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(RESEARCH ARTICLE)

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Formulation and evaluation of an anti-inflammatory gel containing 2.5% *Capparis Brevispina* Extract

ASHA NANDABARAM *, MUVVALA SUDHAKAR, RACHANA NANGUNOORI, DEEPIKA NADIMINTI, NAMITHA NALUVALA, MANOGNA NANDED and SAIKIRAN PANJALA

Department of Pharmacology, MallaReddy college of pharmacy, dhulapally, secunderabad, Telangana, 500100 (Affiliated to Osmania University), India.

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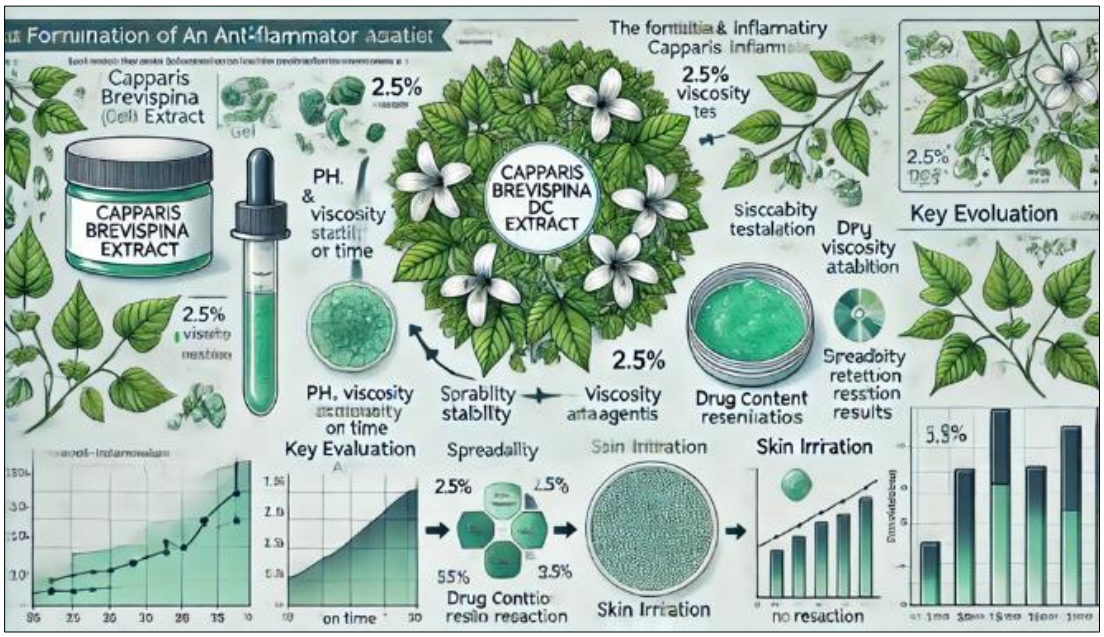
Abstract

This study successfully formulated and evaluated an anti-inflammatory gel containing 2.5% *Capparis Brevispina* extract, traditionally known for its analgesic and anti-inflammatory properties. The goal was to develop a stable, effective, and user-friendly topical gel as a natural alternative for inflammation management. The formulation incorporated appropriate gelling agents, penetration enhancers, and stabilizers to ensure the desired consistency, spreadability, and ease of application. Several formulations were prepared and optimized based on their rheological and physical characteristics. The gel underwent evaluations for pH, viscosity, spreadability, homogeneity, and stability under various storage conditions. The skin-friendly pH minimized irritation, while optimized viscosity ensured easy application and adhesion. Homogeneity tests confirmed uniform distribution of the extract, and spreadability studies indicated smooth application. Stability tests were conducted to assess changes in appearance, texture, or phase separation over time, confirming the gel's integrity under varying humidity and temperature conditions, making it suitable for long-term storage. The findings demonstrated that the gel met pharmaceutical quality standards, validating its potential as a viable herbal formulation for inflammation management. Overall, this study highlights the successful development of a *Capparis Brevispina*-based anti-inflammatory gel with promising therapeutic benefits. Further research and clinical evaluations are necessary to establish its efficacy and safety, contributing to the advancement of herbal-based pharmaceutical formulations.

