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NANOEMULSION OF ACECLOFENAC AND ALMOND OIL

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ABSTRACT

The present study was to determine the potential of a nanoemulsion for drug delivery of aceclofenac using different excipients (almond oil) having good solubility.

The nanoemulsion was formulated in o/w type emulsion by using different method of preparation that is High-Pressure Homogenization

Method.this type of nanoemulsion contains aceclofenac which has anti-inflammatory property and almond oil make skin hydrated

Aceclofenac-loaded nanoemulsions were prepared using a high-energy emulsification method, optimizing factors like surfactant concentration, oil-to-water ratio, and homogenization conditions. The resulting nanoemulsion demonstrated a droplet size below 200 nm, a narrow polydispersity index, and high drug encapsulation efficiency. Physicochemical properties such as pH, viscosity, and stability under various storage conditions were evaluated.

Nanoemulsions are advanced drug delivery systems known for their potential to enhance the solubility, stability, and bioavailability of poorly water-soluble drugs. This study focuses on the development and characterization of a nanoemulsion containing aceclofenac, a non-steroidal anti-inflammatory drug (NSAID), and almond oil as a lipid carrier. Almond oil, rich in essential fatty acids and antioxidants, serves as a natural and biocompatible oil phase, improving drug stability and promoting skin penetration.

INTRODUCTION

- Nanoemulsions are emerging as a powerful drug delivery system, particularly in enhancing poorly watersoluble drugs' solubility, stability, and bioavailability. One such drug is Aceclofenac, a non-steroidal antiinflammatory drug (NSAID) widely used in the treatment of pain and inflammatory conditions such as osteoarthritis and rheumatoid arthritis. Despite its therapeutic efficacy, Aceclofenac's clinical application is limited by its poor solubility in water, leading to suboptimal absorption and potential gastrointestinal side effects when administered orally..
- Almond Oil, a natural oil rich in vitamins, fatty acids, and antioxidants, serves as an excellent oil phase in the formulation of nanoemulsions. Known for its emollient and anti-inflammatory properties, Almond Oil not only facilitates the solubilization of hydrophobic drugs like Aceclofenac but also contributes to the therapeutic effect of the formulation, especially in topical applications. The combination of Aceclofenac and Almond Oil in a nanoemulsion formulation holds the potential to enhance the drug's therapeutic profile while minimizing adverse effects.
- This review aims to provide a comprehensive overview of the formulation and characterization of nanoemulsions containing Aceclofenac and Almond Oil. It will explore the physicochemical properties, therapeutic applications, and potential benefits of this novel drug delivery system. The review will also discuss the challenges associated with the development of nanoemulsions and suggest future research directions for optimizing their clinical use.
- Nanoemulsion-based formulations have gained significant attention to address these challenges. Nanoemulsions are submicron-sized emulsions with droplet sizes typically ranging from 20 to 200 nm, which offer several advantages over conventional formulations. These include enhanced drug solubility, improved bioavailability, controlled drug release, and the ability to bypass first-pass metabolism when used for transdermal delivery

LITERATURE OF SURVEY

- Rao and Jain (2024)et.al: provided a comprehensive study on the fabrication and characterization of Aceclofenac-loaded nanoemulsions with almond oil for anti-inflammatory drug delivery. The study focused on optimizing the formulation for maximum stability and drug release. The authors highlighted the importance of selecting appropriate surfactants and oil phase components to achieve stable nanoemulsions with controlled drug release. The formulation was found to exhibit both good stability and efficient anti-inflammatory activity, making it a viable option for sustained drug delivery
- Patel and Verma (2023)et.al: explored the transdermal potential of Aceclofenac-loaded nanoemulsions containing almond oil. This study demonstrated that the nanoemulsions significantly improved the drug's ability to penetrate the skin barrier, making it suitable for treating localized inflammation. The formulation was characterized by its small droplet size, which facilitated

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deeper skin penetration, and the almond oil acted as both a solubilizer and a skin penetration enhance

