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# Post Formulation Studies of Curcumin Longa Loaded Transethosomes

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## Abstract

This investigation successfully developed and characterised a new transethosomal gel formulation including Curcumin longa extract for improved topical therapeutic use, demonstrating its efficacy as a promising option in controlling effective topical delivery system with potential applications in treating skin-related ailments and infections. The key goals were to optimise the formulation to maximise drug delivery efficiency, stability, and release profile, while also ensuring that the active pharmaceutical ingredient (API) and excipients worked well together. By undertaking extensive pre-formulation and characterisation tests, this study demonstrates the potential of transethosomal technology to overcome bioavailability and stability difficulties often associated with herbal extracts. Curcumin longa L was examined for excipient compatibility, organoleptic characteristics, solubility, melting point, and other key features prior to formulation. FTIR and DSC investigations confirmed that there was no conflict between the API and the excipients, indicating that the formulation is stable and suitable. The solubility investigation indicated that Curcumin longa L was easily soluble in chloroform, acetone and practically insoluble in water which helped to generate the transethosomes. These exploratory investigations provided the basis for developing a stable transethosomal complex that enhances the therapeutic potential of Curcumin longa L extract.The optimisation phase used a $3^3$- response surface methodology to identify the optimal concentrations of phospholipid, ethanol and edge activator for maximal entrapment efficiency and particle size reduction. The optimised transethosomal formulation had an outstanding entrapment effectiveness of 68.70% and a particle size of 270.2nm and PDI 0.352. TEM investigation validated the spherical form of transethosomes, which is required for improved absorption and adhesion to topical tissues. The formulation's zeta potential of -16.6 mV revealed high stability, which is advantageous for the delivery system's long-term integrity.

**Key words: Curcumin longa, Post Formulation, formulation's zeta potential.**

## MATERIALS AND METHODOLOGY

**Table no. 1: List of excipients used in formulation development and study**

| Sr.no | Materials | Source / Provided by / Purchased |
|---|---|---|
| 1 | Curcumin Longa (Gift sample) | Sami sabinsa Ltd Pvt |
| 2 | Ethanol | Changshu Hungering Fine Chemical Co. Ltd, China. |
| 3 | Soya Lecithin Liquid (Gift Sample) | Group pharmaceutical limited, Bangalore |
| 4 | Tween 80 | Thomas Baker (Chemicals)Pvt.Ltd. Mumbai. |
| 5 | Cholesterol | Thomas Baker (Chemicals)Pvt.Ltd. Mumbai. |
| 6 | Carbopol 934 | Loba chemie Pvt Ltd. |
| 7 | Propylene Glycol | Spectrum Reagents& Chemicals Pvt. Ltd. Cochin, India. |
| 8 | Triethanolamine | Merck Pvt.Ltd |
| 9 | Methyl Paraben | Thomas Baker (Chemicals)Pvt.Ltd. |
| 10 | Acetone | Thomas Baker (Chemicals)Pvt.Ltd. Mumbai. |

| | | |
|---|---|---|
| 11 | Chloroform | Thomas Baker (Chemicals)Pvt.Ltd. Mumbai. |
| 12 | Ethyl acetate | Thomas Baker (Chemicals)Pvt.Ltd. Mumbai. |

**MATERIALS:**

**Drug & Excipient Profile:**

***Curcuma longa***

Curcumin, a bright yellow polyphenolic compound, is the primary active ingredient in turmeric (Curcuma longa), a spice widely used In traditional medicine practices, particularly in South Asia. It has garnered attention for its potential therapeutic properties, including anti-inflammatory, antioxidant, and anticancer effects.

**Family:** Zingiberaceae

**Table no:2 overall particle size and PDI**

| Formulation of transethosomes | Particle size | PDI |
|---|---|---|
| F1 | 344.3 | 0.417 |
| F2 | 298.7 | 0.433 |
| F3 | 270.2 | 0.461 |
| F4 | 337.6 | 0.357 |
| F5 | 321.7 | 0437 |
| F6 | 397.9 | 0.277 |
| F7 | 370.7 | 0.232 |
| F8 | 361.6 | 0.348 |
| F9 | **270.2** | **0.352** |
| F10 | 278.3 | 0.300 |
| F11 | 399.7 | 0.202 |
| F12 | 300.9 | 0.434 |
| F13 | 326.9 | 0.236 |
| F14 | 329.1 | 0.223 |
| F15 | 326.8 | 0.253 |

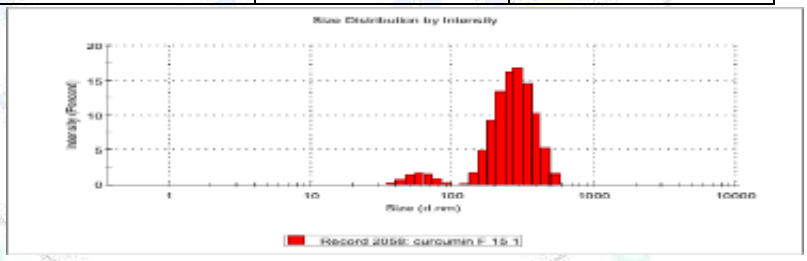


**Figure no. 1: Particle size & PDI Report for Optimized transethosomes**

**1. Entrapment efficacy:**

The Entrapment efficacy obtained for the optimized transethosomes batch is in the percentage of 68.70%

