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Formulation, Development and evaluation of ibuprofen gel by using natural Polymer

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ABSTRACT:

The current study focuses on developing and assessing a topical ibuprofen gel formulation utilizing guar gum as a polymeric agent. The gel was prepared by dispersing guar gum in a water-glycerol mixture containing methyl paraben as a preservative, followed by magnetic stirring to achieve a uniform dispersion. Ibuprofen was added in varying amounts, and the dispersion was neutralized and thickened with triethanolamine.Topical drug delivery systems have gained popularity due to their ability to deliver drugs locally and systemically while minimizing gastrointestinal side effects and first-pass metabolism. Nonsteroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen, are often formulated as topical gels to target the site of action directly. Ibuprofen exhibits potent analgesic and anti-inflammatory effects, making it suitable for treating conditions like osteoarthritis, rheumatoid arthritis, and dental pain.Gels offer advantages over ointments as topical drug delivery systems due to their non-sticky nature and low energy requirements during formulation. The prepared ibuprofen gel was evaluated for various parameters, including drug content, pH, spreadability, and entrapment efficiency. Guar gum and propylene glycol were used as polymer and permeation enhancer, respectively, to optimize the formulation.

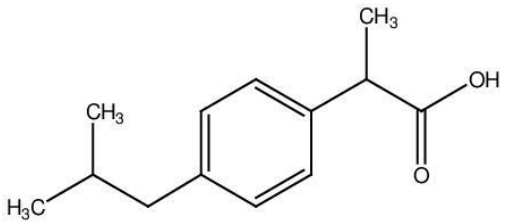
Keywords: Ibuprofen, gel, guar gum, triethanolamine, propylene glycol, evaluation.

Introduction

Drug detail Ibuprofen

Ibuprofen is a derivative of propanoic acid, characterized by a p-isobutyl phenyl group at the 2-position. Its physical properties include a white crystalline appearance with a distinctive odor. Ibuprofen exhibits limited solubility in water but is highly soluble in alcohol and alkaline aqueous solutions.[1-2]In terms of its mechanism, ibuprofen inhibits prostaglandin synthase, resulting in potent analgesic, antipyretic, and anti-inflammatory effects. However, its use can be associated with gastrointestinal side effects, such as nausea, vomiting, and diarrhea.Ibuprofen is commonly used to treat conditions like rheumatoid arthritis, osteoarthritis, and ankylosing spondylitis. It serves as a viable alternative to aspirin for individuals who experience intolerance. Other notable propionic acid derivatives used in clinical practice include naproxen, fenoprofen, ketoprofen, and flurbiprofen[3].

Drug structure



Ibuprofen

Transdermal drug delivery (TDD) offers a promising solution to overcome existing limitations. By bypassing the gastrointestinal tract and liver, TDD enhances bioavailability and reduces the impact of first-pass metabolism. This delivery method also provides sustained and controlled drug release, prolonging therapeutic effects and minimizing dosing frequency. Additionally, TDD reduces systemic side effects by targeting the drug directly to the site of action, making it a safer option for prolonged use. Its non-invasive nature and ease of use also improve patient compliance. Among various transdermal formulations, gels stand out due to their ease of application, skin adhesion, and customizable properties, such as viscosity and spreadability, which enhance drug permeation.[4]

Objective

- The objective is to prepare transdermal topical gel of Ibuprofen using guar gum which can be effectively used For transdermal topical delivery.
- Formulation Development: Prepare ibuprofen gel using polymers (guar gum) and penetration enhancers (propylene glycol).
- Physicochemical Evaluation: Assess pH, viscosity,spreadability to ensure formulation stability and skin compatibility.

MATERIALS AND METHODS [5]

Ibuprofen is a nonsteroidal anti-inflammatory medication that provides relief from pain, fever, and inflammation. It's commonly used to treat various conditions, including menstrual cramps, osteoarthritis, rheumatoid arthritis, and juvenile idiopathic arthritis. While ibuprofen is effective, it can have adverse effects, particularly at high doses, such as increased risk of cardiovascular, kidney, and liver problems.Research suggests that low doses of ibuprofen may not significantly increase heart attack risk, but higher doses may pose a greater risk. Despite these potential risks, ibuprofen remains a widely used and effective medication, recognized by the World Health Organization as an essential medicine due to its efficacy and safety profile. [6]

Propylene glycol is a widely used humectant known for its strong affinity for water. It helps stabilize the water content in various formulations, making it a valuable ingredient in many applications.[7]

Glycerin is a versatile, sweet-tasting liquid with multiple uses in various industries. Its properties as a trihydroxy alcohol make it suitable for numerous applications, particularly in pharmaceutical formulations where its characteristics are valued.[8]

Methylparaben is a widely used preservative that exhibits effective antimicrobial and antifungal properties. Its applications span various industries, including food, cosmetics, and pharmaceuticals, where it helps prevent microbial growth and contamination.[9]

Guar gum is a natural polysaccharide derived from the guar bean, specifically the endosperm of Cyamopsis tetragonolobus. Native to the Indian subcontinent, guar gum is valued for its unique properties as a thickening agent, stabilizer, and emulsifier. Composed primarily of galactomannan, guar gum forms a gel-like substance when mixed with water, making it a versatile ingredient in various applications.Guar gum's uses extend beyond food products, where it serves as a thickener and stabilizer, to industrial applications, such as soil stabilization and fracturing. Its physical properties include a white to yellowish-white powder appearance, bland taste, and limited solubility in organic solvents. When dispersed in water, guar gum rapidly forms a highly viscous solution.[10]

Triethanolamine (TEA) serves as a versatile ingredient in gel formulations, functioning as both a pH regulator and stabilizer to optimize product performance.[11]

Distilled water is purified water that has been stripped of impurities, including mineral ions and microorganisms, making it suitable for various applications, from research to industrial use.[12]

Turpentine oil can be utilized in gel formulations for its potential benefits, including:

- Pain relief: Its anti-inflammatory and analgesic properties may provide relief from pain and inflammation when applied topically.
- Infection prevention: Turpentine oil's antimicrobial properties can help prevent the growth of microorganisms.

