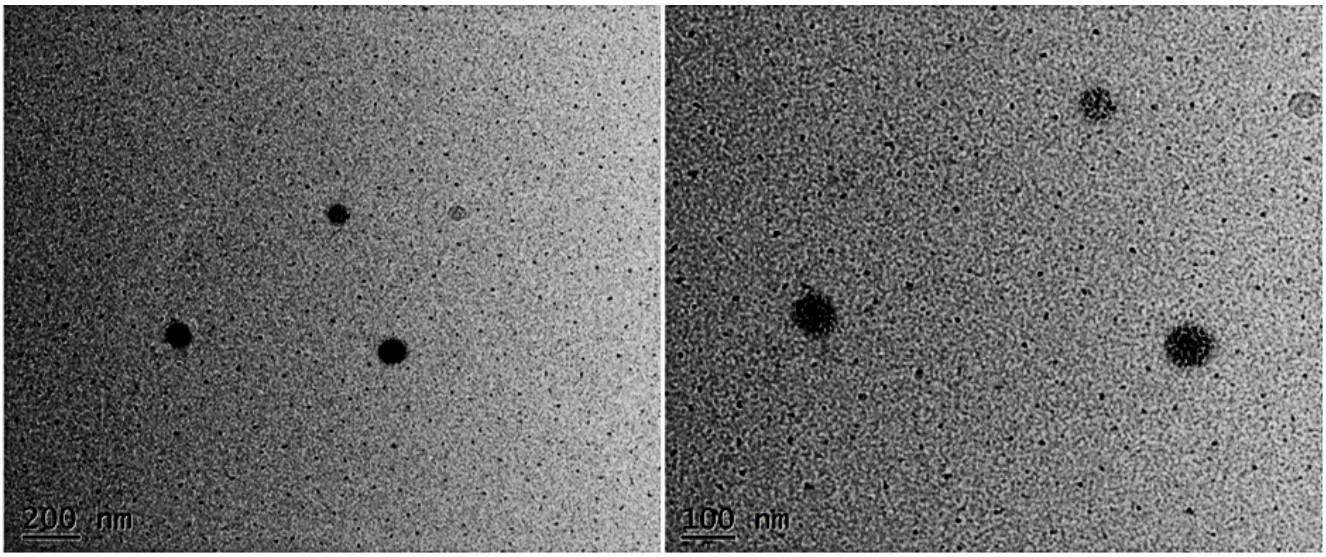


**Figure 2:** Surface Morphology of Optimized DPSE Formulation.

However, smaller globules generate a larger surface area required for absorption, which could be responsible for solubility and bioavailability enhancement. The globule size of optimized DPSE was observed in the nanometer range, indicating better absorption of DPS from the emulgel. The globule size of optimized DPSE was found to be 382.3±4.17 nm with a PDI (0.23±0.010), (Figure 3A).

## Zeta Potential

Zeta potential plays a key role in the stability of the dispersion system. Generally, systems with more negative or more positive zeta potential values become stable by creating resonance with each other in a dispersion system. The merging of oil globules causes an instable emulsion due to coagulation, creaming and cracking, which can be overcome by high electrostatic repulsive forces, which are nothing but the zeta potential of the system. The negative zeta potential value of optimized DPSE revealed good stability.[51,52] The zeta potential of optimized DPSE was found to be -21.8±3.21 mV, (Figure 3B).

## Skin Permeation

For efficient therapy of acne, greater drug permeation within deep layers of skin is crucial as acne develops where high concentration of sebaceous glands and located in the middle layer of skin. Figure 4 displays images of a goat ear skin taken under fluorescence microscope after 6 hr of treatment with Rh6G-emulgel and Rh6G solution (control). On treatment with the Rh6G solution, goat skin showed fluorescence confined only to the superficial subcutaneous *Stratum Corneum* (SC) layer Figure 4A. On the other hand, when treated with Rh6G-emulgel, relatively uniform, bright fluorescence observed throughout the top skin layers, SC, dermis and epidermis Figure 4B. The large rise in intensity of fluorescence from deep skin layers suggests that emulgel is effectively delivered to this deeper skin layers.[53]

## *In vitro* antibacterial activity

### *Determination of MIC and MBC of DPS and DPSE*

The antibacterial activity of DPS and DPSE was assessed against *P. acne* and *S. aureus* strains using the usual broth dilution technique. Both DPS and DPSE have demonstrated substantial inhibitory efficacy against *P. acne* in comparison to S. aureus. The Minimum Inhibitory Concentration (MIC) values for several test samples are displayed in Table 5. DPSE has the lowest Minimum Inhibitory Concentration (MIC) value of 10±1.5 µg/mL, compared to DPS which has a MIC value of 25±2 µg/mL.