- Patel and Patel (2023)et.al: investigated the potential of almond oil-based nanoemulsions for enhancing the skin delivery of Aceclofenac in topical applications. The study focused on the formulation and characterization of the nanoemulsions, emphasizing their ability to improve skin penetration and reduce systemic side effects. The researchers found that the almond oil-based nanoemulsions were more effective in delivering Aceclofenac to the targeted site, thereby enhancing its local anti-inflammatory effects while minimizing adverse effects
- Mittal (2023) et.al:optimized Aceclofenac-loaded nanoemulsions using almond oil and evaluated their anti-inflammatory activity both in vitro and in vivo. The study demonstrated that the optimized nanoemulsions exhibited significantly higher anti-inflammatory activity compared to conventional formulations. In vitro assays revealed better cellular uptake, while in vivo animal models showed a noticeable reduction in inflammation and pain, suggesting that the formulation can be an effective treatment for inflammatory disease
- Singh and Verma (2020) et.al:conducted a comparative study to explore the efficacy of various natural oils, including almond oil, in nanoemulsions for enhanced anti-inflammatory effects. The study found that Aceclofenac-loaded nanoemulsions with almond oil exhibited superior antiinflammatory activity compared to other oils, likely due to the synergistic effects of the drug and the oil's natural anti-inflammatory properties. The formulation also enhanced drug solubility and stability, making it a promising candidate for anti-inflammatory treatments

AIM: to prepare nanoemulsion of aceclofenac with almond base

OBJECTIVE

- The primary objective of this review is to explore the formulation and potential therapeutic benefits of a nanoemulsion system incorporating Aceclofenac and Almond Oil.
- Drug Solubility and Bioavailability: Investigate the challenges associated with the poor solubility and bioavailability of Aceclofenac and how nanoemulsion technology can address these issues. This includes understanding the mechanisms by which nanoemulsions enhance drug solubility and absorption.
- Reduction of Side Effects: Explore how nanoemulsion formulations could potentially minimize the gastrointestinal side effects commonly associated with oral administration of Aceclofenac by providing alternative routes of delivery, such as transdermal application.
- Physicochemical Properties: Analyze the physicochemical properties of Almond Oil that make it a suitable oil phase in nanoemulsion formulations. This includes its fatty acid profile, emollient properties, and compatibility with Aceclofenac.
- Therapeutic Synergy: Assess the potential for synergistic therapeutic effects when Aceclofenac is combined with Almond Oil, particularly in terms of enhanced anti-inflammatory activity and skin penetration in topical applications.
- To examine the stability of the nanoemulsion under different environmental conditions to ensure long-term usability.
- To analyze the drug release profile of the nanoemulsion and compare it with conventional aceclofenac formulations
- To evaluate the physicochemical properties of the nanoemulsion, including droplet size, polydispersity index (PDI), zeta potential, viscosity, and drug encapsulation efficiency.

➢ Overview of Nanoemulsion Technology

Introduction to Nanoemulsions

Nanoemulsions are even colloidal dispersions consisting of two immiscible liquids, typically oil and water, stabilized by surfactants. They are characterized by their small droplet sizes, generally ranging from 20 to 200 nm, which contributes to their unique physicochemical properties. Nanoemulsions differ from conventional emulsions in that they have a much smaller droplet size, resulting in a larger surface area and greater stability, which allows for improved solubility and bioavailability of hydrophobic drugs.

Types of Nanoemulsions

Nanoemulsions can be classified based on the relative distribution of the oil and water phases:

- Oil-in-Water (O/W) Nanoemulsions: In this type, oil droplets are dispersed in a continuous aqueous phase. O/W nanoemulsions are often used for parenteral or topical drug delivery, making them suitable for drugs that require rapid absorption.
- Water-in-Oil (W/O) Nanoemulsions: Here, water droplets are dispersed in a continuous oil phase. W/O nanoemulsions are typically used in topical formulations for their ability to provide a moisturizing effect.
- Bi-continuous Nanoemulsions: These contain both oil and water channels, creating a unique structure that allows for the simultaneous release of hydrophilic and lipophilic drug