Method of preparation [14]

The ibuprofen gel was prepared using a hydration and precipitation method, involving the following steps:

- Ibuprofen was dissolved in propylene glycol at a temperature range of 40-50°C.
- Guar gum and glycerin were added to the mixture, which was then heated to 90°C with constant stirring for 15 minutes.
- The mixture was cooled to room temperature while stirring for 15-30 minutes.
- Triethanolamine (2 drops) was added, followed by the preservative (paraben) and other ingredients.
- The exact composition of the ibuprofen gel formulation can be found in Table 1.

Formulation	F1	F2
Ibuprofen (g)	**1g**	**1.5g**
Propylene glycol(ml)	**3.3ml**	**5ml**
Guar gum(g)	**1.3g**	**2g**
Triethanolamine (ml)	**0.1ml**	**0.1ml**

Methyl paraben(mg)	**266mg**	**400mg**
Pipermentoil (ml)	**0.1ml**	**0.1ml**
Distilled water	**Q.s**	**Q.s**

Ibuprofen

1.Physical Evaluation

Appearance (Color ,Homogeneity)

Procedure:
Each formulation (F1–F2) is visually inspected in natural and artificial light for its color and overall uniformity. The gel is checked for lumps, air bubbles, or particulate matter.
Result:

Formulation	**Colour**	**Homogeneity**
F1	**White**	**Homgeous**
F2	**White**	**Homgeous**

Texture and Feel (Smoothness, Greasiness)
Procedure:
A small quantity of each gel is applied to the back of the hand and gently rubbed. Smoothness And greasy residue are subjectively evaluated.
Result:

Formulation	**Smoothness**	**Grisiousness**
F1	**Smooth**	**No**
F2	**Smooth**	**No**

pH Measurement
Procedure:
1g of gel is dissolved in 10 mL distilled water. The pH is measured using a digital pH meter (calibrated using standard buffers).
Result:

Formulation	**pH Value**
F1	**6.13**
F2	**6.12**

F1

F2

Viscosity

Procedure:

Viscosity is measured using a Brookfield viscometer at 25°C using spindle number 64 at 10, 20, and 50 rpm. Rheological behavior is interpreted based on shear-thinning or thickening.

Result :

Formulation	Viscosity (cp at 20 rpm)
F1	5100
F2	6000

Spreadability Test

Procedure:

A known amount of gel is placed between two glass slides and a 500 g weight is placed for 5 Minutes. The diameter of spread is measured.

Result:

Formulation	Spread Diameter (cm)
F1	6.5
F2	6.0

Homogeneity Test

Procedure:

Each formulation is inspected under bright light and under a microscope (10x) for particulate Matter, phase separation, or inconsistencies.

Results:

Formulation	Visual Homogeneity
F1	Uniform
F2	Uniform

Extrudability Test

Procedure:

A 10g gel sample is filled into a collapsible tube. The force required to extrude the gel (measured by weight or qualitative rating) and the amount extruded in 30 seconds is recorded.

Result:

Formulation	Ease of Extrusion
F1	Easy
F2	Moderate

Moisture Content Assessment

The moisture content of the gel formulation is a critical parameter that impacts its stability, texture, and shelf life. Excessive moisture can lead to microbial growth and physical instability.

Procedure

- Accurately weigh a gel sample (W1).
- Place the sample in a desiccator with a drying agent at room temperature until a constant weight is achieved (W2).
- Calculate the moisture content percentage using the formula: ((W1 – W2) / W1) × 100.

Result:

- Moisture content typically ranges from 1% to 5%, depending on the formulation.
- Lower moisture levels indicate improved stability and reduced risk of microbial contamination.
- Spread Diameter Measurement (Spreadability)
- Spreadability is a crucial parameter that affects patient comfort and uniform drug application. It measures how easily the gel spreads on the skin.

Procedure:

- Place a known amount of gel (1g) between two glass plates.
- Apply a standard weight (125g) to the upper plate.
- Measure the diameter of the spread gel after 1 minute.
- Repeat the measurement in triplicate and calculate the average spread diameter.
- Calculating Spreadability:
- Spreadability (S) can be calculated using the formula: S = m × l / t, where m is the weight applied, l is the length of the glass plate, and t is the time taken to spread.
- Acceptance Criteria: Should spread smoothly and evenly under moderate pressure.
- Weigh 2–5 g of gel, place it between two glass slides.
- Tie the upper slide with a thread and attach a weight pan.
- Add weights gradually until 75 g is reached.
- Measure the time taken by the top slide to move 10 cm.

Use the formula:

- Spreadability Index =$Time(seconds)$ /Weight (g)

Result:

- Time: 15 seconds, Weight: 78 g
- Spreadability Index = 15 / 78= 0.1923 s/g (✓ Acceptable).

Conclusion

The development of Ibuprofen gels offers a promising alternative to traditional oral NSAIDs for managing pain and inflammation. By optimizing gel formulations with polymers like guar gum and penetration enhancers like propylene glycol, we achieved controlled drug release, enhanced skin permeation, and improved patient comfort.

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