*Nanotechnology Perceptions*
*ISSN 1660-6795*
*www.nano-ntp.com*

# Formulation Development And Evaluation Of Curcumin-Loaded Microemulsions To Enhance The Bioavailability And Therapeutic Efficacy

**Kirankumar Dhawale[1], Arulmozhi Sathiyanarayanan[1,*], Bothiraja Chellampillai[2]**

*[1]Department of Pharmacology, Bharati Vidyapeeth (Deemed to be University), Poona College of Pharmacy, Pune, [2]Goa College of Pharmacy, Goa University, 18th June Road, Panaji, Goa-403001*
**Corresponding author*
*Dr. Arulmozhi Sathiyanarayanan*
*Department of Pharmacology,*
*Bharati Vidyapeeth (Deemed to be University),*
*Poona College of Pharmacy, Pune*
*Email- arulmozhi.s@bharatividyapeeth.edu*

Curcumin-loaded microemulsions were developed to enhance the bioavailability and therapeutic efficacy of curcumin, a poorly water-soluble compound. Preformulation studies of curcumin confirmed its purity with a melting point of 183°C and a λmax of 417.2 nm, aligning with expected absorption characteristics. Solubility studies revealed that curcumin is highly soluble in organic solvents, particularly methanol and ethanol, with limited solubility in aqueous solutions, making it suitable for lipid-based formulations. Saturation solubility studies indicated high solubility in oils like Capmul MCM and Isopropyl palmitate, as well as moderate solubility in surfactants. FTIR and DSC analyses confirmed the chemical structure and thermal stability of curcumin. Post-formulation studies of the curcumin-loaded microemulsions (F1 to F13) identified formulation F9 as the optimized batch. F9 exhibited an ideal pH of 7.2, ensuring stability and compatibility with biological systems. Its density of 0.98 g/cc and viscosity of 58.3 cps, the highest among the formulations, make it suitable for applications requiring thicker consistency, such as transdermal delivery. Stability studies confirmed that F9 maintained its key properties over time. ANOVA results highlighted that isopropyl palmitate was the most influential factor in determining the viscosity, suggesting its optimization can further improve the formulation's stability and viscosity. These findings indicate that curcumin-loaded microemulsion F9 is a promising formulation for enhanced curcumin delivery, offering improved bioavailability and therapeutic potential.

**KEYWORDS:** Curcumin, Microemulsion, Solubility, Saturation Solubility, Formulation Optimization, Therapeutic Efficacy.

## 1. INTRODUCTION

Curcumin, the primary bioactive compound derived from the rhizome of Curcuma longa, has long been recognized for its extensive therapeutic properties, including anti-inflammatory, antioxidant, anticancer, antimicrobial, and neuroprotective effects. Despite its vast pharmacological potential, the clinical application of curcumin is severely limited by its poor aqueous solubility, low bioavailability, and rapid systemic elimination. These limitations hinder its effectiveness in treating a variety of diseases, including cancer, arthritis, diabetes, and neurodegenerative conditions. As a result, considerable research has been dedicated to developing novel drug delivery systems to enhance the solubility, stability, and bioavailability of curcumin, thereby improving its therapeutic outcomes. [1-4]

Among the various strategies developed to improve curcumin's bioavailability, microemulsions have emerged as a promising approach. Microemulsions are transparent, thermodynamically stable, and isotropic mixtures of oil, water, surfactants, and co-surfactants. These systems have unique properties, such as their ability to solubilize hydrophobic drugs and enhance drug absorption through biological membranes. Microemulsions are characterized by their small droplet size, typically ranging from 10 to 100 nm, which facilitates the efficient delivery of poorly soluble drugs like curcumin. The nanoscale droplets of the microemulsion can effectively enhance the dissolution rate of curcumin, allowing for improved absorption and bioavailability. [5-8]

The formulation of curcumin-loaded microemulsions involves the selection of an appropriate oil phase, surfactants, and co-surfactants. Commonly used oils include medium-chain triglycerides (MCT), virgin coconut oil, and other lipophilic substances that serve as the base for the microemulsion. Surfactants such as Tween 80, Span 80, and Kolliphor ELP are used to reduce the interfacial tension between the oil and water phases, facilitating the formation of the microemulsion. Co-surfactants, such as polyethylene glycol (PEG) 400 or ethanol, are incorporated to enhance the stability of the system and improve the solubilization capacity of the curcumin. The primary advantage of curcumin-loaded microemulsions is their ability to improve the solubility and stability of curcumin, which is inherently hydrophobic and prone to degradation. By encapsulating curcumin in the microemulsion droplets, the formulation not only protects the drug from degradation but also allows for controlled release, reducing the risk of side effects associated with rapid drug release. Moreover, microemulsions can facilitate the targeted delivery of curcumin to specific sites in the body, further enhancing its therapeutic potential. [9-12]

Curcumin-loaded microemulsions have been explored for various routes of administration, including oral, transdermal, and parenteral delivery. For oral administration, microemulsions have shown significant promise in improving the gastrointestinal absorption of curcumin, which is otherwise poorly absorbed due to its low solubility in aqueous environments. Transdermal formulations of curcumin-loaded microemulsions have been investigated for localized treatment of inflammatory conditions and skin disorders, while parenteral formulations have been developed for the treatment of systemic diseases like cancer. [13-15]

In addition to enhancing bioavailability, curcumin-loaded microemulsions offer several other benefits, such as improved drug stability, reduced toxicity, and the ability to bypass the first-pass metabolism. The small droplet size of the microemulsion enhances the surface area for drug absorption, allowing for faster onset of action and more efficient therapeutic effects.

Furthermore, the use of biocompatible and biodegradable surfactants and co-surfactants ensures that these formulations are safe for long-term use. [16-18]
The potential of curcumin-loaded microemulsions extends beyond improving the bioavailability of curcumin alone. These formulations can be used to deliver other poorly water-soluble drugs, making them a versatile platform for the development of novel drug delivery systems. By incorporating curcumin into microemulsions, researchers can exploit its synergistic effects with other therapeutic agents, thereby enhancing the overall efficacy of the treatment. [19]
In conclusion, curcumin-loaded microemulsions represent a highly promising approach for overcoming the challenges associated with the clinical application of curcumin. By improving its solubility, stability, and bioavailability, these formulations have the potential to revolutionize the use of curcumin in the treatment of various diseases. Furthermore, the versatility of microemulsions as a drug delivery system opens up new possibilities for the formulation of other therapeutic agents, making it an essential area of research in pharmaceutical development.[19-20]

## 2. MATERIALS AND METHODS

### 2.1 MATERIALS

Curcumin was procured from Solanki enterprises, pune. (Capmul MCM (CPM), Castor oil, Isopropyl palmitate, Span 80,Tween 20, polyethylene glycol 400 (PEG 400) ,propylene glycol were purchased from Cosmo Chem. Pvt. Ltd . methanol, ethanol and Potassium Dihydrogen Phosphate were purchased from Cosmo Chem. Pvt. Ltd. All other chemicals were analytical grade.

### 2.2 METHODS

#### 2.2.1 Formulation of Micro-Emulsions [21-22]

Microemulsion was formulated by dissolving the drug in a mixture of solid, lipid, surfactant and co-surfactant. Microemulsion were prepared by a high shear homogenization method. Aqueous phase solution contains co-surfactant and distilled water and oil phase solution contains oil, surfactant, drug and preservative. Both the solutions were heated step by step until it soluble properly. The oil phase was poured drop by drop on to the aqueous phase and homogenization was carried out at 6000 rpm for 15 min using high shear homogenizer. Drug loaded in microemulsion were finally obtained by allowing to cool to room temperature.

#### 2.2.2 EXPERIMENTAL DESIGN [21-22]

In this study, a Response Surface Methodology (RSM) known as Box-Behnken design was utilized with Design Expert® software (Version 13.0). The Box-Behnken design involved three independent variables: the amount of Isopropyl palmitate (ml) (A), Span 80 (B) and PEG 400 (C) .the dependent variables examined were Drug content (%),Viscosity (%) and drug release (%). The Box-Behnken design included factorial points, a center point, and axial points, resulting in a total of 13 experimental runs. The details of the independent variables,

their coded levels, and the Box-Behnken design scheme matrix are provided in the accompanying table.

**Table 1: List of independent and dependent variable in box Behnken design**

| **PARAMETER** | **Level LOW(-)** | **Level HIGH (+)** |
|---|---|---|
| **INDEPENDENT VARIABLE** | | |
| Isopropyl palmitate (A) | 10 | 15 |
| Span 80(B) | 3 | 5 |
| PEG 400(C) | 0.4 | 0.9 |
| **DEPENDENT VARIABLE** | Constraint | |
| Drug Content (%) | Maximize | |
| Viscosity (cps) | Maximize | |
| Drug release (%) | Maximize | |

**Table 2: DOE suggested and Experimental batches**

| **Formulation code** | **Isopropyl palmitate (ml)** | **Span 80(ml)** | **PEG 400(ml)** | **Methyl cellulose(mg)** | **Methyl paraben (mg)** | **Distilled water (ml)** |
|---|---|---|---|---|---|---|
| F1 | 12.5 | 5 | 0.9 | 100 | 25 | Qs |
| F2 | 12.5 | 4 | 0.65 | 100 | 25 | Qs |
| F3 | 12.5 | 3 | 0.9 | 100 | 25 | Qs |
| F4 | 10 | 4 | 0.9 | 100 | 25 | Qs |
| F5 | 15 | 5 | 0.65 | 100 | 25 | Qs |
| F6 | 15 | 3 | 0.65 | 100 | 25 | Qs |
| F7 | 15 | 4 | 0.4 | 100 | 25 | Qs |
| F8 | 12.5 | 3 | 0.4 | 100 | 25 | Qs |
| F9 | 10 | 4 | 0.4 | 100 | 25 | Qs |
| F10 | 10 | 3 | 0.65 | 100 | 25 | Qs |
| F11 | 15 | 4 | 0.9 | 100 | 25 | Qs |
| F12 | 12.5 | 5 | 0.4 | 100 | 25 | Qs |
| F13 | 10 | 5 | 0.65 | 100 | 25 | Qs |

## 3. PREFORMULATION STUDY

### 3.1 Melting Point [23]

The melting point of Curcumin was determined using capillary tube method. Thieles tube containing liquid paraffin solution and then small amount of pure drug was filled in the capillary tube which is sealed at one end using flame. Sample filled in capillary is tied with thread to the thermometer and suspended

into Thieles tube and heated till drug powder melts. Thetemperature at which the pure drug powder started melting was noted.

