



Formulation And Evaluation Of Ibuprofen Gel Using The Solid Lipid Nanoparticles

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Abstract: The study investigates the formulation and evaluation of an Ibuprofen gel incorporating solid lipid nanoparticles (SLNs) to enhance topical drug delivery. Ibuprofen, a widely used nonsteroidal anti-inflammatory drug (NSAID), often faces challenges with skin permeability and release rate when applied topically. SLNs offer a promising Drug Delivery system by improving drug stability, controlled release, and skin penetration. This research details the preparation of ibuprofen-loaded SLN gels, their characterization, and comparative performance evaluation.

Keywords: Ibuprofen, Solid Lipid Nanoparticles, Gel Formulation, Drug Delivery, Topical Application

I Introduction

Ibuprofen is widely known as a nonsteroidal inflammatory drug (NSAID) offering pain relieving and anti-inflammatory properties while also helping reduce fever symptoms in various conditions, like rheumatoid arthritis and muscle pains. Because Ibuprofen works by inhibiting cyclooxygenase enzymes without specificity to a type of enzyme which can lead to side effects, like stomach irritation and other systemic reactions when taken orally despite its effectiveness. Topical forms of ibuprofen have been studied as an approach to reduce side effects and provide specific relief.

The main aim of using ibuprofen is to target the area directly to reduce potential side effects and enhance its effectiveness, in treating inflammation at that specific site. However limited absorption through the skin and rapid release of the drug from the formulation often hinder the effectiveness of ibuprofen. As a result the product needs to be reapplied due to these limitations, which may cause discomfort, for patients and lead to therapeutic outcomes. The study focused on creating a lasting ibuprofen gel with lipid nanoparticles and comparing its release pattern to that of the commercial gel to discover a better option.^{[1][2]}

➤ Advantages of SLN loaded Ibuprofen gel

- Enhanced Drug Stability
- Controlled and Sustained Release
- Improved Skin Penetration
- Reduced Systemic Side Effects
- Uniform Drug Distribution
- Fewer side effects

➤ Disadvantages of conventional ibuprofen gel

- Limited Skin Penetration
- Short Duration of Action
- Drug Instability
- Inconsistent Drug Delivery
- Potential for Skin Irritation
- Systemic Side Effects

Inflammation is a fundamental physiological response of the body's immune system to a range of potentially harmful stimuli. These stimuli include infections (bacterial, viral, fungal), physical injury (cuts, burns, trauma), chemical irritants (toxins, pollutants), and biological factors (allergens, autoimmune triggers). Inflammation serves a critical role in defending the body against these threats, facilitating the removal of damaging agents, and promoting tissue repair.^[2]



Fig 1 : Inflammation

➤ Causes Of Inflammation

Inflammation is a natural response by your body to injury or infection. It serves as a defence mechanism and aids in recovery. On the other hand, chronic or severe inflammation can cause a number of health issues.

Here are some common causes of inflammation: -

- Autoimmune disorders
- Acute inflammation that's left untreated
- Consuming excess alcohol
- Smoke
- Chronic stress
- Not exercising enough or exercising too frequently with maximum intensity
- Having a high body mass index (BMI)

➤ Need and Rational

- Ibuprofen gel is improved to improve skin permeability
- To reduce Gastrointestinal side effects
- To improve bioavailability
- SLN enhance the stability of drug
- SLN reduces the skin irritation

II Material and method

One popular non-steroidal anti-inflammatory medicine (NSAID) that works well for relieving pain and inflammation is ibuprofen. Oral administration, however, may have adverse effects in the gastrointestinal tract. Although topical distribution presents a potential answer, its effectiveness may be limited by issues such as skin penetration and fast drug removal. Solid lipid nanoparticles (SLNs) have shown promise as more effective medication delivery systems with fewer adverse effects.

The goal of our research was to create a new ibuprofen gel loaded with SLN. Colloidal carriers made of physiological lipids, known as SLNs, provide better medication delivery with fewer adverse effects. Our goal was to increase ibuprofen's penetration into the skin and extend its release by integrating SLNs into a gel basis.