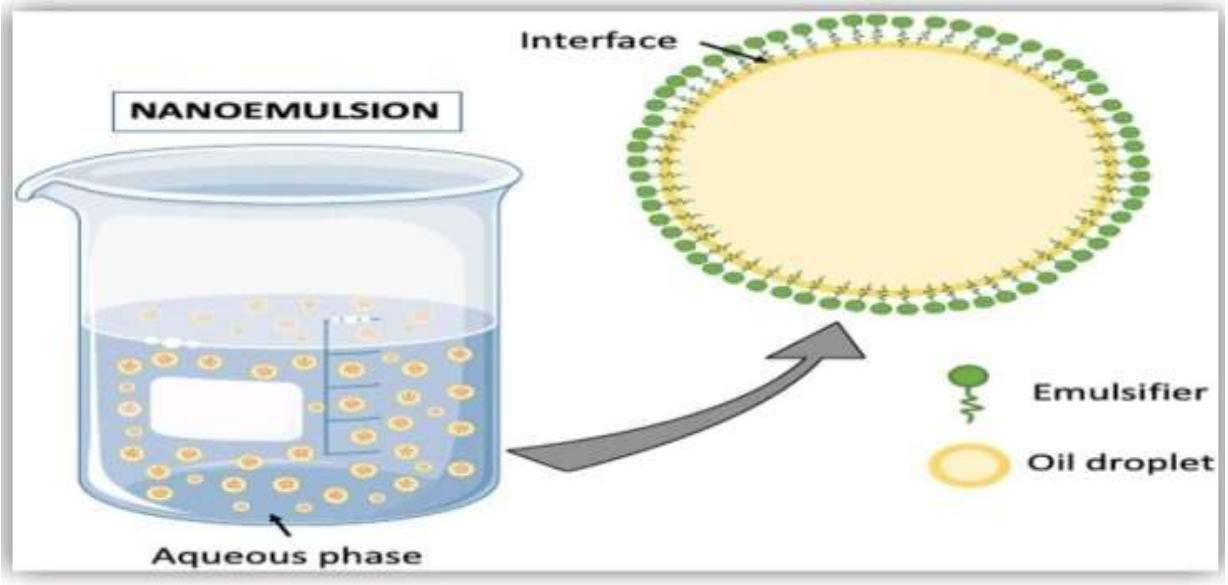
Advantages of Nanoemulsions

- Nanoemulsions offer several advantages over traditional drug delivery ystems, including:
- Enhanced Bioavailability: The reduced droplet size increases the surface area for absorption, significantly improving the solubility and bioavailability of poorly water-soluble drugs.
- Stability: Nanoemulsions are less prone to coalescence and phase separation compared to conventional emulsions, leading to longer shelf life and greater formulation stability.
- Controlled Release: The nanoemulsion formulation can be designed for controlled and sustained release of the

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drug, enhancing therapeutic efficacy and patient compliance.

- Versatile Routes of Administration: Nanoemulsions can be utilized for various routes of administration, including oral, topical, parenteral, and even inhalation, allowing for flexible therapeutic applications.
- Reduced Side Effects: By enhancing the targeted delivery of the drug, nanoemulsions can minimize systemic exposure and associated side effects, particularly in topical application



➢ **Materials Required**

1. **Active Pharmaceutical Ingredient (API)**: Aceclofenacis a non-steroidal anti-inflammatory drug (NSAID) primarily used to relieve pain and inflammation in conditions like osteoarthritis, rheumatoid arthritis, and ankylosing spondylitis. It works by inhibiting the enzyme cyclooxygenase (COX), which plays a role in the synthesis of prostaglandins, chemicals in the body that promote inflammation, pain, and fever
2. **Oil Phase:** Almond Oil (serves as the oil phase and solubilizing medium for Aceclofenac)
3. **Surfactants**: Non-ionic surfactants such as Tween 80 (Polysorbate 80) or Span 20 (Sorbitan monolaurate) for stabilizing the nanoemulsion
4. **Co-Surfactants**: Ethanol, Propylene Glycol, or Polyethylene Glycol (PEG) to enhance the effectiveness of the surfactant
5. **Aqueous Phase**: Purified water or a suitable buffer solution (e.g., phosphate buffer) **6. Preservatives (Optional):** To prevent microbial growth during storage

➢ **Preparation Methods**

There are several methods to prepare a nanoemulsion,

A. High-Pressure Homogenization Method

Step 1: Preparation of the Oil Phase

- Dissolve a pre-weighed amount of Aceclofenac in the Almond Oil. Stir the mixture gently to ensure complete dissolution of the drug.

