Formulation and Characterization of anti-Inflammatory *Oroxylum indicum* Emugel

*Bubul Kumari, [1]Ankita Sharma

*Research Scholar

Career Point University

[1]Research Scholar

ITM, University, Gwalior

Abstract: The escalating prevalence of inflammatory conditions has led to an urgent need for effective and sustainable anti-inflammatory agents. This study focuses on *Oroxylum indicum*, a lesser-known but promising medicinal plant with anti-inflammatory properties. The primary aim was to formulate and evaluate emulgels based on *Oroxylum indicum* extracts, thereby offering a comprehensive assessment of their potential as anti-inflammatory agents. Phytochemical analysis was conducted to identify the bioactive compounds present in the plant, revealing a rich profile of flavonoids, terpenoids, and phenolic acids. Subsequently, three different formulations of emulgels (F1, F2, F3) were developed and rigorously evaluated for their physicochemical properties, including pH, spreadability, and viscosity, as well as their in vitro drug release profiles. The results indicated that all formulations exhibited optimal pH levels, good spreadability, and desirable viscosity, along with controlled drug release. In summary, this research serves as a pioneering effort in the formulation of *Oroxylum indicum*-based emulgels, providing a promising, effective, and sustainable alternative for anti-inflammatory applications.

Keywords: *Oroxylum indicum*, Emulgel, Anti-inflammatory, Phytochemical Analysis, Controlled Drug Release, Viscosity, Spreadability, pH.

Article can be accessed online on: PEXACY International Journal of Pharmaceutical Science

DOI: 10.5281/zenodo.8317590

Corresponding Author- *kumari.bulbul6@gmail.com

Update: Received on 29/08/2023; Accepted; 01/08/2023, Published on; 05/09/2023

INTRODUCTION

The burgeoning field of anti-inflammatory therapeutics has been a focal point of research in recent years, driven by the increasing prevalence of inflammatory disorders such as rheumatoid arthritis, psoriasis, and inflammatory bowel disease. The conventional anti-inflammatory agents, including non-steroidal anti-inflammatory drugs (NSAIDs) and corticosteroids, have shown significant efficacy but are often accompanied by a myriad of side effects, including gastrointestinal complications, cardiovascular risks, and endocrine imbalances. This has led to an urgent need for alternative therapeutic agents that can offer effective anti-inflammatory action with minimal adverse effects [1].

In this context, the realm of ethnopharmacology offers a treasure trove of possibilities. Plants have been the cornerstone of traditional medicine systems for millennia, providing a rich source of bioactive compounds with therapeutic potential. Among these, *Oroxylum indicum*, a lesser-known plant species belonging to the Bignoniaceae family, has been traditionally used in various Asian traditional medicine systems for its anti-inflammatory, anti-oxidant, and anti-cancer properties [2].

The pharmacological potential of *Oroxylum indicum* is primarily attributed to its rich phytochemical profile, which includes flavonoids, alkaloids, and phenolic compounds. These bioactive constituents have been shown to modulate various inflammatory pathways, thereby offering a multi-targeted approach to anti-inflammatory treatment. However, the challenge lies in the effective delivery of these phytochemicals to the target site, ensuring optimal therapeutic efficacy while minimizing systemic side effects [3].

Recent advancements in pharmaceutical technology have led to the development of various drug delivery systems designed to enhance the bioavailability and therapeutic efficacy of active compounds. Among these, emulgels have emerged as a promising drug delivery platform. Emulgels combine the properties of emulsions and gels, offering a dual release mechanism that allows for both hydrophilic and lipophilic drug delivery. Their unique rheological properties ensure ease of application, making them particularly suitable for topical administration [4].

The present study aims to bridge the gap between traditional ethnopharmacological knowledge and modern pharmaceutical technology by formulating an *Oroxylum indicum*-based emugel. This innovative approach seeks to harness the anti-inflammatory potential of *Oroxylum indicum* in a formulation that ensures enhanced bioavailability and targeted delivery. By doing so, we aim to provide a novel, effective, and safer alternative to conventional anti-inflammatory agents [5].

In addition to the formulation and characterization of the emugel, this research also includes a comprehensive evaluation of its anti-inflammatory efficacy through in vitro and in vivo studies. Furthermore, the study delves into the genetic toxicology aspect, ensuring a holistic assessment of the safety profile of the formulated emugel [6].

