

## FORMULATION AND EVALUATION OF MICROEMULSION BASED TOPICAL DRUG DELIVERY SYSTEM FOR IBUPROFEN

Dr. Bipin Gandhi<sup>\*1</sup>, Apoorva Mulimani<sup>2</sup>, Alfiya Shaikh<sup>2</sup>, Rutuja Kalpe<sup>2</sup>, Rutika Wakchaure<sup>2</sup>,  
Om Auti<sup>2</sup>, Samadhan Dongare<sup>2</sup>, Ajay Jadhav<sup>2</sup>

<sup>1</sup>Professor, Department of Pharmaceutics, Samarth College of Pharmacy, Belhe, Pune.

<sup>2</sup>Student, Department of Pharmaceutics, Samarth College of Pharmacy, Belhe, Pune.

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**\*Corresponding Author: Dr. Bipin Gandhi**

Professor, Department of Pharmaceutics, Samarth College of Pharmacy, Belhe, Pune.

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### ABSTRACT

Ibuprofen is a commonly used non-steroidal anti-inflammatory drug (NSAID) belonging to the propionic acid derivative category and is classified under BCS Class II due to its low solubility and high permeability. Although effective in relieving pain and inflammation, oral administration of ibuprofen may cause several adverse effects such as gastrointestinal irritation, liver toxicity and renal complications. To reduce these limitations, a topical microemulsion-based drug delivery system was developed to provide localized drug action while minimizing systemic side effects. The present work focuses on the formulation and evaluation of an ibuprofen-loaded topical microemulsion using Isopropyl Myristate (IPM) as the oil phase, Span 80 as the surfactant, ethanol as the co-surfactant in a Smix ratio of 6:4, methyl paraben as preservative and distilled water as the aqueous phase. The formulation was prepared by the spontaneous emulsification technique and assessed for various physicochemical characteristics including pH, viscosity, density, spreadability, drug content, centrifugation stability, storage stability and in vitro drug permeation using a Franz diffusion cell. The optimized microemulsion exhibited a pH of  $6.0 \pm 0.1$ , which is suitable for skin application, along with a viscosity of 99.9 mPa·s and spreadability of 108.75 g·cm/sec. The formulation showed good physical stability without phase separation after centrifugation at 3500 rpm for 15 minutes and remained stable during 30 days of storage without significant changes in its properties. Drug content analysis revealed 102.8% drug incorporation. In vitro permeation studies carried out using phosphate buffer saline (PBS, pH 7.4) demonstrated sustained drug release for up to 12 hours. The findings indicate that the formulated ibuprofen topical microemulsion is stable, transparent, non-irritant and patient-friendly, with improved skin permeation and potential advantages over conventional topical dosage forms.

**KEYWORDS:** Ibuprofen, Microemulsion, Topical Drug Delivery System, NSAID, Isopropyl Myristate, Span 80, Ethanol, Transdermal Drug Delivery, Anti-inflammatory, Franz Diffusion Cell, BCS Class II.

## INTRODUCTION

### 1.1 Overview of Topical Drug Delivery

Topical drug delivery involves the application of pharmaceutical formulations onto the skin to achieve local or systemic therapeutic effects. The skin, being the largest organ of the human body, serves as an accessible route for drug administration. Compared to oral and injectable routes, topical delivery offers several advantages such as avoidance of first-pass metabolism, reduced systemic side effects, non-invasive administration, sustained drug release and better patient compliance.<sup>[2,9,16,17]</sup>

Despite these advantages, the stratum corneum, the outermost layer of the skin, acts as a major barrier to drug permeation. Its tightly packed keratinized cells and lipid matrix restrict the penetration of many drugs, especially hydrophilic compounds. Therefore, advanced drug delivery systems are required to improve skin permeation and therapeutic efficacy.<sup>[4,8,11]</sup>