**Table no:3 overall entrapment efficacy**

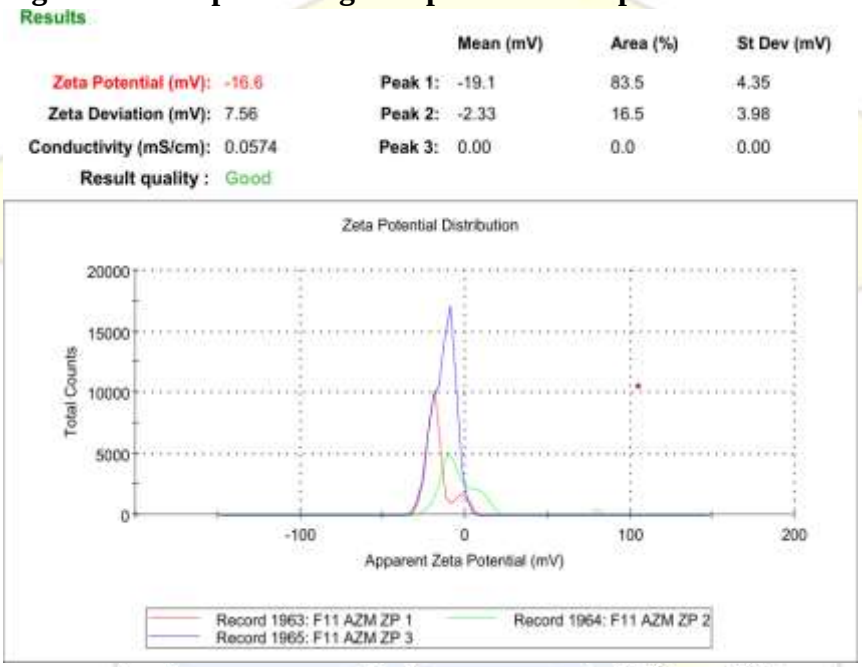
| Formulation of transethosomes | Entrapment efficacy |
|---|---|
| F1 | 61.32 |
| F2 | 55.4 |
| F3 | 65.11 |
| F4 | 66.71 |
| F5 | 63.21 |
| F6 | 76.31 |
| F7 | 79.85 |
| F8 | 69.4 |
| F9 | **68.70** |

| | |
|---|---|
| F10 | 58.3 |
| F11 | 80.11 |
| F12 | 57.7 |
| F13 | 71.88 |
| F14 | 71.07 |
| F15 | 71.77 |

**2. Zeta potential measurement:**

Zeta potential suggests the relative surface charge which provides better stability. High Zeta potential value prevents the vesicle aggregation due to electrostatic repulsion. Transethosomes shows Zeta potential in the range of -18mv to-65.2mv It indicates good stability with less aggregation. The optimal Formulation F9 exhibits a zeta potential of -16.6mv enhancing electrostatic repulsion among vesicles and confirming its potential for topical applications.

**Figure no.2. Representing zeta potential for optimized transethosomes**




**3. Transmission electron microscopy**

Morphological analysis of prepared vesicles was performed with transmission electron microscopy. TEM imaging of prepared vesicular delivery is shown in Fig. It was observed that all the vesicles are almost spherical in shape and they are in nanometer size. with no aggregation and/or fusion among the vesicle. these images also confirms the nanosize and spherical shape of nanovesicular systems.

**Figure no. 3: TEM Photomicrograph of optimized Curcumin Longa loaded Transethosomes**

**4. Drug content**

**Table no. 4: Determination of drug content of Optimized Curcumin longa loaded transethosomes**

| Test Drug Content | Observations | | | Mean (SD) |
|---|---|---|---|---|
| | 1 | 2 | 3 | |
| | 80.5% | 79.9% | 80.2% | 80.2±0.3 |

Drug content in the optimised Curcumin Longa loaded transethosomes was found to be 80.2%.

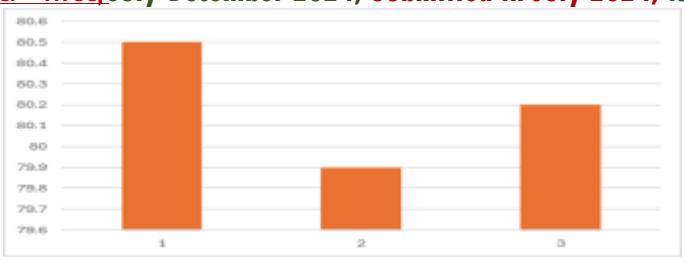



**Figure no. 4: Graph Representing Drug Content of Optimized transethosomes**

**5. In-vitro drug release studies of optimised Curcumin Longa extract loaded transethosomes**

**Table no. 5: Represents In-vitro dissolution studies of optimised Curcumin Longa extract loaded transethosomes**

| Time(min) | Trial 1 | Trial 2 | Trial 3 | % Drug release |
|---|---|---|---|---|
| 0 | 0 | 0 | 0 | 0 |
| 30 | 9.16 | 9.72 | 9.72 | 9.53±0.323 |
| 60 | 19.16 | 19.61 | 19.62 | 19.46±0.262 |
| 90 | 30 | 31 | 31.9 | 30.96±0.950 |
| 120 | 44.5 | 44.59 | 45 | 44.36±0.266 |
| 150 | 59.66 | 60 | 60 | 59.88±0.196 |
| 180 | 76.33 | 77.33 | 77.99 | 77.21±0.835 |

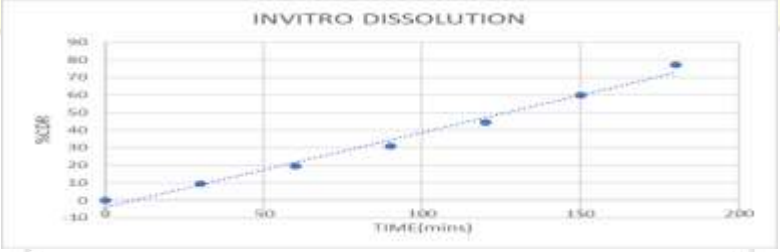



**Figure no. 5: Graph Representing In vitro drug release of Curcumin longa**

**6. Drug Release Kinetics study:**

Results of in-vitro release study are fitted into different release kinetic models: Basically drug follows three drug release behavior, penetration of the dissolution medium into the matrix, dissolution and diffusion of the dissolved drug through the matrix. Higuchi and Korsmeyer Peppas model suggest that drug release follows diffusion of the drug and zero-order kinetics shows that dissolution of the drug is the rate-limiting step, In Peppas prediction, If n=0.5 (Fickian diffusion) and n=0.5-1.0 (Non-Fickian model). For (n >1) it will follows super case II transport mechanism.

