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# Formulation And Characterization Of Herbal Microemulsion Gel Containing Nigella Sativa Oil And Coconut Oil

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*Abstract:* The formulation and characterization of an herbal antifungal microemulsion gel using coconut oil and Nigella sativa oil are presented in this study. The formulation procedure achieved a stable microemulsion by optimizing the amounts of surfactants and co-surfactants with the goal of improving the topical administration and activity of antifungal drugs. To verify the gel's stability, homogeneity, and efficacy, characterization methods such as droplet size analysis, zeta potential measurement, and rheological tests were used. Coconut oil and Nigella sativa oil were selected due to their strong antifungal, anti-inflammatory, and skin-beneficial qualities. The created microemulsion gel showed remarkable skin penetration, stability, and retention, indicating that it could be a viable treatment option for fungal infections. According to the study, this unique herbal mixture may work well as a substitute for traditional antifungal medications, providing more therapeutic advantages with fewer adverse effects.

Keywords: Microemulsion, Nigella sativa oil, Coconut oil, Antifungal, Microemulsion gel.

## I. INTRODUCTION

A transparent, isotropic mixture of oil, surfactant, and co-surfactant that is thermodynamically stable is called a microemulsion, and it is a revolutionary drug delivery mechanism. When it comes to enhancing the solubility and bioavailability of poorly soluble drugs, microemulsion is crucial. Because the microemulsion can raise the drug's permeability and solubility in the GIT, it can improve the drug's oral bioavailability. Its increased penetration rate also enhances the drug's administration via cutaneous transport. (1)

Oil, water, and surfactant mixes that are thermodynamically stable are called microemulsions. Its stability can be attributed to the high concentration of surfactants present. There are three basic forms of microemulsion: (2)

**Oil in water type microemulsion:** In this type oil droplets are dispersed in a continuous aqueous phase.

**Water in oil type microemulsion:** In this type water droplets are dispersed in a continuous oil phase.

**Bi-continuous microemulsion:** This kind of microdomain involves the intermixing of water and oil within the system.

Nigella Sativa and coconut oil are classified as polyunsaturated fatty acids, which have the ability to boost both permeability and solubility. It also inhibits the evaporation of water from the surface and is non-toxic. (3,4)

Oils, surfactant, and co-surfactant screening is necessary for the manufacture of microemulgel. These are chosen using the API's solubility profile as a guide. (5)

Presence of oil leads to more penetration of API in the skin. Microemulsions helps in keeping A broad interfacial area for drug absorption is provided by the drug in its solubilized state and the creation of small sized droplets. (6)

The goal of the current study is to develop and assess a microemulsion-based gel of Nigella sativa oil and coconut oil for improved permeability and solubility with improved antifungal activity through the use of polyunsaturated fatty acids. (7)

## II. Materials and Methods

### Materials:

Nigella Sativa Oil and Coconut oil was purchased from Kazima perfumes, Tween 80 was procured from Modern Industries, Sinnar, propylene glycol was procured from Modern Industries, Sinnar, PEG 400 was procured from Pallavi Chemicals, Carbopol was procured from Pallavi Chemicals, methyl paraben and propyl paraben procured by Oxford Laboratory Reagent and Vishal chemicals. All the chemicals used were of analytical grade.

## III. Preparation of microemulsion gel:

Microemulgel consist of two steps. 1st one is prepared stable Microemulsion and 2nd gel formation. Oil was combined with a combination of cosurfactant and surfactant to create a microemulsion, and water was carefully added to the oil phase while being continuously stirred by a magnetic field, at (70-80) °C. After 24hrs add gelling agent into optimized formulation (stable microemulsion)

