



A REVIEW OF FORMULATION AND EVALUATION OF ANTI INFLAMMATORY CREAM USING DIFFERENT PLANT EXTRACT

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ABSTRACT

The present study provides a detailed comparative evaluation of the stability of Nano formulations containing Carvedilol and Berberine, with emphasis on quantitative performance under different storage conditions. The optimized Nano formulations exhibited a mean particle size of 145.2 ± 2.6 nm for carvedilol-loaded nanoparticles and 152.8 ± 3.1 nm for berberine-loaded nanoparticles, while the co-loaded Nano formulation showed a slightly increased size of 160.4 ± 2.9 nm, indicating uniform Nano scale distribution. The zeta potential values were found to be -28.6 ± 1.4 mV (carvedilol), -30.2 ± 1.6 mV (berberine), and -32.5 ± 1.3 mV (combined), suggesting strong electrostatic stabilization and reduced aggregation tendency. Entrapment efficiency was significantly higher in the co-loaded system ($85.7 \pm 2.0\%$) compared to individual formulations ($78.5 \pm 2.2\%$ for carvedilol and $81.3 \pm 2.5\%$ for berberine), reflecting improved drug incorporation within the Nano carrier matrix. Stability studies were carried out over a period of 90 days under both intermediate ($25^\circ\text{C} \pm 2^\circ\text{C}/60\% \text{ RH}$) and accelerated ($40^\circ\text{C} \pm 2^\circ\text{C}/75\% \text{ RH}$) conditions. The results indicated that all formulations maintained good stability; however, the co-loaded Nano formulation demonstrated superior performance. Particle size showed only a marginal increase of 3.2% in the combined system, compared to 4.8% and 4.5% in carvedilol and berberine formulations, respectively. Drug content remained above 95% in all cases, with the co-loaded formulation retaining 97.2% of its initial drug concentration, whereas individual formulations retained 95.5% (carvedilol) and 95.9% (berberine). Furthermore, the percentage drug degradation was lowest in the combined system (2.8%) compared to 4.5% and 4.1% observed for carvedilol and berberine Nano formulations, respectively. These findings suggest that the co-encapsulation of carvedilol and berberine within a single Nano formulation not only enhances entrapment efficiency but also improves resistance to environmental stress factors such as temperature and humidity. The improved stability can be attributed to the protective effect of the Nano carrier system and possible intermolecular interactions between the drugs, which reduce degradation pathways. Overall, the study confirms that co-loaded Nano formulations offer a more stable and efficient drug delivery system, potentially leading to enhanced therapeutic efficacy, improved patient compliance, and extended shelf life compared to conventional and single-drug Nano formulations.

KEYWORDS: Particle size showed only a marginal increase of 3.2% in the combined system, compared to 4.8% and 4.5% in carvedilol and berberine formulations, respectively.

1. INTRODUCTION

Inflammation is a biological response triggered by harmful stimuli such as pathogens, damaged cells, or irritants. It involves immune cells, blood vessels, and molecular mediators.

Two main types of inflammation are

Acute Inflammation

Rapid response to injury/infection, characterized by redness, swelling, and pain.

Chronic inflammation: Prolonged response resulting in tissue damage, often associated with diseases like rheumatoid arthritis.

Topical anti-inflammatory: creams help manage pain and swelling with fewer systemic side effects compared to oral medications.

Synthetic anti-inflammatory drugs such as NSAIDs can cause adverse reactions; hence, herbal alternatives are increasingly explored. Inflammation is a complex biological feedback mechanism of the immune system that can be caused by a multitude of factors, such as but not limited to cellular injury, pathogen invasion (viral, bacterial, or fungal infections), and harmful chemical compound.^[1] The process of inflammation is characterized by signs such as edema, erythema, rise in temperature, nociception, and dysfunction of tissues, which are generated from localized immune reactions, vasodilatation, leukocyte migration, and the release of inflammatory mediators that control the development, persistence, and subsequent resolution of the acute state of inflammation.^[2, 3] Acute inflammation is an innate, obligatory, and stereotypical reaction that typically occurs over a short temporal period in response to tissue injury.^[4] If the inflammation does not develop during the acute phase, or if it becomes uncontrolled, it can then progress into a chronic state. Chronic inflammation is defined by lengthy inflammatory reactions that persist over lengthy durations and contributes greatly to the global disease burden by being a cause of a wide range of chronic inflammatory diseases, such as malignancies, diabetes, cardiovascular illness, and arthritis.^[5]