Keywords: Anti-inflammatory; *Capparis Brevispina*; Topical gel; Formulation; Stability

* Corresponding author: ASHA NANDABARAM

Graphical Abstract



1. Introduction

1.1. Inflammation

1.1.1. Understanding Inflammation

The immune system's natural reaction to damaging stimuli like infections, wounds, or irritants is inflammation. It is a defense system that facilitates tissue healing and helps eliminate harmful substances. On the other hand, chronic or severe inflammation can result in a variety of inflammatory illnesses, discomfort, and tissue damage. In order to eradicate the source of damage and start the healing process, the inflammatory response entails intricate interactions between immune cells, blood vessels, and chemical mediators. Depending on how long it lasts and what causes it, this process can be either acute or chronic.

1.2. Types of Inflammation

1.2.1. Acute Inflammation

Acute inflammation is a short-term reaction that happens right after tissue damage and is characterized by the classic five signs:

- **Pain (Dolor**): Caused by the release of chemical mediators that activate pain receptors. Because of swelling and pain affecting mobility or function
- **Amplification Phase**: Attracts immune cells (neutrophils, macrophages) to the affected site.
- **Resolution Phase**: Eliminates harmful agents and starts tissue repair mechanisms.
- **Redness (Rubor):** Caused by increased blood flow; Swelling (Tumor): Because of fluid accumulation.
- **Heat (Calor):** Because of increased metabolic activity and blood flow.

1.2.2. Chronic Inflammation

Chronic inflammation is a long-lasting response that occurs when the immune system fails to eliminate the cause of inflammation. It is commonly associated with conditions such as:

Rheumatoid arthritis (RA), Osteoarthritis, Inflammatory bowel disease (IBD),Psoriasis Chronic infections (e.g., tuberculosis, hepatitis)

Unlike acute inflammation, chronic inflammation involves **continuous immune activation**, leading to **tissue damage, fibrosis, and increased risk of chronic diseases** such as cardiovascular diseases, diabetes, and cancer.

1.3. Mechanism of Inflammation

The inflammatory response is mediated by various chemical messengers and cellular interactions. Some of the key players in inflammation include:

1.3.1. Inflammatory Mediators

Prostaglandins (PGs), Leukotrienes, Cytokines (TNF-α, IL-1, IL-6),Histamine, Reactive Oxygen Species (ROS).

2. Methodology

2.1. Plant Extraction

2.1.1. Plant collection and authentication

The *Capparis Brevispina* DC plant was sourced from Tirupati. Plant verification was conducted by Dr. K. Madhava Chetty, a plant taxonomist and assistant professor in the department of botany at Sri Venkateshwara University, Tirupati, A.P., India. A voucher specimen (Ref. No.0157), dated 22/01/2024, has been stored in the herbarium for reference.

2.1.2. Capparis Brevispina DC

Botanical Classification and Morphology:

Indian Caper is a common name. *Capparis Brevispina* is its botanical name. Capparaceae (Caper family) is the family. Cappariswallichiana is a synonym. The plant known as Indian caper is equipped with prickly stipules. The leaves are short stemmed, oval or broad-lance-shaped, mucronate, more or less pointy, and lighter below. On stalks as long as the leaves, flowers are carried individually in the leaf axils. Large, two-inch diameter, white flowers with two yellow-tinged upper petals that turn red as they mature. The anthers are blue. When mature, the berry is smooth and red. On arid rocky terrain, Indian caper is widespread in the Malabar region.

Taxonomy

- **Root:** Root
- **Kingdom:** Plantae
- **Phylum:** Tracheophyta
- **Class:** Magnoliopsida
- **Order:** Capparales
- **Family:** Capparaceae
- **Genus:** *Capparis*
- **Species:** *Capparis Brevispina* DC**. (**India biodiversity portal. *Capparis Brevispina* DC.,n.d.)

