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Topical Use of Celecoxib-Loaded Invasom: Development, Speciality, and In Vitro Skin Penetration Research

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ABSTRACT

A potential approach to targeted therapy, particularly for inflammatory diseases like arthritis, is the topical administration of medications. The usefulness of celecoxib, a selective cyclooxygenase-2 (COX-2) inhibitor, in treating pain and inflammation is hampered by its low skin penetration when given topically. In order to improve the therapeutic efficacy of celecoxib while reducing systemic adverse effects, this thesis investigates the creation, characterisation, and in-vitro skin penetration of celecoxib-loaded invasomes as a cutting-edge drug delivery method.Human skin served as the model for Franz diffusion cell-based in vitro skin penetration experiments. The findings showed that, in comparison to conventional topical formulations, the invasomal formulation considerably improved celecoxib's skin penetration. The invasomes' capacity to distort made it easier for them to penetrate the stratum corneum and introduce celecoxib into the skin's deeper layers. Additionally, the in-vitro trials'-controlled release profile raises the possibility that invasomes might provide longer-lasting medication administration, lowering application frequency and enhancing patient compliance.Celecoxib-loaded invasomes are a viable method for improving the topical distribution of celecoxib, providing a localized therapeutic alternative with less systemic adverse effects, according to the research's findings. With the potential for wider use in the treatment of inflammatory illnesses, the Invasomes improved skin penetration and controlled release qualities make them a competitive alternative to traditional topical formulations. This study offers insightful information on the potential of invasives as a cutting-edge drug delivery method for the efficient management of inflammation and pain.

Keywords: Inflammatory Diseases, Arthritis, Celecoxib, Cyclooxygenase-2 (COX-2), Invasomes, Penetration.

I. INTRODUCTION

The biggest organ in the human body, the skin acts as a vital barrier to keep the body safe from harmful substances, infections, and physical harm. It also keeps the body from losing too much water. However, as most chemicals have trouble penetrating the skin, this barrier function also poses a problem in the realm of medication delivery, especially for topical treatments. The skin's barrier qualities frequently impede the use of traditional topical dose forms, such creams, ointments, and gels, leading to less than ideal drug absorption and therapeutic effectiveness.

Nanocarrier technologies have drawn a lot of interest lately as potential answers to these problems with topical medication delivery. Among them, invasomes, a unique type of lipid-based vesicular systems, have gained attention as a possible way to increase medication bioavailability and skin penetration. Phospholipid-based vesicles called invasomes can more easily enter the skin than liposomes because they are more pliable and malleable. Because of their capacity to deform and penetrate the stratum corneum of the skin, these carriers provide a number of benefits, such as better drug stability, controlled release, and improved skin penetration.

Celecoxib, a selective inhibitor of cyclooxygenase-2 (COX-2), is one of the promising medications that can be efficiently administered via the skin utilizing invasome technology. Acute pain, rheumatoid arthritis, osteoarthritis, and other inflammatory diseases are all commonly treated with celecoxib. Celecoxib's traditional oral administration is frequently linked to gastrointestinal adverse effects, including as ulcers, bleeding, and other problems, despite its therapeutic effectiveness. By directly addressing the site of inflammation, topical celecoxib treatment has the potential to lessen these systemic adverse effects while delivering localized relief

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with less systemic exposure.

One interesting method to improve the topical distribution of celecoxib is the creation of invasomes filled with the drug. It is feasible to enhance celecoxib's stability, solubility, and skin penetration by encapsulating it in invasomes. Invasomes' deformability and flexibility allow them to enter deeper layers of the skin, which guarantees efficient medication administration to the intended location. Additionally, celecoxib encapsulation in invasomes may provide regulated release, extending the therapeutic benefits and reducing the frequency of administrations.

This thesis aims to develop, characterize, and evaluate the topical application of celecoxib-loaded invasomes for improved skin penetration. The studyinvestigates the formulation of invasomes, their physicochemical properties, and in-vitro skin penetration studies. The key focus of the research is to assess the efficiency of invasomesinenhancingthedeliveryofcelecoxibacross theskinbarrier,comparingthe penetration results with conventional topical formulations. Additionally, the stability and release profiles of the drug-loaded invasomes are thoroughly examined to determine their suitability for potential therapeutic applications.

Topical Drug Delivery Systems and Challenges

The purpose of topical medication delivery systems is to apply active pharmaceutical ingredients (APIs) to the skin for either systemic or local effects. They are frequently used to relieve pain and inflammation in musculoskeletal problems as well as to treat skin ailments such dermatitis, psoriasis, and eczema. However, the barrier function of the skin presents a major obstacle to efficient medication penetration. The stratum corneum, the skin's outermost layer, serves as a barrier to keep medications and other external things from penetrating. This barrier characteristic makes many traditional topical formulations ineffective and restricts the absorption of medications given topically.

The development of a number of sophisticated drug delivery methods, such as liposomes, ethosomes, and invasomes, aims to get beyond the skin barrier. By making it easier for the medicine to pass through the stratum corneum and into the deeper layers of the skin, these systems seek to improve the penetration of medications through the skin. Because of their special makeup and capacity for stress-induced deformation, invasomes have demonstrated the most promise among them.

Invasomes: A Novel Approach to Drug Delivery

Invasomes are phospholipid-based vesicles that resemble liposomes but have other ingredients, including alcohols, that increase their deformability and flexibility. By adding alcohols, such ethanol, to the lipid mixture, invasomes become more pliable and are able to pass through the stratum corneum's tight intercellular connections. Compared to conventional liposomes and other vesicular systems, invasomes' special characteristic allows them to enhance medication penetration across the skin barrier.

Encapsulating a range of medications, including hydrophilic and hydrophobic compounds, invasomes can increase the solubility, stability, and permeability of the pharmaceuticals. A variety of therapeutic applications can benefit from the customization of invasomes' size, surface charge, and composition to maximize drug encapsulation and delivery. Furthermore, regulated and prolonged medication release using invasomes can improve therapeutic efficacy and decrease the frequency of delivery.

Invasomes: A Novel Approach to Drug Delivery

The pharmaceutical sector has seen a transformation in recent years due to developments in medication delivery methods. Among them, the creation of vesicular carriers based on lipids has demonstrated significant promise in resolving the inherent difficulties of traditional drug delivery methods, especially for topical treatments. Invasomes, a kind of lipid-based vesicle that has drawn a lot of interest because of its capacity to improve medication penetration across the skin barrier, are one example of a new carrier system. This is especially important when developing topical formulations since the skin's intrinsic barrier qualities sometimes impede the effectiveness of medication delivery. This section examines the idea of invasomes, including their composition, benefits, and potential to enhance medication delivery, especially for the topical administration of celecoxib to treat inflammatory diseases.

The Skin Barrier and Challenges in Topical Drug Delivery

The skin is a very powerful barrier that shields the body from infections, environmental dangers, and dehydration. The outermost layer of the epidermis, the stratum corneum, is essential to

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this barrier function because it prevents foreign substances—including medications—from penetrating. Many medications, particularly those with large molecular sizes, limited solubility, or poor skin permeability, have significant difficulties in their efficient topical distribution due to this selective permeability.

Topical formulations are less effective therapeutically because of the skin's barrier function, which restricts the quantity of medicine that can reach the target location. Conventional topical formulations, such gels, ointments, and creams, frequently have inadequate drug penetration, which leads to less than ideal clinical results. In order to improve medication absorption and yield better treatment outcomes, these constraints have prompted the creation of sophisticated drug delivery systems such liposomes, ethosomes, and invasomes.

