PREPARATION AND EVALUATION OF MICROEMULSION-BASED TRANSDERMAL DELIVERY OF *Clitoria ternatea*

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ABSTRACT-

The present study aimed to develop and evaluate a microemulsion-based transdermal delivery system for the extract of *Clitoria ternatea*, a plant widely recognized for its pharmacological properties. The extractive yield from ethanol, methanol, and water revealed the highest yield with ethanol at 11.10%. The phytochemical screening showed the presence of several valuable compounds such as alkaloids, carbohydrates, saponins, steroids, phenolics, and flavonoids.

Three distinct microemulsion formulations (F1, F2, F3) were prepared, exhibiting pH values within the suitable range for skin application (F1: 6.1±0.2, F2: 5.9±0.2, F3: 6.2±0.1). The viscosity measurements showed F2 as the most viscous formulation (415.7±4.0 cP), which could be suggestive of a controlled drug release profile. Particle size analysis demonstrated the smallest average particle size for F1 (91.3±1.0 nm), potentially indicating better skin permeability. High drug content was observed in all formulations, with values of 91.3±0.6% for F1, 90.3±1.5% for F2, and 91.0±1.0% for F3, indicating their robust capacity as carriers for Clitoria Ternatea extract.

Our results suggest that microemulsion-based transdermal delivery systems could be a promising approach for the application of *Clitoria ternatea* extract, highlighting their potential as efficient drug delivery systems. However, *in-vivo* studies and stability testing are required to validate these findings further.

KEYWORDS: *Clitoria ternatea*, Microemulsion, Transdermal delivery, Phytochemical screening, Viscosity, Particle size, Drug content, Conductivity.

INTRODUCTION

Transdermal drug delivery systems (TDDS) have garnered significant attention in pharmaceutical research due to their potential for providing controlled release of drugs into the systemic circulation. By bypassing the hepatic first-pass metabolism and reducing gastrointestinal side effects, TDDS offer a promising alternative for oral and invasive methods of drug administration [1].

However, designing an efficient TDDS remains a challenge due to the impermeable nature of the stratum corneum, the outermost layer of the skin. Microemulsions have been proposed as a possible solution to this challenge [2]. Microemulsions are clear, thermodynamically stable, isotropic mixtures of oil, water, and surfactant, often in combination with a cosurfactant. Due to their nanometric droplet size, microemulsions can enhance the solubility, stability, and bioavailability of drugs, thus facilitating improved drug penetration through the skin [3].

In this research, we focused on *Clitoria ternatea*, a plant known for its medicinal properties. *Clitoria ternatea*, commonly referred to as the Butterfly pea, has been used in traditional medicine for centuries. The plant is rich in various phytochemicals, including flavonoids, anthocyanins, and tannins, which contribute to its antioxidant, anti-inflammatory, anti-diabetic, and neuroprotective effects. Despite these known benefits, the therapeutic potential of *Clitoria ternatea* has not been fully realized, primarily due to challenges in drug delivery [4].

The aim of this study was to prepare and evaluate a microemulsion-based transdermal delivery system for *Clitoria ternatea*. We explored different formulations and investigated their pH, viscosity, particle size, drug content, and conductivity. This study represents an important step towards exploiting the full medicinal potential of *Clitoria ternatea* and creating an effective, non-invasive drug delivery system [5].

A variety of medicinal plants have served as vital sources of therapeutic agents for centuries. Among these, *Clitoria ternatea* is especially noted for its wide range of bioactive compounds, which have demonstrated remarkable pharmacological effects. However, despite its promising medicinal value, the systemic utilization of *Clitoria ternatea* has been constrained due to the lack of effective and efficient drug delivery systems. An advanced system that can overcome the barriers of conventional drug administration methods is, therefore, highly desired [6].

Transdermal drug delivery systems have emerged as an attractive approach to overcome these challenges. By providing controlled drug release, bypassing gastrointestinal side effects, and avoiding first-pass metabolism, these systems offer a promising alternative to oral and injectable routes of administration. Among the various strategies employed to facilitate transdermal drug delivery, microemulsion systems have shown considerable promise [7].