➤ Formulation

- To identify and select appropriate drug that has been used for managing Inflammation.
- To formulate SLN loaded ibuprofen gel using this drug
- To do evaluation of SLN loaded ibuprofen gel.

➤ Applications: -

- To treat Musculoskeletal Pain
- Dermatological inflammation (e.g., eczema, psoriasis)
- Insect bites and stings
- Pain and inflammation related to athletic activities
- Muscle strains and sprains

A. Ibuprofen



Fig 2: Ibuprofen Chemical

Ibuprofen is a nonsteroidal anti-inflammatory drug (NSAID) commonly used to relieve pain, fever, and inflammation. It works by inhibiting the production of prostaglandins, substances in the body that cause pain and inflammation.^[3]

Chemical Structure and Properties

- **Chemical Name:** 2-(4-Isobutylphenyl) propionic acid
- **Molecular Formula:** $C_{13}H_{18}O_2$
- **Molecular Weight:** 206.28 g/mol
- **Appearance:** White to off-white crystalline powder
- **Solubility:** Soluble in ethanol, slightly soluble in water

B) Carbopol 934



fig 3-Carbopol 934

It is a synthetic polymer used in medicine and cosmetics as a stabilizer, thickener, and gelling agent. Controls viscosity, suspends particles, and produces a texture akin to gel. Frequently found in topical products such as ointments, gels, and creams.^[4]

Chemical Structure and Properties

- **Chemical Name:** Poly(1-carboxy-1-methylethylene)
- **Molecular Formula:** $C_3H_4O_2$
- **Appearance:** White, free-flowing powder.
- **Solubility:** Carbopol 934 is not soluble in water but swells and forms a gel when dispersed in water.

C. Triethanolamine (TEA)



Fig 4:-Triethanolamine

It is an pH adjuster and emulsifier in cosmetics and pharmaceuticals. Improves texture, stabilizes formulations, and neutralizes basic or acidic ingredients. Improves the feel of the skin and the spread ability of the product.^[5]

Chemical Structure and Properties

- **Chemical Name:** 2,2',2''-Nitrilotriethanol
- **Molecular Formula:** $C_6H_{15}NO_3$
- **Molecular Weight:** 149.19 g/mol
- **Appearance:** Colourless to pale yellow, viscous liquid.
- **Solubility:** Highly soluble in water, Soluble in alcohols and some organic solvents.

D. Methyl Paraben



Fig 5:- Methylparaben

- It is an Preservative that prolongs the shelf life of products by preventing microbial growth.
- Effective against food, medicine, and cosmetic products' bacteria, yeast, and Mold.
- Commonly employed at up to 0.3% w/w concentrations.^[6]

Chemical Structure and Properties

- **Chemical Name:** Methyl 4-hydroxybenzoate
- **Molecular Formula:** $C_8H_8O_3$
- **Molecular Weight:** 152.15 g/mol
- **Appearance:** White to off-white crystalline powder or granular solid.
- **Solubility:** Slightly soluble in water; soluble in organic solvents

E. Stearic acid



Fig 6:- Stearic acid

- Stearic acid waxy, solid nature at room temperature helps stabilize the nanoparticles, ensuring they maintain their structure and release active ingredients in a controlled manner.
- Stearic acid is used as a solid lipid matrix material
- Stearic acid improves the SLNs' physical stability, resulting in longer-lasting drug release and compatibility with a wider range of active ingredients. [7]

Chemical Structure and Properties

- **Chemical Name:** Octadecanoic acid
- **Molecular Formula:** $C_{18}H_{36}O_2$
- **Molecular Weight:** 284.48 g/mol
- **Appearance:** White, waxy solid or flakes at room temperature
- **Solubility:** Soluble in organic solvents like ethanol, ether, and chloroform