**Table 4: ANOVA results for various responses of DPS-Emulgel.**

| Source | Responses | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | $Y_1$ (%Cumulative drug release) | | | $Y_2$ (Viscosity) | | | $Y_3$ (Spredability) | | |
| | F-value | *p*-value Prob > F | Adequacy precision | F-value | *p*-value Prob > F | Adequacy precision | F-value | *p*-value Prob > F | Adequacy precision |
| Model | 15.21 | 0.0242 | 37.548 | 18.21 | 0.0188 | 31.128 | 18.37 | 0.0186 | 24.547 |
| $X_1$ | 57.18 | 0.0048 | | 54.53 | 0.0051 | | 33.70 | 0.0102 | |
| $X_2$ | 19.69 | 0.0213 | | 1.00 | 0.3902 | | 10.00 | 0.0508 | |
| $X_1X_2$ | 4.69 | 0.1190 | | 0.4150 | 0.5653 | | 3.80 | 0.1463 | |
| $X_1^2$ | 23.92 | 0.0163 | | 6.24 | 0.0879 | | 73.91 | 0.0033 | |
| $X_2^2$ | 3.63 | 0.1527 | | 13.91 | 0.0336 | | 5.71 | 0.0967 | |

$X_1$ and $X_2$ are coded terms for independent variables; $X_1X_2$ interaction terms; $X_1^2$ and $X_2^2$ are quadratic term.

**Table 5: MIC and MBC values obtained for DPS and DPSE against *S.aureus and P. acne*.**

| Sl. No. | Test Material | MIC (µg/mL) *S. aureus* | MBC (µg/mL) *S. aureus* | MIC (µg/mL) *P. acne* | MBC (µg/mL) *P. acne* |
|---|---|---|---|---|---|
| 1 | DPS | 96±3.5 | 212±5 | 25±2.5 | 51±4 |
| 2 | DPSE | 54±2.5 | 98±4 | 10±1.5 | 21±2 |

**Table 6: Stability study data of evaluation of optimized DPSE.**

| Month | Color | Consistency | %Drug Release | pH | Spread ability (gm.cm/sec) |
|---|---|---|---|---|---|
| 0 | White | Excellent | 93.93±2.87 | 6.62±0.85 | 14.34±1.57 |
| 1 | White | Excellent | 93.63±2.54 | 6.54±0.76 | 14.13±1.87 |
| 2 | White | Excellent | 92.46±2.43 | 6.45±0.67 | 14.63±1.77 |
| 3 | White | Excellent | 92.35±2.12 | 6.32±0.58 | 14.49±1.43 |

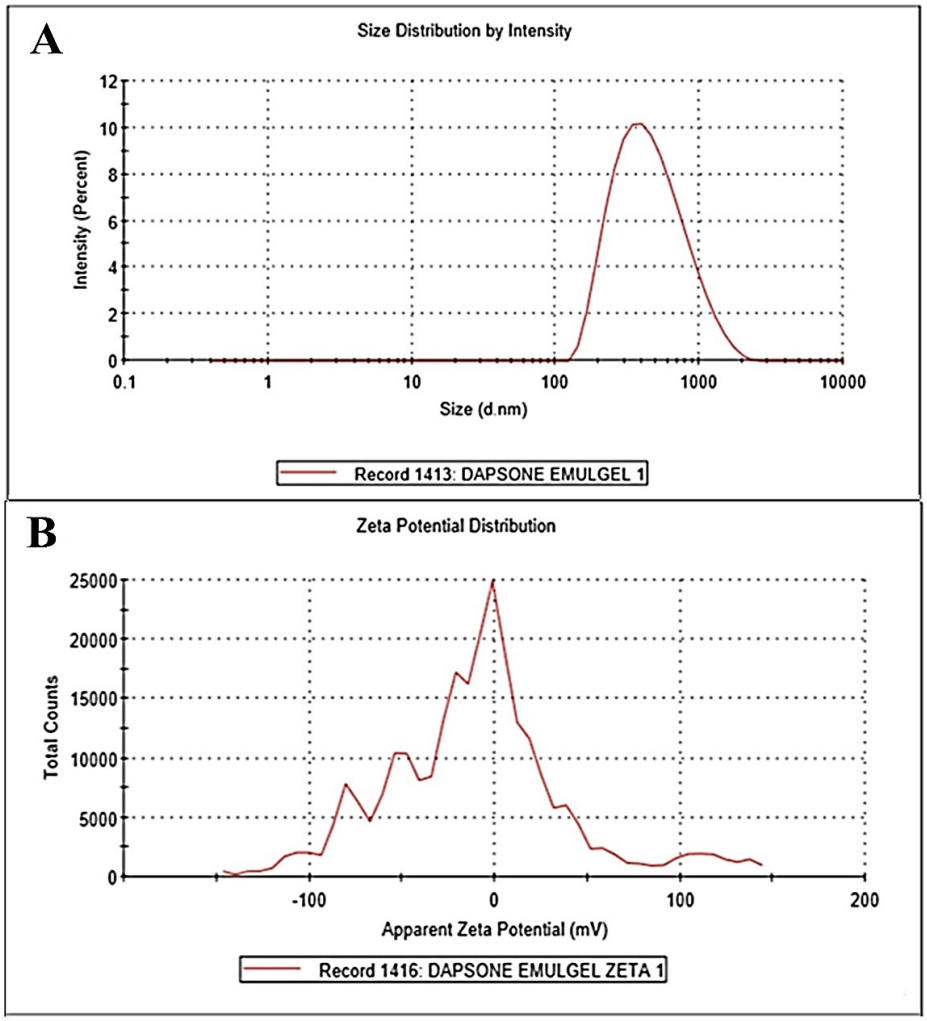


**Figure 3:** DPSE Optimized Formulation A) Globule size B) Zeta potential.

MBC refers to the concentration at which 99.9 percent of viable organisms are eliminated within a brief timeframe, relative to the initial inoculum. The optimized DPSE has the lowest Minimum Bactericidal Concentration (MBC) value of 21±2 µg/mL, in comparison to DPS which has an MBC value of 51±4 µg/mL.