### 3.2 Detection of Absorption Maxima (λ max) [24]

The sample of the standard solution were scanned between 200-400 nm regions on UV spectrophotometer (Jasco V-630). There are stock solutions of the Curcumin sample was prepared by dissolving 25 mg of drug in 25 ml of, methanol respectively. The absorption maximum for distilled water was found to be 417.2 nm.

### 3.3 Solubility study of the Drug (Curcumin) [25]

The solubility of Curcumin was performed in Methanol, ethanol, distilled water,phosphate buffer pH 7.4, Phosphate buffer pH 6.8, Acidic buffer pH 1.2 were taken in different 100 ml conical flask & 50 mg of Cilnidipine were added in it. The conical flask was stirred for 24 hrs. On mechanical shaker at 150 RPM. After 24 hrs. The flask was removed solutions were filtered and absorbance was measured at 417.2 nm.

### 3.4 Solubility study oils, surfactants and co- surfactants [26]

Solubility estimation is done in different oils, surfactants and co- surfactants. Excess amount of drug is added to the specified amount of oil such as (Capmul MCM (CPM), Castor oil, and Isopropyl palmitate) surfactants (Span 80) and co-surfactants (Polyethylene glycol-400).The resulting suspension was agitated on a rotary shaker for 24 h to achieve equilibration. Thereafter, the suspension was centrifuged at 4000 rpm for 15 min. The supernatant suitably diluted with methanol and the dissolved concentration of Curcumin was determined spectrophotometrically at 417.2 nm.

### 3.5 FTIR [27]

The drug excipients compatibility study was performed by FTIR technique. The Curcumin samples were scanned over wave number range of 500-4000 cm-1 with diffraction reflectance scanning technique.

### 3.6 Differential Scanning Calorimetry (DSC) [28]

Differential scanning calorimetric (DSC) measurements were carried out on a modulated DSC (Mettler Toledo, SW STARe, and USA). The Curcumin (drug) were weighed (2-8mg), the aluminum pans were used and hermetically covered with lead. The heating rage was 50-250 °C for sample with constant increasing rate of temperature at 10°C /min under nitrogen atmosphere (50-60ml/min). The resultant thermograms of formulation was obtained.

## 4. POST FORMULATIO STUDY

### 4.1 Organoleptic Characteristics

The Organoleptic properties, including physical appearance, color, texture, phase separation, homogeneity, and immediate skin feel of the selected topical formulations

**4.2 pH Determination [29]**

The pH values of the Microemulsion formulation were measured by immersing the electrode directly into the dispersion using a calibrated pH meter.

**4.3 Density [21-22]**

The specific gravity or density of microemulsion emulsion formulation is two crucial parameters. A decrease in the formulation's density is typically a sign that there is trapped air inside its composition. Density at certain temperatures can be determined with high-precision hydrometers

**4.4 Viscosity [30]**

The viscosity of the microemulsions was determined by Brookfield Viscometer (DVE Viscometer) using a S18 spindle in triplicate at 25°C.

**4.5 Drug content analysis [31-32]**

1 ml of Curcumin loaded Microemulsion was taken in 10 ml volumetric flask containing 1 ml ethanol and Volume was made up to 10 ml with Methanol. From the above solution, 1 ml was further diluted with 10 ml Methanol to get 10 μg/ml. The resultant solution was filtered through Whatman filter paper and absorbance of the solution was measured at 417.2 nm using UV spectrophotometer.

**4.6 Centrifugation [32]**

Those formulations that passed the heating cooling cycle then subjected to were centrifuged test, the microemulsion were centrifuged at 3500 rpm for 5 min. Those formulations that did not show any phase separation some formulation show phase separation test.

**4.7 Freeze Thaw [21-22]**

Freeze-thaw cycle testing is a part of stability testing that allows to determine the microemulsion formulation will remain stable under various conditions. It consists of quick freezing and thawing were to kept in test tube for 24 hrs at freezing temperation and 24 hrs at room temperation and then measured the temperation by using thermometer heating upto 50o C to observed the formulation was stable at under conditions.

**4.8 In-Vitro Diffusion study [33]**

The in vitro diffusion study of the microemulsion was carried out in Franz Diffusion cell using Dialysis membrane (Molecular weight cut off: 12000, pore size: 2.4 nm). The membrane was previously soaked in phosphate buffer pH of 7.4 for 24 hours was clamped carefully to one end of the hollow glass tube of diffusion cell. Then Curcumin loaded microemulsion was pour uniformly on the dialysis membrane in donar compartment. 20 ml of phosphate buffer was taken in a beaker, the donar compartment was kept in contact with receptor compartment. This whole assembly was kept on a magnetic stirrer and the solution on the receptor side was stirred continuously and temperature of the cell was maintained at 37°C. A similar blank set was run simultaneously as a control. Sample (3 ml) was withdrawn at suitable time intervals (1, 2, 3, 4, 5 and 6) and replaced with equal amounts of fresh dissolution media. The Samples were

analyzed spectrophotometrically at 417.2 nm and the cumulative percent drug release was calculated.

### 4.9 Particle Size and Zeta potential [34]

The weighed amount of optimized formulation was taken and mixed with distilled water and sonication was kept for 30 min. The analysis was performed at a temperature of 25°Csame procedure repeated at zeta potential. The prepared formulations were characterized for zeta-potential in order to know the stability of the formulations.

### 4.10 Stability Study [35]

The Curcumin loaded emulsion formulations were stored at room temperature (25°C) and refrigerator temperature (2–8°C) for 3 month and Drug content, Entrapment efficiency (EE%) and Drug Release(%) were determined. The Azelnidipine loaded nanomicelle formulations were stored at room temperature for 90 days, and Viscosity (cps), Drug Content (DI %) and Drug Release (%) is calculated.

## 5. RESULT AND DISCISSION

### 5. 1 PREFORMULATION STUDY

#### 5.1.1 Melting point

The observed melting point of Curcumin **is** 183°C**,** which falls within the reported melting point range of 182-184°C**.**This indicates that the curcumin sample is of good quality and the melting point is consistent with the expected range, suggesting the absence of impurities or degradation in the sample. Therefore, the sample seems to meet the required standards for its melting point.

**Table 3: Observation of melting point**

| Drug name | Observed value | Reported value |
|---|---|---|
| Curcumin | 183°C | 182-184°C |

#### 5.1.2 Detection of Absorption Maxima (λ max)

The λmax of curcumin was determined to be 417.2 nm, which closely aligns with the reported value of 418 nm**.**

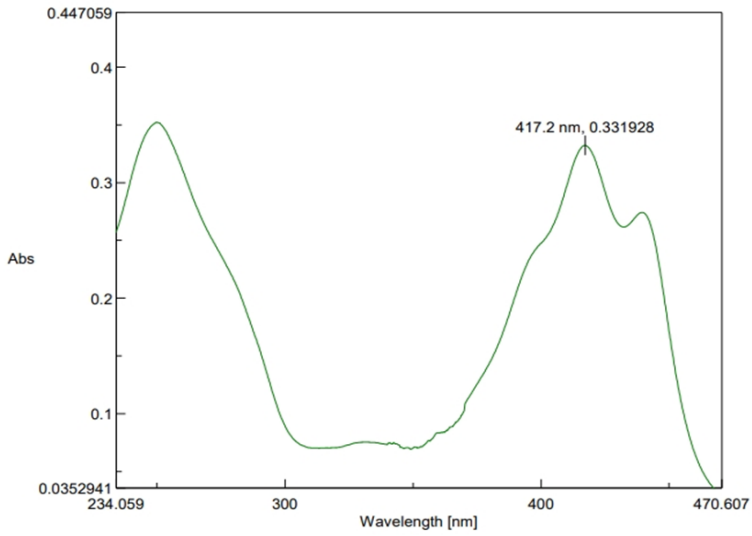


**Figure 1: UV spectra of Curcumin in Methanol**

### 5.1.3 Solubility study of Curcumin

The solubility study of Curcumin in different media reveals that it exhibits varying solubility across solvents. It has the highest solubility in methanol (0.325 µg/mL), followed by ethanol (0.287 µg/mL). In distilled water**,** Curcumin shows moderate solubility (0.214 µg/mL). When tested in buffer solutions, its solubility decreases significantly, with phosphate buffer at pH 6.8 and pH 7.4 showing solubility values of 0.122 µg/mL and 0.114 µg/mL, respectively. The acidic buffer at pH 1.2 demonstrates the lowest solubility at 0.110 µg/mL. These results indicate that Curcumin is more soluble in organic solvents like methanol and ethanol, while its solubility is considerably reduced in aqueous and buffer solutions, particularly under acidic and neutral to slightly basic conditions. This solubility profile is crucial for determining the most suitable formulation approach for Curcumin-based products.