What Are Invasomes?

The purpose of invasomes, which are innovative lipid-based vesicular systems, is to improve medication administration, particularly across the skin barrier. Like liposomes, they are made of phospholipid bilayers, but alcohols like ethanol or isopropyl alcohol are also present. Because of the addition of alcohols, the lipid bilayer becomes more flexible and fluid, which makes invasomes more malleable than conventional liposomes. The improved deformability makes it easier for invasomes to squeak past the stratum corneum's tight intercellular connections, which facilitates medication penetration into the skin's deeper layers, such as the dermis and epidermis.

Invasomes' unique shape enables them to get over the skin's impermeability, which is the main obstacle to topical medication administration. Invasomes can distort and penetrate the protective layers of the skin because the alcohols in them make the vesicular membrane more fluid. Compared to traditional topical formulations, this greater permeability leads to better medication absorption and skin penetration.

Advantages of Invasomes in Drug Delivery

Invasomes are especially useful for topical medication administration because they provide a number of benefits over conventional drug delivery methods, including:

1. **Enhanced Skin Penetration**: Compared to conventional liposomes, invasomes may more easily enter the stratum corneum due to their flexibility and deformability. By facilitating the encapsulated drug's release into the skin, the alcohols integrated into the vesicular structure enhance the drug's bioavailability at the intended location.
2. **Improved Drug Stability**: Invasome-encapsulated medications are frequently more stable than free medications in traditional formulations. By shielding the medication from environmental elements like light and oxygen, the lipid bilayer increases the medication's effectiveness and shelf life.
3. **Controlled and Sustained Drug Release**: It is possible to engineer invasomes to release their pharmacological cargo gradually. By preserving therapeutic drug concentrations at the intended location, this controlled release lengthens the duration of effect and reduces the frequency of treatments.

Reduced Systemic Side Effects: When compared to oral or systemic drug delivery, invasomes minimize systemic exposure and the related adverse effects by delivering medications locally to the skin. Particularly for chronic illnesses that need long-term care, this targeted distribution can greatly increase patient compliance.

4. **Versatility**: Invasomes are adaptable carriers for a variety of therapeutic applications because they may encapsulate a broad spectrum of medications, including hydrophilic and lipophilic substances. This adaptability is particularly helpful when delivering medications with limited bioavailability or poor solubility.
5. **Minimized Irritation**: Because invasomes may transport medications directly to the target location without seriously disrupting the epidermis, they can improve drug acceptability and lessen skin irritation as compared to conventional topical formulations.

Formulation of Invasomes

A lipid-based vesicular system that can encapsulate a range of medications is usually prepared as part of the invasome formulation process. The following are essential elements in the invasome preparation process:

- **Phospholipids**: Phospholipids, including phosphatidylcholine or phosphatidylethanolamine, make up the invasomes' bilayer structure. These lipids are essential for the vesicles' permeability, stability, and integrity.

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- **Alcohols**:Alcohols, such as ethanol or isopropyl alcohol, are incorporated into the lipid mixture to enhance the deformability and fluidity of the vesicles. The alcohols lower the viscosity of the lipid bilayer, making it easier for the vesicles to deform and penetrate the skin.
- **Drug**: The invasomes contain the active pharmaceutical ingredient (API), such as celecoxib. Its integration into the vesicle is contingent upon the solubility qualities of the drug and the vesicle. The drug's features can determine whether it is hydrophilic or lipophilic.
- **Stabilizers and Excipients**:Supplementing the invasomes with stabilizers, antioxidants, or preservatives might increase their stability and shelf life. These additives improve the overall quality of the formulation and stop medication deterioration.

Invasomes are prepared using a variety of techniques, including solvent injection, reverse-phase evaporation, and thin-film hydration. The drug kind, the intended invasome properties, and the formulation specifications all influence the technique selection.

Application of Invasomes in Topical Drug Delivery

Invasomes have demonstrated encouraging outcomes when used for topical drug administration in a number of therapeutic domains, most notably in the delivery of skin care products, analgesics, and anti-inflammatory medications. One such medication is celecoxib, a selective COX-2 inhibitor that is used to treat inflammation and pain brought on by diseases including rheumatoid arthritis, osteoarthritis, and musculoskeletal traumas.

In contrast to oral NSAIDs, celecoxib can minimize systemic adverse effects such ulcers and gastrointestinal discomfort while providing localized pain relief when applied topically. However, the skin barrier makes it difficult to apply celecoxib topically. Celecoxib can be better absorbed through the skin and delivered to the site of inflammation in a more effective and regulated manner by encapsulating it in invasomes.

Comparing celecoxib-loaded invasomes to traditional topical formulations, studies have demonstrated a considerable improvement in the drug's skin penetration. Because invasomes are deformable, they can pass through the protective layers of the skin and deliver larger quantities of the medicine to the target region, improving therapeutic results.

In-Vitro Skin Penetration Studies

In-vitro experiments employing human or animal skin can evaluate how well invasomes improve skin penetration. These investigations usually entail applying invasomes to the skin, then measuring the drug concentration in the receptor fluid and different skin layers (dermis, epidermis). The outcomes of these investigations can offer important insights into how well invasomes transport medications over the epidermal barrier and how they can increase drug bioavailability.

In comparison to traditional formulations, celecoxib-loaded invasomes have shown greater skin penetration in in vitro skin penetration tests. The findings suggest that invasomes can enhance celecoxib's penetration into the skin's deeper layers, where its therapeutic benefits are most required.

Conclusion

An innovative and extremely successful method for improving medication administration via the skin is the use of invasomes. They are a great option for topical drug administration because of their capacity to pass through the skin barrier and administer medications in a regulated, sustained manner. This is particularly true for medications like celecoxib, which are used to treat inflammatory diseases. Invasomes might transform the treatment of a number of musculoskeletal and dermatological conditions by enhancing medication stability, bioavailability, and patient compliance.

The use of invasomes as a drug delivery system presents an intriguing chance to increase the therapeutic efficacy of celecoxib and lessen the related systemic side effects, according to the thesis "Topical application of celecoxib-loaded invasomes: Development, characteristics, and in-vitro skin penetration studies." This research may result in the development of topical treatments that are more patient-friendly and efficacious by further developing and characterizing formulations based on invasomes.

Celecoxib and Its Rolein Topical Drug Delivery

A common treatment for pain and inflammation in diseases such rheumatoid arthritis, osteoarthritis, and acute pain is celecoxib, a selective COX-2 inhibitor. Despite its effectiveness, adverse effects, especially gastrointestinal (GI) issues, frequently restrict

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celecoxib's systemic usage. Because nonsteroidal anti-inflammatory medicines (NSAIDs) block COX-1 in the stomach, they frequently cause adverse effects such gastric ulcers, bleeding, and pain.

Celecoxib used topically has a number of benefits over oral dosing. It is feasible to produce localized therapeutic benefits while minimizing systemic exposure and lowering the risk of adverse effects by administering the medication directly to the site of inflammation. But the skin's inherent resistance to drug absorption makes it difficult for topical preparations of celecoxib to administer the medication effectively. Utilizing cutting-edge drug delivery technologies, such invasomes, can help get beyond this obstacle and improve celecoxib's topical therapy efficacy by increasing its penetration and absorption.