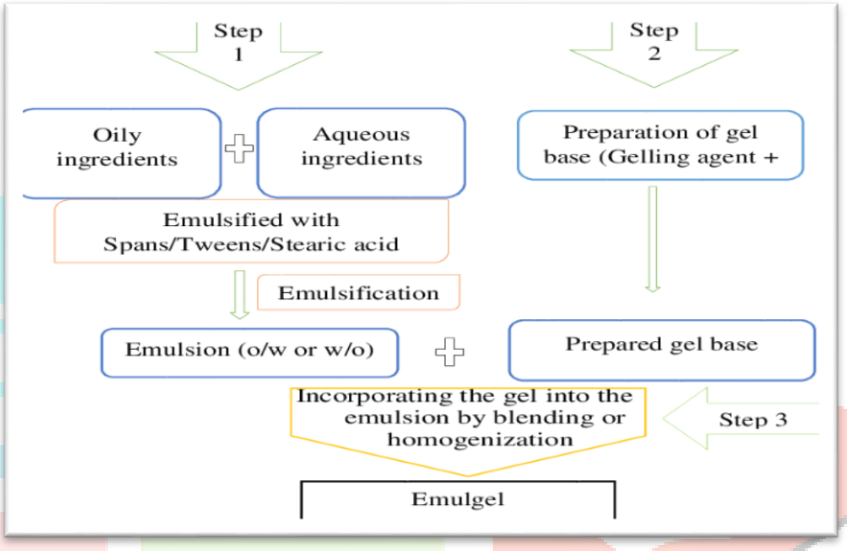



figure 1. formulation chart of microemulgel

## IV. Construct of Ternary Plot Diagram:

First, we construct phase diagram for preparation of microemulsion. Because possible phases and their equilibrium based on a mixture of three components under constant pressure and temperature are displayed on a ternary phase diagram. So, Take Smix in different ratio (1:1, 1:2, 2:1) and finally with the help of ternary phase diagram (ternaryplot.com) we got the ratio of 2:1 is more superior as compare to 1:1 and 1:2 then we carry further Smix in ratio 2:1.

For each phase diagram, nine sections (1:9, 2:8, 3:7, 4:6, 5:5, 6:4, 7:3, 8:2, and 9:1) of oil and surfactant/cosurfactant (2:1) were used.

Under agitation at Sixty rpm, a tiny amt. of water added to the combination in 0.5% w/w increments, and the combination was then given time to equilibrate.

A Microemulsion was considered clear or hardly muddy when the titration was terminated and the water volume was recorded. The mass% of oil, water, and surfactant/cosurfactant were recorded at the end point since the sum was 100%.

Phase diagram microemulsion area sizes were compared; the greater the size, the better the micro-emulsifying ability.

table 1. formulation batches of ternary phase diagram

| Ingredients | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
|---|---|---|---|---|---|---|---|---|---|
| Nigella Sativa oil & Coconut oil (ml) | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |
| Smix (2:1) Tween 80: Polyethylene glycol (ml) | 9 | 8 | 7 | 6 | 5 | 4 | 3 | 2 | 1 |
| Water (ml) | q.s. | q.s. | q.s. | q.s. | q.s. | q.s. | q.s. | q.s. | q.s. |

## V. Formulation of Microemulsion:

The mixture was made with the help of the necessary ratio of surfactants to cosurfactant to create a stable microemulsion. To create an acceptable Smix ratio, Propylene Glycol (as co-surfactant) and Tween 80 (a surfactant) were dissolved to create a unique combination for the microemulsion's Oil Phase. With purified water serving as the aqueous phase and Nigella sativa oil and Coconut oil as the oil phase, the phase behavior was examined using the titration method. Water was added drop by drop against the oil-surfactant phase while being stirred magnetically at room temperature (70–80°C) until turbidity appeared.

table 2. composition of different formulation batches for microemulgel

| Ingredients | GF1 (5:5) | GF2 (5:5) | GF3 (5:5) | GF4 (6:4) | GF5 (6:4) | GF6 (6:4) |
|---|---|---|---|---|---|---|
| Nigella Sativa Oil and Coconut Oil | 35.06 | 35.06 | 35.06 | 36.76 | 36.76 | 36.76 |
| Smix (gm) | 35.06 | 35.06 | 35.06 | 24.51 | 24.51 | 24.51 |
| Methyl Paraben (gm) | 0.15 | 0.15 | 0.15 | 0.15 | 0.15 | 0.15 |
| Propyl Paraben (gm) | 0.30 | 0.30 | 0.30 | 0.30 | 0.30 | 0.30 |
| HPMC (mg) | 1.00 | 1.50 | 2.00 | 1.00 | 1.50 | 2.00 |
| Triethanolamine (ml) | q.s. | q.s. | q.s. | q.s. | q.s. | q.s. |
| Carbopol (gm) | 0.40 | 0.40 | 0.40 | 0.40 | 0.40 | 0.40 |
| Distilled Water (ml) | 29.87% | 29.87% | 29.87% | 38.73% | 38.73% | 38.73% |

## VI. Evaluation of microemulgel:

### i. Visual observation

To verify the parameters, including phase separation and transparency, a visual inspection of the preparation was conducted. For additional examination, the formulations with no phase separation and improved clarity were chosen.

### ii. Measurement of pH

The pH of the prepared microemulsion formulations were determined by using a calibrated digital pH meter.

