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# Formulation Development and Evaluation of Microemulsion Based Celecoxib Gel

Sujit Kakade*[1], Amjadkhan Pathan[2]
[*1] *Research Scholar, Institute of Pharmacy, Shri JJT University, Jhunjhunu, Rajasthan, India.*
[2] *Research Guide and Professor, Institute of Pharmacy, Shri JJT University, Jhunjhunu,Rajasthan, India.*

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**ABSTRACT**
Celecoxib is a nonsteroidal anti-inflammatory medication (NSAID) used to treat joint illnesses such as osteoarthritis. Creating a novel microemulsion formulation of Celecoxib for transdermal distribution was the focus of this study. To choose excipients with excellent drug loading capacity, solubility of drug in different oils, surfactant, and co-surfactant was assessed in preformulation tests. Capmul MCM C8 was chosen as the oil in the microemulsion's formulation, while labrasol and ethanol were chosen as the surfactant and co-surfactant, respectively. From pseudo ternary phase diagrams, the concentration of oil phase, Smix, and distilled water were calculated and subsequently processed for the formulation of Celecoxib microemulsion. Three testsa centrifugation test, a heating and cooling cycle test, and a freeze thaw cycle test were used to determine the optimal formulation. The % transmittance, droplet size, and cloud point of the optimized formulations were also measured.Because of its high % transmittance, the CF2 formulation stands out as the best of the bunch. The smallest globule size seen in CF-2 was 103.2 nm. Zeta potential of CF2 was determined to be -20.5mV. The CF2 formulation released its medication faster than any of the other batches tested in an in vitro diffusion assay, at about 8 hours. Microemulgel was created by adding a gelling agent to the microemulsion at a 1:1.2 ratio (microemulsion: gelling agent). All stability requirements were met by the microemulgel (PC3) under study. Skin irritation investigation indicated that Celecoxib loaded microemulgel formulation (PC3) was nonirritating. These findings suggest that a microemulsion formulation of Celecoxib might be an effective formulation for transdermal distribution.

**KEYWORDS:** Microemulsion, Microemulgel, Celecoxib, Arthritis

## I. INTRODUCTION

Transdermal drug delivery system (TDDS) is a well define a therapeutic system that delivers for the surface region with a programmed quantity of the drug at a predetermined rate of intact, healthy skin. Under this system, drugs would be provided systemically at a conventional rate and time period and can be extended while sustaining the rate. Therefore, this system of delivering drugs is very helpful in reducing the numerous problems connected with oral treatments like hepatic metabolism at the first level impulsive bioavailability, enhanced first pass, dose inflexibility, residence time at comparatively shorter, dose dumping [1, 2].The research findings build up a revolutionary theory over a resistant skin barrier, which persuaded many researchers to establish a rate-controlled drug delivery system which mange transdermal drugs to accomplish the purpose of systemic medication. Microemulsions are thermodynamically stable. Droplet size is >0.15 micron and solution is transparent. Microemulsions require a higher amount of surfactant, in the range of 6-8% by total weight contrasting with a value of 2-3% for emulsions. Phase diagram used for obtaining the microemulsion region. J. Willard Gibbs proposed the phase diagram rules. Titration method used for phase diagram and External phase titrated with internal phase. Cloudiness is obtained at the end of the titration. Lastly, the coarse emulsion will be prepared and titrated by a co-surfactant till a transparent solution is obtained. The co-surfactant showsthe microemulsion region in a different ratio which is stable, called as “pseudo-component”4-7.In autoimmune disease class, rheumatoid arthritis (RA) is one of the devastating diseases where patients suffer acute joint swellings, serious pain, and stiffness. RA effects paired joints and often elbows, ankles, shoulders etc. In acute condition, RA causes bone deformations in affected areas, sometimes it leads to permanent joint damage. Coming to the treatment point of view, there are many wide

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ranges of medicines are available for RA, but doctors prefer painkillers, non-steroidal, anti-inflammatory drugs, disease modifying anti-rheumatoid drugs, steroids etc.

In this experiment, we used celecoxib, a potential cyclooxygenase-2 (COX-2) inhibitor which has very less adverse effect as compare to rofecoxib, valdecoxib etc., Celecoxib mechanism of action is very simple, it selectively inhibits COX-2, due to which COX-2-induced inflammation and prostanoids (Prostaglandin E2) synthesis cleaved. Due to which inflammation, edema and pain end. However, celecoxib has very poor oral bioavailability and aqueous solubility. It is highly soluble in acetonitrile[3,4] The goal of this study was to create an appropriate microemulsion gel system after screening oils, surfactants, and cosurfactants for transdermal delivery of Celecoxib in order to improve its dissolution and skin permeability while maintaining safety.