Release of Curcumin Longa from transethosomes formulation follows Zero order kinetics as it is showing high R2 value (0.) and when all data are fitted into korsmeyer equation they are showing Non fickian diffusion mechanism as the value of (n=0.5 -1)

**Table no. 6: Drug release kinetics**

| Formulation | Zero order kinetics | First order kinetics | Higuchi model | Korsemeyer peppas model | | Mechanism of drug release |
|---|---|---|---|---|---|---|
| Curcumin Longa loaded Transethosomes | $R^2$ | $R^2$ | $R^2$ | $R^2$ | N | Korsemeyer peppas model, Non fickian |
| | 0.9869 | 0.8214 | 0.9869 | 0.9963 | 0.855 | |

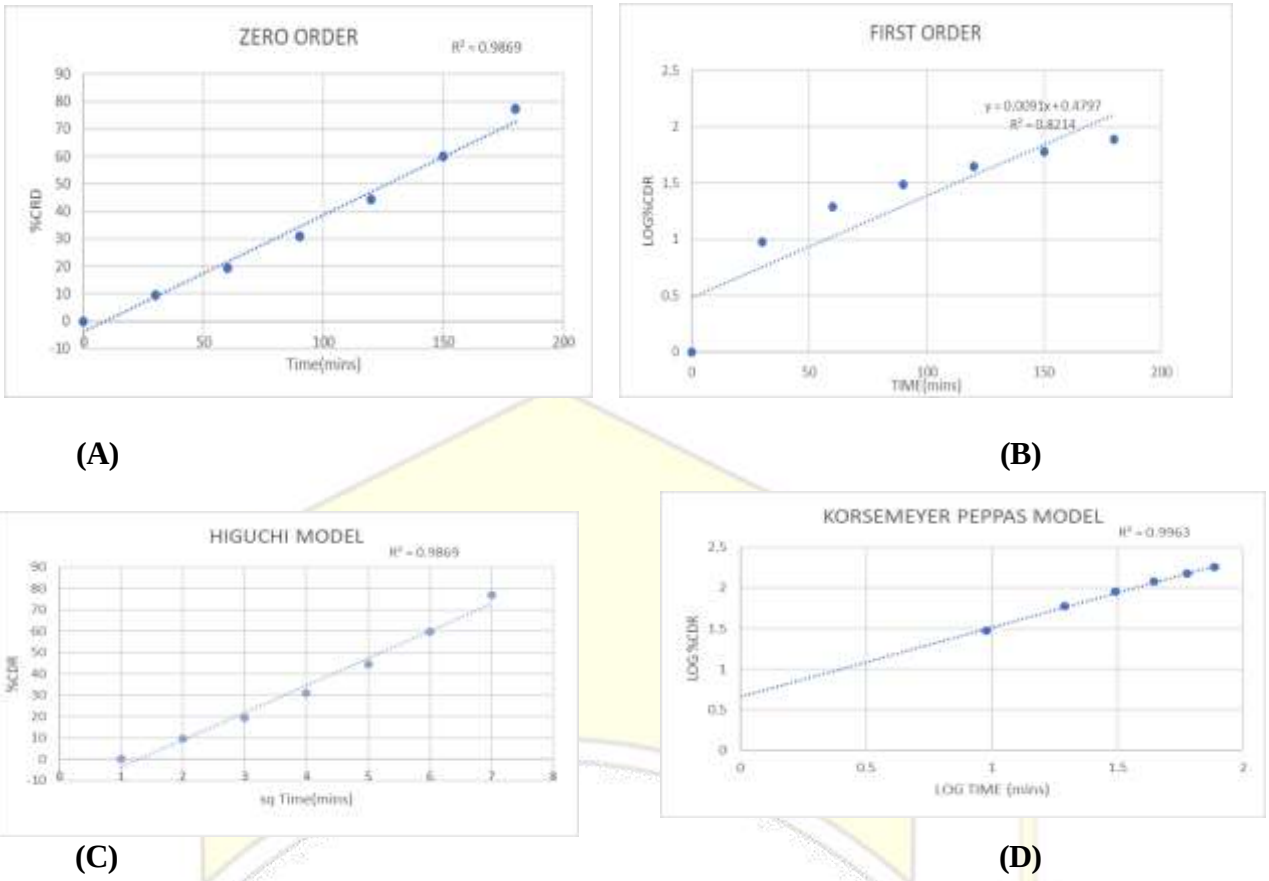



**Figure no. 6: Graph representing the kinetics of drug release plots Fig. A: Zero order, Fig. B: First order,**

**Fig. C: Higuchi plot, Fig. D: Peppas plot**

**Incorporation of optimized formulation in gel:**

Due to rheological properties of suspensions all formulations are converted to gel formulation so that they can retain on skin site for long period of time because of enhanced viscosity and provide better applicability of the formulation to the skin. Carbapol 940 is used as a gelling agent.

**1. Characterization of transethosomal Gel formulations:**

For evaluating the effectiveness of formulation as gel, gels are evaluated for drug content, pH, spreadibility and viscosity of prepared formulation. Because these are very important properties for a gel formulation to be applied topically. Gel formulation must devoid of any type of gritty particle which can cause irritation for this gel must be smooth and all the vesicular gels formulations have a smooth texture, good homogeneity and free from the gritty particle.

**2. pH:**

The pH of the developed gel formulations is very critical aspect for transdermal preparation, because highly acidic/basic nature of transdermal formulations may cause irritation and change the natural environment of the skin. The pH of all the gel formulations was in the range of 5.39 ± 0.02 to 5.51 ± 0.04 which is a suitable pH condition for skin application which proves that these are suitable for topical application on skin.

**3. Viscosity**

The viscosity of developed gel formulations are in the range of 9582 ± 0.21 to 10235± 0.44 cps which indicated that all gels has good consistency.

**4. Spreadibility**

The spreadibility is also a very important parameter for an ideal topical formulation. The spreadibility enhances patient compliance and helps in good spreading of gel formulation to the application site. The spreadibility of all gel formulations was found in the range of 3.21±

0.17 to 4.93 ± 0.11gm.cm/sec indicating easy spread of gel into a larger area. Overall the developed gel formulations showed excellent spreadibility property. Above optimized formulation displayed sufficient viscosity, pH and spreadibility which revealed a good gelling property of gel for topical application which are ideal for the transdermal gel. From below table, it is evident that vesicle gel systems special characteristics are like plain gel in all respect.