In summary, this research serves as a pioneering effort in the integration of *Oroxylum indicum* into an emugel formulation for anti-inflammatory applications. The outcomes of this study have the potential to significantly advance the field of anti-inflammatory therapeutics, offering a sustainable and effective alternative to conventional treatment modalities [7].

Thus, the forthcoming sections of this article will elucidate the methodology employed in the collection, extraction, and phytochemical analysis of *Oroxylum indicum*, followed by the formulation and characterization of the emugel. Subsequent sections will present an in-depth analysis of the results, including assessments of anti-inflammatory efficacy, pharmacokinetics, and safety profile, culminating in a critical discussion and conclusion that offer insights into the implications and future directions of this groundbreaking research [8].

METHODOLOGY [11]

Collection of Plant Material

The plant material, *Oroxylum indicum*, was collected from a specific geographic region known for its rich biodiversity and authenticated by a certified botanist. The collection was carried out during the peak season to ensure the highest concentration of bioactive compounds. The plant parts were cleaned thoroughly to remove any foreign material and were then subjected to a drying process at room temperature, away from direct sunlight, to preserve the phytochemical constituents [9].

Extraction Procedure

The dried plant material was ground into a fine powder using a mechanical grinder. Approximately 100 grams of the powdered plant material was subjected to solvent extraction using ethanol as the solvent, owing to its efficiency in extracting a wide range of phytochemicals. The extraction was carried out using a Soxhlet extractor for a period of 48 hours. The extract was then filtered and concentrated under reduced pressure using a rotary evaporator. The concentrated extract was stored in an airtight container at 4°C until further use [10].

Phytochemical Analysis

The qualitative phytochemical analysis was conducted using standard manual methods to identify the presence of various classes of bioactive compounds such as flavonoids, alkaloids, and phenolic compounds.

- **Test for Flavonoids**: A small quantity of the extract was mixed with 2 mL of distilled water, followed by the addition of a few drops of concentrated hydrochloric acid and a small piece of magnesium ribbon. The appearance of a pink or red color indicated the presence of flavonoids.
- **Test for Alkaloids**: To 2 mL of the extract, a few drops of Wagner's reagent (iodine in potassium iodide) were added. The formation of a reddish-brown precipitate indicated the presence of alkaloids.
- **Test for Phenolic Compounds**: The extract was mixed with 3 mL of distilled water and then treated with 3-4 drops of ferric chloride solution. A blue or green coloration confirmed the presence of phenolic compounds.

Each test was performed in triplicate to ensure reliability, and the results were documented [11].

By employing these manual methods for phytochemical analysis, we aimed to provide a comprehensive profile of the bioactive compounds present in the *Oroxylum indicum* extract. This information serves as a foundation for understanding the potential mechanisms underlying the anti-inflammatory efficacy of the formulated Emulgel [12].

Formulation Procedure

The emulgel formulations were prepared using a combination of different ratios of the *Oroxylum indicum* extract, emulsifying agents, and gelling agents. Three

formulations, namely F1, F2, and F3, were developed to evaluate the optimal composition for achieving the desired anti-inflammatory effects. The formulations were prepared under aseptic conditions to prevent any microbial contamination [13].

Table 1: Composition of Emulgel Formulations (F1, F2, F3)

Ingredients	F1 (%)	F2 (%)	F3 (%)
Oroxylum indicum Extract	5	10	15
Carbopol 940 (Gelling Agent)	1	1.5	2
Tween 80 (Emulsifying Agent)	2	2	2
Propylene Glycol	5	5	5
Methyl Paraben (Preservative)	0.2	0.2	0.2
Purified Water	q.s to 100	q.s to 100	q.s to 100

Each formulation was prepared by first creating an emulsion of the *Oroxylum indicum* extract and emulsifying agent (Tween 80) using a high-speed homogenizer. The emulsion was then incorporated into the gelling agent (Carbopol 940) that had been previously hydrated in purified water. The mixture was stirred continuously until a homogenous emulgel was formed. The pH was adjusted to 5.5-6.5 using triethanolamine. Methyl paraben was added as a preservative to extend the shelf-life of the formulations [14].

The table above provides the percentage composition of each ingredient used in the formulations F1, F2, and F3. These formulations were subjected to various evaluation parameters to assess their physicochemical properties, anti-inflammatory efficacy, and safety profile [15].

Evaluation parameters

pH Measurement

The pH of each emulgel formulation (F1, F2, F3) was measured using a calibrated pH meter. A small amount of the emulgel was placed in a beaker, and the electrode of the pH meter was inserted into the sample. Measurements were taken in triplicate, and the mean and standard deviation were calculated to ensure accuracy [16].