Microemulsion systems are a class of colloidal drug delivery systems which have been found to improve the solubility, permeability, and bioavailability of drugs, allowing them to bypass the skin's stratum corneum layer more effectively. This is particularly significant as the stratum corneum, the outermost layer of the skin, presents a primary barrier to transdermal drug delivery due to its hydrophobic nature [8].

In this research, we aim to develop an innovative microemulsion-based transdermal drug delivery system for *Clitoria ternatea*. This approach seeks to harness the synergistic benefits of microemulsion systems and the therapeutic potential of *Clitoria ternatea* [9].

We believe this investigation will significantly contribute to the exploration of *Clitoria ternatea's* therapeutic potential and the advancement of transdermal drug delivery systems. We anticipate that our research will not only further our understanding of *Clitoria ternatea's* pharmacological properties and their interactions with microemulsion systems but also pave the way for innovative drug delivery strategies that could greatly benefit patients worldwide [10].

Methodology

Preparation of *Clitoria ternatea* Extract [11]

The extraction of *Clitoria ternatea* was performed using three different solvents: water, ethanol, and methanol. The plant material was subjected to sequential extraction using these solvents in increasing order of polarity. The resulting extracts were then concentrated under reduced pressure and evaluated for their yield percentage.

Formulation of Microemulsion [12]

For the microemulsion preparation, we created three different formulations (F1, F2, and F3) using *Clitoria ternatea* extract, surfactants (Tween 20 and Span 20), Linseed oil, and water.

The proportions of the ingredients for each formulation are as follows:

- F1: Extract 500mg, Tween 20 0.25%, Span 20 1%, Linseed oil 5%, and water q.s.
- F2: Extract 500mg, Tween 20 0.5%, Span 20 0.75%, Linseed oil 5%, and water q.s.
- F3: Extract 500mg, Tween 20 0.75%, Span 20 0.50%, Linseed oil 5%, and water q.s.

The process involved dissolving the surfactant and oil phase at room temperature and then slowly adding the aqueous phase under constant stirring until a clear or bluish microemulsion was formed.

Evaluation of Extract [13]

The extractive values were determined using standard procedures. This included determining the water-soluble extractive value, the alcohol-soluble extractive value, and the ash value. Furthermore, we measured acid insoluble ash, water-soluble ash, and loss on drying.

A phytochemical analysis was carried out on the extracts to detect the presence of various constituents, such as alkaloids, carbohydrates, saponins, glycosides, steroids, phenolics, and flavonoids.

Evaluation of Microemulsion

pH Determination [14]

The pH of each microemulsion formulation (F1, F2, F3) was determined using a calibrated pH meter. Prior to measurement, the pH meter was calibrated using standard buffer solutions of pH 4.0, 7.0, and 9.2. Each formulation was then placed in a beaker, and the electrode of the pH meter was immersed in the solution. The pH was measured in triplicate, and the average was reported.

Viscosity Measurement [15]

The viscosity of each microemulsion formulation was measured using a Brookfield viscometer at a controlled temperature of 25°C. Each formulation was placed in the viscometer sample chamber, and the spindle was lowered into the sample. The viscometer was then switched on and allowed to stabilize before readings were taken. Viscosity was measured in centipoise (cP). The process was repeated three times for each formulation, and the mean and standard deviation were calculated.

Particle Size Analysis [16]

The average particle size of each microemulsion was determined using a particle size analyzer. A small quantity of the microemulsion was diluted with a suitable solvent and then subjected to particle size analysis. The process was repeated three times for each formulation, and the mean particle size and standard deviation were calculated.

Drug Content Determination [17]

The drug content in each formulation was analyzed using a suitable analytical method. A known amount of the microemulsion was diluted with a suitable solvent and the solution was then analyzed to determine the amount of *Clitoria ternatea* extract present. This process was repeated three times for each formulation, and the mean drug content and standard deviation were calculated.