**Physical appearance**

**Table no. 7: Physical appearance of Optimized Transethosomal gel formulation**

| **Parameter** | **Optimized Transethosomal gel formulation** |
|---|---|
| Colour | Yellow orange |
| Odor | strong, pungent aroma |

**The prepared formulation gel was assessed for different parameters to check the quality of gel.**

**Table no. 8: Observation of different parameters**

| **Parameter** | **Trial** | **Standard values** | **Observed value** | **Mean (SD)** |
|---|---|---|---|---|
| **pH** | **1** | **5.3-5.6** | **5.39** | **5.39±0.01** |
| | **2** | | **5.41** | |
| | **3** | | **5.39** | |
| **Viscosity** | **1** | **1,000 to 10,000 centipoise (cps)** | **7000** | **7150±129.09** |
| | **2** | | **7200** | |
| | **3** | | **7100** | |
| | **4** | | **7300** | |
| **Spreadibility** | **1** | 3.21to 4.93 **gm·cm/sec** | **4.93** | **4.67± 0.22** |
| | **2** | | **4.6** | |
| | **3** | | **4.5** | |

**Figure no. 7: (1) pH of optimized Transethosomal gel (2a) and (2b) Spreadibility of Transethosomal gel Graphical representation of transethosomal gel assessed with**

**different parameters**

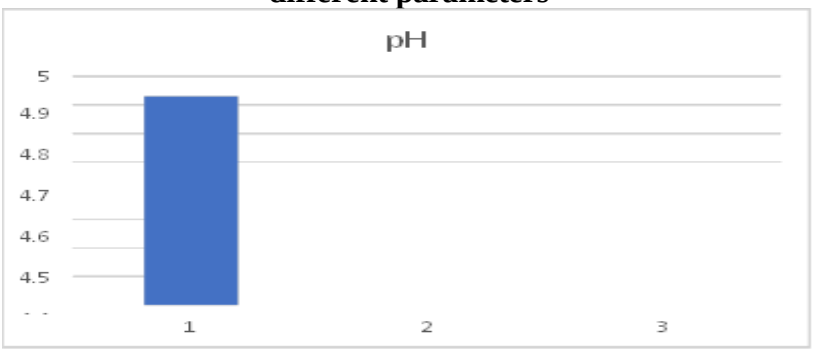



**Figure no. 8: pH graphs of transethosomal gel**

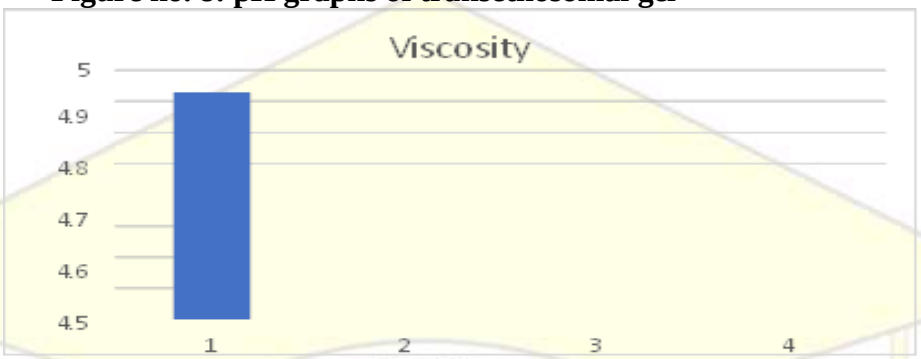



**Figure no. 9: Viscosity graph of transethosomal gel**

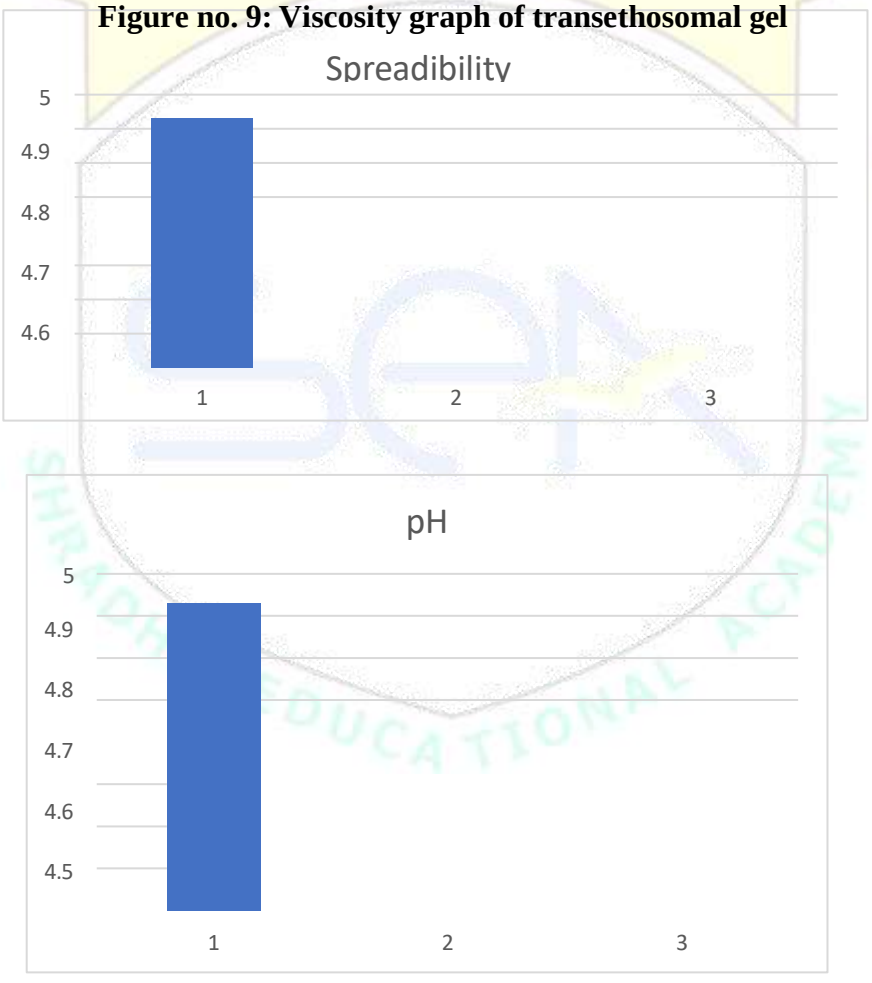



**Figure no. 10: Spreadibility graph of transethosomal gel**

**Drug Content**

Optimized transethosomal formulations has been evaluated for drug content ansd it was found in the range of 80% to 90%. The average drug content of the optimized transethosomal gel

formulation was found to be 85.53%.