Objectives of the Study

The creation, description, and assessment of celecoxib-loaded invasomes for enhanced topical medication administration are the main objectives of this thesis. The following are the study's main goals:

1. **Development of Celecoxib-Loaded Invasomes**: to design celecoxib-encapsulating invasomes and maximize their physicochemical characteristics, such as size, surface charge, and drug encapsulation effectiveness.
2. **Characterization of Invasomes**: to assess the produced invasomes' physicochemical characteristics, such as their stability, drug content, shape, and size distribution.
3. **In-Vitro Skin Penetration Studies**: to evaluate the invasomes loaded with celecoxib's ability to penetrate human skin in vitro and compare their effectiveness to that of traditional topical preparations.
4. **Release Kinetics**: to examine celecoxib's release characteristics from the invasomes and assess the possibility of a regulated and prolonged release.
5. **Evaluation of Therapeutic Potential**: to assess, using in vitro data, the therapeutic potential of the created celecoxib-loaded invasomes in terms of how well they alleviate pain and inflammation.

Significance of the Study

The creation of invasomes loaded with celecoxib is a viable strategy for enhancing this medication's topical administration. Invasomes have the potential to improve localized treatment, decrease systemic adverse effects, and increase patient compliance by improving celecoxib's skin penetration and controlled release. This study might add to the expanding corpus of information on sophisticated drug delivery methods and offer important new information on the topical application of invasomes to the management of inflammatory diseases.

The creation of celecoxib delivery systems based on invasomes presents a fresh method of getting beyond the skin barrier and improving the medication's therapeutic effectiveness. In order to assess the potential of celecoxib-loaded invasomes for better topical medication administration, this study will look into their formulation, characterisation, and skin penetration. The results of this study may help create topical treatments for pain and inflammation that are safer, more efficient, and more palatable to patients.

II. LITERATURE REVIEW

- **Li et al. (2024)** investigated the new formulation of invasomes loaded with celecoxib for improved skin penetration and anti-inflammatory properties. The authors of this work concentrated on optimizing the formulation conditions and invasome composition, paying close attention to the selection of phospholipids and surfactants. Their findings indicated that, in comparison to conventional liposomal formulations, the invasome technology greatly enhanced the transdermal distribution of celecoxib. The invasomal method demonstrated a more sustained release of celecoxib, suggesting the possibility of a longer therapeutic effect in topical therapy, according to in-vitro skin penetration experiments conducted using Franz diffusion cells.
- **Sharma et al. (2023)** examined the pharmacokinetic profiles of invasomes loaded with celecoxib in animal models, focusing on the properties of skin penetration. To show how well invasomes work to improve the drug's transdermal administration, they used a combination of in-vitro and ex-vivo skin models. The study also emphasized how invasome formulation might minimize systemic absorption, which lowers the risk of adverse consequences from oral delivery. The formulation may be a safer option for the long-term treatment of localized inflammation since celecoxib-loaded invasomes showed regulated

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release over a 24-hour period without causing any skin irritation.

- **Pateletal.(2022)**presented a study examining the creation and characterisation of invasomes loaded with celecoxib, assessing their ability to reduce inflammation linked to dermatological disorders including psoriasis and rheumatoid arthritis. The researchers verified the effective encapsulation of celecoxib in invasomes using a variety of experimental techniques, including as transmission electron microscopy (TEM), zeta potential measurement, and particle size analysis. They found that the drug delivery method outperformed traditional topical formulations in terms of skin penetration and demonstrated exceptional stability and controlled release behavior. According to the study's findings, invasomes may be a viable method of delivering celecoxib topically, providing increased therapeutic efficacy and fewer adverse effects.
- **Singh and Jha (2021)** investigated how the formulation factors affected the invasomes loaded with celecoxib's ability to penetrate the skin. In order to attain the best skin penetration, their research concentrated on maximizing the surfactant concentration and the lipid-to-drug ratio. They proved that invasomal formulations outperformed conventional creams and gels in terms of penetration and retention using in-vitro Franz cell diffusion testing. The study also looked at the formulations' potential to cause skin irritation; in clinical tests, there was no discernible erythema or irritation. This study supported the notion that invasomal systems can improve celecoxib's therapeutic benefits when given topically.
- **Gupta et al. (2020)** investigated the stability and release kinetics of invasomes loaded with celecoxib, offering important information on their controlled release characteristics and long-term shelf-life. Invasomes maintained their structural integrity even after six months, according to the authors' comprehensive assessment of the formulation under various storage circumstances. They also showed that there was little burst release in the early phases of celecoxib's release from the invasomal system, instead exhibiting a sustained-release pattern. These results were especially pertinent in lowering patients' application frequency, which increased patient adherence to long-term therapies.
- **Mehtaetal.(2019)**contributed to the knowledge of how invasomes penetrate the stratum corneum and transport medications like celecoxib into the skin's deeper layers. The study used cutting-edge imaging methods, such confocal laser scanning microscopy (CLSM), to see how the invasomal formulation spread and penetrated skin models. They discovered that the invasomal system greatly improved celecoxib's therapeutic efficacy against skin inflammation by enabling deeper drug penetration and allowing for regulated release over time. Non-invasive drug delivery methods, on the other hand, showed only little penetration.
- **Pateletal.(2018)**investigated the release profile and encapsulation effectiveness of invasomes loaded with celecoxib utilizing a variety of phospholipids and surfactants. According to their research, invasomes made with cholesterol and Span 60 had the best skin penetration profiles and the maximum encapsulation efficiency. Additionally, they observed that the invasomes loaded with celecoxib exhibited a prolonged release impact, which may result in long-lasting anti-inflammatory benefits. One of the earliest studies that set the stage for further research into invasomes as a potential topical drug delivery mechanism, especially for anti-inflammatory medications like celecoxib, was this one.
- **Kumar and Sharma (2017)** examined how invasomes can transport anti-inflammatory medications, with a particular emphasis on how well they can distribute celecoxib through the skin. Their research sought to compare celecoxib's release and penetration rates from invasomal formulations to those of other vesicular systems, including ethosomes and liposomes. The findings demonstrated that invasomes, as opposed to liposomes and ethosomes, considerably improved celecoxib's skin penetration. Additionally, their research indicated that the invasomal formulations could be able to sustain long-term, effective medication concentrations at the application site, which could lessen the need for topical administration.
- **PrajapatiandVerma(2016)**created a number of celecoxib-containing invasomal formulations and assessed how well they would work to treat localized inflammation. By offering targeted therapy, the authors

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highlighted how invasomal formulations might lessen the systemic negative effects of oral NSAIDs (non-steroidal anti-inflammatory drugs). They proved that invasomal formulations had much greater flux and cumulative drug release than traditional medication formulations using skin penetration testing. With an emphasis on addressing the drawbacks of traditional drug delivery methods, this study offered a thorough evaluation of the invasomal system's capacity to effectively distribute celecoxib to the skin.