Conductivity Measurement [18]

The conductivity of each microemulsion formulation was measured using a conductivity meter. Prior to measurement, the conductivity meter was calibrated using a standard potassium chloride solution. Each microemulsion was then placed in a beaker, and the electrode of the conductivity meter was immersed in the formulation. The conductivity was measured in triplicate, and the average was reported.

Through these evaluations, we aimed to ensure that the formulations were within acceptable ranges for transdermal application, and that they retained the necessary properties to function as effective drug delivery systems.

RESULTS

Percentage Yield of *Clitoria ternatea* Extract

The extraction process yielded 11.10% for ethanol, 9.02% for methanol, and 10.05% for water. This indicates that ethanol was the most efficient solvent for extracting the plant materials, followed by water, and then methanol.

Extractive Values

We found that the water-soluble extractive value was 1.90%, and the alcohol-soluble extractive was slightly higher at 2.01%. These figures represent the total amount of water-soluble and alcohol-soluble matter present in the plant extract. The ash value was 1%, representing the total inorganic matter present in the extract. The acid-insoluble ash was 2%, and the water-soluble ash was also 2%. These values provide an indication of the cleanliness of the extract and the presence of foreign matter. The loss on drying was 2.3%, indicating the amount of moisture content in the extract.

Phytochemical Analysis

Our analysis revealed the presence of alkaloids, carbohydrates, saponins, steroids, phenolics, and flavonoids in all three extracts (methanol, ethanol, and water). However, the water extract showed a higher presence (+++) of alkaloids, suggesting it may have higher therapeutic potential. None of the extracts tested positive for glycosides.

pH Determination

The pH values for F1, F2, and F3 were 6.1±0.2, 5.9±0.2, and 6.2±0.1, respectively. These values fall within the acceptable range for skin application (4.5 to 7.0), indicating that the formulations are safe for transdermal application.

Table-1: pH determination

Sn.	Microemulsion	pH (Mean±SD)
1	F1	6.1±0.2
2	F2	5.9±0.2
3	F3	6.2±0.1

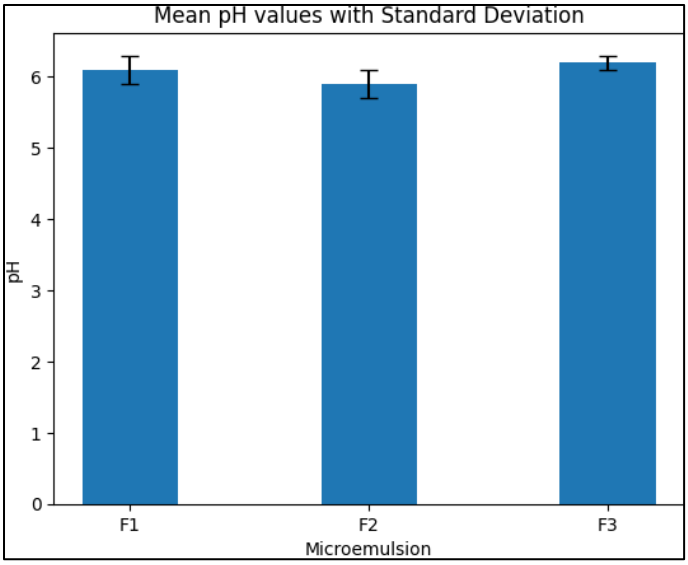

Fig.-1: pH of the Formulations

Viscosity Measurement

The viscosities of the F1, F2, and F3 formulations were 387.7±2.3cP, 415.7±4.0cP, and 399.3±10.5cP, respectively. These results suggest that F2 has the highest viscosity, followed by F3 and F1. Higher viscosity may lead to slower drug release, implying that F2 might offer prolonged release of *Clitoria ternatea* extract.