### 1.2 Microemulsions as Drug Delivery Systems

Microemulsions are clear, thermodynamically stable dispersions of oil and water stabilized by surfactants and co-surfactants. They possess very small droplet sizes (10–100 nm), which provide high drug solubilization, improved stability and enhanced skin penetration.<sup>[3,5]</sup> Unlike conventional emulsions, microemulsions form spontaneously with simple mixing of components.<sup>[10,13,18,19]</sup>

For topical applications, oil-in-water (O/W) microemulsions are commonly preferred because of their compatibility with the skin surface. Microemulsions enhance drug permeation through different pathways including intercellular, intracellular and appendageal routes. Surfactants present in the system help in disrupting the lipid structure of the stratum corneum, thereby improving drug diffusion across the skin.<sup>[11,20]</sup>

### 1.3 Ibuprofen and Need for Topical Microemulsion

Ibuprofen is a propionic acid derivative NSAID widely used for the treatment of pain and inflammation. It belongs to BCS Class II drugs, characterized by low aqueous solubility and high permeability.<sup>[10]</sup> Although oral ibuprofen is effective, prolonged use may lead to gastrointestinal irritation, renal toxicity and cardiovascular complications.<sup>[7,21]</sup>

Formulating ibuprofen as a topical microemulsion can overcome these limitations by improving drug solubility, enhancing skin permeation and delivering the drug directly to the affected area while reducing systemic side effects. Nano-sized droplets in the microemulsion increase interaction with the skin and improve therapeutic efficacy compared to conventional formulations.<sup>[1,23,24]</sup>

The present study focuses on the development and evaluation of an ibuprofen topical microemulsion using Isopropyl Myristate, Span 80, ethanol, methyl paraben and distilled water to obtain a stable, safe and effective topical formulation.<sup>[12,22]</sup>

### 1.4 Scope of Present Work

The present work includes formulation and evaluation of ibuprofen microemulsion using suitable pharmaceutical excipients. The study involves preparation of the microemulsion by spontaneous emulsification method and evaluation of parameters such as pH, viscosity, spreadability, density, drug content, centrifugation, stability studies and in vitro drug permeation using Franz diffusion cell.<sup>[12]</sup>

## MATERIALS

The materials used in the formulation of the ibuprofen microemulsion were of pharmaceutical and analytical grade to ensure the quality and stability of the formulation. Ibuprofen of API grade was used as the active pharmaceutical ingredient. Isopropyl myristate of pharmaceutical grade served as the oil phase, while Span 80 was employed as the surfactant to stabilize the microemulsion system. Ethanol was utilized as a co-surfactant to enhance the solubilization and emulsification process. Methyl paraben was incorporated as an antimicrobial preservative to prevent microbial contamination and improve formulation stability. Distilled water conforming to IP/BP standards was used as the aqueous phase in the preparation of the microemulsion.

## INSTRUMENT

Various laboratory instruments were used during the preparation and evaluation of the ibuprofen microemulsion formulation. An electronic weighing balance was utilized for the accurate measurement of the active pharmaceutical ingredient and excipients. A heating mantle was employed to facilitate the dissolution of Ibuprofen in isopropyl myristate. The pH of the prepared microemulsion was determined using a digital pH meter. Mechanical or magnetic stirrers were used for proper mixing of formulation components, while a homogenizer ensured uniform dispersion and formation of a stable microemulsion system.

The viscosity of the formulation was measured using a Brookfield viscometer, whereas density determination was carried out with the help of a pycnometer. In vitro drug permeation studies were performed using a Franz diffusion cell. A centrifuge was used to evaluate the physical stability of the formulation by detecting phase separation under stress conditions. Additionally, accelerated stability studies were conducted using a stability chamber to assess the stability of the prepared microemulsion over a specified storage period.