### ii. Viscosity

The viscosity of the prepared microemulsions were measured by using Brookfield's viscometer. (8)

### iv. Particle size analysis

Using Nano particle SZ 100, the particle size or globule size of particular formulations was examined. A dynamic light scattering (DLS) technique was used to determine the particle size. The particle size of the sample is assessed by placing it in a cuvette and running it through a particle size analyzer.

### iv. Zeta potential analysis

The surface charge of the microemulsions was measured by the SZ-100 by measuring the zeta potential of a solution. The sample is injected into a cuvette and placed in the particle size analyzer and the zeta potential of the prepared microemulsion were measured. The zeta potential is mostly used to check of dispersion stability of a sample. (9)

### v. Drug content

By dissolving 1g of emulgel into 100 ml of acetone, the drug concentration was determined. 1 milliliter was taken out of this and diluted with acetate buffer to make 10 milliliters. Acetone was chosen since it had the best solubility in acetone and Nigella sativa and coconut oil were insoluble in water. After 30 minutes of sonication, this solution was filtered. Following sonication, the medication disintegrated entirely and no precipitate was seen. used spectrophotometry to measure the absorbance at 326 and 327 nm. (10)

**vi. Spreadability:**

To test spreadability, two 7.5 cm long glass slides were used. Accurate weight measurements of 350 mg of microemulgel were made on a single glass slide. Five centimeters above it was another glass slide. Five grams of weight was maintained on the upper slide, and after a minute, the diameter of the spread circle was measured in centimeter. The type of gel is indicated by the observed diameter. (11)

**vii. Skin Irritation test:**

Microemulsion gel applied on skin and check after irritation.

**viii. In vitro permeation study:**

Laboratory assembly apparatus resembling a Franz diffusion cell was used to determine the release profile of drug from topical microemulgel. The cell consisted of two chambers, the donor and the receptor compartment in which between a diffusion membrane (Fish membrane) was mounted. The donor compartment, with inner diameter 24mm, was open i.e., exposed to the atmosphere at one end and the receptor compartment was such that it permitted sampling. The diffusion medium used was phosphate buffer solution pH 6.8(PBS). 0.5 gm of the drug containing topical microemulgel was placed in the donor compartment separated from the receptor compartment by the fish membrane. The fish membrane was previously soaked for 24hrs, in PBS.

The donor and receptor compartments were held together using a clamp. The position of the donor compartment was adjusted so that fish membrane just touches the diffusion medium. The whole assembly was fixed on a thermostatically controlled magnetic stirrer. It was maintained at 37°C+ 0.50°C and stirred constantly at 50rpm. Samples of 3 ml were collected at predetermined time intervals and analyzed for drug content by uv spectrophotometer at max against blank. The receptor phase was replenished with an equal volume of phosphate buffer at each time of sample withdrawn at suitable time intervals and replaced with equal amounts of fresh dissolution media. Samples were analyzed spectrophotometrically at 327 nm and 326 nm therefore the cumulative % drug release was calculated. (12)

**ix. In vitro antifungal study:**

dissolved nutrient agar in distilled water to prepare the nutrient agar medium. To maintain sterility, the mixture was autoclaved. To create a pure culture, inoculate Candida albicans onto a brand-new nutrient agar plate. The plate was incubated for 24 hours at 37°C. Place a loopful of Candida albicans cells into a tube filled with sterile saline solution using a sterile loop. Suspension turbidity was adjusted to meet the 0.5 McFarland requirement. Using a sterile cotton swab, evenly inoculate the whole surface of a nutrient agar plate with the Candida albicans suspension. Let the plate air dry to guarantee even dispersal. In the agar medium, make wells with a sterile cork borer. made certain that the wells were dispersed and spaced evenly over the agar plate.

noted the outcomes and contrasted the zones of inhibition for various antifungal drug concentrations. (13)

## VII. RESULTS AND DISCUSSION

**i. Physical Appearance:**

table 3. physical appearance

| Sr. No. | Formulation code | Colour | Odor | Phase separation |
|---|---|---|---|---|
| 1. | GF1 | Slightly Brown | Characteristics to NSO | No |
| 2. | GF2 | Slightly Brown | Characteristics to NSO | No |

**ii. Measurement of pH:**

The pH of all formulations was within a range of 5.60 to 6 which in accordance with skin pH indicating compatibility with skin.