Table-2: Viscosity (Mean and SD)

Sn.	Microemulsion	Viscosity (Mean±SD)
1	F1	387.7±2.3
2	F2	415.7±4.0
3	F3	399.3±10.5

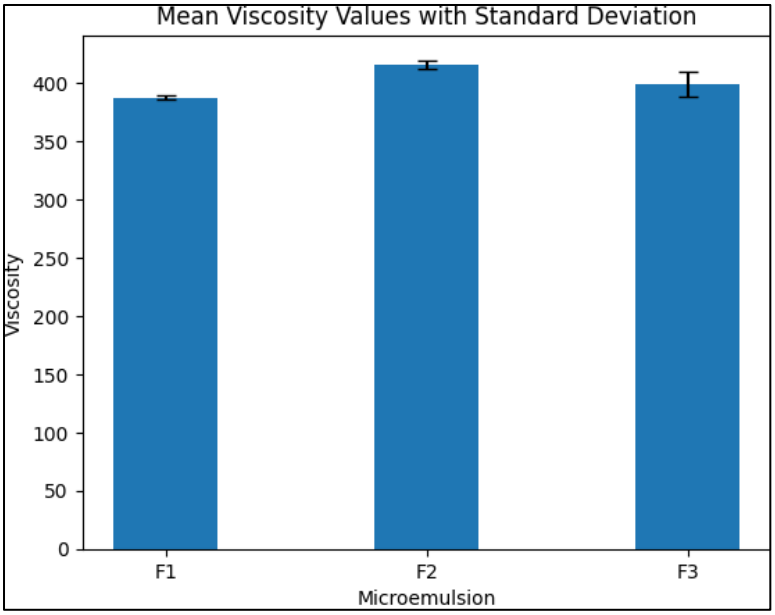

Fig.-2: Viscosity of the Formulations

Particle Size Analysis

The average particle sizes for F1, F2, and F3 were 91.3±1.0nm, 95.7±4.9nm, and 100.0±1.0nm, respectively. The smaller the particle size, the greater the surface area available for absorption, implying that F1 might be absorbed more readily through the skin.

Drug Content Determination

The drug contents in F1, F2, and F3 were 91.3±0.6%, 90.3±1.5%, and 91.0±1.0% respectively. These high drug content values suggest that the microemulsion formulations have a high capacity for carrying the *Clitoria ternatea* extract.

Conductivity Measurement

The conductivity of F1, F2, and F3 was 0.244±0.005 mS/cm, 0.212±0.003 mS/cm, and 0.208±0.003 mS/cm, respectively. These values indicate the presence of ions in the microemulsion, which could enhance the permeation of the drug through the skin.

In summary, all the prepared microemulsion formulations met the acceptable standards and showed potential as transdermal delivery systems for *Clitoria ternatea* extract. However, further in vivo and stability studies are required to confirm their effectiveness and safety.

Sn.	Microemulsion	Particle Size (Mean±SD)	Conductivity (Mean±SD)	Drug Content (Mean±SD)
1	F1	91.3±1.0	0.244±0.005	91.3±0.6
2	F2	95.7±4.9	0.212±0.003	90.3±1.5
3	F3	100.0±1.0	0.208±0.003	91.0±1.0