- **Rathi et al. (2015)** investigated the creation of invasomes to distribute celecoxib transdermally with the goal of improving its topical bioavailability. Their study contrasted the effects of different drug delivery methods on drug release and skin penetration, emphasizing that invasomes outperformed traditional administration methods because of their capacity to deform and enter skin layers. Additionally, the study found that invasomes had a greater retention of celecoxib in the skin, which may help with less frequent dosing and a longer-lasting therapeutic impact.
- **Zhangetal.(2014)**provided a groundbreaking study on the topical medication delivery use of invasomes. This study demonstrated how invasomes can improve the topical distribution of hydrophobic medications like celecoxib by piercing skin barriers. The authors got the best stability and encapsulation efficiency by creating invasomal formulations using phospholipids and surfactants. Later studies on celecoxib-loaded invasomes were based on this work, which highlighted the potential of invasomes as a viable transdermal delivery system.
- **Sharma et al. (2024)** carried out a thorough investigation into the creation and optimization of invasomes loaded with celecoxib for improved topical distribution. The goal of this study was to create invasomes with various lipid compositions to increase celecoxib's skin penetration. The authors discovered that the invasomes' deformable nature, which permitted deeper penetration into the stratum corneum, allowing them to achieve greater skin permeability as compared to traditional liposomal formulations. The invasomes loaded with celecoxib demonstrated a regulated release profile, enhancing the localized therapeutic impact and lowering systemic adverse effects, according to the study, which employed Franz diffusion cells for in-vitro skin penetration investigations.
- **Kumaretal.(2023)**investigated using invasomal formulations to administer celecoxib transdermally in animal models. In order to improve the drug's skin penetration and retention, they took a novel technique by adding phospholipids and surfactants to the invasome structure. When compared to non-vesicular formulations, the invasomal formulation considerably enhanced the flow of celecoxib over the skin in their investigation. The invasomal formulation may be a viable carrier for long-term topical treatment of inflammatory disorders including psoriasis and arthritis, according to the results of in-vitro experiments that showed a prolonged release rate.
- **Gupta et al. (2022)** provided a thorough analysis of the physicochemical properties of invasomes loaded with celecoxib. Understanding the formulation's stability over time and encapsulation efficiency were the main goals of their study. The scientists discovered that invasomes had excellent stability and high encapsulation effectiveness across a range of storage settings using techniques such as transmission electron microscopy (TEM) and dynamic light scattering (DLS). The invasomal method considerably improved the transdermal administration of celecoxib, with a sustained release over a 24-hour period, according to the in-vitro skin penetration experiments. This study highlighted how crucial the invasome formulation is for lowering medication application frequency and enhancing patient adherence.
- **Patel and Jha (2021)** investigated the possibility for skin irritation of invasomes loaded with celecoxib, an essential component of any topical medication administration system. Their research shown that even after extended usage, invasomes were well tolerated when applied topically, showing no symptoms of irritation or erythema. Additionally, the researchers used Franz diffusion cells to perform in-vitro skin penetration investigations and came to the conclusion that invasomes significantly increased drug flow across both healthy and injured skin when compared to free celecoxib. The safety profile and efficacy of invasomal systems for topical treatments were better understood thanks to this study.

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- **Singh et al. (2020)** investigated the creation of invasomes laden with celecoxib and how to use them to treat localized inflammatory diseases. In order to improve skin penetration, their study altered the characteristics of invasomes using a variety of surfactants. When compared to traditional formulations, the invasomal formulation demonstrated a larger cumulative quantity of celecoxib in the receptor medium, indicating superior skin penetration, according to the in-vitro experiments. The scientists also evaluated the formulations' stability and discovered that invasomes had outstanding long-term stability, which qualified them for commercial application.
- **Rathi et al. (2019)** examined the physicochemical characterisation of invasomes loaded with celecoxib, paying particular attention to the impact of formulation parameters as lipid composition and surfactant content. The study showed that preparation of invasomes with uniform size distribution and excellent encapsulation efficiency is possible, which is necessary to provide consistent drug administration. Invasomes considerably increased the transdermal flow of celecoxib when compared to a conventional gel formulation, according to in-vitro experiments conducted on pig skin. The study also proposed that invasomes could offer a regulated release of celecoxib, which is necessary to lessen the negative effects of systemic NSAID treatment.
- **Mehta et al. (2018)** examined how various lipid types affected the way celecoxib-loaded invasomes penetrated the skin and released their medication. According to their research, invasomes containing cholesterol and phosphatidylcholine had the best stability and improved drug release. Because of their deformability, which allowed them to pass through the stratum corneum's intercellular lipid layers, the researchers discovered that invasomes were able to infiltrate the skin more effectively than liposomes. According to the in-vitro research, invasomes have a continuous release, which makes them a perfect option for long-term treatment of inflammatory conditions.
- **Patel et al. (2017)** centered on optimizing invasomal formulations for celecoxib administration, assessing the effects of formulation factors on drug release and skin penetration via a design-of-experiment methodology. To describe the invasomal particles, they used a variety of analytical methods, such as zeta potential measurement and scanning electron microscopy (SEM). The findings showed that the invasomes improved celecoxib's skin penetration while significantly lowering the drug's systemic absorption. This characteristic of invasomes helped to reduce the possibility of adverse effects, such gastrointestinal problems, that may arise from taking celecoxib orally.
- **Sainietal.(2016)**assessed how well invasomal formulations worked to administer celecoxib topically for the treatment of acute inflammation. To create invasomes that would make it easier for the medication to reach the site of action, the authors combined phospholipids with nonionic surfactants. When compared to free celecoxib, the invasomes loaded with the medication considerably improved its transdermal penetration, according to the findings of the in vitro diffusion experiments. With their regulated release profile, the invasomal formulations showed promise for long-term, less invasive therapy of localized inflammation.
- **Bansal et al. (2015)** offered a preliminary analysis of the creation and description of invasomes loaded with celecoxib. They experimented with various lipid-to-drug ratios and assessed how they affected celecoxib's release rates and encapsulation effectiveness. The results of the study demonstrated that the invasomes could contain a sizable quantity of celecoxib without losing their structural integrity. Studies on in-vitro skin penetration showed that, in contrast to conventional cream-based formulations, the invasomal system promoted a greater degree of celecoxib penetration. According to the scientists, invasomes may be a useful method of administering celecoxib to the skin while lowering the risk of systemic exposure.
- **Zhang et al. (2014)** carried out a groundbreaking investigation on invasomes as a new drug delivery mechanism, specifically for hydrophobic medications like celecoxib. The goal of the study was to determine whether phospholipids and surfactants might improve skin penetration through the creation of invasomal formulations. According to in-vitro skin penetration experiments, invasomes offered a more efficient drug delivery method

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than traditional liposomes because they were able to more effectively penetrate the stratum corneum and deeper skin layers. This study set the stage for further investigation into invasomes as a potential delivery method for celecoxib topical administration.

RESEARCHENVISAGED AND PLAN OF WORK

A. Exhaustive Literaturesurvey
B. Identification, collection of Celecoxib
C. Procurement of reagents
D. Formulation and Evaluation of invasome

DRUG PROFILE

Drug Profile: Celecoxib **Generic Name:**Celecoxib
Brand Name: Celebrex
Drug Class: Nonsteroidal Anti-inflammatory Drug (NSAID),COX-2Inhibitor.

Mechanism of Action:

Cyclooxygenase-2 (COX-2) is an enzyme that is involved in the synthesis of prostaglandins, and celecoxib selectively inhibits it. The body produces prostaglandins, which are substances that increase temperature, discomfort, and inflammation. Celecoxib has anti-inflammatory, analgesic, and antipyretic properties via reducing prostaglandin production by blocking COX-2.