III. METHOD OF PREPARATION OF SLN LOADED IBUPROFEN GEL

Table1:- Formulation table of SLN loaded Ibuprofen gel

Sr no.	Ingredient	Concentration(%)	Function
1	Ibuprofen	5%	Active ingredient
2	Solid Lipid Nanoparticles (SLN)	20%	Drug carrier
3	Carbomer 934	1.5%	Gelling Agent
4	Triethanolamine (TEA)	0.5%	Neutralizing agent

5	Water	Q.S	Solvent
6	Methyl Paraben	0.1%	Preservative

Table2:- Formulation table of SLN

Sr no.	Ingredients	Concentrations (%)	Function
1	Stearic acid	5 %	Act as Solid Lipid matrix
2	Propylene glycol	3.5 %	Surfactant
3	Ibuprofen	5%	API
4	Water	Q.S	Dispersion medium



Fig 7:-Chemicals used for formulation

➤ Equipment's used:-

- Weighing Balance /Analytical Balance: It is the most Important equipment used for any formulation. It gives us the accurate weighed quantity of any drug use for the formulation. All ingredients use for formulation are weighed on same.

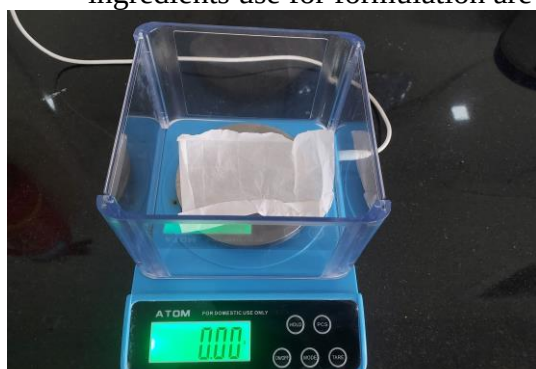


Fig 8:- Analytical balance

- pH meter: pH, which indicates the concentration of hydrogen ions in the solution. Used to check the acidity or alkalinity of a solution. pH meter provides a numerical value.

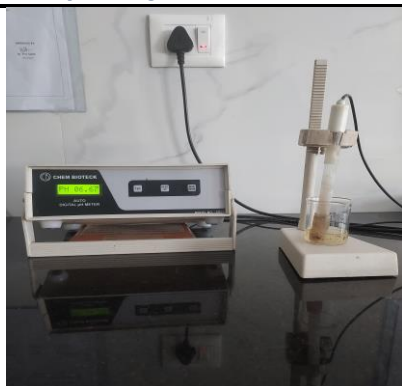


Fig 9:- pH meter

- **Magnetic stirrer:** Magnetic stirrers use a rotating magnetic field to stir liquids. A magnetic bar (or flea) is placed inside the liquid container, and an external magnetic field rotates beneath the container, causing the magnetic bar to spin.



Fig 10:- Magnetic stirrer

➤ Procedure

I) Formation of SLN particles: -

1. In a beaker solid lipid(5%) melted in beaker.
2. In separate beaker add drug and Propylene glycol(3.5%) and mix.
3. Mix both oil an aqueous phase at same temperature 70-80⁰ C.
4. Stir the mixture on magnetic stirrer at 400rpm for 1hr.
4. Allow the mixture to cool to room temperature, while maintaining magnetic stirring.

II) Formation of SLN loaded Ibuprofen gel

1. Prepare SLN dispersion according to the procedure mentioned earlier.
2. Mix carbomer 934 and TEA in a separate beaker.
3. Slowly add SLN dispersion to the carbomer-TEA mixture, stirring continuously.
4. Neutralize with TEA until pH reaches 5.5-6.5.
5. Add preservatives and stir well.
6. Store the gel in a sealed container.^{[8][9]}