**Table 4: Solubility in different Medium**

| **Medium** | **Solubility(µg/ml)** |
|---|---|
| Distilled water | 0.214 |
| Methanol | 0.325 |
| Ethanol | 0.287 |
| Phosphate buffer ph 6.8 | 0.122 |
| Phosphate buffer ph 7.4 | 0.114 |
| Acidic buffer ph 1.2 | 0.110 |

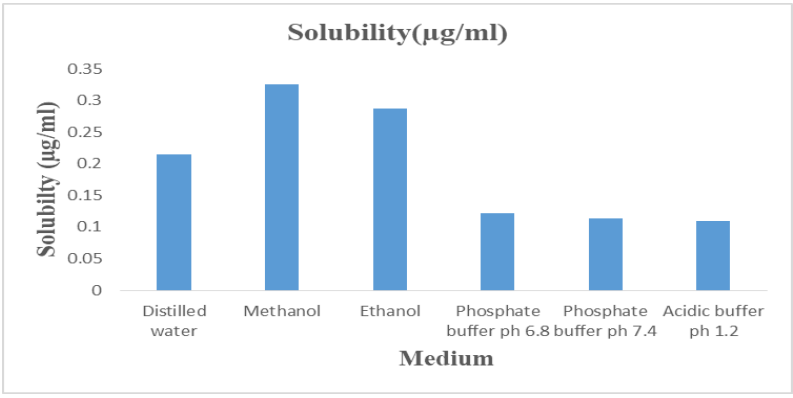


**Figure 2: Solubility in different Medium**

### 5.1.4 Determination of saturation solubility

The solubility of Curcumin in various oils, surfactants, and co-surfactants, as shown in **5**, provides valuable insights into its formulation potential. Levosulpiride exhibits high solubility in oils such as Capmul MCM (8.9 mg/ml) and Isopropyl palmitate (9.2 mg/ml), making them suitable for oil-based formulations. Castor oil also demonstrates good solubility (8.4 mg/ml), though slightly lower than the other oils. In terms of surfactants, Span 80 (3.9 mg/ml) and Tween 20 (2.2 mg/ml) show moderate solubility, indicating their potential for use in emulsions or micellar systems to improve the solubility of levosulpiride in aqueous formulations. Polyethylene glycol-400 (3.2 mg/ml) and Propylene Glycol (0.08 mg/ml) exhibit lower solubility, but they may still be effective as co-surfactants or solvents when combined with other ingredients to enhance formulation stability. Overall, oils like **Capmul MCM** and **Isopropyl palmitate** are the most effective for Curcumin solubilization, while surfactants and co-surfactants can be utilized to optimize formulation performance.

**Table 5: Solubility of Curcumin in various oils, surfactant and co-surfactant.**

| Sr no | Name Of Oil | Solubility (mg/ml) |
|---|---|---|
| 1. | Capmul MCM | 8.9 mg/ml |
| 2. | Isopropyl palmitate | 9.2(mg/ml) |
| 2. | Castor oil | 8.4 mg/ml |
| 3. | Span 80 | 3.9 mg/ml |
| 4. | Tween 20 | 2.2 mg/ml |
| 6. | Polyethylene glycol-400 | 3.2 mg//ml |
| 7. | Propylene Glycol | 0.08 mg/ml |

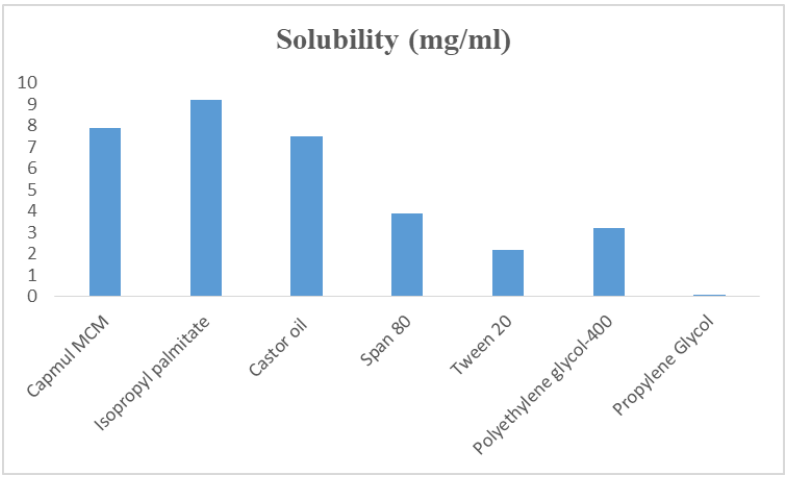


**Figure 3: solubility of oil, Surfactant, Co-surfactant**

### 5.1 .5 Fourier transform infrared spectroscopy FTIR

The FTIR spectra of curcumin reveal key functional groups that align with its chemical structure, confirming its identity and purity. The observed IR ranges and their corresponding functional groups include O-H stretching at 3506.92 $cm^{-1}$, which indicates the presence of a hydroxyl group (-OH) in curcumin. The C=O stretching observed at 1703.8 $cm^{-1}$ corresponds to the carbonyl group (C=O), confirming the conjugated ketone structure. Additionally, the C=C stretching at 1653.66 $cm^{-1}$ is associated with the conjugated double bond (C=C), which is a prominent feature of curcumin's aromatic system. The C-O stretching at 1204.33 $cm^{-1}$ reflects the ether linkage, while the C-H bending at 1427.07 $cm^{-1}$ is typical of aromatic compounds. These findings are consistent with the reported IR values, validating the molecular structure of curcumin and confirming the accuracy of the characterization.

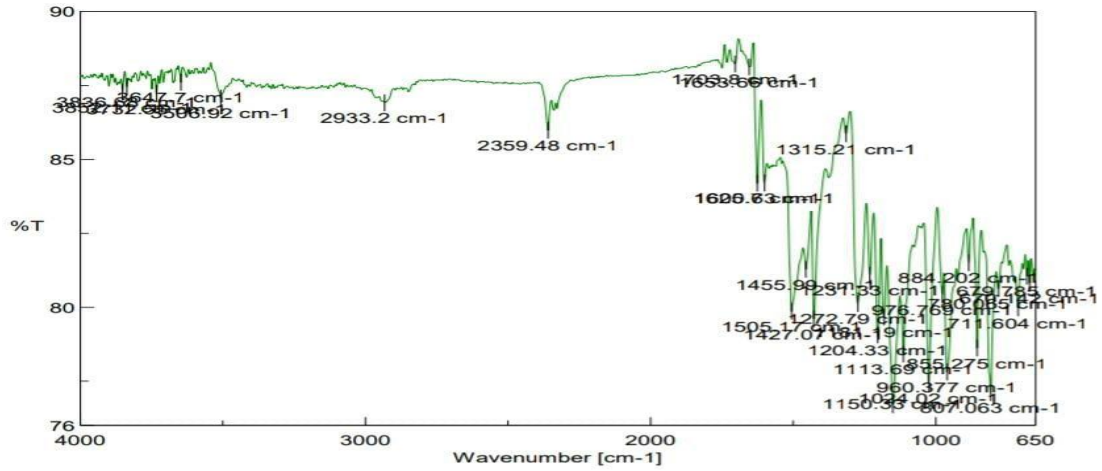

**Figure 4: FTIR Spectrum of curcumin**

### 5.1.6 Differential Scanning calorimetry (DSC)

The Differential Scanning Calorimetry (DSC) thermogram of curcumin reveals important thermal characteristics. The melting point of curcumin is observed at 181.20°C, indicating its crystalline nature, with an onset temperature of 178.29°C and an endset temperature of 183.84°C. The sharp peak and narrow peak width of 3.21°C reflect the high purity of the sample. The enthalpy of melting, represented by an integral value of -349.19 mJ, quantifies the energy absorbed during the phase transition. The absence of additional thermal events beyond the melting point suggests that curcumin does not undergo thermal decomposition within the measured range. These findings confirm curcumin's thermal stability below 178°C and its suitability for applications requiring thermal processing, while also validating its crystalline purity for formulation and drug delivery purposes.

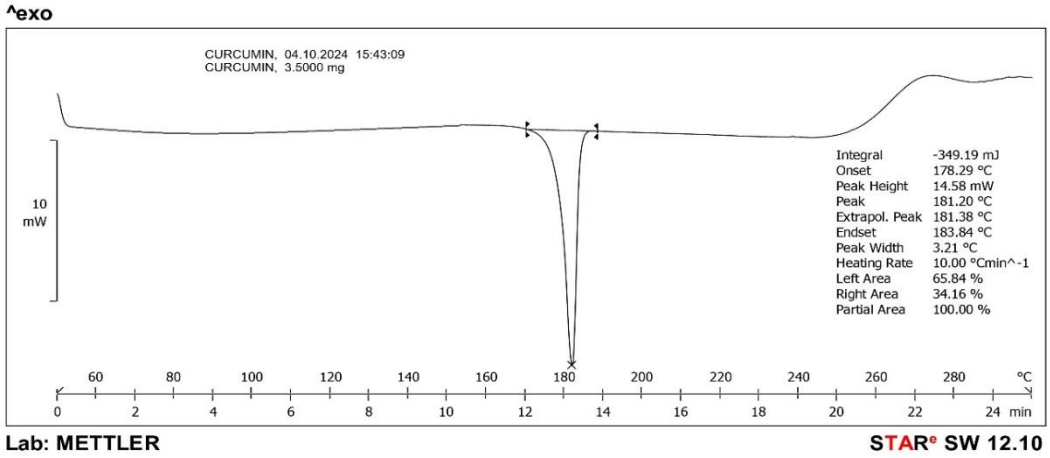


**Figure 5: DSC Thermogram of curcumin**

## 5.2 POST FORMULATION STUDY

### 5.2.1 PH Determination

The pH values of formulations **F1 to F13** range from **5.58 to 7.2**, indicating a variety of formulations with different pH levels. Formulations **F3 (7.1)**, **F7 (7.0)**, **F8 (6.97)**, and **F9 (7.2)** are close to neutral or mildly alkaline, which are typically preferred for stability and compatibility in many pharmaceutical or cosmetic applications. On the other hand, formulations like **F1 (6.52)**, **F2 (6.8)**, **F6 (6.3)**, **F10 (6.54)**, and **F12 (6.0)** fall within a mildly acidic range, which may be suitable for formulations that require slightly acidic conditions. The more acidic formulations, such as **F5 (5.9)**, **F11 (5.58)**, and **F13 (5.7)**, could influence solubility, stability, or absorption, depending on the intended use. Based on these observations, **F3 (7.1)**, **F7 (7.0)**, and **F9 (7.2)** are likely the optimized formulations if a neutral or slightly

alkaline pH is desired, though the final choice should depend on the specific application and desired characteristics of the product.