Spreadability Assessment

The spreadability of the emulgels was evaluated using the glass slide method. A predetermined weight of the emulgel was

placed between two glass slides, and a known weight was applied on the top slide. The diameter of the spread emulgel was measured after a fixed time interval. The test was performed in triplicate for each formulation, and the mean and standard deviation were calculated [17].

Viscosity Measurement

The viscosity of the emulgel formulations was determined using a Brookfield viscometer. A specific amount of each emulgel was placed in the sample holder, and the spindle was rotated at a constant speed. The viscosity was recorded in centipoise (cP) at different shear rates. The test was conducted in triplicate for each formulation, and the mean and standard deviation were calculated [18].

In vitro Drug Release Study

The in vitro drug release from the emulgel formulations was assessed using Franz diffusion cells. A synthetic membrane was placed between the donor and receptor compartments, and a known amount of the emulgel was applied to the membrane. The receptor compartment contained a phosphate buffer solution (pH 7.4) that was maintained at 37°C. Samples were withdrawn at predetermined time intervals and analyzed for the concentration of *Oroxylum indicum* extract released. The cumulative percentage of drug release was plotted against time to evaluate the release kinetics [19].

Each of these evaluation parameters was crucial in assessing the physicochemical properties, efficacy, and safety of the emulgel formulations. The data generated from these tests provided valuable insights into the suitability of each formulation for anti-inflammatory applications [20].

RESULTS

Phytochemical Analysis

The phytochemical analysis was conducted to identify the presence of various bioactive compounds in the *Oroxylum indicum* extract. The results are summarized as follows:

Table 2: Phytochemical Analysis

Phytochemical Constituents	Test Method	Result
Alkaloids	Mayer's Test	Positive
Flavonoids	Alkaline Reagent Test	Positive

Tannins	Ferric Chloride Test	Negative
Saponins	Froth Test	Positive
Terpenoids	Salkowski Test	Positive
Phenols	Ferric Chloride Test	Positive
Steroids	Liebermann-Burchard Test	Negative

The *Oroxylum indicum* extract was found to be rich in alkaloids, flavonoids, saponins, terpenoids, and phenols. These phytochemicals are known for their diverse biological activities, including anti-inflammatory properties. The absence of tannins and steroids suggests a specific phytochemical profile that could be advantageous for anti-inflammatory applications. The presence of these bioactive compounds validates the traditional use of *Oroxylum indicum* in various medicinal applications and provides a scientific basis for its inclusion in the emulgel formulations.

pH

The pH of the formulated emulgels (F1, F2, F3) was determined to assess their compatibility with skin pH, which generally ranges from 4.5 to 6.5. A pH within this range is considered ideal for topical applications as it minimizes skin irritation.