**iii. viscosity:**

Viscosity of microemulsion was determine by Brookfield's viscometer using spindle no 6.

table 4. viscosity of microemulgel

| Sr. | Batch | Viscosity (cp) |
|---|---|---|
| 1. | GF1 | 153.50-210 |
| 2. | GF4 | 180.80-250 |

**iv. Measurement of droplet size, polydispersity index and Zeta potential**

The Malvern particle size analyzer (Zetasizer Ver. 8.02) was used to measure the mean droplet size, polydispersity index, and zeta potential and results are shown in Table.

table 5. droplet size, polydispersity index, and zeta potential of microemulsion

table 5. globule size, pdi and zeta potential

| Sr. No. | Evaluation | F6 (MEF6) |
|---|---|---|
| 1. | Globule size (d. nm) | 117.6 |
| 2. | PDI | 0.237 |
| 3. | Zeta potential (mV) | -17.06 |

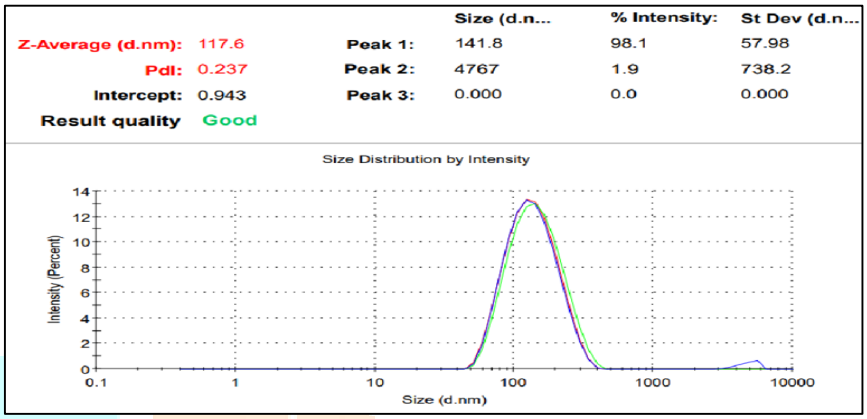



figure 2. globule size and PDI of batch of f6

**Zeta Potential Measurement:**

Zeta potential measurement gives an idea about the potential stability of the colloidal system.

table 6. zeta potential measurement

| Sr. no. | Formulation Batch | Sample Name | Zeta Potential (mV) |
|---|---|---|---|
| 1. | F6 | MEF6 | -17.06 |

**Formulation Batch (MEF6)**

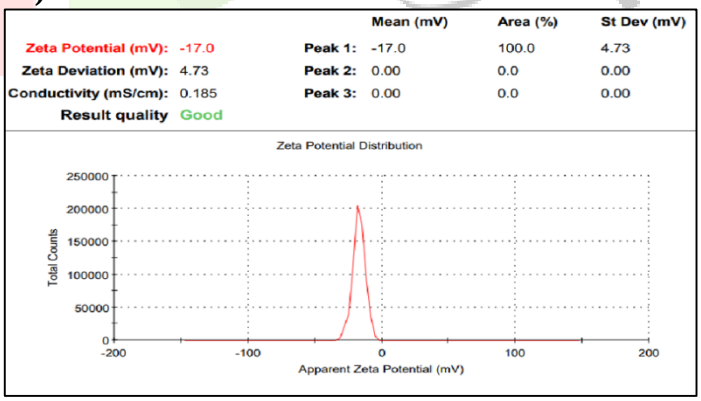



figure 3. zeta potential of batch f6

**v. Drug Content Determination:** The drug content of prepared batches from GF1 was shown in table no. 7

table 7. drug content of microemulgel

| Sr. No. | Formulation Code | Drug | Drug content |
|---|---|---|---|
| 1. | GF1 | Nigella sativa oil | 91.06% |
| 2. | GF1 | Coconut oil | 89.12% |

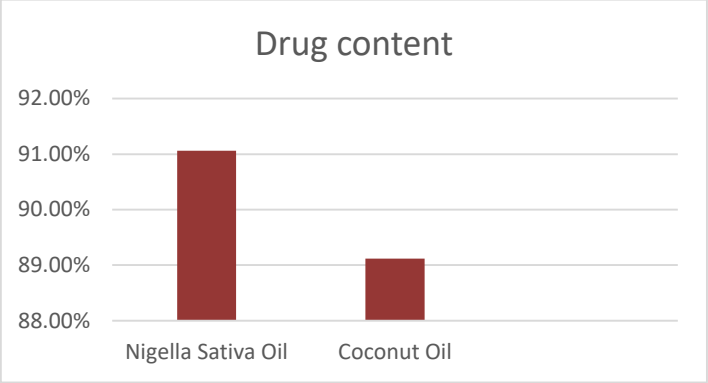



figure 4. drug content percent (%)