Leaves are broadly lanceolate, oval, leathery, smooth, and veined like a net, with a paler underside. Stipules are small and spiky, and they are comparatively straight. A rectangular ovary heavily covered in fine hairs; A nearly spherical and smooth berry as a fruit (Al-Snafi, A.E. et al., 2016). *Capparaceae* family that Indians have long employed. The region's cultural diversity further emphasizes the significance of medicinal herbs.

Figure 1 *Capparis Brevispina* DC- Flower, Leaf, Plant

- **Chemicals and Reagents:** Carbopol (a polymer used for gelling), Polyethylene Glycol (PEG), Propylene Glycol (Humectant and Stabilizer), Water (Aqueous Phase), Triethanolamine (Neutralizer for Carbopol)
- **Equipment:** Heating mantle, Soxhlet apparatus, Weighing balance, pH meter, Magnetic Stirrer, Viscometer, Autoclave, SOXHLET APPARATUS [(Zhang, Q.W. et al., 2018)

2.2. Preparation of plant extract

A 40g sample of *Capparis Brevispina* DC leaf extract was safely fixed inside a porous bag constructed from a sterile cloth of sturdy filter paper.

Water, the extraction solvent, was added to the round-bottom flask, and then by inserting the thimble into the extraction chamber.

The lower solvent was heated in a separate beaker to produce a vapor, which was then transferred to the condenser and subsequently transformed back into liquid before falling into the extraction chamber.

The solvent and extract returned to the flask when the extraction chamber's solvent level reached the siphon level. This cycle went on until there was no longer any residue coming out of the extraction chamber with the solvent, indicating that the compound had been fully extracted. (Dhawan, D. et al.,2017)

2.3. Preparation of Anti-inflammatory Gel

2.3.1. Formulation

Carbopol 940 was carefully dispersed in half of the required distilled water and allowed to hydrate for 2 hours to ensure complete swelling and uniform gel formation. Simultaneously, the ***Capparis Brevispina*** extract was dissolved in ethanol to enhance its solubility, followed by the gradual addition of propylene glycol, glycerin, and polyethylene glycol 6000. These ingredients were mixed thoroughly to achieve a homogenous blend. Meanwhile, methylparaben and propylparaben were separately dissolved in warm water to facilitate proper dissolution and even distribution within the formulation.

The prepared extract and preservative solutions were then slowly incorporated into the fully hydrated Carbopol under continuous stirring to ensure a smooth, lump-free mixture. The pH of the formulation was carefully adjusted to a range of 5.0–6.0 using triethanolamine to achieve optimal skin compatibility. Finally, the total volume of the formulation was adjusted to 100 g with the remaining distilled water.

The final gel was thoroughly mixed to ensure uniformity, transferred into an airtight container, and stored at room temperature to maintain its stability, efficacy, and consistency.

Table 1 Composition table for 100 g Anti-Inflammatory gel containing 2.5% Capparis Brevispina DC extract

Ingredient	Quantity (%w/w)	Amount (g)
Capparis Brevispina Extract	2.5%	2.5 g
Carbopol 940 (Gelling agent)	1.0 %	1.0 g
Polyethylene Glycol 6000 (PEG 6000) (Solubilizer,Moisturizer)	5 %	5 g
Propylene glycol (Humectant & penetration Enhancer)	10 %	10 g
Glycerin (Moisturizer & Hydration Agent)	5 %	5 g
Methyl paraben (preservative)	0.15 %	0.15 g
Propyl paraben (preservative)	0.05 %	0.05 g
Triethanolamine (pH Adjuster,Neutalizing Agent)	0.5 %	0.5 g
Ethanol (Solvent for Extract, Enhances Penetration)	10 %	10 g
Distilled water (Solvent ,Diluent)	q.s. to 100%	65.8 g