In the present study, the bactericidal or bacteriostatic effect of DPSE (Figure 5A), DPS (Figure 5B) is determined at different concentrations against *P. acne* and *S. aureus*. DPS (Figure 5C), DPSE (Figure 5D) respectively. The optimized DPSE treatment has resulted in maximum inhibition (no growth) of *P. acne* when compared to *S. aureus* and a lower number of colony forming units when compared to DPS. The MBC values obtained for different test samples are presented in Table 5. The optimized DPSE displayed better antibacterial potential against *P. acne* when compared to *S. aureus*.[54,55]

## Time-kill assay

A time-kill test was used to assess the antibacterial activity of DPS and DPSE against *P. acne*. When compared to DPS the time-kill test findings showed that DPSE had significant bactericidal effects against the *P. acne* strain at the MBC concentration. Increases in the concentration of DPS and DPSE, as well as incubation duration, resulted in increased bacterial inhibition. In motile bacteria like *P. acne*, bacterial adhesion is the first stage in biofilm formation. Certain protein interactions between the bacterial surface and human matrix aided the attachment process.[56,57] For this test, the bacteria were exposed to concentrations of DPS and DPSE at the MBC and MIC levels for several time intervals. At the MIC concentration, bacterial growth was inhibited in a time-dependent manner, but at the MBC concentration, 100 percent inhibition was reached in 48 hr (Figure 6A).

## Biofilm reduction and crystal violet assay

Antibiotics cannot penetrate biofilm because bacterial cells are entrenched inside the exopolymeric matrix. The pre-formed *P. acne* biofilm was strongly inhibited in a dose-dependent manner by DPSE at MIC and MBC concentrations.[58] In comparison to the control and DPS at MBC and MIC concentrations DPSE significantly reduced *P. acne* adhesion capacity. No cell reduction

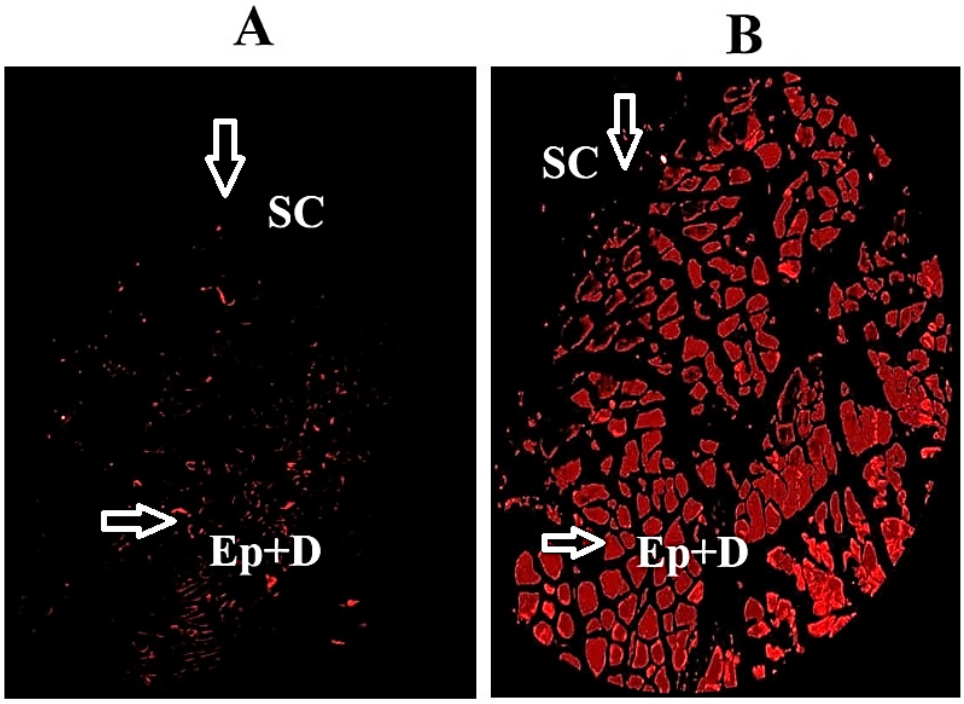


**Figure 4:** Fluorescence photomicrographs of goat skin after 8 hr application of A) Rhodamine-6G Solution B) DPSE loaded with Rhodamine 6G. Images display the distribution of fluorescence into different skin layers.