**Table no. 9: Observation for Drug Content studies of gel formulation**

| Test | Drug Content | Observations | | | Mean (SD) |
|---|---|---|---|---|---|
| | | 1 | 2 | 3 | |
| | 85.53% | 84.5% | 85.9% | 86.2% | 85.53±0.907 |

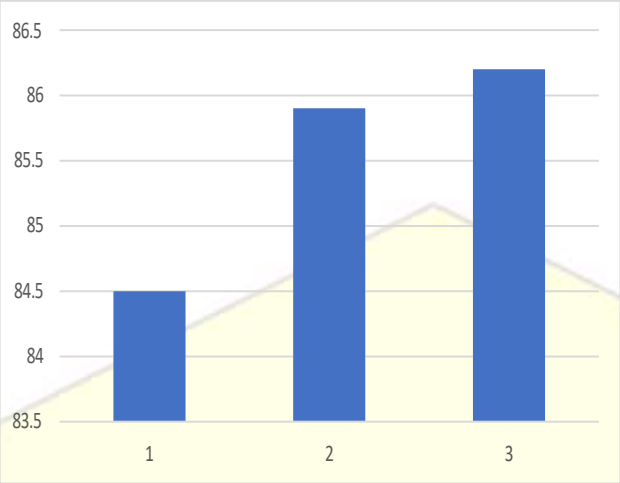



**Figure no. 11: Graph Representing Drug Content of Optimized Transethosomal gel formulation**

**DSC Studies:**

The DSC curve of pure drug Curcumin longa L and optimized formulation of transethosomal gel were recorded.

Curcumin longa showed a Characteristic sharp Endothermic peak at 177.68°C, indicating the melting point of the drug. The obtained DSC curve for optimized transethosomal gel formulation shows the endothermic peak at 109.38°C.

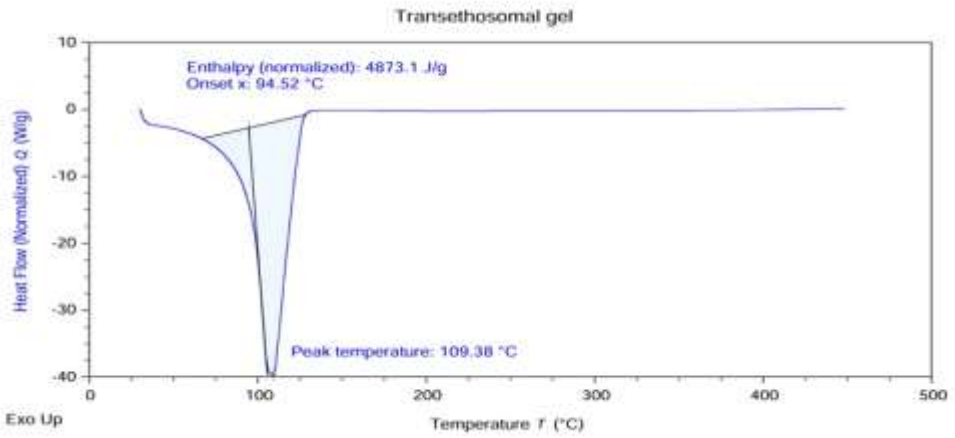



**Figure no. 12: DSC thermogram of transethosomal gel formulation**

**FTIR Studies:**

The FTIR spectra of the pure drug and the optimized formulation of transethosomal gel formulations were recorded in between 400-4000 wave numbers (cm-1).

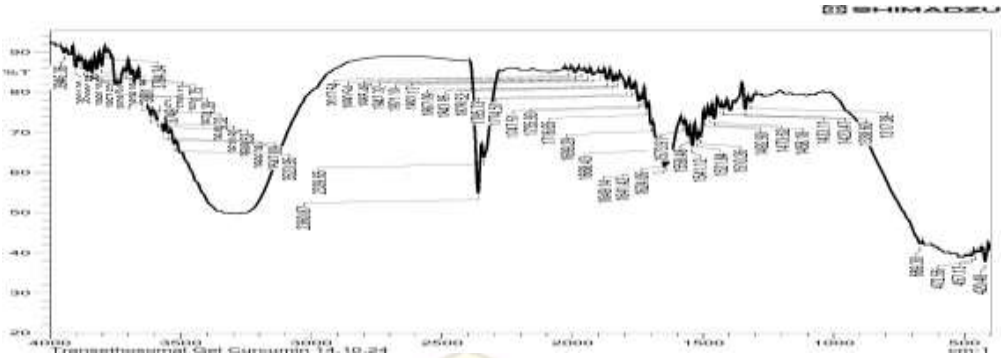


**Figure no. 13: FTIR Spectrum of transethosomal gel formulation**

**Table no. 10: Observations for Drug & Excipient mixture& formulation compatibility study**

| FUNCTIONAL GROUP | wavenumber or frequency range ($cm^{-1}$) | OBSERVED PEAKS | |
|---|---|---|---|
| | | Observed wavenumber of Curcumin longa L extract with mixture ($cm^{-1}$) | Formulation |
| O-H Stretching | 3400-2400 | 2923 | 2990.7 |
| C=C Stretching | 1600-1450 | 1462 | 1473.62 |
| C-O Stretching | 1350-1000 | 1088 | 1317.38 |
| C-O-C Stretching | 1250-1050 | 1048 | 3122.92 |
| Aromatic ring | 1650-1500 | 1628 | 1624.06 |