## II. MATERIALS AND METHODS

### Materials

celecoxib was received as a gift sample from RPG Life Sciences Ltd., Mumbai. Capmul MCM was obtained from Abitech Corporation, U.S.A., Cremophore RH40, Tween 80 and Tween 20 was procured from BASF, Mumbai, and Propylene glycol was obtained from Pure Chem Lab, Pune. All other chemicals were of analytical grade.

### Methods

### Solubility Study

The solubility of celecoxibin various oils (Capmul MCM, Isopropyl myristate, Aniseed oil, Oleic acid, Castor oil, and Olive oil), surfactants (Cremophore RH 40, Tween 20, Tween 80, and Span 20) and co-surfactant (PEG400, Transcutol HP, and Polyethylene glycol) it was determined. In a vial, 2 ml of required solvent and excess quantity of the drug was added. The mixture was removed, filtrate and analyze by using UV spectrophotometerat 255nm. All measurements were done in triplicates [5].

### Preparation of microemulsion of Celecoxib:

1gram solution of celecoxib was added to an oil-surfactant-cosurfactant combination. A high-pressure homogenizer was used to break down the mixture until a clear solution was achieved.

**Table 01:**Optimized formulation of microemulsion for 100 ml.

| Batch No. | Celecoxib | Capmul MCM C8 | Labrasol | Ethanol | Water |
|---|---|---|---|---|---|
| **CF1** | 1 | 5 | 36 | 24 | 34 |
| **CF2** | 1 | 10 | 32 | 21 | 36 |
| **CF3** | 1 | 20 | 28 | 18 | 33 |
| **CF4** | 1 | 25 | 24 | 15 | 35 |
| **CF5** | 1 | 30 | 20 | 12 | 37 |
| **CF6** | 1 | 35 | 16 | 9 | 39 |
| **CF7** | 1 | 40 | 12 | 6 | 41 |
| **CF8** | 1 | 45 | 8 | 3 | 43 |
| **CF9** | 1 | 5 | 45 | 24 | 25 |
| **CF10** | 1 | 10 | 41 | 21 | 27 |
| **CF11** | 1 | 20 | 37 | 18 | 24 |
| **CF12** | 1 | 25 | 23 | 15 | 36 |
| **CF13** | 1 | 30 | 29 | 12 | 28 |
| **CF14** | 1 | 35 | 25 | 9 | 30 |
| **CF15** | 1 | 40 | 21 | 6 | 32 |
| **CF16** | 1 | 45 | 17 | 3 | 34 |
| **CF17** | 1 | 5 | 39 | 24.5 | 30.5 |
| **CF18** | 1 | 10 | 35 | 21.5 | 32.5 |
| **CF19** | 1 | 20 | 31 | 18.5 | 29.5 |
| **CF20** | 1 | 25 | 27 | 15.5 | 31.5 |
| **CF21** | 1 | 30 | 23 | 12.5 | 33.5 |
| **CF22** | 1 | 35 | 19 | 9.5 | 35.5 |
| **CF23** | 1 | 40 | 15 | 6.5 | 37.5 |

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| | | | | | |
|---|---|---|---|---|---|
| **CF24** | 1 | 45 | 11 | 3.5 | 39.5 |

All values are in ml

**Optimization of Microemulsion:-**

**Thermodynamic Stability of microemulsion:**

When the medicine precipitates in an excipient matrix, the performance of the microemulsion formulation might be severely impacted. In addition, inadequate formulation physical stability may lead to excipient phase separation, which affects both formulation and visual performance.Thermodynamic Stability study of microemulsion (CF1-CF24) were performed as per procedure mentioned below

**Heating cooling cycle:**

Six cycles between refrigerator temperature i.e. 4 $^0$C and 45 $^0$C with storage at each temperature of not less than 48 h were studied. Those formulations, which were stable at these temperatures, were subjected to a centrifugation test.

**Centrifugation:**

Those formulations that complied with the heating cooling cycling test were centrifuged at 3500 rpm for 30 min. Those formulations which did not show any phase separation were taken for the freeze-thaw stress test.

**Freeze-thaw cycle:**

Three freeze-thaw cycles between -21 $^0$C and +25 $^0$C with storage at each temperature for not less than 48 h were done for the formulations. The result of the stability study of amlodipine and nifedipine loaded microemulsion was reported in Tables 22 and 42 respectively.Phase separation in the resulting formulations was then monitored. The optimal formulations are the ones that pass these three tests with the lowest concentration of Smix.

**Characterization of Microemulsion [6,7]: -**

**1. Percentage transmittance: -**

Microemulsions of celecoxib were diluted one hundred times with distilled water and examined visually for turbidity. The UV-VIS spectrophotometer was then used to determine its percent transmittance at 331nm using distilled water as a blank.