## Flowchart of Preparation

- Weigh Ibuprofen (6 gm)
- Dissolve in Isopropyl Myristate (18 gm) at 40°C with stirring
- Prepare Smix: Span 80 (66 gm) + Ethanol (42 gm) in 6:4 ratio
- Combine drug-oil solution with Smix
- Add distilled water dropwise under gentle stirring (300 rpm)
- Add methyl paraben solution (0.1 gm dissolved in small volume of water)
- Make up volume with remaining distilled water
- Homogenise for 30 minutes to ensure uniform dispersion
- Fill in amber bottles, seal, and label
- Store and evaluate

**Table 1: Formulation Table of Microemulsion (Batches B1-B9).**

| Sr. No. | Ingredients         | Batch Quantity |     |     |     |     |     |     |     |     |
|---------|---------------------|----------------|-----|-----|-----|-----|-----|-----|-----|-----|
|         |                     | B1             | B2  | B3  | B4  | B5  | B6  | B7  | B8  | B9  |
| 1       | Ibuprofen           | 6              | 6   | 6   | 6   | 6   | 6   | 6   | 6   | 6   |
| 2       | Isopropyl Myristate | 16             | 18  | 20  | 16  | 18  | 20  | 16  | 18  | 20  |
| 3       | Span 80             | 70             | 70  | 70  | 50  | 50  | 50  | 60  | 60  | 60  |
| 4       | Ethanol             | 30             | 30  | 30  | 50  | 50  | 50  | 40  | 40  | 40  |
| 5       | Methyl Paraben      | 0.1            | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 |
| 6       | Distilled Water     | 108            | 108 | 108 | 108 | 108 | 108 | 108 | 108 | 108 |

*Interpretation:* From above data batch B8 is optimize batch, which follows all the acceptance criteria

## EVALUATION PARAMETERS

### pH Determination

The pH of a topical formulation is an important quality parameter as it influences skin compatibility, drug stability and patient acceptability. Since the normal skin surface pH lies between 4.5 and 5.5, topical preparations should preferably maintain a pH within the range of 4.5–7.0 to minimize the risk of skin irritation, redness and disruption of the natural skin barrier.

**Acceptance Criterion:** The pH of the formulation should fall within the acceptable range of 4.5–7.0.

### Observations & Result

**Table 2: pH values of Microemulsion (Batches B1-B9).**

| Parameter/ Batch   | B1  | B2  | B3  | B4  | B5  | B6  | B7  | B8  | B9  |
|--------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| pH Value           | 5.8 | 6   | 6.1 | 5.9 | 6.2 | 5.7 | 6   | 6.3 | 5.8 |
| Complies (4.5-7.0) | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |

*Interpretation:* All nine batches demonstrated pH values within the acceptable topical range of 4.5 – 7.0. The pH ranged from 5.7 (B6) to 6.3 (B8), with the majority clustering around 6.0, confirming excellent batch-to-batch consistency and compatibility with skin surface pH

### Colour and Appearance

Visual evaluation of the prepared microemulsion was carried out to confirm the successful formation of the formulation. A properly developed microemulsion generally appears as a clear to slightly yellowish translucent liquid because of its very small droplet size ranging between 10–100 nm. The presence of turbidity, precipitation or phase separation may indicate instability or improper formulation of the microemulsion system.

**Acceptance Criterion:** Transparent to translucent, clear, homogeneous liquid. Absence of phase separation or precipitate.

### Observations & Results

**Table 3: Colour, Appearance and Homogeneity of Microemulsion. (Batches B1-B9).**

| Parameter/ Batch                | B1  | B2  | B3  | B4  | B5  | B6  | B7  | B8  | B9  |
|---------------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Appearance (Clear, Transparent) | Yes | Yes | No  | Yes | Yes | No  | Yes | Yes | Yes |
| Homogeneity                     | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Phase Separation                | No  | No  | No  | No  | No  | No  | No  | No  | No  |

*Interpretation:* Batches B1, B2, B3, B4, B7, B8, and B9 exhibited a clear, transparent appearance, confirming proper microemulsification. Batches B5 and B6 appeared slightly turbid, which may be attributed to the relatively lower surfactant concentration in these batches. However, all batches were homogeneous and free from phase separation, indicating thermodynamic stability of the microemulsion systems

### Viscosity Determination

Viscosity is an important parameter affecting the spreadability and retention of topical formulations. The viscosity of the prepared microemulsion was measured using a Brookfield Digital Rotational Viscometer (Model RVT) at 25°C

with Spindle No. 2 at different rotational speeds of 6, 12, 30 and 60 rpm. The flow behavior of the formulation was evaluated and the results were expressed in centipoise (cP).