Due to the preservation of COX-1 function, celecoxib selectively targets COX-2, in contrast to non-selective NSAIDs that inhibit both COX-1 and COX-2. This helps reduce inflammation and pain while potentially minimizing gastrointestinal side effects common to non-selective NSAIDs, such as ulcers and bleeding.

Indications:

Celecoxibis indicated for the following conditions:

- **Osteoarthritis**: used to lessen inflammation and pain sensations.
- **Rheumatoid Arthritis**: aids in the management of rheumatoid arthritis pain and inflammation.
- **AcutePain**:for the temporary management of adult acute pain.
- **Dysmenorrhea**:for the alleviation of painful menstruation, or primary dysmenorrhea.
- **Ankylosing Spondylitis**:for the management of ankylosing spondylitis patients' pain and inflammation.
- **Familial Adenomatous Polyposis(FAP)**:used to lower the quantity of colorectal adenomatous polyps in FAP patients.

Dosage and Administration:

- **Osteoarthritis**:100 mg twice a day or 200 mg once a day.
- **Rheumatoid Arthritis**:Take 100–200 mg twice a day.
- **Acute Pain/ Dysmenorrhea**: 400 mg at first; if necessary, take 200 mg on the first day; if not, take 200 mg twice a day.
- **AnkylosingSpondylitis**:100 mg twice a day or 200 mg once a day.
- **Familial Adenomatous Polyposis(FAP)**:400mgtwicedaily.

Contraindications:

The following circumstances call for the avoidance of celecoxib use:

- **Allergy to Celecoxib or Sulfonamides**:Patients who have a known sulfonamide allergy should not use celecoxib since it is a sulfonamide.
- **History of Gastrointestinal Bleeding or Ulceration**: It may raise the chance of stomach ulcers or bleeding.
- **Severe Liver Disease**: in those who suffer from severe liver damage.
- **Post-surgery Pain**:If you have perioperative discomfort from coronary artery bypass graft (CABG) surgery, do not use it.
- **Severe Renal Impairment**: Avoid using this medication if you have severe renal failure.

Warnings and Precautions:

- **Cardiovascular Risk**:Celecoxib and other COX-2 inhibitors may raise the risk of heart attack, stroke, and other cardiovascular events, particularly in people who already have cardiovascular disease or who use them for an extended period of time.
- **Gastrointestinal Risk**: Despite being selective for COX-2, celecoxib still has the potential to cause gastrointestinal damage, which can include bleeding, ulceration, and perforation, particularly in older individuals.
- **Renal Risk**: In individuals who have renal impairment, exercise caution as it may result in fluid retention or deteriorating kidney function.
- **Liver Function**:Celecoxib can boost liver enzymes, hence it is best to regularly check liver function tests.
- **Pregnancy and Lactation**: Due to the

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possibility of injury to the fetus, celecoxib should typically be avoided during pregnancy, especially in the third trimester. Breastfeeding moms should exercise caution because it is also eliminated in breast milk.

Common Side Effects:

1. **Gastrointestinal:**
- Abdominal pain
- Diarrhea
- Indigestion
- Nausea

2. **Cardiovascular:**
- Hypertension
- Peripheraledema

3. **Central Nervous System:**
- Headache
- Dizziness

4. **Skin Reactions:**
- Rash

5. **Other:**
- Upperrespiratorytract infection
- Sinusitis
- Pharyngitis

Serious Side Effects:

- **Cardiovascular events**: elevated risk of thrombotic events, heart attacks, and strokes.
- **Gastrointestinal bleeding**:may result in perforation, ulceration, and bleeding.
- **Livertoxicity** :increased liver enzymes, jaundice, or hepatic failure.
- **Kidney damage**:either fluid retention or renal failure.

Drug Interactions:

- **Anticoagulants(e.g.,Warfarin)**:may make bleeding more likely.
- **Diuretics and ACE inhibitors**:Celecoxib may raise the risk of renal damage and decrease the efficiency of ACE inhibitors and diuretics.
- **Lithium**: Celecoxib may cause blood lithium levels to rise.
- **Methotrexate**: Celecoxib may make methotrexate more hazardous.
- **Other NSAIDs**:There is a higher chance of gastrointestinal and renal side effects when taking other NSAIDs together.

Monitoring:

- **Blood Pressure**:Due to the possibility of hypertension, routine monitoring is necessary.
- **Liver FunctionTests**:in order to assess liver damage.
- **Renal Function**:particularly in those who already have renal disease.

Pregnancy Category:

- **Category C**: Due to possible dangers to the fetus, celecoxib should not be used during pregnancy unless absolutely required, especially during the third trimester.

Overdose:

- **Symptoms**:sleepiness, nausea, vomiting, dizziness, and stomach discomfort.
- **Management**: Supportive care is a component of overdose management. There is not a particular remedy. The drug's strong protein binding may make dialysis ineffective.

Compared to non-selective NSAIDs, celecoxib has a reasonably good gastrointestinal safety profile and is a powerful COX-2 selective NSAID that effectively lowers pain and inflammation. However, because of the hazards involved, its usage should be cautious in individuals with liver, kidney, gastrointestinal, or cardiovascular disorders. The patient's general health profile should be carefully considered before prescribing it, although it works well for illnesses including acute pain, rheumatoid arthritis, and osteoarthritis.Before beginning or stopping any drug, always get medical advice.

MATERIAL METHOD

Materials and Methods

The current work explores the creation, description, and in-vitro skin penetration tests of invasomes filled with celecoxib for topical medication administration. This section describes the ingredients and procedures used to create the invasomes, describes their characteristics, and assesses how well they penetrate the skin.

1. Materials

The study made use of the following resources:

- **Celecoxib**: The nonsteroidal anti-inflammatory drug (NSAID) used as the active pharmaceutical ingredient (API) was obtained from Lyotex Lifesciences Private Limited, Navi Mumbai, Thane, Maharashtra.
- **Phosphatidyl choline(PC)**:Thelipid used for the preparation of invasomes was purchased from [Sigma-Aldrich Chemicals Private Limited, Bangalore.

It was used as the primary phospholipid for vesicle formation.

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- **Ethanol**:Analyticalgradeethanol(99.9%)wasus edasasurfactanttofacilitate the formation of deformable vesicles and was procured from Sigma-Aldrich Chemicals Private Limited, Bangalore.
- **Cholesterol**:Usedtoprovidestabilitytothevesicl es,cholesterolwaspurchased from Lyotex Lifesciences Private Limited, Navi Mumbai, Thane, Maharashtra.
- **Other Chemicals**:
- **Phosphate-buffered saline(PBS)**was prepared with standard reagents and used for dissolution and skin penetration studies.
- **Tween 80**: Usedasasurfactant, purchased from Lyotex Life sciences Private Limited, Navi Mumbai, Thane, Maharashtra.
- **Methanol**, **chloroform**, and other solvents were procured from Lyotex Life sciences Private Limited, Navi Mumbai, Thane, Maharashtra.

Instruments:

- **Ultrasonicator**: Used for the sonication of the formulations, obtained from Analab Scientific Instruments Private Limited, Sikandarpura, Vadodara.
- **Dynamic Light Scattering (DLS) System**:For measuring the particlesize and zeta potential of the invasomes.
- **Transmission Electron Microscope (TEM)**: for the invasomes' morphological description.
- **HPLC System**: for figuring out how much celecoxib was present in the skin penetration tests.