**2. Cloud point measurement: -**

Microemulsions that had been optimised were diluted with distilled water at a 1:250 ratio, then heated in a water bath. The point at which clouds suddenly become visible was identified as the cloud point using a UV-vis spectrophotometer to measure transmittance and ocular observation.

**3. Droplet size determination**

In a beaker, 10 milligrammes of CF1-CF24 microemulgel formulation was diluted with 50 millilitres of deionized water while being stirred with a glass rod. Analyses of particle size were performed on the resulting emulsion. Dynamic light scattering (DLS) using a zetasizer is used to quantify the size of the resulting droplets (Nano ZS, Malvern Instruments, UK). 25 degrees Celsius; red He-Ne laser; 4.0 milliwatts; 633 nanometers.

**4. Zeta Potential Determination**

Laser diffraction examination using a particle size analyser was used to ascertain the Zeta potential of the winning formulation (Malvern Zetasizer Nano Series ZS 90). The samples were diluted with distilled water at a ratio of 1:100 (v/v) and stirred for 1 minute. There were three sets of each experiment.

**Preparation of Microemulgel of formulation**

**Selection of microemulsion and polymer Ratio:**

Microemulsion and polymer ratios, including 1:0.5, 1:1, 1:1.2, and 1:1.5, were tested for free-flowing microemulgel before being narrowed down using the table below. Utilize a high pressure homogenizer to completely dissolve a mixture of microemulsion and polymer at varying ratios of 1:0.5, 1:1, 1:1.2, and 1:1.5. This strategy relies on experimentation and close visual inspection.

**Method of Preparation of Trial Batches:**

Firstly, microemulsions take in test tube on high pressure homogenizer. The carbopol 940 was then added with constant stirring, and the gel was kept at room temperature for 15 min to obtain a good microemulgel.

**Preparation of trial batches:**

**Preparation of trial batches using different combination of microemulsion and polymer to selection of ratio.**

On the basis of literature survey and laboratory work preliminary trials are design.

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**Table 02:** Ratio of microemulsion and polymer

| Trial Batch | Polymer | Ratio(O:P) |
|---|---|---|
| O1 | Carbopol 940 | 1:0.5 |
| O2 | Carbopol 940 | 1:1 |
| O3 | Carbopol 940 | 1:1.2 |
| O4 | Carbopol 940 | 1:1.5 |
| O5 | Carbopol 940 | 1:2 |

On the basis of literature survey, preliminary trials and there results the following trials are design.

**Characterization of microemulgel:**

**A) Physical appearance:**

Color, homogeneity, consistency, and pH were checked visually in the microemulgel formulations after they were created.

**1. pH**

Digital pH metre readings were taken from the microemulgels to establish their pH levels (Labindia Instruments, GMPH). After continuously monitoring the microemulgel composition, the electrode was dipped into it. Triplicate pH readings were taken for each batch.

2. **Appearance of microemulgel**

The formulas' aesthetic appeal was evaluated by holding them up to the light and taking a look at how they reflected it.

Where + average, ++ good, +++ excellent

**3. Spreadability**

The spreadability instrument was used to quantify this quality. The equipment consists of two slides: one is securely fastened in a wooden frame, while the other glides effortlessly over its surface. We stuffed two grammes of microemulgel (2 gm) in between the apparatus's slides. After letting a 1 kilogramme weight sit on the slide for 5 minutes, the air was forced out from between the slides and a homogenous sheet of microemulgel formed. Carefully, we wiped the slides' borders to get rid of the extra gel. An 80-gm weight was pulled on the upper slide while the lower slide was securely fastened. Observe how long it takes the top slide to travel a distance of 5 centimetres (in seconds). Higher Spreadability is associated with shorter intervals.

Spreadability was then calculated using the following formula:

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

Where, S = is the spreadability,

M = is the weight in the pan (tied to the upper slide),

L = is the length moved by the glass slide and

T = represents the time in seconds taken to separate the slide completely.

**4. Extrudability**

After the microemulgels were created, they were poured into the compressible tubes. The formula's extrudability has been tested.

Where + average, ++ good, +++ excellent

**B) Rheological study:**

Spindle speeds of 0.5, 1.0, 2.0, 2.5, 4.0, 5.0, 10.0, 50.0, and 100.0 revolutions per minute were used on a Brookfield Viscometer (Model RVT, Brookfield Engineering Laboratories, Inc., USA) to examine the flow behaviour of the gel compositions. At 251 °C, the flow behaviour of the various formulations was evaluated by analysing the location of the upward and downward curves in the rheogram.