**Table 6: PH of F1-F13**

| Formulation code | PH |
|---|---|
| F1 | 6.52 |
| F2 | 6.8 |
| F3 | 7.1 |
| F4 | 6.2 |
| F5 | 5.9 |
| F6 | 6.3 |
| F7 | 7.0 |
| F8 | 6.97 |
| F9 | 7.2 |
| F10 | 6.54 |
| F11 | 5.58 |
| F12 | 6.0 |
| F13 | 5.7 |

### 5.2.2 Density

The density values of formulations **F1 to F13** range from **0.82 g/cc to 0.98 g/cc**, indicating slight variations in the formulations. Formulations **F7 (0.98 g/cc)**, **F9 (0.98 g/cc)**, and **F13 (0.98 g/cc)** have the highest density, suggesting they may have a more compact structure or higher solid content. In contrast, formulations **F6 (0.82 g/cc)** and **F8 (0.82 g/cc)** have the lowest density, indicating they may be less compact or have a higher volume relative to their mass. The remaining formulations, such as **F1 (0.85 g/cc)**, **F3 (0.87 g/cc)**, **F4 (0.92 g/cc)**, and others, fall within a moderate density range, which may offer a balance of physical properties for different applications.

The choice of optimized batch would depend on the specific requirements of the formulation, such as desired texture, release profile, or stability. If a higher density is preferred for more stable or compact formulations, **F7**, **F9**, and **F13** could be considered. However, formulations with lower densities like **F6** and **F8** may be suitable for applications requiring lighter or more porous structures.

**Table 7: Density (g/cc) of F1-F13**

| Formulation code | Density (g/cc) |
|---|---|
| F1 | 0.85 |
| F2 | 0.96 |
| F3 | 0.87 |
| F4 | 0.92 |
| F5 | 0.96 |

| | |
|---|---|
| F6 | 0.82 |
| F7 | 0.98 |
| F8 | 0.82 |
| F9 | 0.98 |
| F10 | 0.92 |
| F11 | 0.89 |
| F12 | 0.93 |
| F13 | 0.98 |

### 5.2.3 Viscosity (cps)

Formulation **F9** has the highest viscosity among all the batches at **58.3 cps**, indicating that it is the thickest formulation in the group. This high viscosity could be beneficial for applications requiring a more gel-like or viscous consistency, such as for better retention, slow release, or a more substantial texture. If the intended use of the formulation demands a thicker consistency, **F9** could be considered the **optimized batch**. However, the suitability of **F9** as the optimized batch depends on the specific requirements of the product's intended use. If a higher viscosity is desired for the formulation's performance, stability, or texture, **F9** would be appropriate. On the other hand, if a thinner, more fluid formulation is required for easier application or spreading, a formulation with lower viscosity may be preferred.

**Table 8: Viscosity (cps) of F1-F13**

| **Formulation code** | **Viscosity (cps)** |
|---|---|
| F1 | 42.52 |
| F2 | 40.5 |
| F3 | 39.6 |
| F4 | 28.5 |
| F5 | 26.5 |
| F6 | 6.6 |
| F7 | 13.2 |
| F8 | 10.25 |
| F9 | 58.3 |
| F10 | 46.5 |
| F11 | 8.5 |
| F12 | 15.4 |
| F13 | 46.5 |

**ANOVA for Linear model**

**Response 2: Viscosity**

| **Source** | **Sum of Squares** | **df** | **Mean Square** | **F-value** | **p-value** | |
|---|---|---|---|---|---|---|
| **Model** | 2111.25 | 3 | 703.75 | 4.22 | 0.0402 | significant |
| A-Isopropyl palmitate | 1953.13 | 1 | 1953.13 | 11.73 | 0.0076 | |
| B-Span 80 | 97.79 | 1 | 97.79 | 0.5871 | 0.4632 | |
| C-PEG 400 | 60.34 | 1 | 60.34 | 0.3622 | 0.5621 | |
| **Residual** | 1499.16 | 9 | 166.57 | | | |
| **Cor Total** | 3610.41 | 12 | | | | |

Factor coding is **coded**.
Sum of squares is **Type III - Partial**

The **Model F-value** of 4.22 implies the model is significant. There is only a 4.02% chance that an F-value this large could occur due to noise.

**P-values** less than 0.0500 indicate model terms are significant. In this case A is a significant model term. Values greater than 0.1000 indicate the model terms are not significant. If there are many insignificant model terms (not counting those required to support hierarchy), model reduction may improve your model.

**Fit Statistics**

| | | | | |
|---|---|---|---|---|
| **Std. Dev.** | 12.91 | | **$R^2$** | 0.5848 |
| **Mean** | 29.45 | | **Adjusted $R^2$** | 0.4464 |
| **C.V. %** | 43.82 | | **Predicted $R^2$** | 0.4384 |
| | | | **Adeq Precision** | 5.3418 |

**Final Equation in Terms of Coded Factors**

| Viscosity | = |
|---|---|
| +29.45 | |
| -15.63 | A |
| +3.50 | B |
| +2.75 | C |

The equation in terms of coded factors can be used to make predictions about the response for given levels of each factor. By default, the high levels of the factors are coded as +1 and the low levels are coded as -1. The coded equation is useful for identifying the relative impact of the factors by comparing the factor coefficients.

**Final Equation in Terms of Actual Factors**

| Viscosity | = |
|---|---|
| +86.45129 | |
| -6.25000 | Isopropyl palmitate |
| +3.49625 | Span 80 |
| +10.98500 | PEG 400 |

The equation in terms of actual factors can be used to make predictions about the response for given levels of each factor. Here, the levels should be specified in the original units for each factor. This equation should not be used to determine the relative impact of each factor because the coefficients are scaled to accommodate the units of each factor and the intercept is not at the center of the design space.