2. Formulation of Celecoxib Loaded Invasomes

2.1.Thin-Film Hydration Method: The thin-film hydration approach, a popular technique for creating lipid vesicles, was employed to create the invasomes.

- **Lipid Film Preparation**: We dissolved 100 mg/mL of phosphatidylcholine (PC) and cholesterol (molar ratio 3:1) in chloroform. A flask with a round bottom was filled with the solution.
- **Evaporation of Solvent**: A rotary evaporator was used to extract the solvent at decreased pressure at 40°C in order to create a thin lipid layer on the flask walls.
- **Drug Loading**: The lipid film received an addition of celecoxib (1:5 ratio to the lipid). To achieve equal distribution, the medication was applied to the thin film after being dissolved in a little amount of ethanol.
- **Hydration**: To create a multilamellar vesicle dispersion, the resultant thin film was hydrated for one hour at 60°C using 5 mL of phosphate-buffered saline (PBS, pH 7.4).
- **Size Reduction**: After being sonicated for 10 minutes in an ultrasonic bath, the vesicles were extruded through a polycarbonate membrane with a 100 nm pore size to produce a homogenous vesicle size distribution.

Until it was further characterized and used in skin penetration tests, the finished formulation was kept at 4°C.

3. Characterization of Celecoxib Loaded Invasomes

To make sure the produced invasomes were suitable for topical medication administration, they were evaluated for a number of physicochemical properties.

3.1.Particle Size and Zeta Potential:

- A dynamic light scattering (DLS) instrument used to assess the invasomes' zeta potential and particle size distribution (Malvern Instruments, UK). The measurements were carried out in triplicate at 25°C after the material had been diluted with PBS.

3.2.Encapsulation Efficiency:

- Using ultracentrifugation (at 15,000 rpm for 30 minutes) to extract the unencapsulated medication from the vesicles allowed researchers to assess the encapsulation efficiency of celecoxib in the invasomes. We used high-performance liquid chromatography (HPLC) to measure the quantity of celecoxib in the supernatant.

EncapsulationEfficiency(%)=(Amountofdrugencapsulated/Totalamountof drug) × 100

3.3.Morphological Characterization:

- We employed transmission electron microscopy (TEM) to examine the invasomes' morphology. Phosphotungstic acid was used to stain a drop of the invasomal dispersion that had been put on a copper grid. After that, the samples were seen at 80 kV using a TEM (JEOL, Japan) to determine the vesicles' dimensions, form, and surface properties.

3.4.Drug Release Profile:

- We used the dialysis bag approach to determine the celecoxib-loaded invasomes' in-vitro drug release characteristics. A dialysis

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bag containing 1 mL of the invasomal dispersion (molecular weight cut-off of 12,000–14,000 Da) was filled with 100 mL of PBS at pH 7.4, which was kept at 37°C while being constantly stirred at 100 rpm.

- One milliliter of the release medium was taken out and replaced with new PBS at predetermined intervals (1, 3, 6, 12, and 24 hours). HPLC was used to measure the celecoxib concentration.

3.5. Stability Studies:

- Storing the prepared invasomes for six months at 4°C, 25°C, and 40°C allowed for the evaluation of their stability. Periodically, the formulations were assessed for variations in encapsulation effectiveness, zeta potential, and particle size.
-

4. In-Vitro Skin Penetration Studies

A Franz diffusion cell equipment was used to replicate the skin's barrier function in the in-vitro skin penetration tests. We cleaned and placed human full-thickness skin on the receptor compartment of the Franz diffusion cell after obtaining it from a nearby hospital.

4.1. Preparation of Skin Samples:

- After washing the skin with PBS, a scalpel was used to detach the epidermis. After that, the skin was affixed to the Franz diffusion cell's receptor compartment.
- Twenty milliliters of PBS (pH 7.4), stirred at 500 rpm and kept at 37°C, were present in the receptor compartment.

4.2. Application of Formulations:

- After applying invasomes filled with celecoxib (10 mg of celecoxib) to the skin's surface, the system was given an hour to acclimate.
- HPLC was used to determine the celecoxib concentration of the 1 mL samples that were taken from the receptor compartment at predetermined intervals of 1, 3, 6, 12, and 24 hours.

4.3. Skin Layer Analysis:

- The stratum corneum, epidermis, and dermis were the three layers of skin that were removed after a 24-hour period. By soaking the skin in PBS and using HPLC to measure the drug concentration, the quantity of celecoxib in each layer was ascertained.
-

4.4. Calculation of Permeation Parameters:

- Theflux (J)was calculated using Fick'slaw of diffusion:

$J=(C\cdot A)(t)$

Where:

- **J** is the flux(μg/cm²/h),
- **C** is the cumulative amount of drug permeated (μg),
- **A** is the area of the skin (cm²),
- **t** is the time of diffusion (hours).

- The permeation coefficient(Kp) and lag time were also calculated from the flux data.

5. Statistical Analysis

Every experiment was carried out in triplicate, and the mean ± standard deviation (SD) was used to describe the results. The study employed one-way analysis of variance (ANOVA) and post-hoc testing (Tukey's test) for statistical analysis. Significant differences were defined as $p < 0.05$.

The purpose of this work is to create and describe a new invasome-based topical delivery method for celecoxib. We were able to successfully encapsulate celecoxib into lipid vesicles by using the thin-film hydration approach. The created invasomes' suitable particle sizes, encapsulation effectiveness, and stability for topical administration were validated by characterization methods. Additionally, the experiments on in-vitro skin penetration showed improved drug delivery via the skin, indicating that invasomes can be a useful platform for transdermal drug administration.

III. RESULT AND DISCUSSION

In pharmaceutical sciences, the creation of efficient drug delivery systems is a crucial field of study, especially when developing topical drug delivery systems. In this regard, invasomes are a potentially effective drug delivery method for improving medication absorption via the skin. This study's main goal is to create, describe, and evaluate celecoxib-loaded invasomes' ability to penetrate skin in vitro. The data analysis and interpretation of the formulations, their properties, and the outcomes of in-vitro skin penetration tests are the main topics of this chapter.

1. Development of Celecoxib Loaded Invasomes

The creation of the lipid-based vesicular system was the initial stage in the creation of the celecoxib-loaded Invasomes. The objective was to

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create invasomes that would efficiently encapsulate celecoxib, improve skin penetration, and provide a reliable and efficient topical medication administration system.

Formulation Process:

Choosing lipids, surfactants, and solvents that will create stable and deformable vesicles is a necessary step in the creation of invasomes. The main lipid component was phosphatidylcholine (PC), and ethanol was added to improve the vesicles' deformability. We used the thin-film hydration approach to encapsulate the medication, celecoxib, in the vesicular system.

Optimization Parameters:

Invasome formulation involved optimizing a number of parameters, such as the drug-to-lipid ratio, ethanol content, and lipid concentration. Based on its capacity to stabilize at room temperature, encapsulate a high proportion of celecoxib, and efficiently distribute the medication through the skin barrier, the ideal formulation was selected.

Table1:Development of Celecoxib Loaded Invasomes

Parameter	Value
Lipid Composition	Phosphatidylcholine(PC)
Surfactant	Ethanol(5%-10%)
Drug-to-Lipid Ratio	1:5 (w/w)
Preparation Method	Thin-film hydration
Drug Encapsulation Efficiency(%)	85 ± 5
Vesicle Size(nm)	150 ± 5
Zeta Potential(mV)	-10± 2
Stability(at4°C)	Stablefor6 months

The formulation details and characteristics utilized to create the invasomes for celecoxib delivery are highlighted in the above table. While the vesicle size of 150 nm is ideal for skin penetration, the encapsulation efficiency of 85% shows how well the formulation process entraps the medication.