**C) Drug content determination: -**

The 10 mg of Celecoxib microemulgel was dissolved in 10 ml of dimethyl acetate in a separate 10 ml volumetric flask; the 0.1 ml of stock solution was then properly measured, transferred to a second 10 ml volumetric flask, and filtered using Whatman filter paper. Celecoxib concentrations in the aforementioned solutions were measured using a UV Spectrophotometer (Shimadzu UV 1800) set to lambda max 252nm, respectively. Standard calibration curves of Celecoxib were used to calculate the exact concentrations of each drug in the formulation.

**D) In vitro drug release study: -**

The experiment employed a Franz diffusion cell that had an effective diffusion area of 7.1 $cm^2$. Franz diffusion cell having donor compartment on the outside and receptor compartment on the inside, with the egg membrane between them. The release patterns of Celecoxib were measured after being applied to the stratum corneum in the forms of ME (1%, w/w D), MBG (0.5%, w/w D), and 0.1 gm and 0.05 gm, respectively. In order to stimulate receptor activity, 25 ml of physiological saline solution was injected into the receptor chamber (pH 6.8 phosphate buffer). The receptor medium was magnetically

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agitated at 50 rpm and kept at 37 1 C. Taken at regular intervals, the samples were filtered through a cellulose membrane filter with a pore size of 0.45 m before being subjected to ultraviolet (UV) analysis. After each sample was taken, the buffer solution in the receptor chamber was immediately changed with new. Both the ME and MBG formulations' cumulative drug accumulation in the receptor chamber was shown vs time (t, h).

**E) Stability of microemulgel**

Clarity and phase separation observation, as well as UV assays of Celecoxib, were used to determine the stability of a microemulgel containing the two drugs at 45 $^{o}$C for three months. For the same purpose of gauging physical stability, centrifuge tests were also performed. 15 minutes of centrifugation at 10,000 rpm were applied to the microemulgel samples.

**Table 03**: **Stability protocol**

| **Stability study (conditions)** | | |
|---|---|---|
| 45°C ± 2°C / 75 % RH ± 5% RH | | |
| 1 Month | 2 Months | 3 months |

## III. RESULT AND DISCUSSION

**Drug Authentification:**

**Appearance, and color:**

Celecoxib is a white to off-white powder.

**Solubility:**

It is freely soluble in methanol, soluble in ethanol, and practically insoluble in water.

**Melting point determination: -**

There was a good match between the melting point of the sample and the values reported in the literature, suggesting that the medication was of high quality.

**Table 04:**Melting point of Celecoxib

| **Drug** | **Melting point** | |
|---|---|---|
| | **Practical** | **Standard** |
| **Celecoxib** | 164$^{o}$C | 162$^{o}$C-164$^{o}$C |

**FTIR of Celecoxib:-**

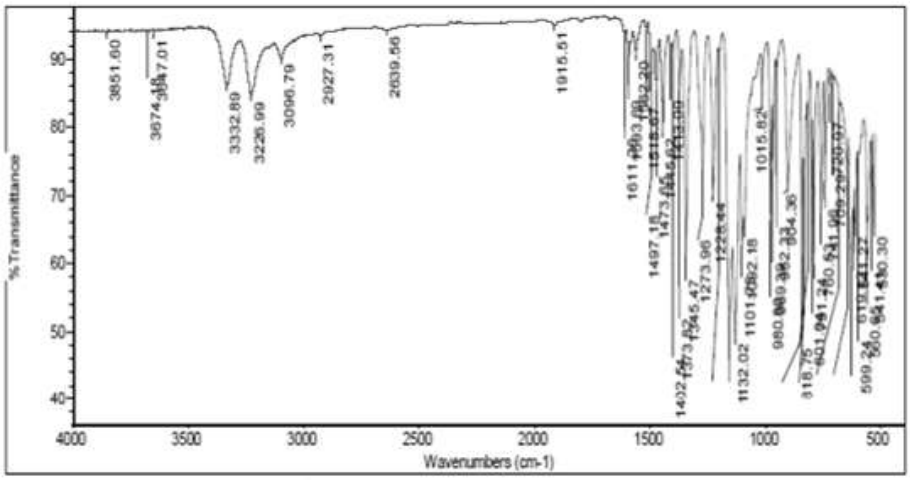


**Figure 01:** FTIR Spectra of Celecoxib

Celecoxib's FTIR spectrum displayed distinctive peaks at the vibrational frequencies of its major functional groups, including NH2 stretching, H stretching, Aromatic CH stretching, and S=O stretching (Sulfonamide group). Celecoxib's functional group was confirmed by comparing the primary peaks. Since Celecoxib was

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the correct drug for the sample, the identification was made.