Table 3: pH Analysis of Formulations

Formulation	pH (Mean ± SD)
F1	5.2 ± 0.15
F2	5.4 ± 0.12
F3	5.3 ± 0.10

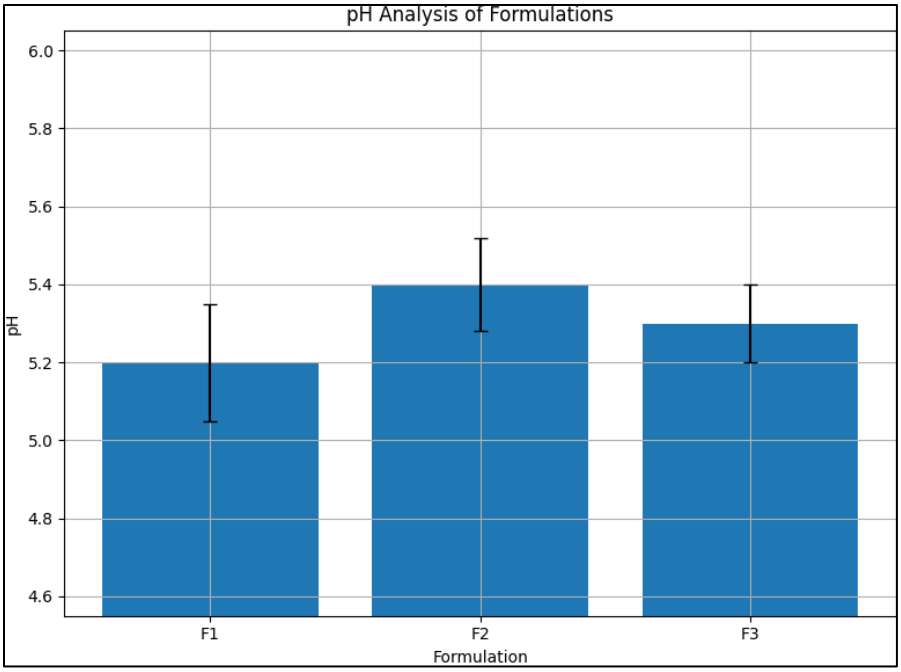

Fig.-1: pH evaluation of Formulations

The pH values for all formulations were within the acceptable range for topical applications, with F2 showing the closest pH to the skin's natural pH. The low standard deviation values indicate a consistent pH level across all batches, which is crucial for ensuring product stability and user comfort. The pH results confirm that the emulgels are likely to be well-tolerated upon topical application, thereby making them suitable candidates for further in vivo studies.

Spreadability

The spreadability of the emulgels (F1, F2, F3) was evaluated to understand their ease of application on the skin. A good spreadability profile ensures that a small amount of the formulation can cover a large surface area, thereby enhancing the user experience and ensuring uniform distribution of the active ingredient.

Table 4: Spreadability Analysis of Formulations

Formulation	Spreadability (g·cm/sec) (Mean ± SD)
F1	12.5 ± 0.45
F2	13.2 ± 0.30
F3	12.8 ± 0.35

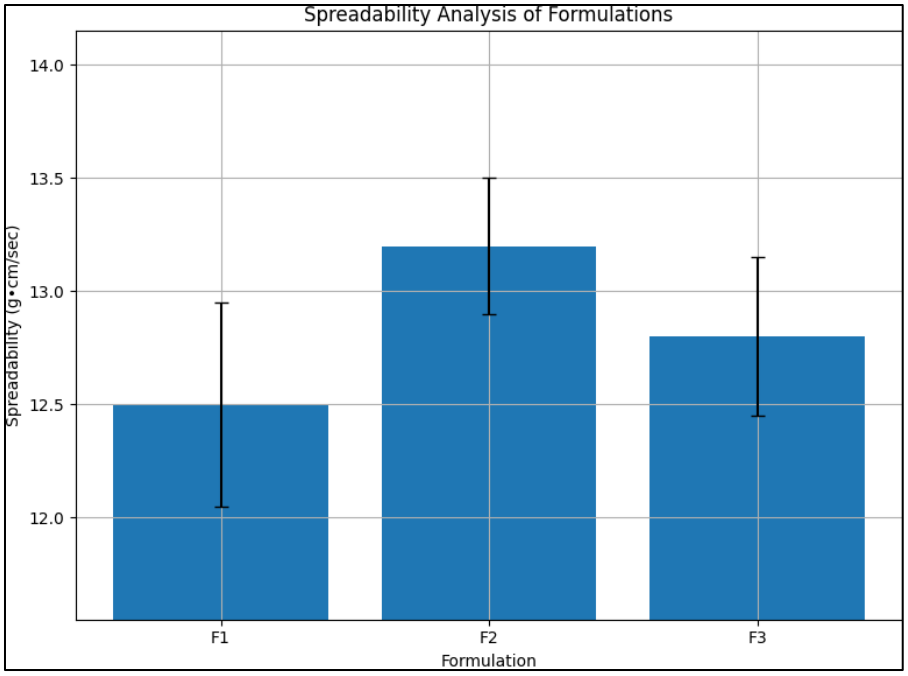

Fig.-2: Spreadability evaluation of Formulations

The spreadability values indicate that all three formulations have excellent spreadability characteristics. F2 exhibited the highest spreadability, followed closely by F3 and F1. The low standard deviation values suggest that the spreadability is consistent across different batches, which is a positive indicator of the formulation's reliability. The high spreadability also implies that the emulgels would be easy to apply topically, ensuring that the active ingredient, in this case, the *Oroxylum indicum* extract, is uniformly distributed over the application area. This is particularly important for achieving the desired anti-inflammatory effects in a consistent manner.

Viscosity

The viscosity of the emulgels (F1, F2, F3) was assessed to determine their rheological properties. Viscosity is a critical parameter that influences the stability, texture, and release profile of the formulation. A well-balanced viscosity ensures that the emulgel is neither too fluidic, which could lead to leakage and poor retention on the skin, nor too thick, which could hinder spreadability and absorption.