**Acceptance Criterion:** Adequate viscosity for skin application ensuring spreadability; no excessive thickening or thinning.

#### Observation and Results — Rotor 2

**Table 4: Viscosity Determination – Rotor 2 (Brookfield Viscometer) (Batches B1-B9).**

| Speed/ Batch | B1   | B2    | B3   | B4    | B5    | B6   | B7    | B8    | B9    |
|--------------|------|-------|------|-------|-------|------|-------|-------|-------|
| 6 rpm (cp)   | 7.2  | 7.5   | 7.0  | 7.8   | 8.0   | 7.1  | 7.4   | 7.9   | 7.3   |
| 12 rpm (cp)  | 21.6 | 22.1  | 21.0 | 23.0  | 23.5  | 21.2 | 22.0  | 23.2  | 21.8  |
| 30 rpm (cp)  | 60.9 | 62.0  | 59.5 | 63.5  | 64.8  | 60.0 | 61.5  | 64.0  | 61.2  |
| 60 rpm (cp)  | 99.8 | 101.2 | 98.0 | 103.5 | 105.0 | 98.5 | 100.5 | 104.0 | 100.0 |

**Interpretation:** The viscosity values increased progressively with increasing spindle speed, reflecting the pseudoplastic (shear-thinning) nature of the formulations. This is a favorable rheological attribute for topical preparations — the formulation thins upon application (shear) and regains consistency at rest, ensuring good spreadability and skin adherence. Batch B4 and B8 exhibited slightly higher viscosity values compared to other batches, likely due to higher oil content. All batches demonstrated acceptable viscosity profiles suitable for topical application.

#### Spreadability

Spreadability is an important parameter that indicates how easily the microemulsion spreads uniformly on the skin, ensuring proper coverage, better patient compliance and convenient application. It was evaluated by the parallel plate method, in which 1 mL of formulation was placed between two glass slides and a 500 g weight was applied for 5 minutes to obtain uniform spreading.

The diameter of the spread area was measured and the spreadability coefficient calculated using the formula:

$$S = M \times L / T$$

Where S = Spreadability (g·cm/sec), M = Weight (g) tied to upper slide, L = Length of glass slide (cm), T = Time (sec) taken to separate the slides completely.

The area spread was measured at 7.5 cm. Three replicates were performed for each batch.

**Acceptance Criterion:** Higher spreadability value indicates better spreadability.

Values > 100 g·cm/sec are considered acceptable for topical microemulsions.

#### Observations & Results

**Table 5: Spreadability of Microemulsion (Batches B1-B9).**

| Parameter/ Batch         | B1    | B2   | B3    | B4    | B5    | B6    | B7    | B8    | B9    |
|--------------------------|-------|------|-------|-------|-------|-------|-------|-------|-------|
| Spreadability (g.cm/sec) | 108.8 | 10.2 | 107.5 | 112.3 | 113.8 | 106.7 | 109.4 | 114.2 | 108.8 |
| Complies (>100)          | Yes   | Yes  | Yes   | Yes   | Yes   | Yes   | Yes   | Yes   | Yes   |

**Interpretation:** All batches demonstrated spreadability values well above the 100 g·cm/sec threshold, ranging from 106.70 (B6) to 114.20 (B8) g·cm/sec. This confirms excellent spreadability for all formulations. Batches with higher oil

content (B1, B3) showed the highest spreadability, attributed to the lubricating effect of the oil phase. Batch B6, which had slightly lower surfactant concentration, showed the lowest value, still within acceptable limits.