**UV spectrophotometric method for Celecoxib**
**Determination of $\lambda_{max}$:-**
**Preparation of stock solution:**
**Calibration curve**

Celecoxib was weighed out at 10mg and then dissolved in 100ml of methanol to achieve a concentration of 100g/ml. Ten millilitres were taken out of the solution and the rest was added to make up to a hundred millilitres. This final solution was used as a stock solution, and subsequent solutions with concentrations ranging from 5-30ug/ml were prepared by diluting the stock solution with methanol as needed. UV Spectrophotometer was used to examine the aforementioned solutions at a max wavelength of 252nm.

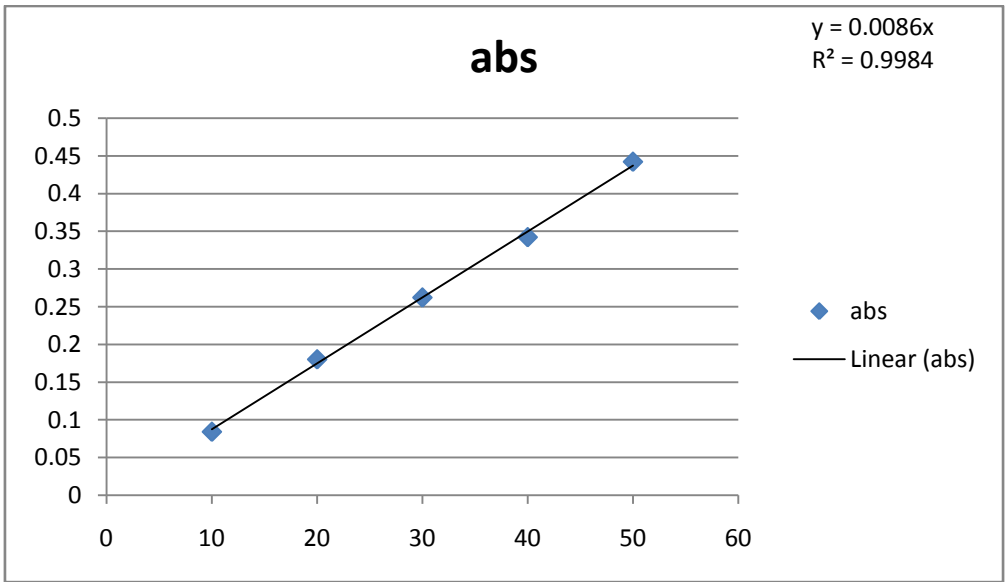


**Figure 02:** Calibration curve for Celecoxib

**Compatibility study: -**

Preformulation compatibility studies of Celecoxib with all excipients were carried out prior to preparation microemulsion. The daily observations of compatibility study for 14 days were taken for colour changes, cake formation, liquefaction, and gas formation.

**Table 05:**Excipients + Celecoxib Compatibility Study

| Sr.no | Physical Mixture | Observations | | | |
|---|---|---|---|---|---|
| | | Colour Change | Cake Formation | Liquefaction | Gas formation |
| 1 | Celecoxib + Moisture | No | No | No | No |
| 2 | Celecoxib + Capmul MCM C8 | No | No | No | No |
| 3 | Celecoxib + Labrasol | No | No | No | No |
| 4 | Celecoxib + Ethanol | No | No | No | No |
| 5 | Celecoxib + Carbopol 940 | No | No | No | No |

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**Evaluation of Optimization of microemulsion:-**

Centrifugation force is used to determine the separation behavior of the colloidal particles under the influence of gravitational field, as there was no separation observed the stability of developed microemulsion confirmed

**Table 06:**Optimization of microemulsion -Celecoxib

**Ratio- 1:1**

| Formula no. | Oil:Smix | After centrifugation test | Heating cooling cycle | Freeze thaw cycle |
|---|---|---|---|---|
| CF 1 | 1:9 | Stable | Stable | Stable |
| CF 2 | 2:8 | Stable | Stable | Stable |
| CF 3 | 3:7 | Stable | Stable | Stable |
| CF 4 | 4:6 | Stable | Stable | Stable |

**Ratio 2:1**

| Formula no. | Oil:Smix | After centrifugation test | Heating cooling cycle | Freeze thaw cycle |
|---|---|---|---|---|
| CF 10 | 1:9 | Stable | Stable | Stable |
| CF 12 | 3:7 | Stable | Stable | Stable |
| CF 13 | 4:6 | Stable | Stable | Stable |

**Ratio 3:1**

| Formula no. | Oil:Smix | After centrifugation test | Heating cooling cycle | Freeze thaw cycle |
|---|---|---|---|---|
| CF 20 | 2:8 | Stable | Stable | Stable |
| CF 21 | 3:7 | Stable | Stable | Stable |