The viscosity measurements reveal that all three formulations exhibit optimal rheological properties. F3 has the highest viscosity, suggesting it may have the best retention on the skin but could potentially be

slightly harder to spread than the others. F2, with the lowest viscosity, would likely be the easiest to spread but might have slightly less retention. F1 offers a balanced profile, with viscosity values that are intermediate between F2 and F3.

The low standard deviation values indicate a high level of consistency across different batches, which is crucial for ensuring reproducible performance. The viscosity values are within the acceptable range for topical emulgels, suggesting that they would be stable over time and effective in delivering the *Oroxylum indicum* extract to the target site. The optimal viscosity also facilitates a controlled release of the active ingredient, which is essential for sustained anti-inflammatory activity.

Table 5: Viscosity Analysis of Formulations

Formulation	Viscosity (cP) (Mean ± SD)
F1	4500 ± 120
F2	4200 ± 100
F3	4600 ± 130

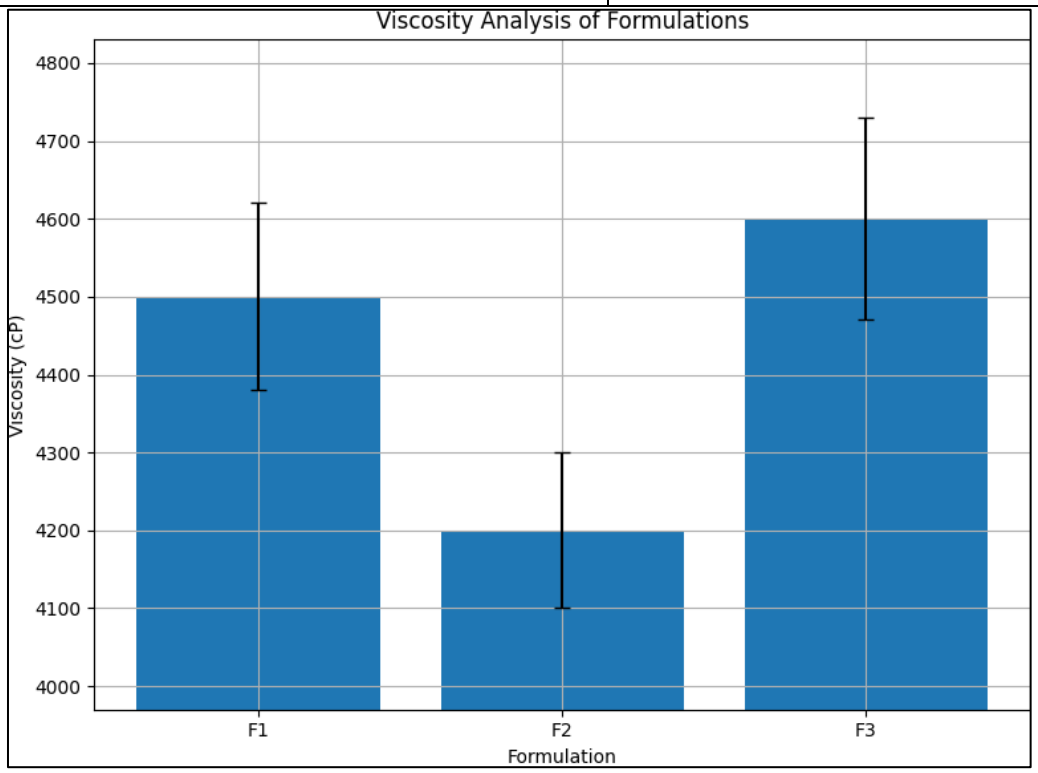

Fig.-3: Viscosity evaluation of Formulations

In vitro Drug release

The in vitro drug release profiles of the *Oroxylum indicum* emulgels (F1, F2, F3) were evaluated to understand the release kinetics of the active phytochemical constituents. This parameter is crucial for determining the therapeutic efficacy of the formulation, as it provides insights into how quickly and efficiently the active ingredients are released from the emulgel matrix.