Step 2: Preparation of the Aqueous Phase

- In a separate container, mix the surfactant (e.g., Tween 80) and co-surfactant (e.g., Ethanol) with purified water or buffer solution. Stir the mixture until the surfactants are fully dissolved.

Step 3: Emulsion Formation

- Gradually add the oil phase (containing Aceclofenac and Almond Oil) to the aqueous phase while stirring continuously. This pre-emulsion should be stirred at a moderate speed to avoid phase separation

Step 4: High-Pressure Homogenization

- Pass the pre-emulsion through a high-pressure homogenizer. This process typically involves forcing the emulsion through a narrow gap at high pressure (e.g., 5000-20,000 psi). The high shear forces generated help reduce the droplet size to the nanometer range.

Step 5: Cooling and Adjustment

- After homogenization, allow the nanoemulsion to cool to room temperature. Adjust the pH if necessary using a pH adjuster to ensure the formulation is suitable for the intended route of administration (e.g., topical, oral).

Step 6: Filtration (Optional)

- For parenteral applications, sterile filtration may be necessary to remove any particulate matter

B. Ultrasonication Method

Step 1: Oil Phase Preparation

- Similar to the high-pressure homogenization method, dissolve Aceclofenac in Almond Oil.

Step 2: Aqueous Phase Preparation

- Mix the surfactants and co-surfactants in the aqueous phase as described above.

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Step 3: Pre-Emulsion Formation

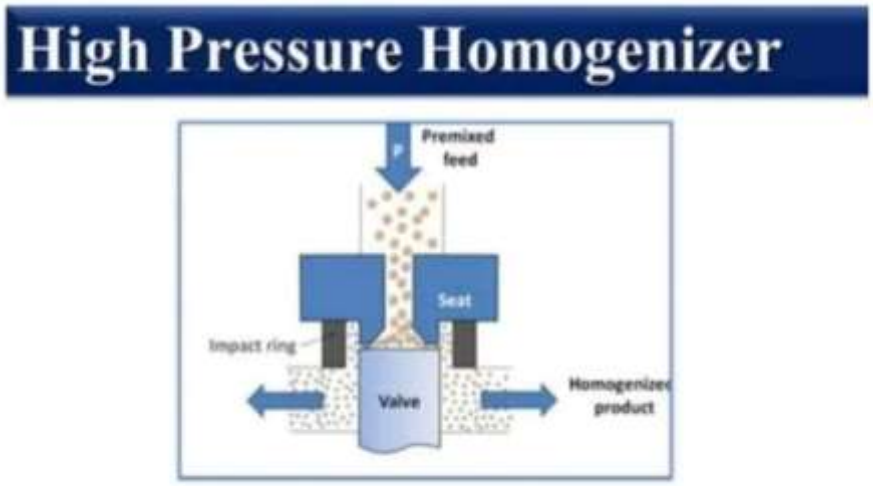
- Combine the oil phase with the aqueous phase under gentle stirring to form a coarse emulsion.

Step 4: Ultrasonication

- Subject the coarse emulsion to ultrasonication using a probe sonicator. Typically, sonication is performed at a frequency of 20 kHz for 10-15 minutes. Ensure that the mixture is kept in an ice bath to prevent overheating during sonication, which could degrade the Aceclofenac.

Step 5: Final Adjustments

- After ultrasonication, allow the nanoemulsion to cool. Adjust the pH and viscosity as needed to meet the desired space



➢ **Mechanisms of Action of Aceclofenac**

Aceclofenac is a widely used non-steroidal anti-inflammatory drug (NSAID) that exerts anti-inflammatory, analgesic, and antipyretic effects. It is commonly prescribed for conditions like osteoarthritis, rheumatoid arthritis, and ankylosing spondylitis. The therapeutic action of Aceclofenac is primarily mediated through the inhibition of inflammatory processes.