Similarly, CF5-CF9, CF14-CF19, CF22-CF24 were found unstable after centrifugation process. No changes in the formulation CF1-CF4, CF10-CF13, CF20-CF21 are observed stable and subjected for further study. Formulation CF5, CF6, and CF14 in heating cooling cycle undergo creaming due to the proportion oil and CF1-CF4, CF10-CF13, CF20-CF21 are found stable and examined for freeze thaw cycle. Among this formulation increase toxicity due to which formulation CF1, CF10 and CF20 contain higher proportion of surfactant and co-surfactant.Six formulations, CF2, CF3, CF4, CF12, CF13, and CF21 from different Smix (1:1, 2:1, 3:1) ratios, were chosen for further study of percent transmittance, Cloud point measurement, globule size analysis, and in vitro release studies

**Characterization of microemulsion: -**

**1. Percentage transmittance: -**

100 µl of microemulsion dissolved in 250 ml of distilled water stir the solution up to 2 min and take the absorbance of solution with the help of UV spectrophotometer at 252nm.

**Table 07.** Percentage transmittance of formulation of optimized formulation

| Sr no. | Formula no. | % transmittance |
|---|---|---|
| 1 | CF2 | 96.22±0.22 |
| 2 | CF3 | 99.11±0.45 |
| 3 | CF4 | 69.12±0.78 |
| 4 | CF12 | 94.18±0.63 |
| 5 | CF13 | 69.20±0.55 |
| 6 | CF21 | 73.56±0.12 |

From the above study it can be concluded that all formulation shows the percent transmittance in between 50-100% which indicated that droplet size was nanometer range and transparent microemulsion was formed.

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**2. Cloud point measurement**

Formation of a stable nano-emulsion is due in large part to the cloud point in a Microemulsion made up of non-ionic surfactants. The cloudiness of the preparation caused by the dehydration of the polyethylene oxide moiety occurs at temperatures over the cloud point, leading to an irreversible phase separation and a negative impact on Celecoxib absorption. Therefore, Microemulsion's cloud point should be above 37$^{o}$C so that phase separation doesn't occur on the skin.

**Table 08.** Cloud Point of Optimized Formulation

| Formulation | Cloud Point Temperature |
|---|---|
| CF2 | 56 |
| CF3 | 71 |
| CF4 | 69 |
| CF12 | 59 |
| CF13 | 66 |
| CF21 | 72 |

From the above study it can be concluded that all the formulation forms a stable microemulsion even at physiological temperature.

**3. Droplet size measurement of microemulsion**

Mean globule size of optimized formulation is given in Table no 09. CF-2 was showing least globule size of 103.2nm shown in figure.

**Table 09. Globule Size (nm) of liquid Formulation**

| Formulation | Avg. Globule Size (nm) |
|---|---|
| CF2 | 103.2nm |

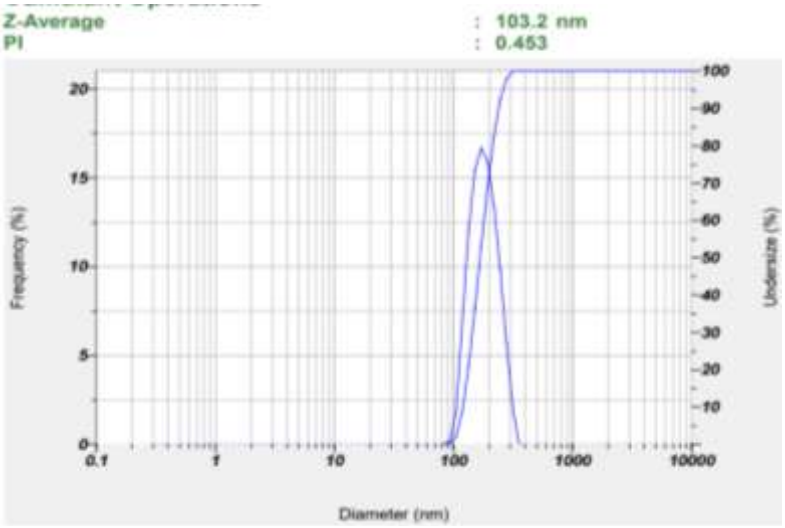


**Figure 03: Graph of globule size determination**

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**4. Zeta potential (ZP) measurement of microemulsion**

Zeta potential of CF2 was found to be -20.5 mV.