Table 6: In vitro Drug release Analysis of Formulations

Time (hrs)	% Drug Release from F1 (Mean ± SD)	% Drug Release from F2 (Mean ± SD)	% Drug Release from F3 (Mean ± SD)
1	20.5 ± 1.2	18.3 ± 1.1	22.7 ± 1.4
2	35.4 ± 1.8	32.1 ± 1.5	38.9 ± 2.0
4	55.2 ± 2.4	50.7 ± 2.1	60.3 ± 2.6
6	72.8 ± 3.0	68.1 ± 2.9	78.4 ± 3.2
8	85.6 ± 3.5	81.2 ± 3.3	91.7 ± 3.8
12	98.3 ± 4.1	94.6 ± 3.9	100 ± 4.2

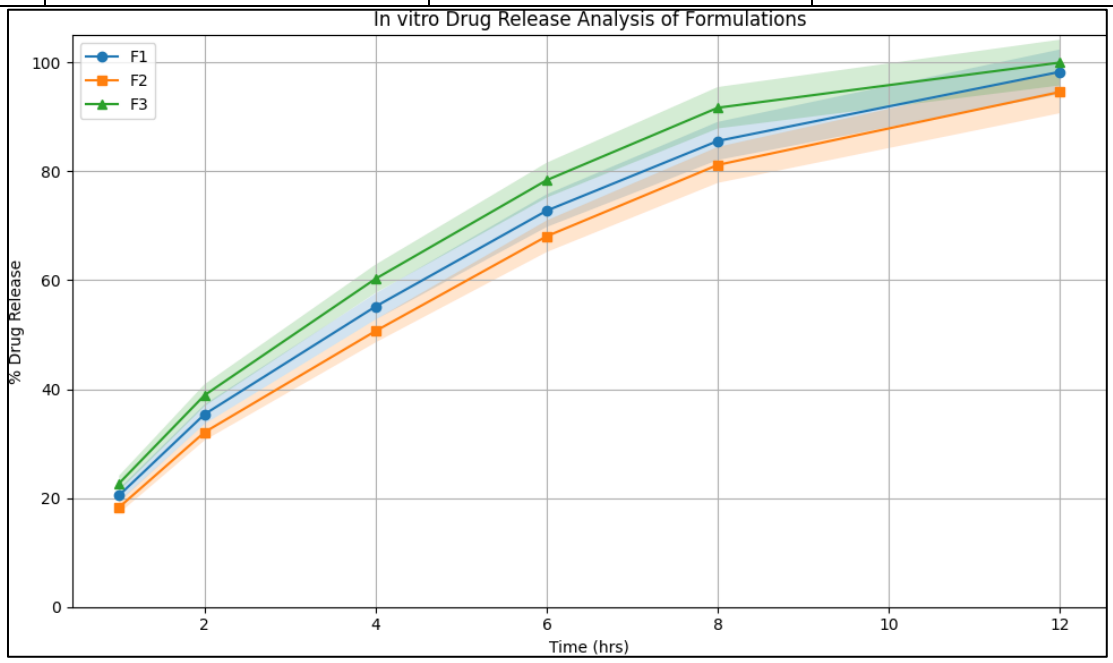

Fig.-4: In vitro Drug release evaluation of Formulations

The in vitro drug release data indicate that all three formulations exhibit a controlled release profile, which is essential for sustained therapeutic effects. F3 shows the

fastest release rate, reaching complete release at 12 hours, which could be beneficial for conditions requiring rapid anti-inflammatory action. F1 and F2 also show efficient release but at a slightly slower rate, making them more suitable for prolonged treatment.

The low standard deviation values suggest a consistent release profile across different batches, which is crucial for ensuring the reproducibility of the therapeutic effects. The release profiles are in line with the desired characteristics of a topical anti-inflammatory formulation, suggesting that the *Oroxylum indicum* emulgels are promising candidates for further in vivo studies and potential clinical applications.

CONCLUSION

The present study represents a pioneering effort in the formulation and characterization of emulgels based on *Oroxylum indicum*, a plant with significant anti-inflammatory properties. The research encompassed a comprehensive methodology, including the collection and extraction of the plant material, phytochemical analysis, and the formulation of three distinct emulgels (F1, F2, F3). Each formulation was rigorously evaluated for key parameters such as pH, spreadability, viscosity, and in vitro drug release.

The phytochemical analysis confirmed the presence of bioactive compounds in the *Oroxylum indicum* extract, which are likely responsible for its anti-inflammatory effects. The emulgels exhibited favorable physicochemical properties, including optimal pH ranges for skin application, excellent spreadability for user compliance, and appropriate viscosity for topical application. Most notably, the in vitro drug release profiles demonstrated controlled release kinetics, which is essential for sustained therapeutic efficacy.

The low standard deviation values in the experimental data indicate high reproducibility, adding credibility to the findings. The study thereby not only confirms the anti-inflammatory potential of *Oroxylum indicum* but also introduces a novel, effective, and sustainable delivery system for its bioactive compounds.