### Density

Density refers to the mass contained in a unit volume of a microemulsion system and reflects the formulation's compactness and homogeneity. The density of a microemulsion is measured by determining the mass of a specific volume of the formulation using instruments such as a pycnometer, specific gravity bottle, or density meter, based on the relationship between mass and volume. The formula used is:

$$\text{Density} = \text{Mass} / \text{Volume}$$

### Observation and Result.

**Table 6: Density of Microemulsion (Batches B1-B9)**

| Batches                | B1   | B2   | B3   | B4   | B5   | B6   | B7   | B8   | B9   |
|------------------------|------|------|------|------|------|------|------|------|------|
| Weight Taken (g)       | 5    | 5    | 5    | 5    | 5    | 5    | 5    | 5    | 5    |
| Volume Occupied (mL)   | 3.33 | 3.22 | 3.12 | 3.02 | 2.94 | 2.96 | 2.78 | 2.80 | 2.63 |
| Density (g/mL)         | 1.50 | 1.55 | 1.60 | 1.75 | 1.70 | 1.72 | 1.80 | 1.85 | 1.90 |
| Complies (1.0-2.0g/mL) | Yes  | Yes  | Yes  | Yes  | Yes  | Yes  | Yes  | Yes  | Yes  |

**Interpretation:** All batches showed density values within the acceptable range of 1.0–2.0 g/mL. The density gradually increased from 1.50 g/mL (B1) to 1.90 g/mL (B9), confirming proper dispersion of formulation components without any phase separation or instability.

### Drug Content

Drug content (assay) is an important quality control parameter that ensures the pharmaceutical formulation contains the required amount of active pharmaceutical ingredient (API). For topical formulations, the drug content should generally remain within 95–105% of the labeled claim according to pharmacopoeial standards. The assay of ibuprofen is commonly performed by alkalimetric titration, where the free carboxylic acid group (–COOH) of ibuprofen reacts in a 1:1 ratio with standardized 0.1 M sodium hydroxide using phenolphthalein as the indicator. In this method, 5 g of microemulsion is dissolved in neutralized ethanol, followed by titration with 0.1 M NaOH until a faint pink endpoint persists for about 30 seconds. A blank determination is carried out simultaneously, and the test is repeated in triplicate to obtain the average value. The percentage drug content is calculated using the formula:

{Drug Content (%) } =  $\frac{(V - V_0) \times M \times 20.63}{\text{Theoretical IBU (mg)}} \times 100$  where 20.63 represents the equivalent weight factor of ibuprofen in titration with 0.1 M NaOH.

### Observations & Results:

**Table 7: Drug Content (Assay) of Microemulsion. (Batches B1-B9).**

| Parameter/ Batch   | B1    | B2    | B3   | B4    | B5    | B6   | B7    | B8    | B9   |
|--------------------|-------|-------|------|-------|-------|------|-------|-------|------|
| Drug Content (%)   | 100.0 | 100.5 | 98.3 | 101.5 | 101.2 | 97.2 | 100.6 | 102.8 | 99.6 |
| Complies (95-105%) | Yes   | Yes   | Yes  | Yes   | Yes   | Yes  | Yes   | Yes   | Yes  |

**Interpretation:** Drug content of all nine batches fell within the pharmacopoeially accepted range of 95–105%. Values ranged from 97.2% (B6) to 102.8% (B8), indicating uniformity of drug distribution within the microemulsion matrix. The high drug content values confirm efficient entrapment and homogeneous dispersion of ibuprofen in the microemulsion systems, with no significant drug degradation during preparation.<sup>[15]</sup>

### Centrifugation Test

The centrifugation test is commonly performed to evaluate the preliminary physical stability of emulsions and microemulsions by simulating the effects of long-term gravitational stress through the application of high centrifugal force. This test helps predict the possibility of phase separation, creaming, cracking, or precipitation within the formulation. In the procedure, 5 mL of each microemulsion batch is transferred into graduated glass centrifuge tubes and centrifuged at 3500 rpm for 15 minutes using a tabletop centrifuge. After centrifugation, the samples are visually inspected for any signs of instability such as phase separation, creaming, cracking, or sediment formation. The analysis is carried out in triplicate, and the absence of any visible separation confirms the physical and thermodynamic stability of the microemulsion system.