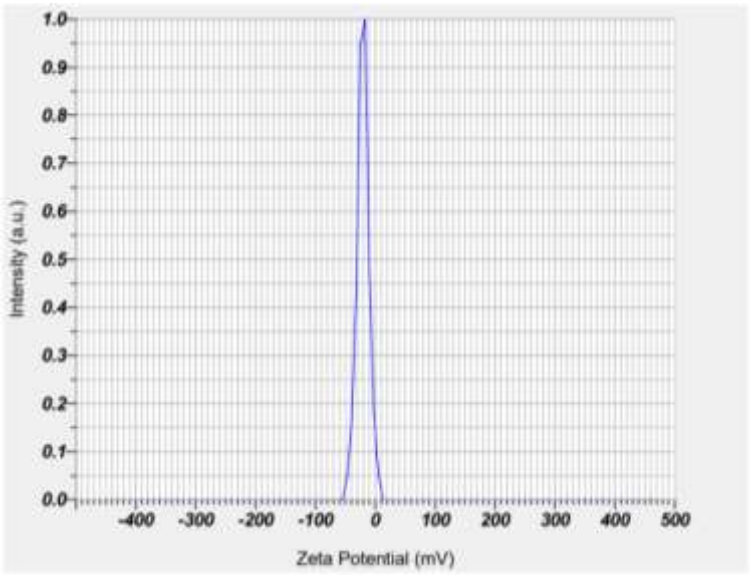


**Figure 04:** Zeta potential of Microemulsion

**5. In vitro drug release study of Microemulsion**

Studying the in vitro drug release of six different microemulsion formulations, it was found that Formulation CF2 had the highest drug release, at 97.85%.

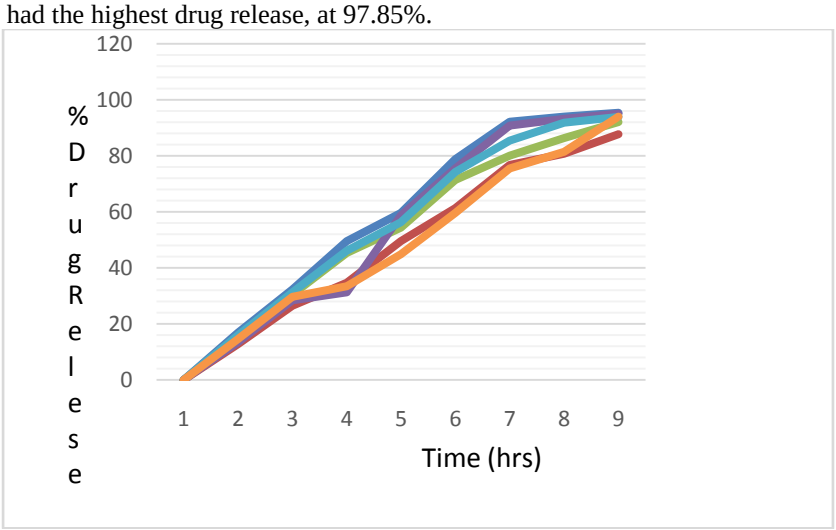


**Figure 05:**Drug Release Profile of Optimized microemulsion formulation

In the image above, you can see how six different batches of the medication preparation compare in terms of how much of the drug is released. The CF2 batch's medication release is greater than that of previous formulation batches. When comparing medication release rates over 8 hours, the CF2 formulation clearly excels.

Based on the aforementioned analysis, it was determined that the CF2 formulation batch would be used for the final formulation batch due to its superior thermodynamic stability, percentage transmittance, drug content, and cloud point.

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**6. In vitro drug release study of Microemulgel**

Formulation PC3 showed the highest drug release (97.75%) when tested in vitro for drug release from microemulgels.

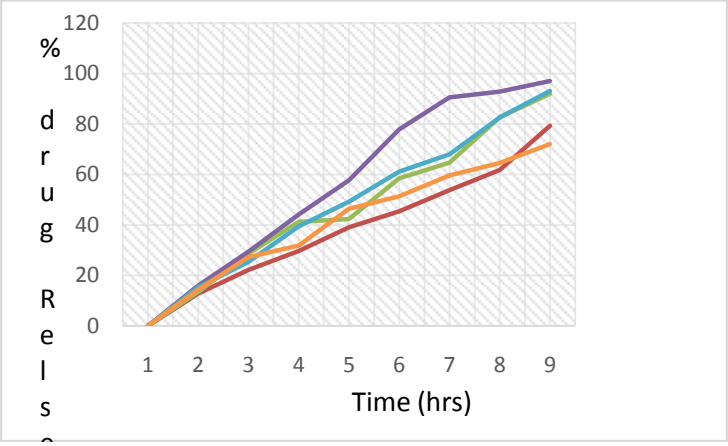


**Figure 06:** Drug Release Profile of Optimized microemulgel formulation

In above figure shows comparison of drug release of five preparation batches. In prepare drug release of PC3 is higher as compare to other formulation batches.

**Characterization of microemulgel: -**

**A) Physical appearance:**

**a) pH**

After immersing the glass electrode into the microemulgel, the pH was measured digitally. A table containing the measured values is provided. The pH level shows whether or not the microemulgel may be used topically.

**b) Viscosity**

We used a Brookfield viscometer set to spindle no. 5 and 50 rpm to measure the viscosity of each microemulgel formulation at 25°C. The table displays the microemulgel's viscosity from the first to the fifth performance category.