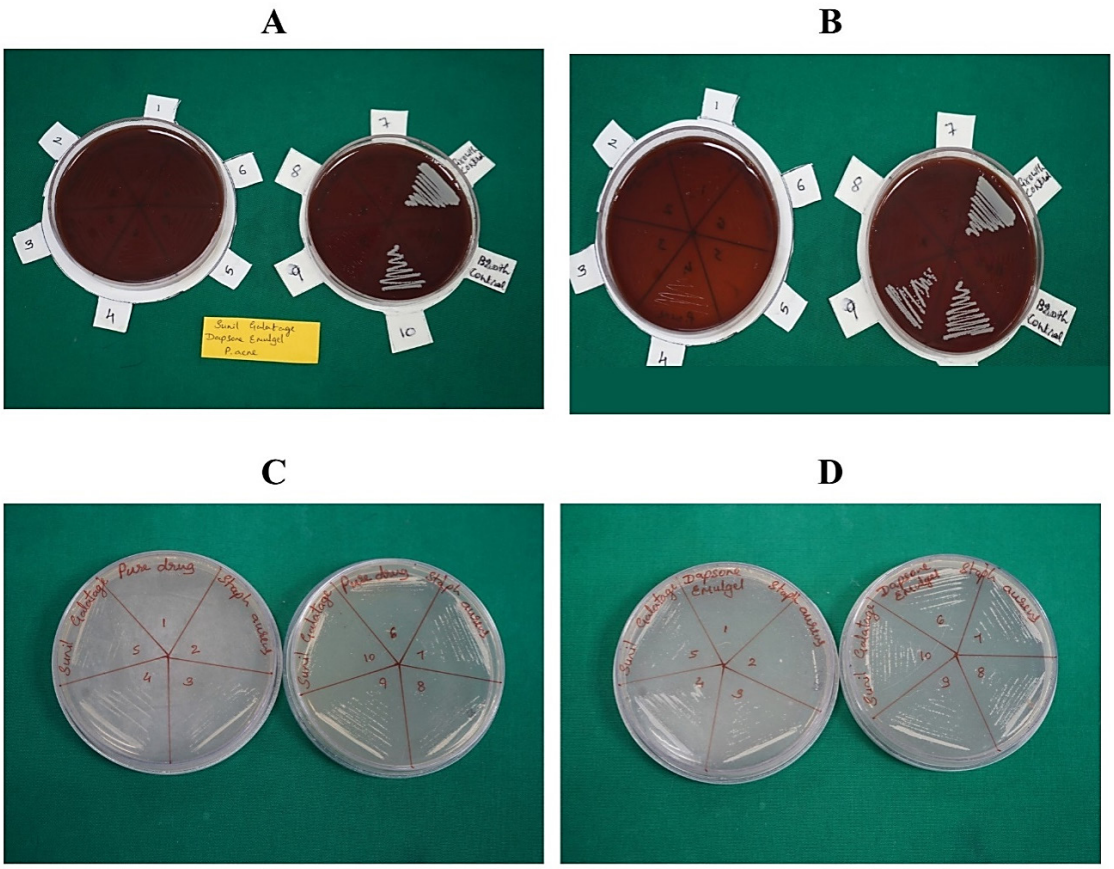


**Figure 5:** Determination of MBC of A) DPS B) Optimized DPSE. against *P.Acne*; C) DPS D) Optimized DPSE against *S.aureus*. The numbers 1 to 10 present on culture plates indicates bacteria adhered zones (1 to 10) that are treated with different concentrations of DPS and Optimized DPSE.

was observed in the control group. The biofilm reduction crystal violet assay has displayed a prominent effect at MIC and MBC concentrations of DPS on *P. acne* cells. The significant ($p$<0.001) cells reduction (70.70±3.32%) was observed with DPS at MIC and at MBC, the cell reduction was 40.08±2.32%. In contrast, DPSE, showed significant ($p$<0.001) cell reduction observed at MIC and MBC was up to 62.91±3.12% and 31.54±1.32% respectively (Figure 6B).

### Accelerated Stability Study

We observe no significant changes in the physicochemical properties of optimized DPSE after storage of 3 months at 40°C±2°C and 75%±5% RH. The physicochemical properties such as color, consistency; pH, spread ability and drug release of optimized DPSE after 1, 2 and 3 months of storage are depicted in Table 6.

## DISCUSSION

The DPSE formulation was optimized via $3^2$ CCD. The two independent factors selected were concentration of carbopol-934 and liquid paraffin and dependent factors (responses) chosen were viscosity, spreadability and *in vitro* drug release. Based on these responses, batch F7 of DPSE was selected as the optimized batch. The carbopol-934 demonstrated positive effect (increase in concentration showed increase in viscosity and vice-versa) on viscosity of emulgel formulation.[27] Hence, the formulation F7 was found to have good viscosity, spreadability and drug release 39481±2.645 cps, 14.68±0.02 and 93.87±0.5% respectively. The spreadability assumes an imperative job in the patient compliance and all dapsone emulgel formulations have excellent spread ability.[28] Decrease in the release of DPS from emulgel may be owing to the concentration of carbopol-934 (gelling agent) used. As the amount of gelling agent increases, it negatively (decreases) impact drug release form emulgel formulation and vice versa.[29] The compatibility of topical formulation with the skin pH is of huge importance for better patient compliance. The pH of optimized DPSE (6.8) found to be compatible with skin pH so it is nonirritant to skin.

The surface morphology analysis of optimzed DPSE revealed presence of sphere-shaped stable oil globules surrounded by the thick film monolayer. This layer prohibits coalescence and drug precipitation and thereby offers stability to developed DPS emulgel formulation.[30] The optimized DPSE displayed better antibacterial potential against *P. acne* and *S. aureus*. This remarkable activity against bacterial strain could be due to utmost entrapment efficiency of DPS in the emulgel. Besides, the rapid release of DPS from the emulgel may responsible for better antibacterial activity.[31] Efficacy of emulgel is critically measured by globule size which primly controls rate and amount of drug release. However smaller globules generate larger surface area required for absorption which could be responsible for solubility and bioavailability enhancement.[32] The globule size of optimized DPSE was observed in nanometer indicating better absorption of DPS from the emulgel. Zeta potential plays key role in stability of the dispersion system. Generally systmes with more negative or mire positive zeta potential values becomes stable by creating repusion with eachother in dispersion system. Merging of oil globules causes instable emulsion due to coagulation,creaming and cracking which can be overcome by high electrostatic repulsive forces which are nothing but zeta potetial of the system. -Ve zeta potential value of optimized DPSE revealed good stability.[33,34]