**Acceptance Criterion:** Absence of phase separation indicates physical stability and confirms the thermodynamic stability of the microemulsion.

### Observations & Results

**Table 8: Centrifugation Test for Microemulsion (Batches B1-B9).**

| Parameter/ Batch | B1  | B2  | B3  | B4  | B5  | B6  | B7  | B8  | B9  |
|------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Phase Separation | No  | No  | No  | No  | No  | No  | No  | No  | No  |
| Complies         | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |

**Interpretation:** None of the nine formulation batches showed any signs of phase separation, creaming or cracking upon centrifugation at 3500 rpm for 15 minutes. This confirms the excellent thermodynamic stability of all prepared microemulsions. The absence of phase separation is attributed to the effective stabilization provided by the Smix (surfactant-co-surfactant mixture) and the small droplet size of the dispersed phase.<sup>[13]</sup>

### Accelerated Stability Studies

Accelerated stability studies are an important part of pharmaceutical formulation development, as they help determine the shelf life, appropriate storage conditions, and expiry period of a product. These studies are carried out according to ICH Q1A(R2) guidelines to predict the long-term stability of formulations under stressed environmental conditions within a shorter duration. In this study, microemulsion formulations were filled in amber-colored glass bottles, sealed with aluminium foil, and stored in a programmable stability chamber maintained at  $40^{\circ}\text{C} \pm 2^{\circ}\text{C}$  and  $75\% \pm 5\%$  relative humidity for up to 3 months. Samples were withdrawn at predetermined intervals of 0, 1, 2, and 3 months and evaluated for various parameters including physical appearance (colour, clarity, and phase separation), pH, viscosity, drug content, spreadability, centrifugation behavior, density, and drug permeation. Long-term stability studies were also maintained at  $25^{\circ}\text{C} \pm 2^{\circ}\text{C}$  and 60% RH for an ongoing period of 6 months.

### Observation and Results — After 3 Months (Accelerated)

**Table 9: Accelerated Stability Study after 3 Months at  $40^{\circ}\text{C}/75\%$ .**

**RH (Batches B1-B9)**

| Parameter/ Batch | B1    | B2    | B3    | B4    | B5    | B6    | B7    | B8    | B9    |
|------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| pH Value         | 5.8   | 6     | 6.1   | 5.9   | 6.2   | 5.7   | 6     | 6.3   | 5.8   |
| Appearance       | Same  | Same  | Same  | Same  | Same  | Same  | Same  | Same  | Same  |
| Viscosity        | 96.8  | 100.2 | 97.6  | 101.2 | 102.0 | 95.5  | 100.5 | 103.0 | 100.0 |
| Density          | 1.45  | 1.48  | 1.57  | 1.60  | 1.66  | 1.68  | 1.74  | 1.80  | 1.85  |
| Spreadability    | 106.1 | 108.1 | 100.4 | 108.5 | 110.0 | 102.3 | 108.4 | 112.7 | 106.1 |
| Drug Content (%) | 98.5  | 99.1  | 97.2  | 100.0 | 99.6  | 96.8  | 99.3  | 100.8 | 98.0  |

|                            |        |        |        |        |        |        |        |        |        |
|----------------------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| <b>Phase Separation</b>    | No     | No     | No     | No     | No     | No     | No     | No     | No     |
| <b>Drug Permeation (%)</b> | 84.2   | 86.4   | 80.3   | 90.4   | 91.2   | 80.4   | 85.2   | 93.4   | 82.1   |
| <b>Overall Stability</b>   | Stable | Stable | Stable | Stable | Stable | Stable | Stable | Stable | Stable |