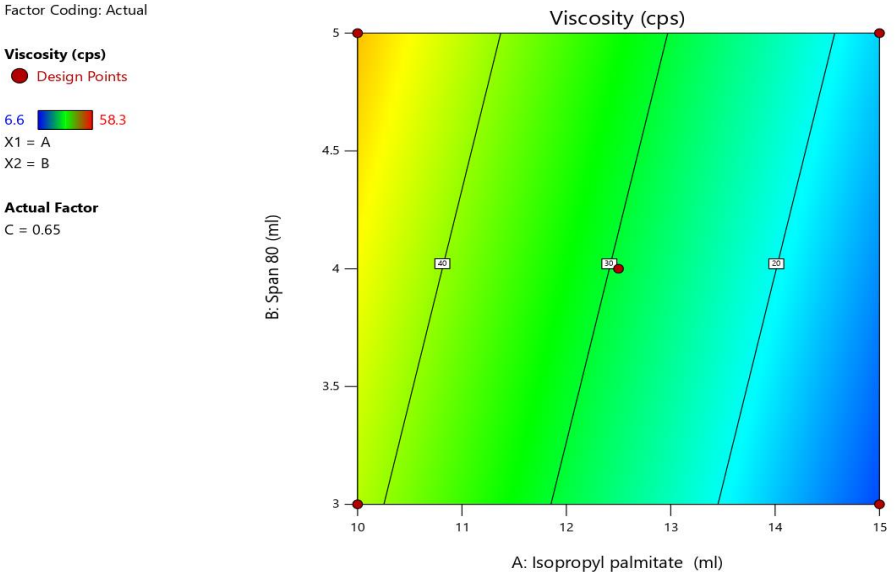


**Figure 6:Counter plot**

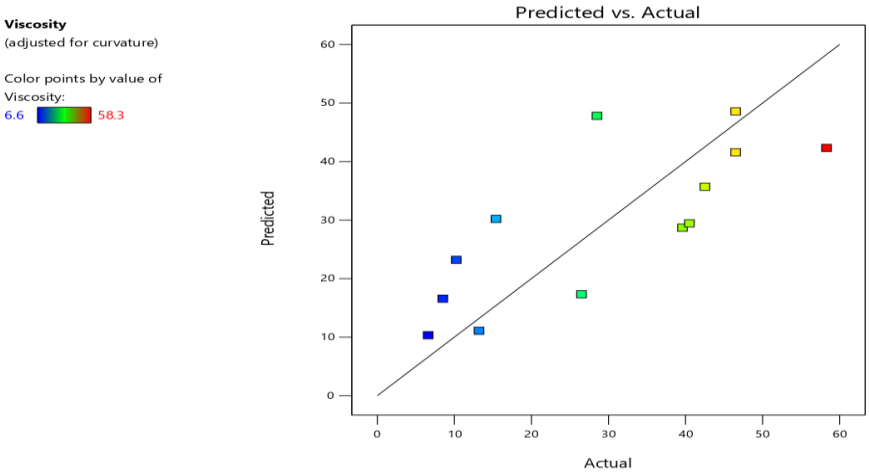


**Figure 7:Predicted vs Actual plot**

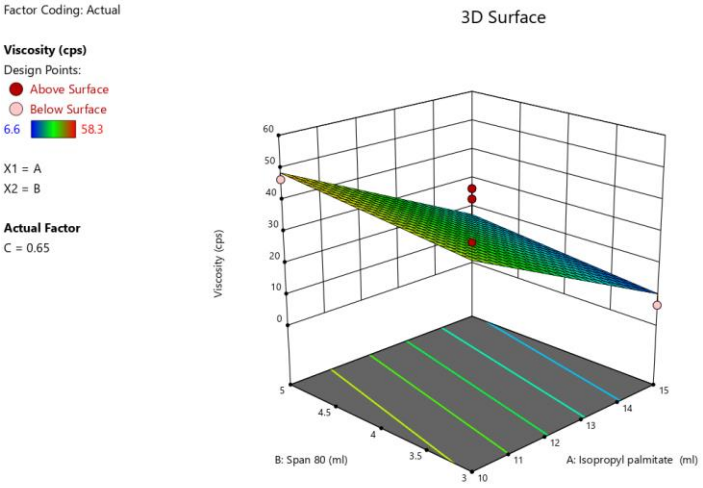


**Figure 8 :3D Surface plot**

### 5.2.4 Drug content analysis

Formulation F9 has the highest drug content at 96.52%**,** making it the most concentrated formulation in terms of active ingredient. This is a significant factor in determining the optimized batch, as higher drug content typically suggests better efficacy and performance, assuming it aligns with the intended dosage and therapeutic goals. In comparison, formulations like F6 (68.95%) and F5 (79.63%) have much lower drug content, which may not be ideal for the desired therapeutic effect. Therefore, based on drug content alone, F9 stands out as the optimized batch, as it offers the highest concentration of the active ingredient. In conclusion, **F9** can be considered the optimized batch due to its superior drug content, which is crucial for ensuring the desired therapeutic effect and efficacy of the formulation.

**Table 9: Drug content (%) of F1-F13**

| Formulation code | Drug content (%) |
|---|---|
| F1 | 90.12 |
| F2 | 89.63 |
| F3 | 85.23 |
| F4 | 80.12 |
| F5 | 79.63 |
| F6 | 68.95 |
| F7 | 72.56 |
| F8 | 86.32 |
| F9 | 96.52 |
| F10 | 91.23 |
| F11 | 85.47 |
| F12 | 90.25 |
| F13 | 89.89 |

**ANOVA for 2FI model**

**Response 1: Drug Content**

| Source | Sum of Squares | df | Mean Square | F-value | p-value | |
|---|---|---|---|---|---|---|
| **Model** | 622.16 | 6 | 103.69 | 5.39 | 0.0299 | significant |
| A-Isopropyl palmitate | 327.04 | 1 | 327.04 | 17.00 | 0.0062 | |
| B-Span 80 | 41.22 | 1 | 41.22 | 2.14 | 0.1936 | |
| C-PEG 400 | 2.77 | 1 | 2.77 | 0.1441 | 0.7173 | |
| AB | 36.12 | 1 | 36.12 | 1.88 | 0.2197 | |
| AC | 214.77 | 1 | 214.77 | 11.16 | 0.0156 | |
| BC | 0.2304 | 1 | 0.2304 | 0.0120 | 0.9164 | |
| **Residual** | 115.45 | 6 | 19.24 | | | |
| **Cor Total** | 737.61 | 12 | | | | |

Factor coding is **coded**.

Sum of squares is **Type III - Partial**

The **Model F-value** of 5.39 implies the model is significant. There is only a 2.99% chance that an F-value this large could occur due to noise.

**P-values** less than 0.0500 indicate model terms are significant. In this case A, AC are significant model terms. Values greater than 0.1000 indicate the model terms are not significant. If there are many insignificant model terms (not counting those required to support hierarchy), model reduction may improve your model.

**Fit Statistics**

| | | | | |
|---|---|---|---|---|
| **Std. Dev.** | 4.39 | | **$R^2$** | 0.8435 |
| **Mean** | 85.07 | | **Adjusted $R^2$** | 0.6870 |
| **C.V. %** | 5.16 | | **Predicted $R^2$** | 0.6799 |
| | | | **Adeq Precision** | 8.5255 |

**Final Equation in Terms of Coded Factors**

| Drug Content | = |
|---|---|
| +85.07 | |
| -6.39 | A |
| +2.27 | B |
| -0.5887 | C |
| +3.01 | AB |
| +7.33 | AC |
| +0.2400 | BC |

The equation in terms of coded factors can be used to make predictions about the response for given levels of each factor. By default, the high levels of the factors are coded as +1 and the low levels are coded as -1. The coded equation is useful for identifying the relative impact of the factors by comparing the factor coefficients.

**Final Equation in Terms of Actual Factors**

| Drug Content | = |
|---|---|
| +267.34377 | |
| -14.98610 | Isopropyl palmitate |
| -13.37900 | Span 80 |
| -152.74500 | PEG 400 |
| +1.20200 | Isopropyl palmitate * Span 80 |
| +11.72400 | Isopropyl palmitate * PEG 400 |
| +0.960000 | Span 80 * PEG 400 |

The equation in terms of actual factors can be used to make predictions about the response for given levels of each factor. Here, the levels should be specified in the original units for each factor. This equation should not be used to determine the relative impact of each factor because the coefficients are scaled to accommodate the units of each factor and the intercept is not at the center of the design space.

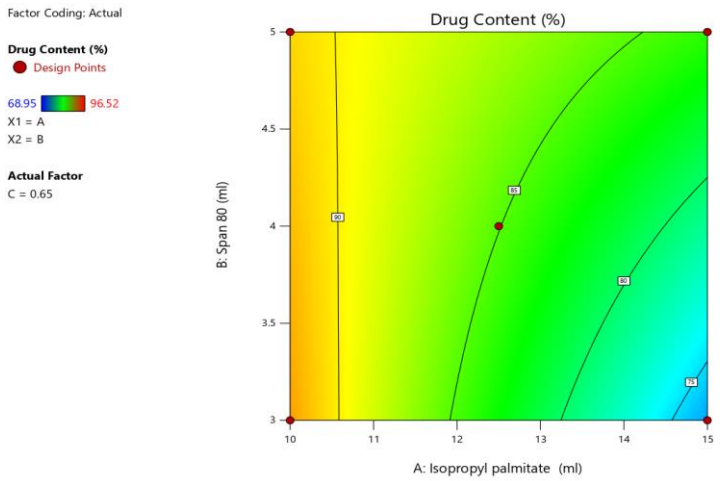


**Figure 9:Counter plot**

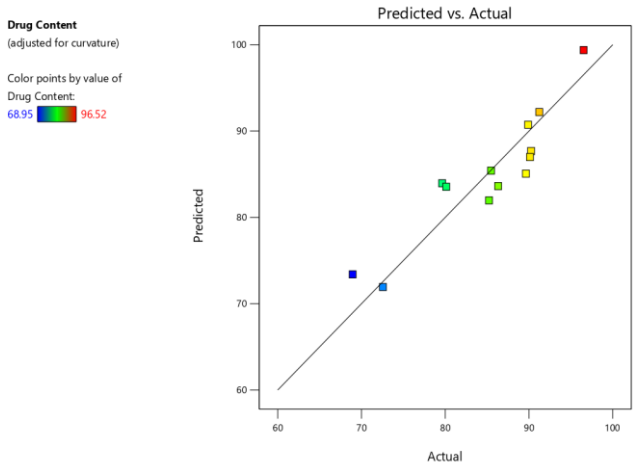


**Figure 10 :Predicted vs Actual plot**

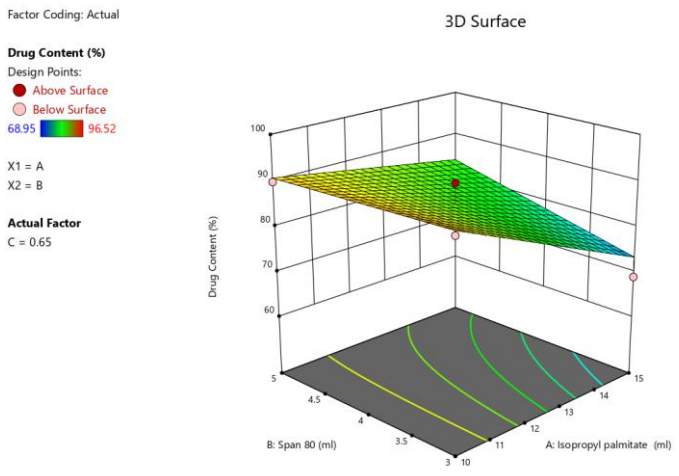


**Figure 11:3D Surface plot**

### 5.2.5 Centrifugation

Based on the centrifugation stability results at **3500 rpm**, the formulations **F3** and **F11** showed **phase separation**, indicating instability under centrifugation conditions. This suggests that these formulations may not maintain uniformity or stability over time, which could affect their performance and reliability. On the other hand, formulations **F1, F2, F4, F5, F6, F7, F8, F9, F10, F12,** and **F13** were **stable**, indicating that they maintained their integrity and uniformity even under centrifugation. Stability under centrifugation is a good indicator of formulation robustness, as it suggests that these batches can withstand stress without significant separation or degradation. In conclusion, **F9** stands out as an optimized batch due to its stability under centrifugation, along with its high drug content and other desirable characteristics. Therefore, **F9** can be considered the most stable and optimized batch based on these parameters.