Emulgel are effectively delivered to these deeper skin layers. This could be due to presence of surfactant and permeation enhancers which changes the way the lipids in the SC are organized and improves the fluidity of the SC. Emulgel releases the drug within innermost deep skin layers and their absorption of transdermal arises from the emulsion fusion with skin lipids as well as releasing the drug at different points along the paths of penetration. Improved permeation mainly due to presence of oils and surfactants which changes the way the lipids in the SC are organized and improves the fluidity of the SC. Additionally, narrow globule size of emulgel may enhances to pass through the SC altered structure and carry the medicine into the innermost layers of skin.[53]

The MBC and MIC values of DPSE against *P. acne* and *S.aureus* demonstrated its remarkable antimicrobial potential. When

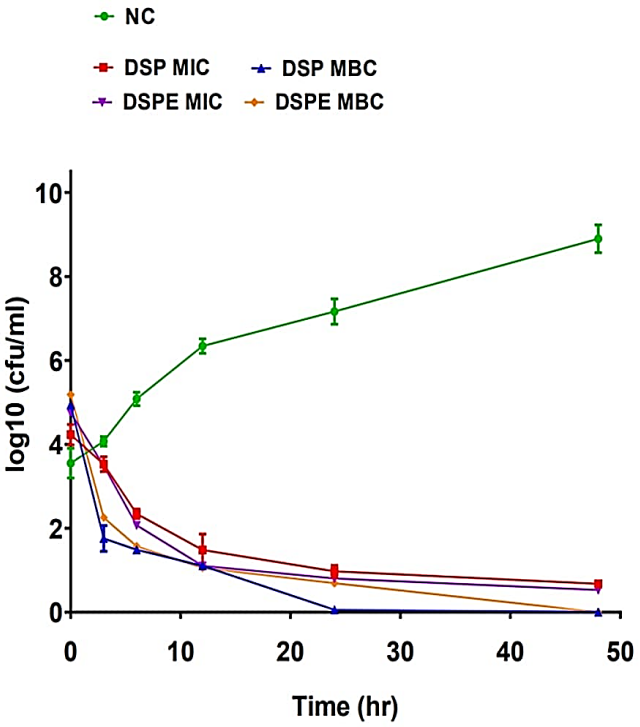


**Figure 6A:** Time kill curve showing time dependent bacterial inhibition and bactericidal activity of DPS, DPSE and ACN on *P. acne*. Data are mean±SD of three independent experiments. MIC: Minimum Inhibitory Concentration, MBC: Minimum Bactericidal Concentration.

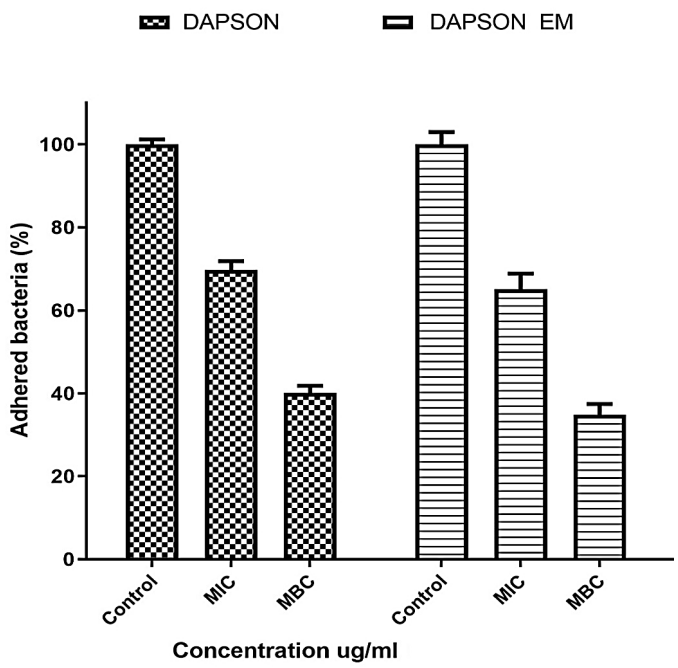


**Figure 6B:** Effect of DPS and DPSE on the bacterial inhibition on microtiter plate. Data are mean±SD of three independent experiments.

compared to DPS, the time-kill test findings showed that DPSE had significant bactericidal effects against the *P. acne* strain at MBC concentration. This remarkable activity against a bacterial strain could be due to the utmost entrapment efficiency of DPS in the emulgel. Besides, the rapid release of DPS from the emulgel may be responsible for better antibacterial activity. Increases in the concentration of DPS and DPSE, as well as incubation duration, resulted in increased bacterial inhibition. In motile bacteria like *P. acne*, bacterial adhesion is the first stage in biofilm formation. Certain protein interactions between the bacterial surface and human matrix aided the attachment process.[35,36] When compared to control, DPS the MBC and MIC concentrations of DPSE exhibited a considerable reduction in *P. acne* adhesion capacity. Antibiotics cannot penetrate the biofilm because bacterial cells are entrenched inside the exopolymeric matrix. The pre-formed *P. acne* biofilm was strongly inhibited in a dose-dependent manner by DPSE at MBC and MIC concentrations. Biofilm inhibition of *P. acne* produced similar findings, which were verified by fluorescence microscopy experiments. When compared DPS; DPSE has superior in lowering the number of live bacteria at MBC and MIC values, indicating that it exhibits effective anti-biofilm as well as bactericidal activities. As a result, DPSE may be utilized to effectively inhibit *P. acne* biofilm.[37,38] Biofilm inhibition of *P. acne* produced similar findings, which were verified by time kill experiments.