2.4. Tests

2.4.1. Physicochemical Tests

Appearance & Homogeneity –Visual Inspection

To assess the physical appearance and homogeneity of the gel, the evaluation is conducted using a transparent glass container, white and black background sheets, and a spatula. The gel is first observed under normal light to check for any lumps, phase separation, or precipitation. A small amount of the gel is then spread onto a glass slide and examined against both white and black backgrounds to assess uniformity. Observations regarding color, texture, and consistency are recorded to ensure the formulation meets the required standards. The gel must be smooth, uniform, and free from any visible lumps or phase separation to be considered acceptable for further use.

pH Measurement -Digital pH Meter

To ensure skin compatibility, the pH of the gel is measured using a digital pH meter. A 1 g sample of the gel is dispersed in 10 mL of distilled water in a beaker and stirred thoroughly before being left to stand for 30 minutes. The pH meter is calibrated with standard buffer solutions of pH 4.0, 7.0, and 9.0 to ensure accurate readings. The electrode is then inserted into the gel sample, and the pH value is recorded. This procedure is repeated three times, and the average pH is calculated. For the gel to be considered suitable for topical application, its pH must fall within the acceptable range of 4.5 to 6.5, aligning with the natural pH of the skin.

Spreadability Test -Glass Slide Method

The spreadability of the gel is assessed to determine how easily it can be applied to the skin. A 1 g sample of the gel is placed between two glass slides, and a 100 g weight is applied for one minute to ensure uniform spreading. After removing the weight, the diameter of the spread gel is measured using a ruler. This procedure is repeated three times to obtain an average spreadability value. The gel should exhibit a spreadability range of 5.0 - 7.0 g.cm/sec to ensure smooth application and adequate coverage on the skin.

2.4.2. Viscosity Test -Brookfield or Capillary Viscometer

The viscosity of the gel is measured to ensure optimal consistency for application and stability. Using a Brookfield Viscometer, 50 g of the gel is transferred into a beaker, and spindle No. 6 is immersed in the sample. The viscometer is set to 10 RPM, and the viscosity is recorded in centipoise (cP). Three readings are taken to obtain an average value. The gel should have a viscosity between 3000 - 5000 cP, ensuring it is neither too thick nor too runny, allowing for smooth application and effective skin adherence.

2.4.3. Stability Studies

Short-Term Stability -Room Temp & 40°C, 4 Weeks

The viscosity of the gel is a crucial factor influencing its application, spreadability, and stability. To measure viscosity, 50 g of the gel is placed in a 100 mL beaker, and spindle No. 6 is attached to a Brookfield Viscometer. The spindle is immersed in the gel, and the viscometer is set to 10 RPM. The viscosity is recorded in centipoise (cP), and three readings are taken to ensure accuracy. The ideal viscosity range for easy application is 3000 - 5000 cP, ensuring the gel is neither too thick nor too runny, allowing for smooth and consistent skin coverage.

Freeze-Thaw Stability -Extreme Temperature Cycles, 3 Weeks

The stability of the gel under extreme temperature variations is essential to ensure its durability and effectiveness. To assess this, the gel is subjected to alternating temperature cycles, stored at 5°C for 24 hours and then transferred to 40°C for another 24 hours. This process is repeated for three weeks to simulate real-world storage conditions. Throughout the test, the gel is closely observed for any signs of phase separation, precipitation, or texture changes. The formulation is considered stable if no visible degradation or separation occurs, ensuring its long-term usability and consistency.

Drug Content Analysis -UV-Visible Spectrophotometry

To determine the percentage of drug content in the gel, 1 g of the formulation is accurately weighed and dissolved in 10 mL of ethanol to ensure complete extraction of the active ingredient. The solution is then filtered to remove any

undissolved particles. The absorbance of the filtrate is measured using a UV-Vis spectrophotometer at the λmax specific to

Capparis Brevispina extract. The drug content percentage is calculated using a pre-established calibration curve, ensuring that the formulation maintains consistent and accurate drug concentration for effective therapeutic action.