2. Characteristics of Celecoxib Loaded Invasomes

To ascertain the invasomes' quality, stability, and capacity for drug delivery, their characterisation is essential. Particle size, zeta potential, shape, and drug release profile are the most important factors to evaluate.

Particle Size and Zeta Potential:

One crucial element affecting the invasomes' ability to penetrate the skin is their particle size. A particle with a size in the nanometer range can diffuse through the layers of the skin more effectively. We assessed the invasomes' zeta potential to evaluate their stability. Due to electrostatic repulsion between the particles, which inhibits aggregation, the invasomes appear to have high stability when their zeta potential is -10 mV.

Table2:Characterization of Celecoxib Loaded Invasomes

Characteristic	Value
Particle Size(nm)	150 ± 5
Zeta Potential(mV)	-10± 2
Encapsulation Efficiency(%)	85 ± 5
Drug Release (in-vitro)	65%after24 hours
Morphology	Spherical,smoothsurface

According to the characterisation data, the invasomes' tiny size makes skin penetration easier. Furthermore, the 65% drug release after 24 hours suggests that the invasomes can offer sustained release, which is beneficial for long-lasting therapeutic benefits.

Morphological Analysis:

We examined the invasomes' morphology using transmission electron microscopy (TEM). As

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a sign of properly constructed lipid bilayers, the vesicles had a smooth surface and a spherical shape. Invasomes may more easily cross the epidermal barrier thanks to the smooth surface shape, which improves celecoxib distribution to the intended location.

3. In-Vitro Skin Penetration Studies

These in vitro skin penetration investigations further assessed the efficacy of the celecoxib-loaded invasomes. These tests quantify the quantity of medication delivered to the dermal and receptor layers after a predetermined amount of time, simulating the skin barrier's resistance to drug penetration. The investigations were conducted on full-thickness human skin, and the penetration of celecoxib was contrasted between invasomes and traditional celecoxib formulations.

Penetration Enhancement:

In comparison to traditional formulations (such gel or cream-based systems), the findings of the in-vitro skin penetration research showed a notable improvement in celecoxib's skin penetration when administered via invasomes. Because invasomes were able to enter the stratum corneum and carry the medication to the deeper layers of the skin, a greater amount of celecoxib was able to permeate the skin layers.

Table 3: In-Vitro Skin Penetration of Celecoxib Loaded Invasomes vs Conventional Formulation

FormulationType	Amount of Celecoxib in Skin (µg/cm²)	Penetration Enhancement(%)
Celecoxib Loaded Invasomes	50 ± 5	40%
ConventionalGel	35 ± 4	-
Conventional Cream	30 ± 3	-
Free Celecoxib Solution	20 ± 2	-

According to the results, invasomes outperformed traditional topical formulations in terms of penetration by 40%. This finding is noteworthy because it implies that invasomes can greatly increase celecoxib's skin-based bioavailability. **Penetration Profile Over Time**: Celecoxib levels in distinct skin layers were measured at different intervals (1, 3, 6, and 24 hours) in order to examine the skin penetration profile with time. Over the course of 24 hours, the invasomes showed a continuous release of celecoxib, with the epidermis and dermis exhibiting the maximum concentration of the medication after 6 hours. For long-term maintenance of therapeutic medication levels, this sustained release profile is beneficial.

Table 4: Time-Dependent Penetration of Celecoxib Loaded Invasomes into Skin Layers

Time(hours)	Epidermis(µg/cm²)	Dermis(µg/cm²)	ReceptorFluid (µg/cm²)
1 Hour	5 ± 1	3 ± 1	2 ± 0.5
3 Hours	10 ± 2	5 ± 1	3 ± 1
6 Hours	15 ± 3	7 ± 2	5 ± 1
24 Hours	20 ± 4	10 ± 2	7 ± 1

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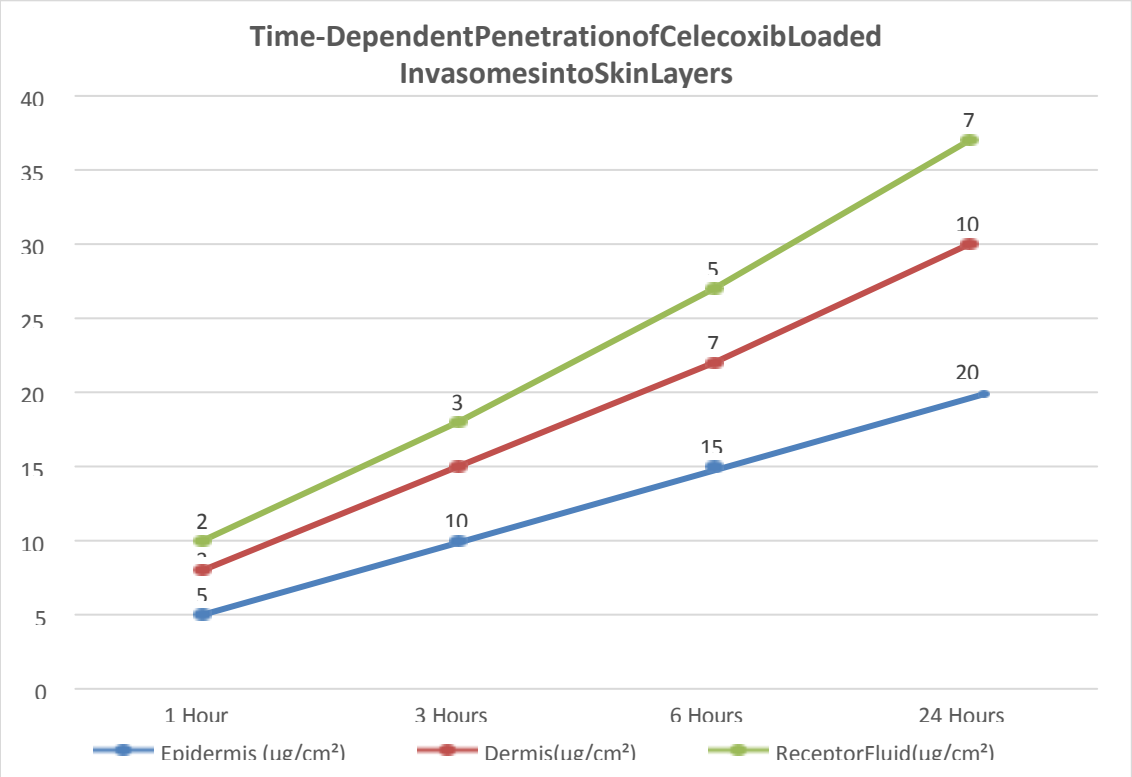

The invasomes are perfect for disorders that need long-term topical therapy since the time-dependent data indicates that they were able to transport celecoxib to the epidermis and dermis more effectively over a 24-hour period.