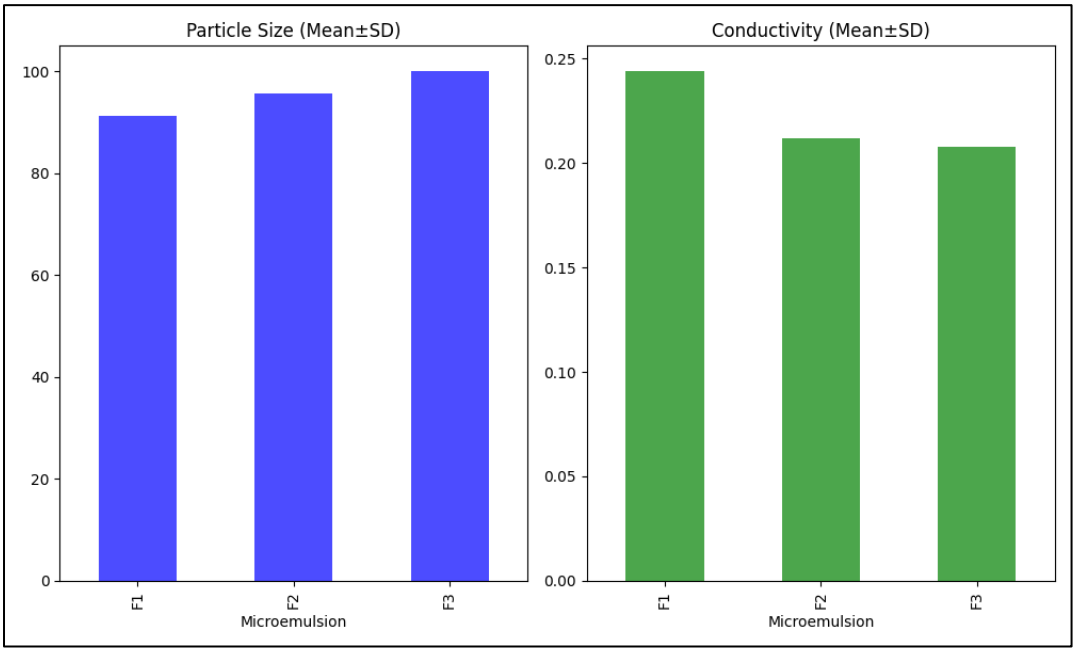

Fig.-3: Particle size and Conductivity of the Formulations

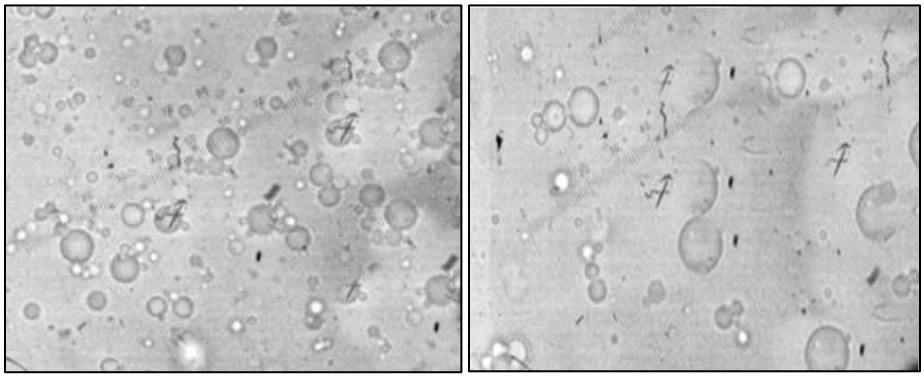

Fig.-4: Particle Size of Formulations

Conclusion

In this study, we successfully developed and characterized microemulsion-based transdermal

delivery systems for *Clitoria ternatea* extract. The exploration of *Clitoria ternatea* for medicinal use has been of significant interest due to its known biological and pharmacological activities. Given the limitations associated with conventional drug delivery systems, the use of transdermal microemulsion systems could potentially offer a more efficient and patient-friendly approach.

The extractive yield from *Clitoria ternatea* demonstrated that ethanol was the most effective solvent, followed by water and methanol. These extracts were rich in phytochemicals, including alkaloids, carbohydrates, saponins, steroids, phenolics, and flavonoids, which are potentially valuable compounds with therapeutic properties.

Three microemulsion formulations (F1, F2, F3) were formulated with varying ratios of surfactants (Tween 20 and Span 20) and oil (Linseed Oil), with each formulation demonstrating distinct physicochemical properties. Importantly, all formulations exhibited pH values within the acceptable range for skin application, ensuring their compatibility with the skin's natural pH and minimizing the risk of skin irritation.

The viscosity of the microemulsions was also examined, with formulation F2 exhibiting the highest viscosity, which could potentially lead to a more controlled and sustained release of the active compound. The particle size analysis revealed that formulation F1 had the smallest particle size, suggesting it might have better skin permeability. High drug content was observed in all formulations, underscoring their potential for effective transdermal drug delivery.