## CONCLUSION

In the current study, DPSE was prepared and optimized using central composite design. Optimized DPSE displayed excellent viscosity, spread ability and controlled and maximum release; this was selected as the optimized batch. The globule size of optimized DPSE was found to be in the nanometer range, with a negative zeta potential. Moreover, this DPSE displayed acceptable appearance, pH and extrudability. Furthermore, optimized DPSE displayed significant anti-bacterial activity against *P. acne* when compared to pure DPS. Thus, DPSE can be a competent alternative for the treatment of acne vulgaris. However, further *in vivo* studies are mandatory to establish its efficacy in the treatment of acne vulgaris.

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## CONFLICT OF INTEREST

The authors declare that they have no conflict of interests.

## ABBREVIATIONS

**DPS:** Dapsone; **DPSE:** Dapsone emulgel; **MIC:** Minimum inhibitory concentrations; **MBC:** Minimum bactericidal concentrations; **CCD:** Central composite design.

## AUTHORS CONTRIBUTION

**STG and GP:** Investigation, Methodology, Writing-original draft, review and editing Visualization, Validation, Conceptualization, Resources, Supervision, Project administration. **ASM and AS:** Methodology, Writing-review and editing, Supervision, Visualization. **SSH and RK:** Writing-review and editing, Software, Visualization, Investigation, Methodology. **SS and RJK and SD:** Investigation, Methodology Software. **KG and PS:** Writing-review, editing, Conceptualization, Resources, Supervision.

## SUMMARY

Acne vulgaris is a disorder related to the skin, which is mainly caused by the formation of seborrhea, comedones, etc. It mainly affects the face, back, head and oil glands. In spite of the potent antimicrobial, anti-inflammatory and antibacterial potential of dapsone, it has hurdles like poor water solubility and bioavailability. Current research develops dapsone emulgel for the treatment of acne vulgaris. Results reveled that the optimized DPSE can be used as a competent alternative to a current treatment for effective management of acne vulgaris. However, further *in vivo* studies are required to establish its efficacy in the treatment of acne vulgaris.