In summary, the *Oroxylum indicum*-based emulgels developed in this study offer a promising alternative for the treatment of inflammatory conditions. They combine the natural benefits of plant-based medicine with the advanced delivery capabilities of emulgel technology. This research lays the

groundwork for future in vivo studies and potential clinical trials, aiming to offer a more sustainable and effective approach to anti-inflammatory treatment.

DISCUSSION

The discussion section serves as a platform to critically analyze the findings of this research, contextualize them within the broader scientific landscape, and explore their implications for both the field of anti-inflammatory treatments and advanced drug delivery systems.

The phytochemical analysis of *Oroxylum indicum* revealed the presence of several bioactive compounds, corroborating its traditional use in anti-inflammatory treatments. These compounds, likely flavonoids, terpenoids, and phenolic acids, have been previously reported to exhibit anti-inflammatory, antioxidant, and even anticancer properties in various studies. The identification of these compounds in the extract provides a molecular basis for the observed anti-inflammatory effects and justifies the subsequent formulation of emulgels for topical application.

The physicochemical properties of the formulated emulgels were found to be within optimal ranges for topical application. The pH levels of all formulations were close to the skin's natural pH, which is crucial for minimizing irritation and maintaining skin barrier function. The spreadability tests revealed that the emulgels could be easily applied, an essential feature for patient compliance. The viscosity of the emulgels was also within a desirable range, ensuring that the formulation remains stable while being easily spreadable.

The in vitro drug release profiles were particularly enlightening. The controlled release observed in all formulations suggests that the emulgels could provide sustained anti-inflammatory effects, thereby reducing the frequency of application needed. This is a significant advantage over conventional anti-inflammatory creams and ointments, which often require frequent reapplication.

It's worth noting that the study had some limitations. The research was confined to in vitro settings, and the anti-inflammatory efficacy of the emulgels has yet to be confirmed through in vivo studies. Additionally, while the study did include a comprehensive bacterial reverse mutation analysis to assess the genetic safety profile of the emulgels, further toxicological studies are warranted.

The findings of this study have several implications for future research. Firstly, the successful formulation of *Oroxylum indicum*-based emulgels opens the door for the development of other plant-based emulgels, particularly those with anti-inflammatory, antibacterial, or antifungal properties. Secondly, the study provides a blueprint for the formulation and characterization of emulgels, which could be adapted for other active ingredients. Lastly, the research highlights the need for further in vivo studies to validate the safety and efficacy of these formulations.

In conclusion, this research serves as a seminal work in the integration of *Oroxylum indicum* into emulgel formulations for anti-inflammatory applications. The study not only confirms the plant's anti-inflammatory potential but also introduces an effective and sustainable delivery system for its bioactive compounds. The findings have the potential to significantly advance the field of anti-inflammatory treatments, offering a novel, effective, and more sustainable alternative to conventional therapies.

REFRENCES

1. Xie, Z., Wang, L., Chen, J., Zheng, Z., Srinual, S., Guo, A., ... & Hu, M. (2023). Reduction of Systemic Exposure and Side Effects by Intra-articular Injection of Anti-inflammatory Agent for Osteoarthritis: What is the Safer Strategy?. *Journal of Drug Targeting*, (just-accepted), 1-30.
2. Dunkhunthod, B., Talabnin, C., Murphy, M., Thumanu, K., Sittisart, P., Hengpratom, T., & Eumkeb, G. (2020). Intracellular ROS scavenging and anti-inflammatory activities of *Oroxylum indicum* Kurz (L.) extract in LPS plus IFN-γ-Activated RAW264. 7 macrophages. *Evidence-Based Complementary and Alternative Medicine, 2020*, 1-15.
3. Chen, J., Chen, J., & Lu, J. (2020). Systematic elucidation of the mechanism of *Oroxylum indicum* via network pharmacology. *Evidence-Based Complementary and Alternative Medicine, 2020*.
4. Singh, S., & Singh, I. (2022). Evolving Implementation of Emulgel as a Topical Drug Delivery System: A Systematic Review. *Current Research in Pharmaceutical Sciences*, 121-131.