2.4.4. Skin Irritation Study -Patch Test

To assess the safety of the gel, 0.5 g of the formulation is applied to the inner forearm of five volunteers and covered with a patch for 24 hours. After the exposure period, the area is carefully examined for any signs of redness, swelling, or irritation. The absence of severe erythema, edema, or itching confirms the gel's suitability for topical use. This test ensures that the formulation is non-irritating and safe for human application, minimizing the risk of adverse skin reactions.

3. Results

3.1. Physicochemical Evaluation

The pH of the gel remained within the acceptable range (5.46), ensured skin compatibility. The spreadability exhibited a slight decrease over time but remained within the ideal range at (6.1), indicating consistent application properties. The viscosity also showed a minimal reduction, with a final recorded value of (3250 cP), suggesting only slight structural degradation while maintaining overall stability.

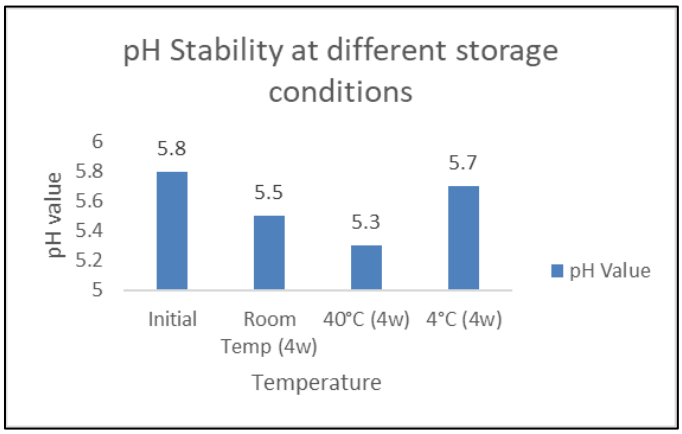


Figure 2 pH Stability

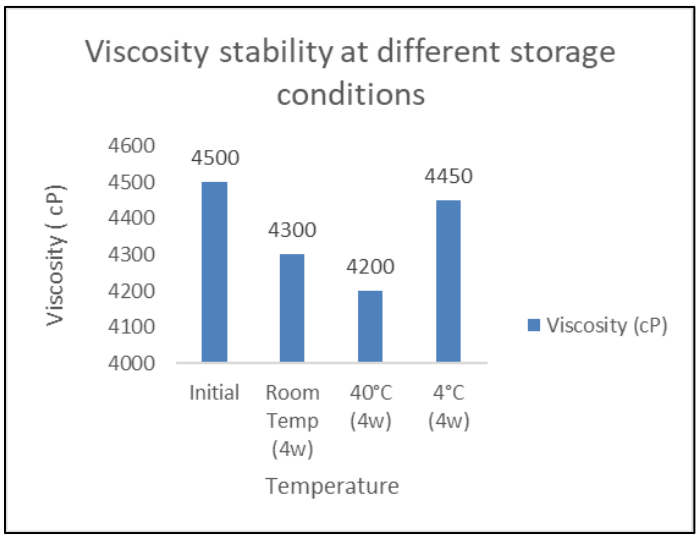


Figure 3 Viscosity Stability

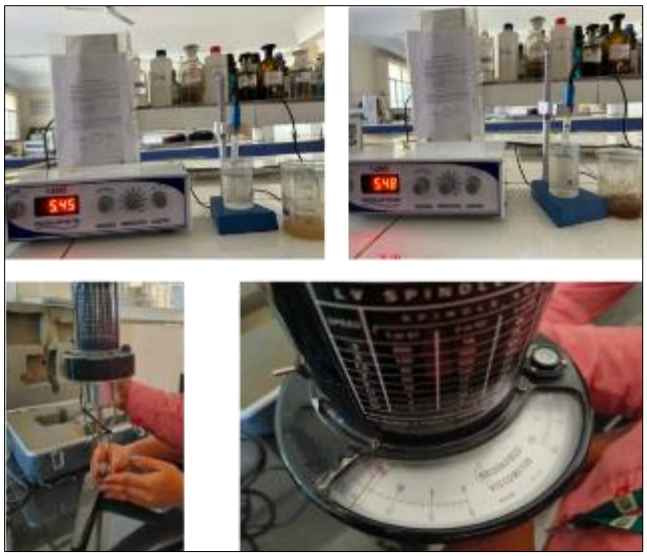


Figure 4 Physicochemical properties of formulated gel

3.1.1. Drug Content Analysis

The drug content remained above **95%,** confirmed the formulation's stability and effectiveness over time. Although a slight decrease was observed, it is a normal occurrence for herbal extracts due to natural degradation. Despite this, the retention of active compounds within the acceptable range ensures the gel's efficacy throughout the study period.

3.1.2. Skin Irritation Test Results

No significant redness, swelling, or itching was observed during the study, indicating that the gel is well-tolerated on the skin. The absence of any adverse reactions confirms its safety for topical application, making it suitable for regular use without causing irritation or discomfort.

3.1.3. Microbial Load Test Results

No significant microbial contamination was observed throughout the study, ensured the formulation's safety and integrity. The microbial counts remained well within acceptable limits, confirming that the preservative system was effective. Overall, the formulation remained microbiologically stable, making it safe for prolonged use.