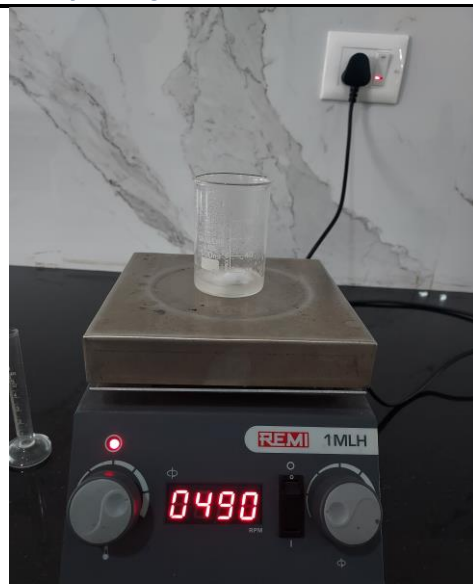


Fig 11:- Stirring

➤ Evaluation

Quality control tests, such as pH measurements as well as visual inspection, were carried out to examine the generated formulations. In order to ensure the quality of the products, various testing were conducted for Ibuprofen formulation.

- *Physical Appearance/ Visual Inspection:*

The formulations prepared were evaluated in terms of their, Colour odour, texture, solubility and thickness.^[10]

- *Determination of Ph:-*

The pH of 10% Ibuprofen solution in distilled water was determined at room temperature 25°C.^[11]

- *Determination of particle size of SLN:-*

An optical microscope equipped with an ocular micrometer was used to measure the particle size of SLNs. A coverslip was used to protect a drop of the SLN dispersion that had been put on a glass slide. A stage micrometer was used to calibrate the micrometer once the particles had been located under a 1000x magnification. Aligning the particles with the micrometer scale allowed for the determination of particle size, which was then repeated for five to ten particles. Next, the average particle size was determined.^{[13][14]}

- *Spreadability test:-*

The objective is to evaluate the spreadability of SLN-loaded Ibuprofen Gel. Required apparatus includes a spreadability meter, glass plate, spatula, weighing balance, and thermometer. Use SLN-loaded Ibuprofen Gel and distilled water. Weigh 1g of gel and place it on the glass plate at room temperature.^[12]

- *Determination of viscosity:-*

A Brookfield viscometer (Model DV-II) was used to measure the viscosity of the SLN gel. A tiny quantity of the gel was put in a sterile container and allowed to equilibrate at 25°C. A suitable spindle was installed in the viscometer, and its speed was adjusted to 10 rpm. After three to five minutes of measurement, the viscosity reading (in cP) was noted. In order to evaluate shear-thinning behaviour, measurements were made again at various speeds (e.g., 100 rpm).^[15]

- *Microbial contamination test:-*

The objective is to detect microbial contamination in SLN-loaded Ibuprofen Gel using the Streak Plate method. Take 1g of SLN-loaded Ibuprofen Gel and mix with 9ml of distilled water (1:10 dilution). Sterilize the inoculation loop, take a small sample from the gel mixture, and streak it onto the NA or TSA plate in a zig-zag pattern. Incubate at 30-35°C for 48-72 hours.^[16]

IV .Result and discussion:-

A. Formulation of SLN loaded ibuprofen gel

The SLN dispersion was prepared by using chemicals in Table 2 in which stearic acid is an solid matrix and Propylene glycol acts as an solvent. After that using this SLN dispersion the SLN loaded ibuprofen gel was prepared using Table 2 . A small amount of methyl paraben was added in the formulation to further preserve it.

B.Evaluation of SLN loaded Ibuprofen gel: -

➤ *Physical Appearance/ Visual Inspection:*

Like any other Gel preparation, a SLN loaded ibuprofen gel should look well. Physical attributes including colour, odour, and transparency of the developed and marketed gels were assessed (Table 3). Our designed gel was smooth, Creamy white in colour, and had a mildly unpleasant odour.

Table 3: Physical Appearance

Sr no.	Test	Observation
1	Colour	Creamy white
2	Odour	Odourless
3	Texture	Smooth
4	Solubility	Water soluble
5	Thickness	Uniform

➤ *pH*

The pH Evaluation Test for SLN-loaded Ibuprofen Gel is crucial to ensure the product's safety, efficacy, and stability. The primary objective is to maintain the skin's natural pH range, preventing potential irritation or discomfort. Additionally, the test helps prevent degradation of ibuprofen and SLN components, which could impact product potency. It was discovered that the pH of formulated SLN loaded ibuprofen gel was almost 6.10.