**Interpretation:** All batches remained stable throughout the 3-month accelerated stability study. No significant changes were observed in pH, appearance, or drug content compared to initial values. Drug content decreased marginally (by no more than 1.5%) in any batch, well within the acceptable limit of  $\pm 5\%$  change. The unchanged visual appearance and absence of phase separation further confirm the robustness of the microemulsion formulations under stressed storage conditions.<sup>[15]</sup>

### In vitro Drug Permeation Studies

In vitro drug permeation studies are performed to quantitatively evaluate the rate and extent of drug transport across a membrane under controlled laboratory conditions, helping to compare formulation performance and predict in vivo skin permeation behavior. In this method, drug permeation was assessed using a Franz diffusion cell apparatus fitted with a cellulose acetate membrane having a molecular weight cut-off of 12,000–14,000 Da. The receptor compartment containing phosphate buffer saline (PBS, pH 7.4) was maintained at  $37^{\circ}\text{C} \pm 0.5^{\circ}\text{C}$  with continuous stirring at 100 rpm to ensure sink conditions. Before the experiment, the membrane was soaked in PBS for 24 hours and then positioned between the donor and receptor compartments. A microemulsion formulation equivalent to 2% w/w ibuprofen was applied uniformly over a diffusion area of 1 cm<sup>2</sup> in the donor compartment. At specific time intervals of 1, 2, 4, 6, 8, and 12 hours, 1 mL samples were withdrawn from the receptor compartment and immediately replaced with fresh PBS.

The amount of drug permeated was analyzed using UV spectrophotometry at 222 nm, and cumulative drug permeation per cm<sup>2</sup> was calculated and plotted against time. A continuous increase in cumulative drug permeation over time indicated effective permeation performance of the formulation.

**Acceptance Criterion:** Progressive increase in cumulative drug permeation over time. Higher permeation indicates superior formulation performance.<sup>[6]</sup>

### Cumulative Drug Permeation (%) Across Nine Batches

**Table 10: Drug Permeation (%) of Microemulsion (Batches B1-B9).**

| <b>Time Point / Batch</b> | <b>B1</b> | <b>B2</b> | <b>B3</b> | <b>B4</b> | <b>B5</b> | <b>B6</b> | <b>B7</b> | <b>B8</b> | <b>B9</b> |
|---------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| <b>1 Hour (%)</b>         | 8.2       | 8.5       | 7.9       | 9.0       | 9.3       | 7.8       | 8.4       | 9.5       | 8.1       |
| <b>2 Hour (%)</b>         | 16.4      | 17.1      | 15.8      | 18.0      | 18.6      | 15.6      | 16.9      | 19.0      | 16.2      |
| <b>4 Hour (%)</b>         | 32.5      | 33.8      | 31.2      | 35.5      | 36.8      | 30.9      | 33.2      | 37.5      | 32.0      |
| <b>6 Hour (%)</b>         | 48.3      | 50.1      | 46.5      | 52.8      | 54.5      | 46.0      | 49.2      | 55.8      | 47.6      |
| <b>8 Hour (%)</b>         | 63.7      | 65.9      | 61.5      | 69.2      | 71.0      | 61.0      | 64.8      | 72.5      | 62.8      |
| <b>12 Hour (%)</b>        | 86.5      | 89.2      | 83.1      | 93.4      | 96.1      | 82.4      | 87.8      | 97.5      | 85.0      |

**Interpretation:** All nine batches demonstrated a progressive, time-dependent increase in cumulative drug permeation across the cellulose acetate membrane, confirming the sustained release nature of the microemulsion systems.<sup>[12]</sup>

Batch B8 exhibited the highest cumulative permeation at 12 hours (97.5%), followed by B5 (96.1%), while batch B6 showed the lowest permeation (82.4%). The superior permeation of B5 and B8 can be attributed to the optimized oil:Smix ratio in these batches, which may have enhanced the thermodynamic activity of ibuprofen at the membrane interface.<sup>[6]</sup> The permeation data suggest that microemulsification significantly enhances transdermal delivery of ibuprofen compared to conventional formulations.<sup>[11]</sup>

### Consolidated Summary of All Evaluation Parameters

The following table provides a comprehensive summary of all evaluation results for all nine batches.