**c) Appearance**

All five batches (PC1 through PC5) seemed to be the same yellowish viscous translucent preparation that was uniform and shiny.

**d) Spreadability**

Table 10 displays the results of a measurement of spreadability from PC1 to PC5. It can be seen that the spreadability of a solution decreases as the concentration of carbopol 940 rises.

**e) Extrudability**

After the gels were made, they were placed in dismantlable tubes. This formulation's extrudability has been tested, and the findings are listed in Table 10.

**Table 10:**Physical appearance of microemulgel

| Batch code | pH | Viscosity (cps) | Appearance | Spreadability | Extrudability |
|---|---|---|---|---|---|
| PC1 | 7.1±0.61 | 11205±0.56 | + | 33.26±0.21 | + |
| PC2 | 7.2±0.63 | 11526±0.22 | + | 34.59±0.78 | + |
| PC3 | 7.0±0.33 | 11478±0.14 | ++ | 35.14±1.20 | ++ |
| PC4 | 6.9±0.21 | 11698±0.56 | + | 33.15±0.56 | + |
| PC5 | 7.1±0.47 | 11452±0.33 | + | 33.20±1.60 | + |

From the above study, it was concluded that the batch PC3 was selected as the promising formulation on the basis of pH, viscosity, appearance, spreadability, and extrudability.

**f) Drug content determination: -**

All formulations of celecoxib had drug contents between 96% and 99.9% in microemulgel, indicating full drug solubilization.

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**Table 11:**Drug content Determination

| Formulation | Drug content (%) |
|---|---|
| PC1 | 96.23±0.55 |
| PC2 | 97.45±0.23 |
| PC3 | 99.10±0.14 |
| PC4 | 98.44±0.59 |
| PC5 | 96.55±0.56 |

From the above study it can be concluded that PC3 formulation shows the higher drug content it means that is degradation of drug and complete solubilization of drug.

**g) Stability Study**

**Batch No**.: PC3 was put on stability as below mentioned condition.

**Condition:** Batch PC3 at 45°C ± 2°C / 75% RH ± 5 % RH

**Packaging:** Aluminum collapsible tube

**Description**:Transparent light yellow colored microemulgel.

**Table 12:First, Second- & Third-month Stability Data of Tablet at 45°C ± 2°C / 75% RH ± 5 % RH.**

| Parameters | | Initial | 1 Months | 3 Months |
|---|---|---|---|---|
| Drug content (%) | | PC3 | PC3 | PC3 |
| | | 99.70±1.02 | 99.11%±0.78 | 98.20±1.54 |
| Diffusion (%) Medium: 25ml of pH 6.8 phosphate buffer, egg's membrane, 50 rpm. | 0Hr | 0 | 0 | 0 |
| | 1hr | 12.72±0.95 | 13.52±0.56 | 13.32±0.47 |
| | 2 hr | 28.95±0.26 | 28.69±0.47 | 29.11±0.36 |
| | 3 hr | 40.25±1.89 | 41.12±0.22 | 41.56±0.85 |
| | 4 hr | 55.26±1.55 | 55.23±2.01 | 54.87±1.04 |
| | 5 hr | 72.56±1.05 | 71.55±1.06 | 71.69±0.26 |
| | 6 hr | 86.98±1.89 | 87.44±0.59 | 87.63±1.45 |
| Clarity | | Clear | Clear | Clear |
| Phase separation | | No phase separation | No phase separation | No phase separation |
| Centrifugation test | | Stable | Stable | Stable |

Microemulgel were evaluated for physical appearance, diffusion study, clarity, Phase separation, centrifugation test. There is no change in description of microemulgel after 3-month stability study. There were no variation observed in Clarity, phase separation and centrifugation test.

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## IV. CONCLUSION

Preformulation studies were performed to determine the solubility of the drug in various oils, surfactants, and co-surfactants in order to select excipients with high drug loading capacity. Capmul MCM C8 was used as the oil in the microemulsions formulation, while labrasol and ethanol were used as the surfactant and co-surfactant, respectively. The concentrations of the oil phase, Smix, and distilled water used in the production of the Celecoxib microemulsion were calculated using pseudo ternary phase diagrams. To make microemulgel, a gelling agent was added to the microemulsion at a 1:1.2 ratio (microemulsion: gelling agent). When tested under various strength settings, the microemulgel (PC3) in question performed well. In vitro investigations demonstrated that the Celecoxib-containing microemulgel formulation (PC3) did not cause skin irritation. Based on these findings, it appears that a Celecoxib microemulsion formulation could be a viable transdermal administration option.

**CONFLICT OF INTERESTS**

None declared by the authors.

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