Fig 12:- pH of gel

➤ *Determination of particle size of SLN: -*

Upon observation, individual SLN particles appeared spherical and were evenly dispersed in the dispersion medium. The size range of the particles was between 200 nm to 700 nm. In order to determine the average particle size, many particles were measured across the slide using the eyepiece micrometer's calibration, where one division was equivalent to 0.1 μm at 1000x magnification. One particle that was five divisions across on the micrometer scale, for example, was 0.5 μm (500 nm) in size. With a size range of 200–700 nm, the mean particle size, determined from observations of 10 particles, was 350 nm. This finding implies that the sample's particle sizes are distributed very uniformly.

➤ *Spreadability test: -*

The spreadability of SLN-loaded Ibuprofen Gel on the skin's surface is assessed using the Spreadability Test. It evaluates the bioavailability, formulation stability, and patient comfort. A number of variables, including as viscosity, pH, temperature, humidity, and formulation makeup, can affect spreadability.

Place 1g of gel between two glass plates (25mm diameter, 5mm thick). Weigh down the top plate. After 5 minutes, measure the diameter of the spread gel in mm. The formulated SLN ibuprofen gel shows good spread ability.



Fig 13:- Spreadability of gel

➤ *Determination of viscosity:-*

The SLN gel exhibited shear-thinning behaviour, with viscosity decreasing at higher spindle speeds. At **10 rpm**, the viscosity was **350 cP**, and at **100 rpm**, it was **150 cP**. The average viscosity was **250 cP**, indicating the gel had moderate viscosity suitable for topical application, with good spreadability at higher shear rates

➤ *Microbial contamination test:-*

The Microbial Contamination Test for SLN-loaded Ibuprofen Gel ensures the product's safety and quality. sterilize an inoculation loop and take a 1-2 mL gel sample. Next, streak the gel onto a nutrient agar plate in a zigzag pattern, typically 4-6 streaks. Incubate the plate at 30-35°C for 24-48 hours. After incubation, No growth of microorganisms was found.



Fig14:- Before incubation



Fig15 · After incubation

V. Conclusion

The goal of this current study was to create a SLN loaded ibuprofen gel that would enhance solubility and bioavailability, sustained drug release, and improve stability. Solid lipid nanoparticles (SLNs) were shown to be a viable method for improving the solubility, stability, and therapeutic efficacy of ibuprofen gel formulation. The gel that was created exhibited advantageous physical characteristics, such as an ideal pH and spreadability, along with a prolonged drug release profile. In order to ensure compatibility with skin tissue and minimize irritation, the formulation's pH was modified to fall within the range appropriate for topical administration. Additionally, the gel's spreadability was determined to be satisfactory, meaning that it can be administered to affected areas with ease and aid in the efficient distribution of drugs.

To verify the formulation's stability and safety, microbial contamination tests were carried out. The results showed that the gel complied with safety requirements and was devoid of dangerous microbes. This factor is crucial for topical formulations since they frequently come into contact with environmental toxins that could jeopardize the safety of the product.

Table 4: - Formulation,development,and evaluation of Ibuprofen gel using Solid lipid nanoparticles

CONTENT	TITLE OF FIGURES & TABLES
Fig no. 1	Inflammation
Fig no.2	Ibuprofen
Fig no.3	Carbachol
Fig no.4	Triethanolamine
Fig no.5	Methyl paraben
Fig no.6	Stearic acid
Fig no.7	Chemicals used in formulation
Fig no.8	Analytical balance
Fig no.9	pH meter
Fig no.10	Magnetic stirrer
Fig no.11	Stirring
Fig no.12	pH of gel
Fig no.13	Spread ability of gel
Fig no.14	Before incubation
Fig no.15	After incubation
Table no.1	Formulation table of SLN loaded ibuprofen gel
Table no.2	Formulation Table of SLN
Table no.3	Physical appearance

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