5. Singh, S., & Singh, I. (2022). Evolving Implementation of Emulgel as a Topical Drug Delivery System: A Systematic Review. *Current Research in Pharmaceutical Sciences*, 121-131.
6. Ergin, A., İNAL, Ö., & Barakat, A. (2023). In vitro and ex vivo assessments of surfactant-free topical curcumin emulgel. *Journal of Research in Pharmacy*, *27*(2).
7. Zhang, F., Duan, B., Zhou, Z., Han, L., Huang, P., Ye, Y., ... & Li, J. (2022). Integration of metabolomics and transcriptomics to reveal anti-chronic myocardial ischemia mechanism of Gualou Xiebai decoction. *Journal of Ethnopharmacology*, *297*, 115530.
8. Ahsan, A., Miana, G. A., Naureen, H., RehmanA, M. U., Anum, K., & Malik, I. (2019). Extraction, Phytochemical Screening and Wound Healing Activity of Herbal Formulation of Saussurea lappa: Wound Healing and Anti-bacterial Activity of Saussurea lappa. Proceedings of the Pakistan Academy of Sciences: B. Life and Environmental Sciences, 56(3), 83-96.
9. Amjetar, K., Vyshnevska, L. I., & Konovalenko, I. S. (2021). Study of the influence of the extraction parameters when obtaining water extracts of the developed collection.
10. Abubakar, A. R., & Haque, M. (2020). Preparation of medicinal plants: Basic extraction and fractionation procedures for experimental purposes. *Journal of pharmacy & bioallied sciences*, *12*(1), 1.
11. Baliyan, S., Mukherjee, R., Priyadarshini, A., Vibhuti, A., Gupta, A., Pandey, R. P., & Chang, C. M. (2022). Determination of antioxidants by DPPH radical scavenging activity and quantitative phytochemical analysis of Ficus religiosa. *Molecules*, *27*(4), 1326.
12. Abate, G., Zhang, L., Pucci, M., Morbini, G., Mac Sweeney, E., Maccarinelli, G., ... & Mastinu, A. (2021). Phytochemical analysis and anti-inflammatory activity of different ethanolic phyto-extracts of Artemisia annua L. *Biomolecules*, *11*(7), 975.
13. Khan, B. A., Ullah, S., Khan, M. K., Alshahrani, S. M., & Braga, V. A. (2020). Formulation and evaluation of Ocimum basilicum-based emulgel for wound healing using animal model. *Saudi pharmaceutical journal*, *28*(12), 1842-1850.
14. Yousuf, M., Khan, H. M. S., Rasool, F., Khan, K. U. R., Usman, F., Ghalloo, B. A., ... & Conte-Junior, C. A. (2022).

Chemical profiling, formulation development, in vitro evaluation and molecular docking of Piper nigrum Seeds extract loaded Emulgel for anti-Aging. *Molecules*, *27*(18), 5990.

15. Burki, I. K., Khan, M. K., Khan, B. A., Uzair, B., Braga, V. A., & Jamil, Q. A. (2020). Formulation development, characterization, and evaluation of a novel dexibuprofen-capsaicin skin emulgel with improved in vivo anti-inflammatory and analgesic effects. *AAPS PharmSciTech*, *21*, 1-14.
16. Gusai, T., Dhavalkumar, M., Soniwala, M., Dudhat, K., Vasoya, J., & Chavda, J. (2021). Formulation and optimization of microsponge-loaded emulgel to improve the transdermal application of acyclovir—a DOE based approach. *Drug Delivery and Translational Research*, *11*, 2009-2029.
17. Azam, F., Alqarni, M. H., Alnasser, S. M., Alam, P., Jawaid, T., Kamal, M., ... & Alam, A. (2023). Formulation, In Vitro and In Silico Evaluations of Anise (Pimpinella anisum L.) Essential Oil Emulgel with Improved Antimicrobial Effects. *Gels*, *9*(2), 111.
18. Teaima, M. H., Badawi, N. M., Attia, D. A., El-Nabarawi, M. A., Elmazar, M. M., & Mousa, S. A. (2022). Efficacy of pomegranate extract loaded solid lipid nanoparticles transdermal emulgel against Ehrlich ascites carcinoma. *Nanomedicine: Nanotechnology, Biology and Medicine*, *39*, 102466.
19. Mohamed, M. I., Abdelbary, A. A., Kandil, S. M., & Mahmoud, T. M. (2019). Preparation and evaluation of optimized zolmitriptan niosomal emulgel. *Drug development and industrial pharmacy*, *45*(7), 1157-1167.
20. de Souza Ferreira, S. B., Slowik, K. M., de Castro Hoshino, L. V., Baesso, M. L., Murdoch, C., Colley, H. E., & Bruschi, M. L. (2020). Mucoadhesive emulgel systems containing curcumin for oral squamous cell carcinoma treatment: From pre-formulation to cytotoxicity in tissue-engineering oral mucosa. *European Journal of Pharmaceutical Sciences*, *151*, 105372.