**Antimicrobial activity**

**Table no. 11: Inhibitory activity of test compounds against test organisms**

| Test Organisms | Test Compounds | Conc. per well | Zone of inhibition (cm) |
|---|---|---|---|
| Staphylococcus aureus | (A) Control | 30µl | Nil |
| | (B) Standard disc | 15mcg | 0.5 |
| | (C)Sample | 30µl | 2.4 |

**Figure no. 14: Inhibitory activity of test sample against Staphylococcus aureus**

5. **In-Vitro characterization of prepared novel vesicular carrier system Table no. 12: In-vitro diffusion studies on Transethosomal gel**

| Time | Trial 1 | Trial 2 | Trial 3 | %Drug release |
|---|---|---|---|---|
| 0 | 0 | 0 | 0 | 0 |
| 30 | 8.33 | 8.12 | 8.33 | 8.26±0.121 |
| 60 | 17.15 | 17.1 | 17.15 | 17.13±0.028 |
| 90 | 28.24 | 28.12 | 28.24 | 28.2±0.069 |
| 120 | 42.94 | 41.32 | 42.94 | 42.73±0.093 |
| 150 | 57.96 | 57.61 | 57.96 | 57.84±0.202 |

| | | | | |
|---|---|---|---|---|
| 180 | 74.63 | 73.99 | 74.63 | 74.41±0.369 |

In vitro diffusion profile of Curcumin longa L extract from transethosmal gel was conducted in diffusion medium (6.8 pH buffer) The formulation has shown 8.26% - 74.41% drug release from 30 minutes to 180 minutes time period of 30 minutes interval.

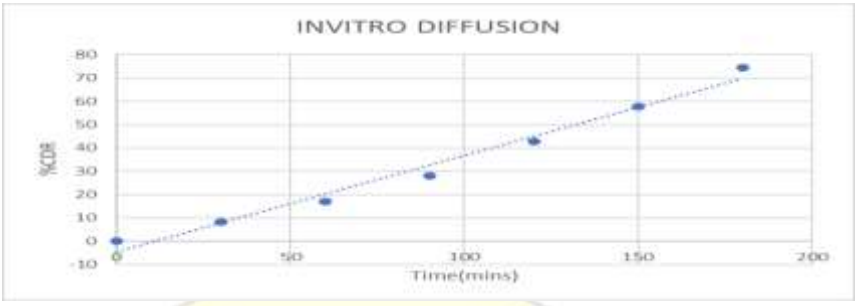


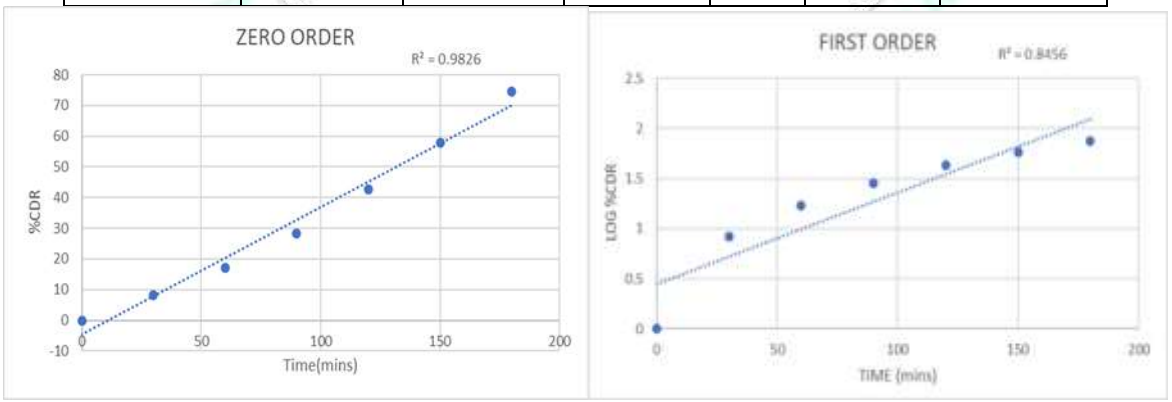

**Figure no.15: Graph representing the In vitro diffusion drug release of transethosomal gel**

**Drug Release Kinetics of diffusion studies on transethosomal gel:**

Results of in-vitro release study are fitted into different release kinetic models: basically drug follows three drug release behavior, penetration of the dissolution medium into the matrix, dissolution and diffusion of the dissolved drug through the matrix. Higuchi and Korsmeyer Peppas model suggest that drug release follows diffusion of the drug and zero-order kinetics shows that dissolution of the drug is the rate-limiting step, In Peppas prediction , If n=0.5 (Fickian diffusion) and n=0.5-1.0 (Non-Fickian model). For (n >1) it will follows super case II transport mechanism. Release of Curcumin Longa L from transethosomes formulation follows Zero order kinetics as it is showing high R2 value (0.9826) and when all data are fitted into korsmeyer equation they are showing Non fickian diffusion mechanism as the value of (n=0.5 -1)

**Table no. 13: Drug release kinetics**

| Formulation | Zero order kinetics | First order kinetics | Higuchi model | Korsemeyer peppas model | | Mechanism of drug |
|---|---|---|---|---|---|---|
| Curcumin Longa L loaded Transethosomal gel | $R^2$ | $R^2$ | $R^2$ | $R^2$ | N | Zero Order model, Non fickian |
| | 0.9826 | 0.8456 | 0.8334 | 0.9653 | 0.414 | |