Conductivity measurements indicated the presence of ions in the microemulsions, which may enhance the permeability of the drug across the skin. Although the significance of this property for transdermal drug delivery needs further investigation, these preliminary results are promising.

In conclusion, our findings suggest that microemulsion-based transdermal delivery could be a viable strategy for the application of *Clitoria ternatea* extract. The developed microemulsions demonstrated suitable physicochemical properties and high drug content, rendering them potential candidates for further development into therapeutic products. However, further research, including in vivo studies and stability testing, is crucial to validate these initial findings and move towards the potential commercial development of these formulations.

The scope of this research opens up an intriguing field of study into the use of microemulsions as transdermal drug delivery systems for herbal extracts, potentially leading to more effective, patient-friendly therapeutic options. The path from laboratory to clinical application is long and complex, but the results of this study suggest it could be a journey worth taking.

Discussion

Our study involved the formulation and evaluation of microemulsion-based transdermal delivery systems for the extract of *Clitoria ternatea*, a plant known for its broad therapeutic potential. This innovative approach was designed to overcome some limitations of conventional drug delivery methods and to enhance the bioavailability and efficacy of the active compounds in *Clitoria ternatea*.

In the initial phase, we extracted the active constituents of *Clitoria ternatea* using ethanol, methanol, and water. The results showed that ethanol extraction was most efficient, yielding the highest percentage of extract. While this indicates a higher efficiency of ethanol as a solvent, it's important to note that different solvents may extract different phytoconstituents, affecting the final therapeutic properties of the extract. Therefore, the choice of solvent must consider the intended therapeutic application.

Phytochemical screening of the extracts revealed the presence of alkaloids, carbohydrates, saponins, steroids, phenolics, and flavonoids. All these components have established pharmacological activities, underscoring the potential therapeutic utility of *Clitoria ternatea*. Interestingly, alkaloids, known for their wide range of pharmacological properties, were most prevalent in the water extract. This observation might steer future research towards an exploration of water-based extraction for certain therapeutic applications.

The microemulsion formulations were prepared with varying compositions of surfactants and oil, resulting in three distinct formulations: F1, F2, and F3. All formulations showed pH values within the acceptable range for transdermal application, ensuring compatibility with skin physiology and minimizing potential irritation. This is a critical parameter in transdermal formulations, as a deviation from the skin's natural pH can disrupt skin barrier function and cause discomfort or harm.

Evaluation of viscosity revealed that F2 had the highest viscosity among the formulations. A higher viscosity implies a thicker formulation, which can potentially influence the rate of drug release and permeation through the skin. F2 might, therefore, provide a more controlled and sustained release profile, which could be beneficial for long-term management of chronic conditions.

Particle size analysis demonstrated the smallest average particle size for F1, suggesting it may have the highest potential for skin permeation and absorption. Small particle size increases the surface area available for interaction with the skin, promoting better absorption and ultimately, potentially improved therapeutic efficacy.

In terms of drug content, all formulations showed high values, indicating their robust capability as carriers of *Clitoria ternatea* extract. High drug content is advantageous as it allows for a smaller amount of formulation to deliver the desired dose, improving patient compliance.

The conductivity of the microemulsions, representing the presence of ions, could also contribute to enhanced skin permeation, although the role of conductivity in transdermal delivery is an area that warrants further exploration.

Taken together, these results reflect the promising potential of microemulsion-based transdermal delivery of *Clitoria ternatea* extract. However, it's important to remember that these are in vitro findings, and while they provide a strong foundation, further in vivo and stability studies are required to fully understand these formulations' efficacy, safety, and durability.

The results of this study are consistent with the growing body of research suggesting that microemulsion systems can offer a superior alternative to conventional dosage forms, especially for the delivery of herbal medicines. The enhanced solubility, stability, and bioavailability offered by these systems could open new horizons in the field of drug delivery and therapeutics.

It is hoped that these findings will provide impetus for further research in this area, with the ultimate aim of improving therapeutic outcomes for patients through innovative and effective drug delivery systems.

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