**Table 10: Centrifugation of F1-F13**

| **Formulation code** | **Centrifugation((3500 rpm))** |
|---|---|
| F1 | Stable |
| F2 | Stable |
| F3 | Phase separation |
| F4 | Stable |
| F5 | Stable |
| F6 | Stable |
| F7 | Stable |
| F8 | Stable |
| F9 | Stable |

| | |
|---|---|
| F10 | Stable |
| F11 | Phase separation |
| F12 | Stable |
| F13 | Stable |

### 5.2.6 Freeze thaw

Formulation F9 has been identified as the optimized batch in terms of stability under freeze-thaw conditions. It remained stable, showing no phase separation, unlike some other formulations such as F3 and F11, which exhibited instability. This stability suggests that F9 may be the most reliable formulation for long-term storage and use under varying temperature conditions.

**Table 11: Freeze thaw of F1-F13**

| **Formulation code** | **Freeze thaw** |
|---|---|
| F1 | Stable |
| F2 | Stable |
| F3 | Phase separation |
| F4 | Stable |
| F5 | Stable |
| F6 | Stable |
| F7 | Stable |
| F8 | Stable |
| F9 | Stable |
| F10 | Stable |
| F11 | Phase separation |
| F12 | Stable |
| F13 | Stable |

### 5.2.7 In-Vitro Diffusion study

The drug release profiles of formulations F1 to F7 and F8 to F13 reveal distinct performance trends. Among F1 to F7, F1 exhibited the highest cumulative drug release at 6 hours (89.53%), followed by F2 (85.2%), while F6 showed moderate release (72.45%), and F7 had the lowest release (80.17%). In the F8 to F13 group, F9 demonstrated the highest cumulative release at 6 hours (96.78%), surpassing all other formulations, with F12 (92.56%) and F13 (93.48%) also showing significant release. Comparatively, F9 exhibited a superior release profile, making it the optimized formulation among the F8-F13 group, while F1 emerged as the best-performing formulation in the F1-F7 group. These findings suggest that F1 and F9 are promising candidates for applications requiring rapid drug release, while formulations with slower release profiles, such as F6 and F11, may be more suitable for sustained or controlled-release

applications. Further optimization and stability studies on F1 and F9 could provide additional insights into their long-term efficacy and therapeutic potential.

**Table 12: Drug release of F1-F7**

| Time (hrs) | F1 | F2 | F3 | F4 | F5 | F6 | F7 |
|---|---|---|---|---|---|---|---|
| 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 1 | 12.35±0.12 | 10.58±0.05 | 9.89±0.98 | 9.55±0.02 | 10.15±0.16 | 9.56±0.06 | 8.56±0.03 |
| 2 | 27.65±0.03 | 24.56±0.47 | 26.47±0.54 | 22.56±0.01 | 21.48±0.58 | 20.18±0.58 | 23.87±0.28 |
| 3 | 41.56±0.56 | 39.87±0.65 | 35.48±0.63 | 31.45±0.36 | 35.49±0.36 | 34.59±0.87 | 32.58±0.34 |
| 4 | 58.96±0.78 | 54.58±0.02 | 45.89±0.02 | 42.15±0.89 | 44.87±0.47 | 48.78±0.63 | 46.58±0.09 |
| 5 | 72.56±0.23 | 70.15±0.03 | 65.23±0.49 | 60.48±0.19 | 64.89±0.27 | 67.89±0.24 | 72.43±0.02 |
| 6 | 89.53±0.53 | 85.2±0.47 | 78.12±0.35 | 78.56±0.02 | 77.45±0.64 | 72.45±0.14 | 80.17±0.18 |

**Table 13: Drug release of F8-F13**

| Time (hrs) | F8 | F9 | F10 | F11 | F12 | F13 |
|---|---|---|---|---|---|---|
| 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 1 | 11.45±0.52 | 13.26±0.85 | 10.78±0.65 | 9.87±0.89 | 11.48±0.86 | 12.56±0.35 |
| 2 | 28.45±0.36 | 30.18±0.46 | 22.45±0.87 | 27.51±0.25 | 29.58±0.35 | 25.36±0.47 |
| 3 | 40.89±0.87 | 48.36±0.34 | 39.73±0.65 | 43.58±0.47 | 41.58±0.47 | 40.45±0.36 |
| 4 | 64.56±0.01 | 56.59±0.12 | 52.52±0.78 | 57.89±0.62 | 50.48±0.36 | 51.15±0.12 |
| 5 | 73.59±0.12 | 75.69±0.63 | 69.87±0.71 | 71.45±0.32 | 83.56±.084 | 79.89±0.23 |
| 6 | 88.56±0.35 | 96.78±0.87 | 90.56±0.03 | 86.78±0.12 | 92.56±0.25 | 93.48±0.01 |

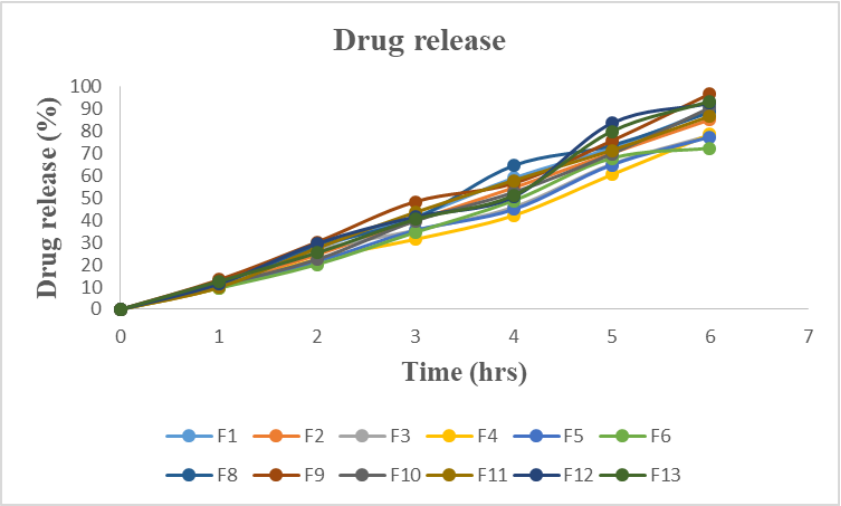


**Figure 12: Drug release of F1-F13**

**ANOVA for Linear model**

**Response 3: Drug release**

| Source | Sum of Squares | df | Mean Square | F-value | p-value | |
|---|---|---|---|---|---|---|
| **Model** | 372.76 | 3 | 124.25 | 3.90 | 0.0489 | significant |
| A-Isopropyl palmitate | 226.10 | 1 | 226.10 | 7.09 | 0.0259 | |
| B-Span 80 | 68.04 | 1 | 68.04 | 2.13 | 0.1781 | |
| C-PEG 400 | 78.63 | 1 | 78.63 | 2.47 | 0.1508 | |
| **Residual** | 286.95 | 9 | 31.88 | | | |
| **Cor Total** | 659.71 | 12 | | | | |

Factor coding is **Coded**.
Sum of squares is **Type III - Partial**

The **Model F-value** of 3.90 implies the model is significant. There is only a 4.89% chance that an F-value this large could occur due to noise.

**P-values** less than 0.0500 indicate model terms are significant. In this case A is a significant model term. Values greater than 0.1000 indicate the model terms are not significant. If there are many insignificant model terms (not counting those required to support hierarchy), model reduction may improve your model.

**Fit Statistics**

| | | | | |
|---|---|---|---|---|
| **Std. Dev.** | 5.65 | | **$R^2$** | 0.5650 |
| **Mean** | 85.40 | | **Adjusted $R^2$** | 0.4201 |
| **C.V. %** | 6.61 | | **Predicted $R^2$** | 0.4100 |
| | | | **Adeq Precision** | 5.3965 |

**Final Equation in Terms of Coded Factors**

| Drug release | = |
|---|---|
| +85.40 | |
| -5.32 | A |
| +2.92 | B |
| -3.14 | C |

The equation in terms of coded factors can be used to make predictions about the response for given levels of each factor. By default, the high levels of the factors are coded as +1 and the low levels are coded as -1. The coded equation is useful for identifying the relative impact of the factors by comparing the factor coefficients.

**Final Equation in Terms of Actual Factors**

| Drug release | = |
|---|---|
| +108.46725 | |
| -2.12650 | Isopropyl palmitate |
| +2.91625 | Span 80 |
| -12.54000 | PEG 400 |

The equation in terms of actual factors can be used to make predictions about the response for given levels of each factor. Here, the levels should be specified in the original units for each factor. This equation should not be used to determine the relative impact of each factor because the coefficients are scaled to accommodate the units of each factor and the intercept is not at the center of the design space.