A B

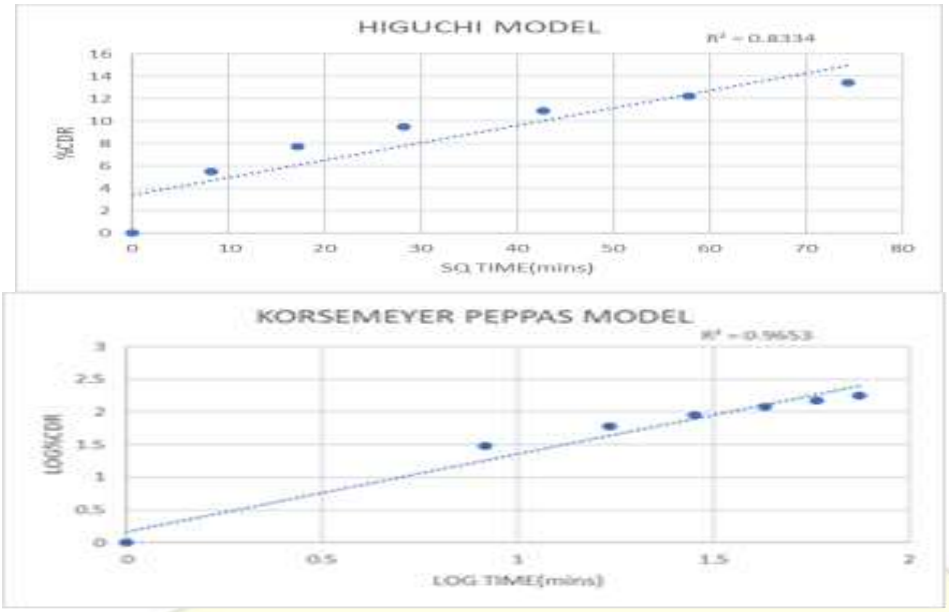



**Figure no. 16: Graph Representing the kinetics of drug release plots Fig. A: Zero order, Fig. B: First order**
**Fig. C: Higuchi plot Fig. D: Peppas plot,**

**Post formulation of transethosomes:**

**Particle size and PDI**

Determination of mean average particle size of transethosomes and PDI was performed by using Horiba instrument. The particle size optimized batch transethosomes was found to be 270.2 nm and PDI was found to be 0.352 are shown table no:20

**Entrapment efficacy:**

The Entrapment efficacy obtained for the optimized transethosomes batch is in the percentage of 68.70% are shown table no:21

**Zeta potential**

The zeta potential is an important measure of colloidal system stability because it reflects the particles relative surface charge. In this work, zeta potential values for Curcumin longa L extract loaded transethosomes ranged potential around -10 mV to -40 mV. Specifically, the optimised formulation has a zeta potential of -16.6 mV, indicating a significant negative surface charge. This high zeta potential implies good stability, since larger absolute values are linked with less aggregation and better dispersion of transethosomes in the medium. A zeta potential of -16.6 mV as shown in fig. no. 28, indicates that the transethosomes repulsive forces are strong enough to avoid flocculation, ensuring the formulation's integrity throughout time. In clinical applications, such stability is necessary to provide constant therapeutic effectiveness and bioavailability.

**Transmission electron microscopy**

Morphological analysis of the prepared vesicles was conducted using Transmission Electron Microscopy (TEM), a powerful tool for visualizing nanostructures at high resolution. The TEM images of the formulated vesicular delivery systems are presented in Figure no 29. Upon examination, it was observed that all vesicles exhibited a predominantly spherical morphology, consistent with the desired characteristics of nanovesicular systems designed for drug delivery in topical applications. The size of the vesicles was confirmed to be within the nanometer range, which is critical for enhancing therapeutic efficacy and bioavailability, particularly in targeting topical layers.

**Drug content**

Drug content of Curcumin longa L extract sample was done thrice, and it was found to be 80.2%which was near to standard reference of prior research article. This high percentage shows that the active component was successfully incorporated into the transethosomes, which is required to sustain the formulation's therapeutic effectiveness.

**In- Vitro dissolution studies of Curcumin longa L extract loaded transethosomes**:

The results of dissolution study depend on concentration of phospholipid. The formulated Curcumin longa L extract loaded transethosomes are subjected to In vitro dissolution test for evaluating drug release from the formulation. The In vitro dissolution test was carried out in 900 ml of phosphate buffer pH 7.4 in USP-II paddle type apparatus at 50 rpm and 37±0.5 C. The results of dissolution study depend on concentration of phospholipids. Formulations containing Excipients (Active pharmaceutical ingredient, Soya lecithin, ethanol, tween 80 and distilled water). Optimized Curcumin longa L extract loaded transethosomes shows drug release 77.21±0.835 in 3 hours Shown in Table no. 23

**Kinetics modelling of drug dissolution profiles:** To study the In-vitro drug release kinetics, data obtained from in-vitro dissolution studies of prepared optimized Curcumin longa L extract loaded transethosomes are plotted in various kinetic models such as Zero order, First order, Higuchi model and Korsmeyer peppas model. The release of Curcumin longa L extract from the transethosomal formulation demonstrated a Korsmeyer Peppas model kinetic profile, indicated by a high coefficient of determination ($R^2$ = 0.9963). it suggests that the drug release rate is independent of its concentration of the drug remaining in the formulation. Additionally, when the release data were analyzed using the Korsmeyer equation, the results indicated a non Fickian diffusion mechanism shown in Table no. 24, characterized by an exponent value (n) ranging from

0.5 to 1. This finding implies that the release process is governed by a combination of diffusion and erosion mechanisms, which can enhance the therapeutic efficacy of the formulation by providing a sustained release of the active compound.

**Incorporation of optimized Curcumin longa L extract transethosomes in gel formulation**

Due to their desirable rheological attributes, all formulations have been transformed into gel formulations to improve their retention at the topical site for a prolonged period of time. Carbopol 934P employed gelling agent enhanced viscosity, which improves the formulation's application for topical diseases. This enhanced viscosity not only improves adherence to the topical site, but also assures long-term release of the active components. As a consequence, this technique is probable to improve therapeutic outcomes in treating ailments such as topical disease by allowing greater duration of contact with skin regions, enhancing the efficacy of Curcumin longa L extract and its beneficial qualities. This version emphasises on the effectiveness of Carbopol 934P in increasing viscosity and its implications for therapeutic effectiveness in topical applications.