## REFERENCES


1. Gorle AP, Gattani SG. Development and evaluation of ocular drug delivery system. Pharmaceutical development and technology. 2010;15(1):46-52.
2. Meenakshi D. Emulgel A novel approach to topical drug delivery. Int J Pharma Bio Sci. 2013;1:847-56.
3. Wesley Z, Gude R. Formulation, design, development and evaluation of emulgel for topical delivery of meloxicam in the treatment of rheumatoid arthritis. Indo Am J Pharm Res. 2015;5:1271-6.
4. Estabragh MA, Bami MS, Dehghannoudeh G, Noudeh YD, Moghimipour E. Cellulose derivatives and natural gums as gelling agents for preparation of emulgel-based dosage forms: A brief review. International Journal of Biological Macromolecules. 2023;241:124538.
5. Pravallika A, Priyanka R. Formulation and Evaluation of Aceclofenac Topical Emulgel. International Journal of Advanced Technology and Innovative Research. 2019;11(2):43-8.
6. Mohamed MI. Optimization of chlorphenesin emulgel formulation. The AAPS journal. 2004;6:81-7.
7. Wozel VG. Innovative use of dapsone. Dermatologic clinics. 2010;28(3):599-610.
8. Joseph J, PA D GB, R PR TN, Carla B. EMULGEL: A novel trend in topical drug delivery system. World Journal of Pharmaceutical and Medical Research. 2017;3(4):35-9.
9. Swami VJ, Kuchekar BS, Jagdale SC. Development and optimization of site targeted topical delivery of norfloxacin emulgel.2015: 22-34.
10. Haneefa KM, Easo S, Hafsa PV, Mohanta GP, Nayar C. Emulgel: An advanced review. Journal of pharmaceutical sciences and research. 2013;5(12):254.
11. Laithy HM. El shaboury KMF. The development of Cutina Lipogels and gel microemulsion for topical administration of fluconazole. Ame Pharm Sci. PharmSciTech. 2003;3:10-25.
12. Viswanath V, Shiva M, Narasimha Rao B, Gnana Prakash K. Formulation Development and Invitro Evaluation of Clarithromycin Topical gel. Int. J. Pharm. Sci. Rev. Res. 2017;42(1):91-6.
13. Galatage ST, Hebalkar AS, Dhobale SV, Mali OR, Kumbhar PS, Nikade SV, *et al.* Silver nanoparticles: properties, synthesis, characterization, applications and future trends. Silver micro-nanoparticles—Properties, synthesis, characterization and applications. 2021;6:1-8.
14. Bhatt P, Gnanaranjan G. Emulgel: A novel formulation approach for topical delivery of Hydrophobic drugs. International research journal of pharmacy. 2013;4(2):12-6.
15. Jagdale S, Pawar S. Gellified emulsion of ofloxacin for transdermal drug delivery system. Advanced pharmaceutical bulletin. 2017;7(2):229.
16. Gorle A, Pawara K. Formulation, development and evaluation of antiacne dapsone gel. WJ Phar And Pharmaceutical Sci. 2017;8:1664-79.
17. Kasliwal N, Derle D, Negi J, Gohil J. Effect of permeation enhancers on the release and permeation kinetics of meloxicam gel formulations through rat skin. Asian Journal of Pharmaceutical Sciences. 2008;3(5):193-9.
18. Bhanu PV, Shanmugam V, Lakshmi PK. Development and optimization of novel diclofenac emulgel for topical drug delivery. Int J Comp Pharm. 2011;2(9):1-4.
19. Sah SK, Badola A, Mukhopadhyay S. Development and evaluation of tioconazole loaded emulgel. Int J Appl Pharm. 2017;9(5):83-90.
20. Rathod HJ, Mehta DP, Yadav JS. A Review on stomach specific floating *in situ* gel. International Journal of Pharmaceutical Research. 2014;6(4):19.
21. Malavi S, Kumbhar P, Manjappa A, Disouza J, Dwivedi J. Emulgel for improved topical delivery of Tretinoin: Formulation design and characterization. InAnnales Pharmaceutiques Françaises 2022;80(2):157-68.
22. Galatage ST. Development and characterization of microparticles of sumatriptan succinate drug carrier system via nasal route. International Journal of Pharmaceutical Sciences and Research. 2019;10(9):4194-200.
23. Varma VN, Maheshwari PV, Navya M, Reddy SC, Shivakumar HG, Gowda DV. Calcipotriol delivery into the skin as emulgel for effective permeation. Saudi Pharmaceutical Journal. 2014;22(6):591-9.
24. Galatage ST, Hebalkar AS, Gote RV, Mali OR, Killedar SG, Bhagwat DA, *et al.* Design and characterization of camptothecin gel for treatment of epidermoid carcinoma. Future journal of pharmaceutical sciences. 2020;6:1-1.
25. Galatage ST, Killedar SG, Katakar RB, Kumbhar RB, Sharma M, Shirote PJ. Developement and Characterization of Floating Tablets of Nizatidine for Peptic Ulcer. Journal of Advances in Medical and pharmaceutical sciences. 2020;21(4):1-2.
26. Snehal P, Manish S. Formulation development and evaluation of Indomethacin emulgel. Der pharmacia sinica. 2013;4:31-45.
27. Kumbar VM, Peram MR, Kugaji MS, Shah T, Patil SP, Muddapur UM, *et al.* Effect of curcumin on growth, biofilm formation and virulence factor gene expression of *Porphyromonas gingivalis*. Odontology. 2021;109(1):18-28.
28. Bhagwat DA, Swami PA, Nadaf SJ, Choudhari PB, Kumbar VM, More HN, *et al.* Capsaicin loaded solid SNEDDS for enhanced bioavailability and anticancer activity: *in vitro, in silico* and *in vivo* characterization. Journal of Pharmaceutical Sciences. 2021;110(1):280-91.
29. Galatage ST, Hebalkar AS, Gote RV, Mali OR, Killedar SG. Silver nano particles by green synthesis: an overview. Research Journal of Pharmacy and Technology. 2020;13(3):1503-10.
30. Sonam V, Charu S, Easwari TS, Shukla VK. Emulgel based gel technique: Novel approach for enhancing topical drug delivery of hydrophobic drugs. Int J Pharm Res Sch. 2014;3:1-2.
31. Singh S, Rohilla BD. Formulation and Evaluation of Herbal Gel from Different Parts of *Cyamposis tetragonoloba* (L.) Taub. For Wound Healing. World Journal of Pharmacy and Pharmaceutical Sciences. 2015;5(3):740-52.
32. Khullar R, Kumar D, Seth N, Saini S. Formulation and evaluation of mefenamic acid emulgel for topical delivery. Saudi pharmaceutical journal. 2012;20(1):63-7.