**vi. Spreadability:** The gel formulation GF1 produced good Spreadability than the GF3 formulation. Spreadability of microemulgel were found to have in the range of 19 to 21gm.cm/s indicating good Spreadability.

table 8. spreadability of microemulgel

| Sr. No. | Formulation Batch | Spreadability (gm.cm/cm) |
|---|---|---|
| 1. | GF1 | 20.18±1.08 |
| 2. | GF3 | 19.17±1.67 |

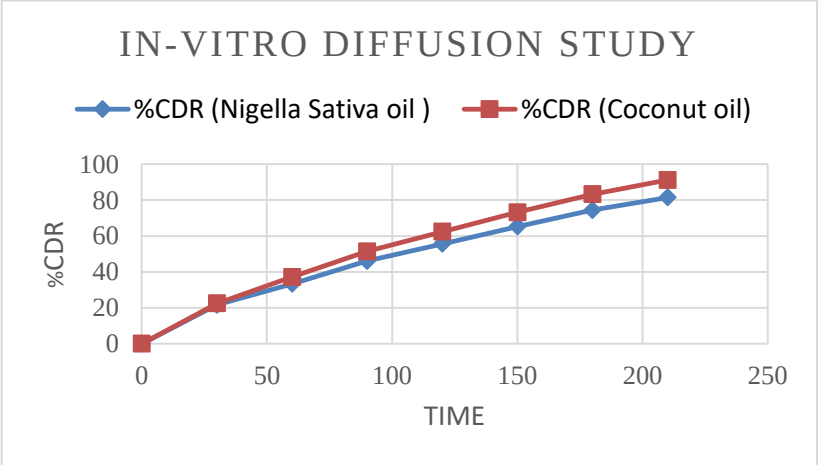
**vii. Skin Irritation test:** After 2hrs Skin doesn't get irritation or any other side effect.

**viii. In-vitro Study: In Vivo Study:**

table 9. in-vitro drug release

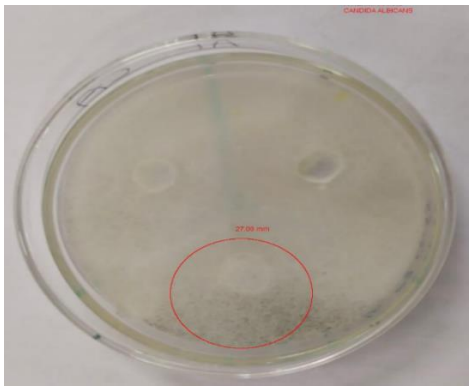
| Time (Min) | %CDR (Nigella Sativa oil) | %CDR (Coconut oil) |
|---|---|---|
| 0 | 0 | 0 |
| 30 | 21.72 | 22.5 |
| 60 | 33.38 | 37.17 |
| 90 | 46.09 | 51.39 |
| 120 | 55.62 | 62.43 |
| 150 | 65.26 | 73.13 |
| 180 | 74.39 | 83.26 |
| 210 | 81.43 | 91.13 |
| 240 | 89.47 | 96.13 |

figure 5. in-vitro drug release



**ix. Antifungal Activity:**

figure 6. zone of inhibition (nigella sativa oil & coconut oil of microemulgel)



**Observation:**

**Microorganism:** Candida Albicans

**Zone of Inhibition:** 27.00 mm

**Interpretation of Results:** The diffusion method was employed to assess the antimicrobial activity of samples against different microorganisms. The diameter of the zones of inhibition was measured for each combination of microorganism and sample. The results indicated varying levels of effectiveness against the tested microorganisms. The Microorganism Candida albicans exhibited sensitivity by providing a clear zone of inhibition. The sample was found to exhibit strong activity against the tested species.

**Results:** sample is found to have a potent anti-fungal effect on tested Candida albicans.

**Conclusion:** The Nigella sativa oil and coconut oil microemulsion, prepared with Tween 80 and propylene glycol and incorporated into HPMC, formed a microemulsion gel with a pH of 6 and good viscosity and rheological properties. The optimized batch GF1 showed 96.13% drug release in 4 hours and had better antifungal activity compared to GF4. The gel was stable for 3 months and can be a viable alternative to current treatments for candidiasis. Its therapeutic potential against candida infections has been demonstrated, and it could also be effective against other fungal strains like superficial fungal infections. Therefore, microemulgel is an excellent topical drug delivery system.

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