**Evaluation of transethosomal Gel formulations:**

**Physical appearance**

Colour of optimized transethosomal gel observed that appears as orange yellow, odor was strong and pungent aroma.

**The prepared gel formulation was evaluated for various parameters to ensure its quality and effectiveness.**

pH, Spreadibility and viscosity of optimized Curcumin longa L extract loaded transethosomal gel was found to be 5.39±0.01(pH), 7150±129.09(viscosity) and 4.67±0.22 (Spreadibility) mentioned in Table no.26 which was near to standard reference of research article range.

**FTIR**

When analyzing the FTIR spectrum of Curcumin longa L extract and Curcumin longa L with excipients (Figure 14,15), it is clear that the peaks at 2923cm-1 due to the O-H Streching, 1462 cm-1 due to C=C Streching, 1088 cm-1 due to C-O group, 1048cm-1 characteristic to C-O-C Stretching, 3007 cm-1 due to C-H group and 1628 cm-1 characteristic to Aromatic Stretching. The optimized transethosomal gel formulation FTIR spectra (Figure no. 39) reveled a peak at 3523 (O- H stretch in Curcumin longa L extract), 1445 (C=C stretch), 1317(C-O Stretch), 1317(C-O-C), 1624 (Aromatic Stretch).

The FTIR spectra of optimized transethosomal gel showed changes in specific regions like O-H stretching frequency of Curcumin longa L extract with excipients at 2923 cm−1

changed to 3523 cm−1 in the optimized transethosomal gel, indicating the presence of stronger intermolecular interaction during the formulation of transethosomal gel and other peaks are showing good stability.

**DSC**

To investigate the possible physical interaction between drug and excipients, DSC studies were carried out. Pure drug showed sharp endothermic peak at 177.68 $^{o}$C, indicating the melting point of the drug. The sharp endothermic peak of sample Curcumin longa L extract was nearly to the standard peak of Curcumin longa Laccording to the USP monographs. The optimised transethosomal gel formulation is taken and the thermal behaviour of sample is determined using differential scanning calorimeter, endothermic peak obtained is at 109.38$^{o}$C. No significant change in the endotherm of the drug was observed in optimised transethosomal gel. From this it was inferred that there was no interaction between the drug and excipients, shown in fig no. (11 and 38).

**Antimicrobial activity**

The antimicrobial activity of the test drug against Staphylococcus aureus has been assessed using the well diffusion technique, with the results described in Table 29 and illustrated in Figure no. 38. The observed zone of inhibition demonstrates that the sample has significant inhibitory effect against pathogenic bacterium. This information suggests the formulation has potential therapeutic uses for reducing Staphylococcus aureus infections, demonstrating its antibacterial potency. The size of the inhibition zone is a qualitative metric of antimicrobial efficacy, illustrating the compound's relevance in the development of effective medical treatments for bacterial infections.

**In-vitro diffusion studies on optimized Curcumin longa L extract loaded in transethosomal gel**

The results of dissolution study depend on concentration of excipients. The formulated Curcumin longa L extract loaded transethosomal gel are subjected to In vitro diffusion test for evaluating drug release from the formulation. The In vitro diffusion test was carried by using egg membrane in franz diffusion cell as a dissolution media, phosphate buffer with a pH of 7.4 was poured into the device and kept at 37°C ± 0.5°C. The results of diffusion study depend on concentration of excipients . Formulations containing Excipients (Active pharmaceutical ingredient, Soya lecithin, ethanol and Tween 80). Optimized Curcumin longa L loaded transethosomal gel shows drug release 74.41±0.36 in 3 hours Shown in Table no. 30

**Kinetics modelling of drug diffusion profiles**:

To study the In-vitro diffusion drug release kinetics, data obtained from in-vitro diffusion studies of prepared optimized Curcumin longa L extract loaded transethosomal gel are plotted in various kinetic models such as Zero order, First order, Higuchi model and Korsmeyer peppas model. The release of Curcumin longa L extract from the transethosomal gel formulation demonstrated a zero order kinetic profile, indicated by a high coefficient of determination ($R^2$ = 0.9826). This suggests that the drug is released at a constant rate over time, independent of its concentration. Additionally, when the release data were analyzed using the Korsmeyer equation, the results indicated a non Fickian diffusion mechanism shown in Table no.31, characterized by an exponent value (n) ranging from 0.5 to 1. This finding implies that the release process is governed by a combination of diffusion and erosion mechanisms, which can enhance the therapeutic efficacy of the formulation by providing a sustained release of the active compound.

**CONCLUSION**

This investigation successfully developed and characterised a new transethosomal gel formulation including Curcumin longa extract for improved topical therapeutic use, demonstrating its efficacy as a promising option in controlling effective topical delivery system with potential applications in treating skin-related ailments and infections. The key goals were to optimise the formulation to maximise drug delivery efficiency, stability, and release profile, while also ensuring that the active pharmaceutical ingredient (API) and excipients worked well

together. By undertaking extensive pre-formulation and characterisation tests, this study demonstrates the potential of transethosomal technology to overcome bioavailability and stability difficulties often associated with herbal extracts.

Curcumin longa L was examined for excipient compatibility, organoleptic characteristics, solubility, melting point, and other key features prior to formulation. FTIR and DSC investigations confirmed that there was no conflict between the API and the excipients, indicating that the formulation is stable and suitable. The solubility investigation indicated that Curcumin longa L was easily soluble in chloroform, acetone and practically insoluble in water which helped to generate the transethosomes. These exploratory investigations provided the basis for developing a stable transethosomal complex that enhances the therapeutic potential of Curcumin longa L extract.

The optimisation phase used a $3^3$- response surface methodology to identify the optimal concentrations of phospholipid, ethanol and edge activator for maximal entrapment efficiency and particle size reduction. The optimised transethosomal formulation had an outstanding entrapment effectiveness of 68.70% and a particle size of 270.2nm and PDI 0.352. TEM investigation validated the spherical form of transethosomes, which is required for improved absorption and adhesion to topical tissues. The formulation's zeta potential of -16.6 mV revealed high stability, which is advantageous for the delivery system's long-term integrity.

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