33. Galatage ST, Manjappa AS, Waghmode RR, Harale SS, Katkar RB, Desai SA, *et al.* Role of Drug Repurposing in Cancer Treatment and Liposomal Approach of Drug Targeting. InDrug Repurposing-Advances, Scopes and Opportunities in Drug Discovery 2023 Feb 22. IntechOpen.
34. Abd-Elhakeem E, Teaima MH, Abdelbary GA, El Mahrouk GM. Bioavailability enhanced clopidogrel-loaded solid SNEDDS: development and *in vitro/in vivo* characterization. Journal of Drug Delivery Science and Technology. 2019;49:603-14.
35. Kugaji MS, Kumbar VM, Peram MR, Patil S, Bhat KG, Diwan PV. Effect of Resveratrol on biofilm formation and virulence factor gene expression of *Porphyromonas gingivalis* in periodontal disease. Apmis. 2019;127(4):187-95.
36. Nazzal S, Nutan M, Palamakula A, Shah R, Zaghloul AA, Khan MA. Optimization of a self-nanoemulsified tablet dosage form of Ubiquinone using response surface methodology: effect of formulation ingredients. International journal of pharmaceutics. 2002;240(1-2):103-14.
37. Galatage ST, Killedar SG, Katakar RB, Kumbhar RB, Sharma M, Shirote PJ. Developement and Characterization of Floating Tablets of Nizatidine for Peptic Ulcer. Journal of Advances in Medical and pharmaceutical sciences. 2020;21(4):1-2.
38. Nekkanti V, Karatgi P, Prabhu R, Pillai R. Solid self-microemulsifying formulation for candesartan cilexetil. Aaps Pharmscitech. 2010;11:9-17.
39. Tan J. Dapsone 5% gel: a new option in topical therapy for acne. Skin Therapy Letter. 2012;17(8):1-3.
40. Shahzad M, Millhouse E, Culshaw S, Edwards CA, Ramage G, Combet E. Selected dietary (poly) phenols inhibit periodontal pathogen growth and biofilm formation. Food and function. 2015;6(3):719-29.
41. Kala BS, Gunjan C, Disha N, Shobha P. Treatment of periodontal disease-a herbal approach. Int J Pharm Sci Rev Res. 2015;33(2):126-36.
42. Donlan RM. Biofilms: microbial life on surfaces. Emerging infectious diseases. 2002;8(9):881.
43. Jaiswal S, Mishra P. Antimicrobial and antibiofilm activity of curcumin-silver nanoparticles with improved stability and selective toxicity to bacteria over mammalian cells. Medical microbiology and immunology. 2018;207:39-53.
44. Kodoli RS, Galatage ST, Killedar SG, Pishwikar SA, Habbu PV, Bhagwat DA. Hepatoprotective activity of *Phyllanthus niruri* Linn. endophytes. Future Journal of Pharmaceutical Sciences. 2021;7(1):97.
45. Killedar SG, Bhagwat DA, Choudhari A, Saboji JK, Chougule PC, Galatage ST. Development and Characterization of Microsponge of Amphotercin B for Topical Drug Delivery. Research journal of pharmaceutical biological and chemical sciences. 2019;10(1):1288-300.
46. Galatage ST, Manjappa AS, Kumbhar PS, Salawi A, Sabei FY, Siddiqui AM, Patil RV, Akole VS, Powar RD, Kagale MN. Synthesis of silver nanoparticles using *Emilia sonchifolia* plant for treatment of bloodstream diseases caused by Escherichia coli. In Annales pharmaceutiques francaises 2023;81(4):653-66.
47. Galatage ST, Hebalkar AS, Gote RV, Mali OR, Killedar SG, Bhagwat DA, Kumbhar VM. Design and characterization of camptothecin gel for treatment of epidermoid carcinoma. Future journal of pharmaceutical sciences. 2020;6:1-1.
48. Galatage ST, Trivedi R, Bhagwat DA. Characterization of camptothecin by analytical methods and determination of anticancer potential against prostate cancer. Future Journal of Pharmaceutical Sciences. 2021;7(1):104.
49. Khan BA, Ullah S, Khan MK, Alshahrani SM, Braga VA. Formulation and evaluation of *Ocimum basilicum*-based emulgel for wound healing using animal model. Saudi pharmaceutical journal. 2020;28(12):1842-50.
50. Manjappa AS, Kumbhar PS, Kasabe R, Diwate SK, Disouza JI. Ameliorated *in vitro* anticancer efficacy of methotrexate D-α-Tocopheryl polyethylene glycol 1000 succinate ester against breast cancer cells. Future Journal of Pharmaceutical Sciences. 2019;5:1-0.
51. Bandgar SA, Jadhav NR, Manjappa AS. A remarkable *in vitro* cytotoxic, cell cycle arresting and proapoptotic characteristics of low-dose mixed micellar simvastatin combined with alendronate sodium. Drug delivery and translational research. 2020;10:1122-35.
52. Peram MR, Jalalpure S, Kumbar V, Patil S, Joshi S, Bhat K, Diwan P. Factorial design based curcumin ethosomal nanocarriers for the skin cancer delivery: *in vitro* evaluation. Journal of liposome research. 2019;29(3):291-311.
53. Kumbhar P, Kole K, Yadav T, Bhavar A, Waghmare P, Bhokare R, *et al.* Drug repurposing: An emerging strategy in alleviating skin cancer. European Journal of Pharmacology. 2022;926:175031.
54. Kumbhar P, Manjappa A, Shah R, Jha NK, Singh SK, Dua K, *et al.* Inhalation delivery of repurposed drugs for lung cancer: approaches, benefits and challenges. Journal of Controlled Release. 2022;341:1-5.

55. Deshantri AK, Fens MH, Ruiter RW, Metselaar JM, Storm G, Mandhane, *et al.* Complete tumor regression by liposomal bortezomib in a humanized mouse model of multiple myeloma. HemaSphere. 2020;4(5):e463.
56. Sambamoorthy U, Manjappa AS, Eswara BR, Sanapala AK, Nagadeepthi N. Vitamin E oil incorporated liposomal melphalan and simvastatin: approach to obtain improved physicochemical characteristics of hydrolysable melphalan and anticancer activity in combination with simvastatin against multiple myeloma. AAPS PharmSciTech. 2022;23:1-6.
57. Galatage ST, Manjappa AS, Bhagwat DA, Trivedi R, Salawi A, Sabei FY, *et al.* Oral self-nanoemulsifying drug delivery systems for enhancing bioavailability and anticancer potential of fosfestrol: *In vitro* and *In vivo* characterization. European Journal of Pharmaceutics and Biopharmaceutics. 2023;193:28-43.
58. Galatage ST, Trivedi R, Bhagwat DA. Characterization of camptothecin by analytical methods and determination of anticancer potential against prostate cancer. Future Journal of Pharmaceutical Sciences. 2021;7(1):104.

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