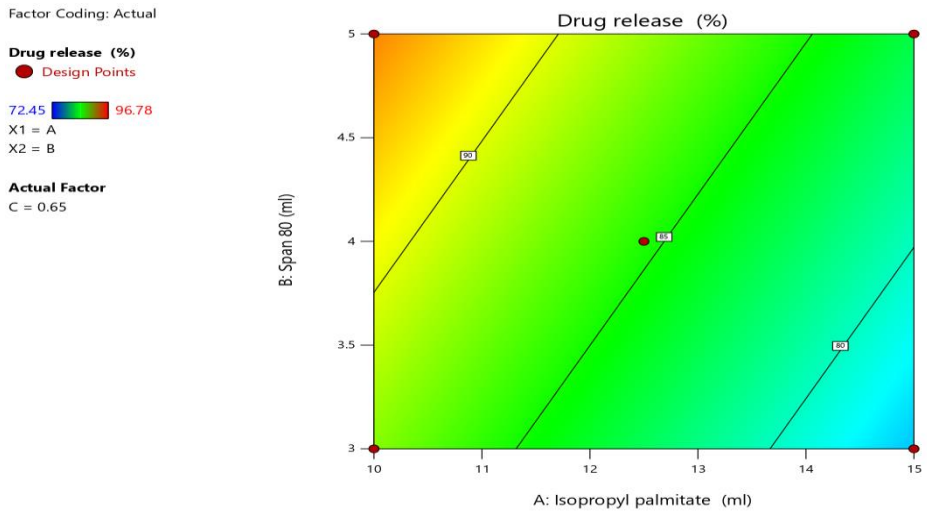


**Figure 13:Counter plot**

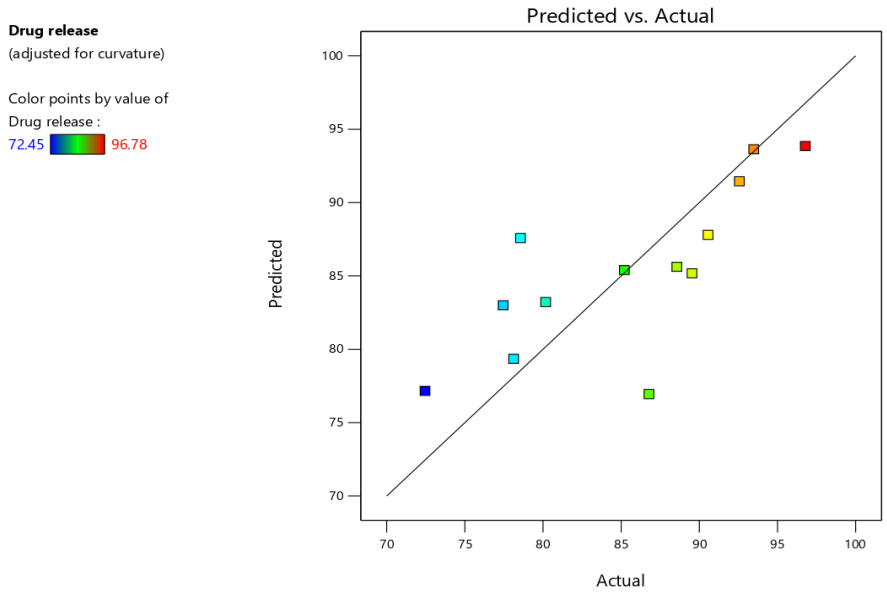


**Figure 14 :Predicted vs Actual plot**

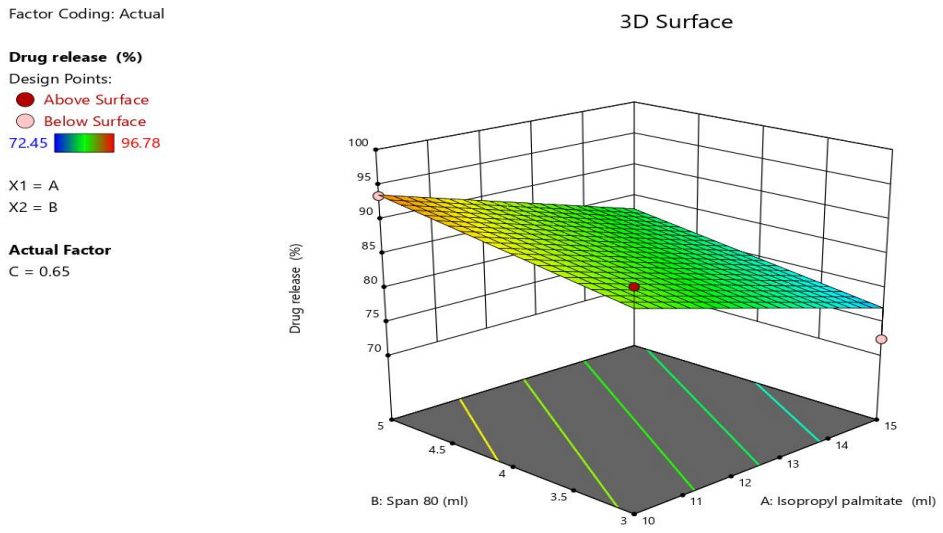


**Figure 15:3D Surface plot**

### 5.2.8 Particle size and Zeta potential

The optimized batch **F9** demonstrated excellent characteristics with a particle size of **29.5 µm**, indicating the formation of nanosized particles suitable for enhanced drug delivery. The polydispersity index (PDI) value of **0.112** suggests a narrow size distribution, confirming the uniformity and stability of the formulation. Additionally, the zeta potential value of **-26.8 mV** indicates good colloidal stability due to sufficient repulsive forces between particles, reducing the likelihood of aggregation. These parameters collectively highlight the suitability of batch F9 for further development and potential therapeutic applications.

**Table 14: Particle size and Zeta potential of optimized batch F9**

| Optimized batch | Particle Size (µm) | PDI | Zeta potential (mV) |
|---|---|---|---|
| F9 | 29.5 | 0.112 | -26.8 |

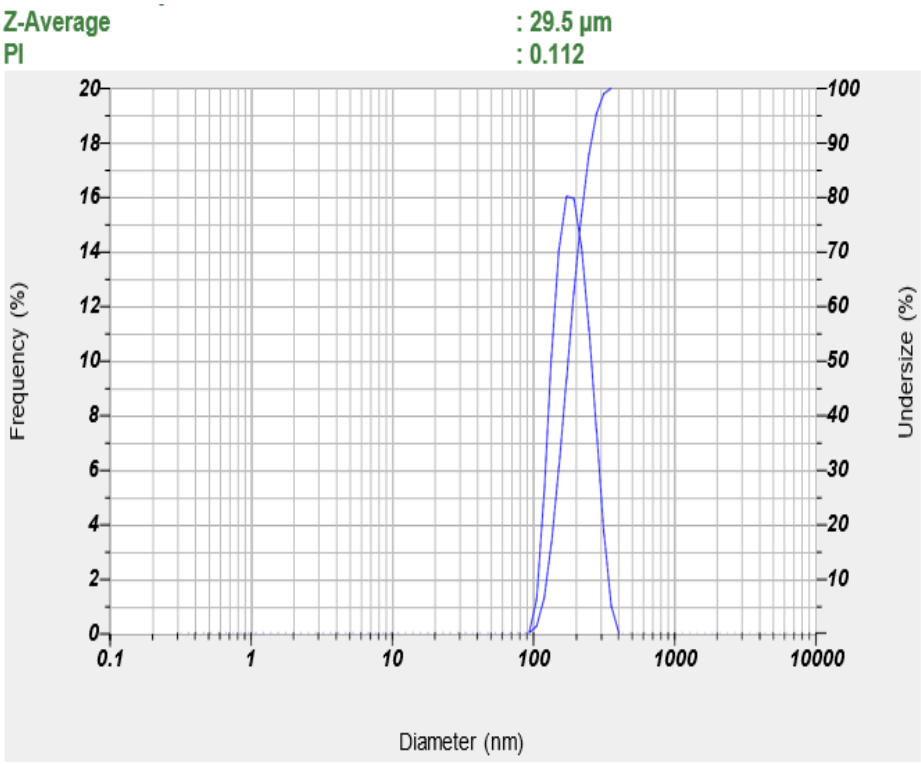


**Figure 16: Particle size of optimized batch F9**

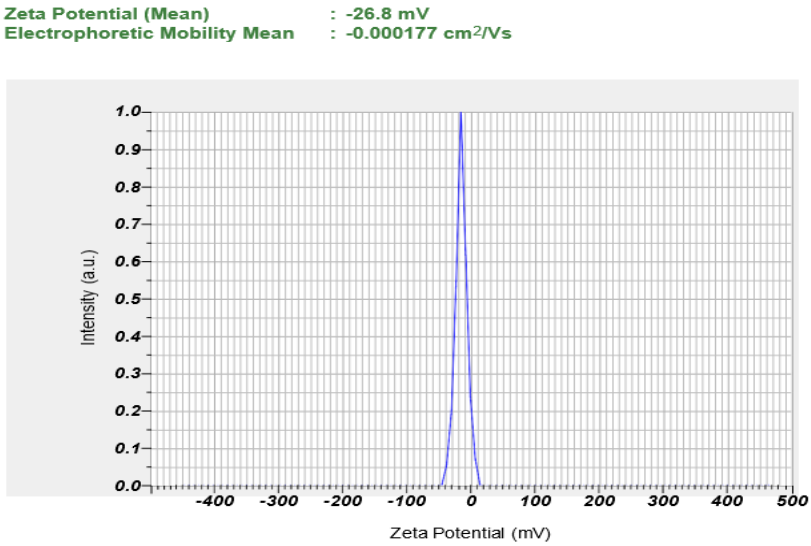


**Figure 17: Zeta potential of optimized batch F9**

### 5.2.8 Stability Study

The stability study of the optimized batch F9 over three months indicates excellent stability in terms of viscosity, drug content, and drug release. The viscosity remained consistent, with negligible variation from the initial value of 58.3 cps. Drug content showed no significant changes, remaining stable at approximately 96.52%**,** demonstrating the formulation's robustness in maintaining its chemical integrity. Similarly, drug release remained consistent, with only a minor change from 96.78% to 96.74%**,** indicating sustained release characteristics over the study period. These results confirm that the optimized batch F9 exhibits excellent physical, chemical, and functional stability under the tested conditions, making it suitable for long-term storage and therapeutic applications.