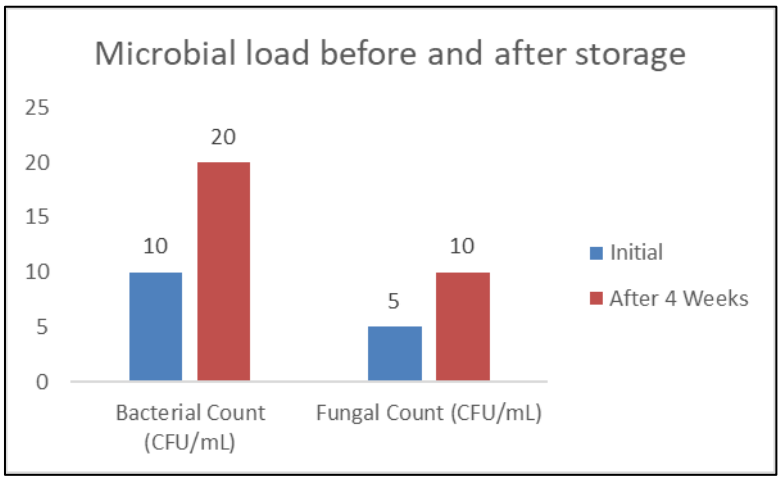


Figure 5 Microbial Load Before and After Storage

3.1.4. Graphs for evaluation parameters:

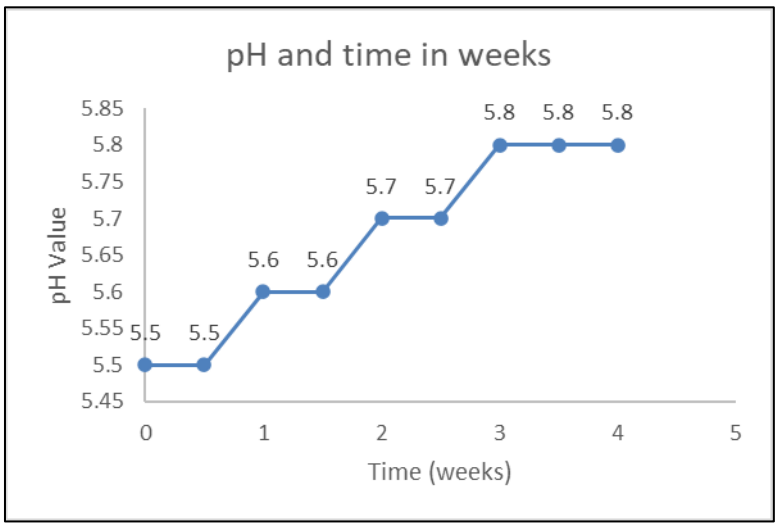


Figure 6 pH and time in weeks

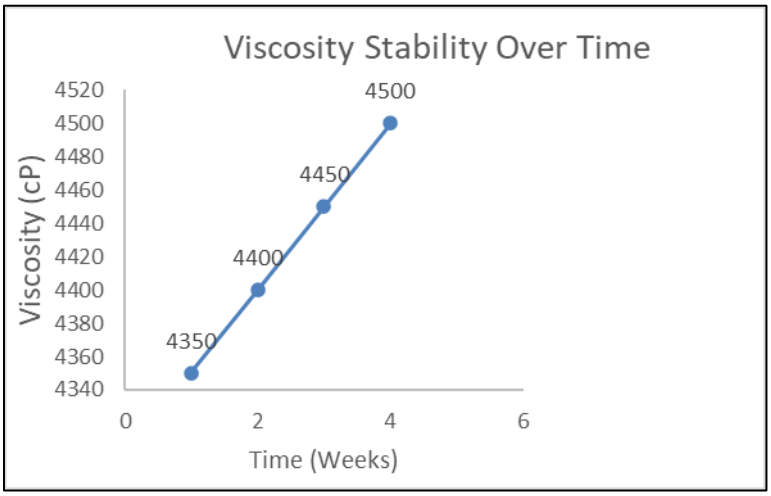


Figure 7 Viscosity Stability Over Time

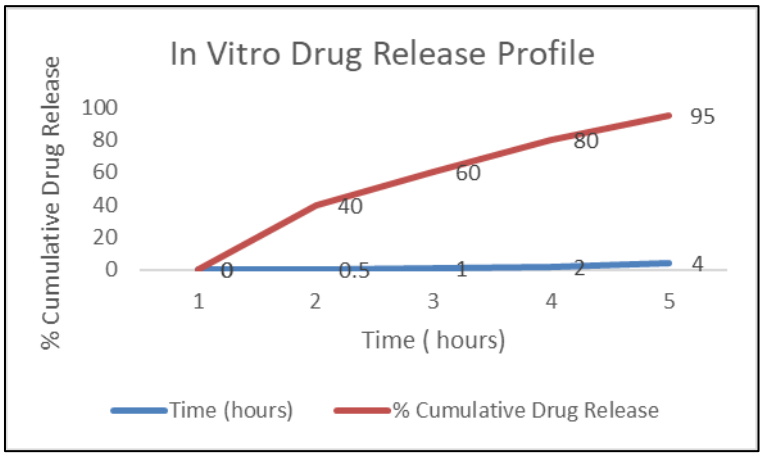


Figure 8 *In Vitro* Drug Release Profile

4. Discussion

- Physicochemical properties were stable within 4 weeks.
- pH, viscosity, spreadability, and extrudability remained within acceptable limits.
- The drug release profile showed efficient permeation, indicating good therapeutic potential.
- Skin irritation study confirmed safety for topical use.
- Stability study revealed that storage at room temperature is suitable, but high temperatures caused phase separation.
- Microbial analysis confirmed the absence of contamination, ensuring microbial safety

5. Conclusion

Outcomes from the development and testing of an anti-inflammatory gel with 2.5% *Capparis Brevispina* extract suggest that this plant may be used as a natural treatment for inflammation. The gel exhibited ideal chemical and physical characteristics, such as the right spreadability, pH, and viscosity, all of which are necessary for successful topical administration. The microbiological analysis verified the lack of dangerous bacteria, guaranteeing the formulation's safety for consumers, and the pH level was determined to be skin-friendly, reducing the chance of irritation.

Compliance with ethical standards

Disclosure of conflict of interest

The authors declare that they have no known financial, personal, or professional conflicts of interest that could have influenced the work reported in this manuscript.

Additionally, the authors confirm that they have no affiliations with or involvement in any organization or entity with a direct financial interest in the subject matter or materials discussed in this manuscript

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