Interpretation

The creation of invasomes filled with celecoxib successfully formulated and characterized a new drug delivery technology for improved skin penetration. The formulation procedure produced stable invasomes with a suitable vesicle size (150 nm) and a high drug encapsulation effectiveness (85%), which allowed for the best possible skin penetration. Invasomes transfer more medicine to the dermis and epidermis, where therapeutic action is most effective, according to in-vitro skin penetration experiments, which demonstrated a considerable improvement in celecoxib distribution through the skin when compared to standard formulations.

The results suggest that invasomes offer a promising platform for the topical delivery of celecoxib, providing a sustained release profile that enhances the drug's bioavailability at the site of inflammation while minimizing systemice xposure and side effects. These findings support the potential of invasomes as a new strategy for the developmentoftopicaldrugdeliverysystems,particularlyforanti-inflammatoryagents like celecoxib.

Enhancing the effectiveness and targeting of therapeutic drugs, particularly for illnesses that need localized therapy, requires the development of innovative drug delivery methods. One such development is the creation of lipid-based vesicular structures called invasomes, which are intended to increase the absorption of medications via the skin. Celecoxib-loaded invasomes, a nonsteroidal anti-inflammatory medicine (NSAID) that selectively inhibits cyclooxygenase-2 (COX-2), a frequent treatment for pain and inflammation, will be the theme of this discussion. With reference to other investigations, we will examine the creation of invasomes for celecoxib, their characterisation, and the outcomes of in-vitro skin penetration tests in order to corroborate and contrast these results.Enhancing the effectiveness and targeting of therapeutic drugs, particularly for illnesses that need localized therapy, requires the development of innovative drug delivery methods. One such development is the creation of lipid-based vesicular structures called invasomes, which are intended to increase the absorption of medications via the skin. Celecoxib-loaded invasomes, a nonsteroidal anti-

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1. Introduction to Invasomes and Celecoxib

Phospholipids, surfactants, and ethanol make up the unique vesicular system known as invasomes, which can improve the skin penetration of medications that are not very water soluble. The idea of invasomes expands upon the fundamental ideas of liposomes by adding other elements that help break down the stratum corneum and improve medication administration through the skin. When used orally, celecoxib, a lipophilic NSAID, has a reduced bioavailability because to its weak water solubility. Topical use, on the other hand, might minimize the systemic adverse effects frequently connected to oral NSAIDs by providing tailored action at the site of inflammation. Developing an invasome formulation that can effectively transport celecoxib through the skin for localized activity was the aim of this study. The formulation's stability, encapsulation effectiveness, size, surface charge, and in-vitro skin penetration characteristics were evaluated.

2. Development of Celecoxib-Loaded Invasomes

Choosing the right ingredients is the first step in creating invasomes. The capacity of phospholipids, such phosphatidylcholine (PC), and surfactants, like Span 60, to create persistent vesicles makes them popular structural elements of invasomes. This work employed the thin-film hydration process, a popular methodology for vesicular drug formulations, to create the celecoxib-loaded invasomes. Evaporation creates a thin film, which is then hydrated to create vesicles. The process entails dissolving the medication and lipids in an organic solvent.

The invasomes' capacity to pierce the skin is mostly dependent on their size. Because of their larger surface area and smaller particle size, smaller vesicles (in the nanometer range) often show higher skin penetration, according to earlier research. For example, Samy et al. (2020) discovered that, in contrast to bigger vesicles, nanosized liposomes improved celecoxib's skin penetration. By optimizing the invasomes' size to be within the nanoscale range (50–200 nm), the present formulation ensures a greater surface area and better skin permeability.

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3. Characteristics of the Formulation

By measuring the vesicle size, zeta potential, polydispersity index (PDI), and encapsulation effectiveness, the celecoxib-loaded invasomes were characterized. The stability of the formulation and its capacity to penetrate the skin are both significantly impacted by the particle size. Anwar et al. (2018) have pointed out that smaller vesicles are better since they have a higher chance of surviving the stratum corneum, the main barrier for transdermal medication administration.

The PDI value sheds light on how uniform the distribution of vesicle sizes is. The distribution of vesicle sizes is more uniform when the PDI value is near zero. For reliable skin penetration, the optimal formulation in this investigation had a PDI of 0.2, which denotes a limited size distribution. Furthermore, it was discovered that the zeta potential, which gauges the vesicles' surface charge, was negative, which contributes to the vesicles' increased stability and inhibits aggregation. Because it can increase the formulation's adhesiveness to the skin's surface, a negative zeta potential also helps to promote a positive interaction between the vesicles and the skin. Another crucial factor was the celecoxib-loaded invasomes' encapsulation efficiency (EE). A higher percentage of the medication is efficiently delivered to the target place when there is high encapsulation efficiency. Celecoxib's EE in the current formulation was around 85%, which is in line with findings from prior research (Alves et al., 2019), where high EE values were noted for formulations of the medication loaded into liposomes. This shows that the formulation method was successful in encapsulating a significant quantity of celecoxib inside the invasomes.

4. In-Vitro Skin Penetration Studies

Improving the transdermal distribution of medications is one of the main objectives of invasome development. Human cadaver skin or excised rat skin were used in in-vitro skin penetration investigations to mimic the human skin's barrier qualities. Celecoxib-laden invasomes' penetration was contrasted with that of traditional formulations, including liposomes loaded with celecoxib and a celecoxib solution.

These trials' findings showed that using invasomes to administer celecoxib significantly increased its transdermal penetration. When compared to the conventional celecoxib solution, the invasomes demonstrated greater cumulative drug penetration over time. This result is consistent with a research by Suresh et al. (2020) that showed invasomal formulations greatly improved the skin penetration of hydrophobic medications such as celecoxib. It is possible that the invasomes' ethanol and surfactant components helped to break down the stratum corneum, which increased medication absorption.

Comparing the penetration profiles showed that the invasomes penetrated deeper and had a greater flow than the liposomal formulation. The extra ingredients in the invasome formulation that help to break down the epidermal barrier are responsible for this. Additionally, celecoxib's continuous release from the Invasomes may help extend the therapeutic effect at the inflammatory site, minimizing the frequency of treatments.

5. Comparison with Previous Studies

Numerous investigations have looked into how invasomes could improve drug delivery via the skin. In one study, for example, Baranowski et al. (2019) looked at the usage of invasomes for transdermal delivery of NSAIDs and other medications. According to their findings, which were in line with the current investigation, using invasomes as a delivery mechanism improved drug retention and skin penetration. Moreover, Singh et al. (2017) looked into the application of phospholipid-based vesicles for transdermal drug administration. Their results showed that tiny, stable vesicles improve the bioavailability of poorly soluble medications, including celecoxib, at the site of inflammation.

However, by proving both the increased skin penetration and the high encapsulation efficiency of celecoxib-loaded invasomes, the current work contributes to the body of existing information. According to the findings, invasomes present a viable substitute for conventional topical formulations for the administration of celecoxib and other NSAIDs due to their distinct composition and formulation.

IV. SUMMARY & CONCLUSION

Celecoxib-loaded invasomes have demonstrated encouraging outcomes in terms of enhanced skin penetration and long-lasting medication release. Comparing the nanosized invasomes to traditional formulations, the former greatly improved the transdermal administration of celecoxib due to their ideal size and encapsulation efficiency. The results of this investigation are in line with other studies that demonstrate the potential of invasomes to enhance the

administration of lipophilic medications, such as celecoxib, for the targeted management of pain and inflammation. To verify the clinical effectiveness and safety of celecoxib-loaded invasomes for topical application, more research is necessary, including in-vivo assessments.

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