**Table 15: Stability study of optimized batch F9**

| **Parameter** | **Initial** | **1 month** | **2 month** | **3 month** |
|---|---|---|---|---|
| Viscosity (cps) | 58.3±0.01 | 58.3±0.14 | 58.2±0.02 | 58.2±0.03 |
| Drug Content (DI %) | 96.52±0.02 | 96.52±0.02 | 96.51±0.04 | 96.52±0.03 |
| Drug Release (%) | 96.78±0.32 | 96.78±0.31 | 96.78±0.31 | 96.74±0.30 |

## CONCLUSION

The Preformulation and post-formulation studies of curcumin-loaded microemulsions have successfully identified the optimized batch (F9) with favorable characteristics, including a neutral pH, high density, and optimal viscosity for transdermal applications. The formulation demonstrated excellent stability and bioavailability potential, with isopropyl palmitate being a key factor influencing viscosity. These findings highlight F9 as the most promising formulation for enhanced curcumin delivery, offering a stable and effective system for therapeutic applications.

## CONFLICT OF INTEREST

All authors declare that there is no any conflict of interest.

## REFERENCES

1. Sharifi-Rad J, Rayess YE, Rizk AA, Sadaka C, Zgheib R, Zam W, Sestito S, Rapposelli S, Neffe-Skocińska K, Zielińska D, Salehi B. Turmeric and its major compound curcumin on health: bioactive effects and safety profiles for food, pharmaceutical, biotechnological and medicinal applications. Frontiers in pharmacology. 2020 Sep 15;11:550909.
2. Hewlings SJ, Kalman DS. Curcumin: A review of its effects on human health. Foods. 2017 Oct;6(10):92.
3. Kocaadam B, Şanlier N. Curcumin, an active component of turmeric (Curcuma longa), and its effects on health. Critical reviews in food science and nutrition. 2017 Sep 2;57(13):2889-95.
4. Kocaadam B, Şanlier N. Curcumin, an active component of turmeric (Curcuma longa), and its effects on health. Critical reviews in food science and nutrition. 2017 Sep 2;57(13):2889-95.
5. Sabet S, Rashidinejad A, Melton LD, McGillivray DJ. Recent advances to improve curcumin oral bioavailability. Trends in Food Science & Technology. 2021 Apr 1;110:253-66.

6. Tabanelli R, Brogi S, Calderone V. Improving curcumin bioavailability: Current strategies and future perspectives. Pharmaceutics. 2021 Oct 17;13(10):1715.
7. Racz LZ, Racz CP, Pop LC, Tomoaia G, Mocanu A, Barbu I, Sárközi M, Roman I, Avram A, Tomoaia-Cotisel M, Toma VA. Strategies for improving bioavailability, bioactivity, and physical-chemical behavior of curcumin. Molecules. 2022 Oct 13;27(20):6854.
8. Shahbaz M, Imran M, Hussain M, Alsagaby SA, Momal U, Naeem H, Abdelgawad MA, El-Ghorab AH, Al Abdulmonem W, Waqar AB, Ghoneim MM. Curcumin: a bioactive compound with molecular targets for human malignancies. Food and Agricultural Immunology. 2023 Dec 31;34(1):2280524.
9. Amuti A, Wang X, Zan M, Lv S, Wang Z. Formulation and characterization of curcumin-loaded microemulsions: Evaluation of antioxidant stability and in vitro release. Journal of Molecular Liquids. 2021 Aug 15;336:116881.
10. Luna-Canales IC, Delgado-Buenrostro NL, Chirino YI, Nava-Arzaluz G, Piñón-Segundo E, Martínez-Cruz G, Ganem-Rondero A. Curcumin-loaded microemulsion: Formulation, characterization, and in vitro skin penetration. Drug Development and Industrial Pharmacy. 2023 Jan 2;49(1):42-51.
11. Bergonzi MC, Hamdouch R, Mazzacuva F, Isacchi B, Bilia AR. Optimization, characterization and in vitro evaluation of curcumin microemulsions. LWT-Food Science and Technology. 2014 Nov 1;59(1):148-55.
12. Jiang T, Charcosset C. Encapsulation of curcumin within oil-in-water emulsions prepared by premix membrane emulsification: Impact of droplet size and carrier oil on the chemical stability of curcumin. Food Research International. 2022 Jul 1;157:111475.
13. Amuti A, Wang X, Zan M, Lv S, Wang Z. Formulation and characterization of curcumin-loaded microemulsions: Evaluation of antioxidant stability and in vitro release. Journal of Molecular Liquids. 2021 Aug 15;336:116881.
14. Hassan SF, Asghar S, Ullah Khan I, Munir R, Khalid SH. Curcumin Encapsulation in Geranium Oil Microemulsion Elevates Its Antibacterial, Antioxidant, Anti-Inflammatory, and Anticancer Activities. ACS omega. 2024 Jan 23;9(5):5624-36.
15. Luna-Canales IC, Delgado-Buenrostro NL, Chirino YI, Nava-Arzaluz G, Piñón-Segundo E, Martínez-Cruz G, Ganem-Rondero A. Curcumin-loaded microemulsion: Formulation, characterization, and in vitro skin penetration. Drug Development and Industrial Pharmacy. 2023 Jan 2;49(1):42-51.
16. Chang R, Chen L, Qamar M, Wen Y, Li L, Zhang J, Li X, Assadpour E, Esatbeyoglu T, Kharazmi MS, Li Y. The bioavailability, metabolism and microbial modulation of curcumin-loaded nanodelivery systems. Advances in Colloid and Interface Science. 2023 Aug 1;318:102933.
17. Paolino D, Vero A, Cosco D, Pecora TM, Cianciolo S, Fresta M, Pignatello R. Improvement of oral bioavailability of curcumin upon microencapsulation with methacrylic copolymers. Frontiers in Pharmacology. 2016 Dec 21;7:485.
18. Joshi SD, Chavan RR, Jadhav AS, Thorat VH, Gaikwad KV. A review of different approaches for improving curcumin bioavailability. Journal of Drug Delivery and Therapeutics. 2023 Dec 15;13(12):238-44.
19. Amuti A, Wang X, Zan M, Lv S, Wang Z. Formulation and characterization of curcumin-loaded microemulsions: Evaluation of antioxidant stability and in vitro release. Journal of Molecular Liquids. 2021 Aug 15;336:116881.
20. Zielińska A, Alves H, Marques V, Durazzo A, Lucarini M, Alves TF, Morsink M, Willemen N, Eder P, Chaud MV, Severino P. Properties, extraction methods, and delivery systems for curcumin as a natural source of beneficial health effects. Medicina. 2020 Jul 3;56(7):336.

21. JADHAV, K. R.; SHETYE, S. L.; KADAM, V. J. Design and evaluation of microemulsion based drug delivery system. International journal of Advances in pharmaceutical Sciences, 2010, 1.2.
22. Patil V, Mhamane S, More S, Pawar A, Arulmozhi S. Exploring the protective effect exhibited by curcumin-loaded coconut oil microemulsion in the experimental models of neurodegeneration: an insight of formulation development, in vitro and in vivo study. Future Journal of Pharmaceutical Sciences. 2022 Dec 2;8(1):51.
23. Kasgavada P, Swapnil M. Formulation and evaluation of fast dissolving tablet of Ciprofloxacin. Int J Adv Pharm. 2016;5:52-60.
24. Singh S, Garg K, Sharma N, Sharma S, Arora S. Development and validation of uv-spectroscopy analytical method for estimation of lafutidine in solid nano-dispersion. Plant Arch. 2020;20(2):2291-7.
25. Savale SK. Curcumin as a model drug: conformation, solubility estimation, morphological, in vitro and in vivo biodistribution study. Journal of PharmaSciTech. 2017;7:31-5.
26. Priya S, Koland M, Kumari S. Nanoemulsion components screening of quetiapine fumarate: Effect of surfactant and co surfactant. Asian J Pharm Clin Res. 2015;8(6):136-40.
27. FABIAN, JUNE. PREFORMULATION AND DEXCHLORPHENIRAMINE DEVELOPMENT OF A FORM. 1994. PhD Thesis. Faculty of Medicine, University of the Witwatersrand, Johannesburg.-
28. NARENDAR, D.; KISHAN, V. Candesartan cilexetil nanoparticles for improved oral bioavailability. Ther deli, 2017, 8.2: 79-88.
29. Nirmala MJ, Allanki SR, Mukherjee AM, Chandrasekaran N. Enhancing the solubility of ramipril using a new essential oil based microemulsion system. Int J Pharm Pharm Sci. 2013;5(4):322-3.
30. Azeem A, Rizwan M, Ahmad FJ, Iqbal Z, Khar RK, Aqil M, Talegaonkar S. Nanoemulsion components screening and selection: a technical note. Aaps Pharmscitech. 2009 Mar;10:69-76.
31. MEGALINGAM, Arumugampillai, et al. Viscosity measurements in semi-solid metal processing: current status and recent developments. The International Journal of Advanced Manufacturing Technology, 2022, 119.3: 1435-1459.
32. Chaudhari VM, Patel MS, Patel MR. Formulation and evaluation of microemulsion based gel of clotrimazole. International Journal of Universal Pharmacy and Bio Sciences. 2014;3(3):268-300.
33. DURGUN, Meltem Ezgi; YAPAR, Evren Algin. A critical step for the cosmetic industry: scale-up. Universal Journal of Pharmaceutical Research, 2021.
34. LEE, Jaehwi, et al. Formulation of microemulsion systems for transdermal delivery of aceclofenac. Archives of pharmacal research, 2005, 28: 1097-1102.
35. HASHEM, Fahima M., et al. Formulation, characterization, and clinical evaluation of microemulsion containing clotrimazole for topical delivery. Aaps Pharmscitech, 2011, 12: 879-886.