**Table 11: Summary of All Evaluation Parameters (Batches B1 - B9).**

| Time Point / Batch     | B1     | B2     | B3     | B4     | B5     | B6     | B7     | B8     | B9     |
|------------------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| pH                     | 5.8    | 6.0    | 6.1    | 5.9    | 6.2    | 5.7    | 6.0    | 6.3    | 5.8    |
| Appearance             | Clear  | Clear  | Clear  | Clear  | Clear  | Clear  | Clear  | Clear  | Clear  |
| Spreadability (g.cm/s) | 106.90 | 110.20 | 107.50 | 112.35 | 113.80 | 108.75 | 109.40 | 114.20 | 108.10 |
| Density                | 1.50   | 1.55   | 1.60   | 1.65   | 1.70   | 1.75   | 1.80   | 1.85   | 1.90   |
| Drug Content (%)       | 100.0  | 100.5  | 98.3   | 101.5  | 101.2  | 97.2   | 100.6  | 102.8  | 99.6   |
| Phase Separation       | No     | No     | No     | No     | No     | No     | No     | No     | No     |
| Permeation (12 Hour %) | 86.5   | 89.2   | 83.1   | 93.4   | 96.1   | 82.4   | 87.8   | 97.5   | 85.0   |
| Viscosity              | 99.8   | 101.2  | 98.0   | 103.5  | 105.0  | 98.5   | 100.5  | 104.0  | 100.0  |
| Overall Stability      | Pass   | Pass   | Pass   | Pass   | Pass   | Pass   | Pass   | Pass   | Pass   |

## RESULT AND DISCUSSION

### Best Formulation Batch

Based on the comprehensive evaluation of all physicochemical parameters, drug content, centrifugation test, accelerated stability and in vitro drug permeation data, Batch B8 emerges as the optimized formulation. It demonstrated:

1. pH: 6.3 - within acceptable range, no skin irritation expected<sup>[10]</sup>
2. Appearance: Clear and transparent - confirms complete microemulsification<sup>[3]</sup>
3. Highest Spreadability (114.20 g·cm/sec) - ensures uniform skin application
4. Highest Drug Content (102.8%) - excellent drug entrapment and uniformity<sup>[15]</sup>
5. Maximum Cumulative Permeation at 12 hours (97.5%) - superior transdermal delivery<sup>[12]</sup>
6. Excellent stability across 3 months accelerated conditions<sup>[14]</sup>
7. Density: 1.85 - within acceptable range, confirms good consistency, and reproducibility
8. None of the nine formulation batches showed any signs of phase separation, creaming, or cracking<sup>[13]</sup>
9. The optimized microemulsion formulation exhibited a viscosity of 104.0 cp indicating satisfactory rheological behavior, good flow properties, and stability of the microemulsion system<sup>[9]</sup>

## CONCLUSION

The present study successfully developed and evaluated a topical ibuprofen microemulsion using Isopropyl Myristate as the oil phase, Span 80 as the surfactant, ethanol as the co-surfactant, methyl paraben as the preservative, and distilled water as the aqueous phase. The formulation was prepared by the spontaneous emulsification method, which is simple, economical, and reproducible. The prepared microemulsion showed satisfactory physicochemical properties and met the required evaluation criteria. Compared to conventional oral ibuprofen therapy, the topical microemulsion offers advantages such as avoidance of first-pass metabolism, reduction of gastrointestinal side effects, targeted drug delivery, and lower systemic exposure. Therefore, the developed formulation may serve as a safe and effective alternative for the management of localized pain and inflammation.

Further studies including in vivo skin permeation studies, skin irritation testing, and longer-term stability studies are recommended to confirm the clinical potential of this formulation.

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