1. Inhibition of Cyclooxygenase (COX) Enzymes

- The primary mechanism of action of Aceclofenac is the inhibition of the cyclooxygenase (COX) enzymes, which are key in the synthesis of prostaglandins. Prostaglandins are lipid compounds that play a crucial role in promoting inflammation, pain, and fever. There are two main types of COX enzymes:
- COX-1: Involved in the production of prostaglandins that protect the stomach lining, maintain kidney function, and support platelet aggregation.
- COX-2: Induced during inflammatory processes and is primarily responsible for the production of pro-inflammatory prostaglandins.

2. Reduction of Prostaglandin Synthesis

- By inhibiting COX-2, Aceclofenac effectively reduces the production of prostaglandins, especially Prostaglandin E2 (PGE2), which is a major mediator of inflammation. The reduction in prostaglandin levels leads to the following therapeutic effects:
- Anti-inflammatory effect: Decreased levels of PGE2 and other inflammatory mediators result in reduced swelling, redness, and inflammation in the affected tissues.
- Analgesic effect: By lowering prostaglandin levels in the central nervous system and at peripheral sites of injury, Aceclofenac reduces pain perception.
- Antipyretic effect: Inhibition of PGE2 in the hypothalamus leads to a decrease in fever by regulating the body's temperature set poi **3. Inhibition of Free Radicals and Oxidative Stress**
- Aceclofenac may exhibit antioxidant properties by reducing the production of reactive oxygen species (ROS) and free radicals generated during the inflammatory response. This reduction in oxidative stress helps prevent further tissue damage and inflammation

➢ **Future Prospects of Nanoemulsion of Aceclofenac**

Nanoemulsion technology offers a promising future for the formulation of poorly water-soluble drugs like Aceclofenac. As a non-steroidal anti-inflammatory drug (NSAID) used to manage pain and inflammation, Aceclofenac's therapeutic effectiveness can be enhanced through nanoemulsion systems, which improve solubility, stability, and bioavailability

1. Enhanced Bioavailability

One of the major challenges with Aceclofenac is its poor water solubility, which limits its oral bioavailability. Nanoemulsions, with droplet sizes in the nanometer range, increase the surface area for absorption, leading to enhanced drug solubility and better gastrointestinal absorption. This technology has the potential to improve the oral bioavailability of Aceclofenac, resulting in faster onset of action, reduced dosing, and improved patient compliance.

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2. Improved Drug Targeting and Controlled Release

Nanoemulsion systems can be engineered to provide site-specific drug delivery. This can be particularly beneficial for treating localized inflammation in conditions such as osteoarthritis or rheumatoid arthritis. By incorporating Aceclofenac into a nanoemulsion, the drug can be directed more efficiently to inflamed tissues, potentially improving efficacy and reducing systemic side effects.

3. Reduction in Side Effects

The selective action of nanoemulsions can help reduce the systemic side effects associated with

NSAIDs, such as gastrointestinal irritation and ulceration. By improving the absorption and bioavailability of Aceclofenac, smaller doses may be required to achieve therapeutic efficacy, thereby minimizing the risks of adverse effects. In the future, nanoemulsion-based Aceclofenac formulations may offer safer alternatives for long-term pain and inflammation management.

4.Use in Injectable Formulations

Aceclofenac nanoemulsions could also be formulated as injectable preparations for more rapid and direct administration into the bloodstream, bypassing the gastrointestinal system altogether. Injectable nanoemulsions could be used in scenarios requiring rapid pain relief, such as postoperative pain or acute inflammatory episodes. This method can improve drug bioavailability while reducing the volume of injections due to the highly concentrated nanoemulsion.

CONCLUSION

- The development of a nanoemulsion of aceclofenac using almond oil as a carrier offers promising benefits due to their small droplet size and high surface area, improve drug absorption and provide a more controlled release profile compared to traditional. Formulations almand oil is base which also give antioxidant effect also benefit the make skin hydration
- aceclofenac in a nanoemulsion can also potentially reduce its gastrointestinal side effects, which are a common concern in oral NSAID therapy.
- Future research should focus on optimizing formulation parameters, evaluating long-term storage conditions, and conducting comprehensive in vivo studies to fully understand the pharmacokinetics and therapeutic potential of aceclofenac nanoemulsions.

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