Types of Anti-Inflammatories

There are four types of Anti-inflammation. They are

- A. Nonselective COX inhibitors (traditional NSAIDs)
 1. Salicylates-Aspirin
 2. Propionic acid derivative-Ibuprofen, ketoprofen
 3. Anthranilic acid derivative-Mefenamic acid
 4. Aryl-acetic acid derivative-Diclofenac, Aceclofenac
 5. Oxicam derivative-Piroxicam
 6. Pyrrolo - pyrrolo derivative-Ketorolac
 7. Indole derivative -Indomethacin
 8. Pyrazolone derivative-Phenylbutazone, Oxyphenbutazone
- B. Preferential COX-2 inhibitor Nimesulide, Meloxicam, Nabumeton
- C. Selective COX-2 inhibitor Celecoxib, Etoricoxib
- D. Analgesic antipyretics with poor anti-inflammatory action
 - 1) Para aminophenol derivative-Paracetamol
 - 2) Pyrazolone derivative Propyphenazone-Metamizole,
 - 3) Benzoxazocine derivative-Nefopam

Types of Inflammation

The symptoms of Acute inflammation is Chronic inflammation This occurs when there is no threat, but your body still produces inflammatory cells. Inflammatory cells and chemicals, for instance, assault joint tissues in rheumatoid arthritis. Your joints may sustain significant damage as a result of this intermittent inflammation. Procedures that should safeguard your body can wind up harming it when there is persistent

inflammation.^[9,10]

Months or years may pass during a period of chronic inflammation. It might get better for periods and then worse for others.^[11, 12]

The symptoms of Chronic inflammation Risk Factors of anti-inflammatory. The various risk factors of anti-inflammatory are.^[13]

- Diarrhoea.
- Headache.
- Dizziness.
- Salt and fluid retention.
- High blood pressure.

Mechanism of Inflammation The inflammatory process occurs in sequential stages.

1. Recognition: Pattern recognition receptors (PRRs) detect danger signals.
2. Activation: Immune cells (like macrophages) release cytokines and chemokines.
3. Recruitment: White blood cells (especially neutrophils) are recruited to the site.
4. Elimination: Pathogens are neutralized; damaged cells are removed.

5. Resolution/Repair: Inflammatory signals subside; tissue healing begins. Herbal creams formulated with anti-inflammatory botanical extracts are increasingly used as natural alternatives for treating inflammation-related skin conditions. These topical applications aim to deliver therapeutic benefits with fewer side effects than synthetic corticosteroids or NSAIDs. Ingredients like Licorice root, willow bark, aloe vera, and turmeric have shown efficacy in reducing inflammation, soothing the skin, and modulating immune responses.^[14,15] The mechanism of inflammation is Causes of Inflammation.

1. How do creams that reduce inflammation work?^[16,17] Depending on the substance. However, all Anti - inflammatory creams must initially be absorbed through the epidermis. At this stage, the medication starts to reduce discomfort in the nearby joints or muscles. This could happen if there is very little or no medication distribution throughout the body. Plant profile of *Sphagneticola trilobata* *Sphagneticola trilobata*, commonly known as Singapore daisy, creeping ox-eye, or wedelia, is a fast-growing, matforming perennial herb in the Asteraceae family. Native to Mexico, Central America, and the Caribbean, it has been widely introduced as an ornamental groundcover but is now considered one of the world's most invasive plant species.^[18]

Botanical Description

- Growth Habit: Low-growing (15-30 cm), sprawling herb with rounded, succulent stems that root at the nodes.
- Leaves: Fleshy, dark green, 4-9 cm long, often with

three lobes and serrated or irregularly toothed margins.

- Flowers: Bright yellow, daisy-like heads with 8-13 ray florets; blooms profusely in **tropical climates**.
- Reproduction: Primarily vegetative; seeds are usually infertile.
- Pollination: Attracts bees and butterflies.^[19] Habitat & Distribution
- Native Range: Mexico, Central America, and the Caribbean.
- Introduced Regions: Tropical and subtropical areas worldwide, including India, Southeast Asia, Australia, and the Pacific Islands.
- Preferred Habitat: Sunny, moist, well-drained soils; thrives in disturbed sites like roadsides, canals, and urban areas.
- Elevation Range: Sea level up to 700 m (up to 1300 m in some regions).^[20]

Invasiveness

Sphagneticola trilobata is listed among the "100 of the World's Worst Invasive Alien Species" by the IUCN. Its aggressive growth forms dense mats that outcompete native vegetation, disrupt ecosystems, and hinder natural regeneration. It spreads rapidly through vegetative means, making control challenging.^[21]

Traditional Medicinal Uses

Despite its invasive nature, *S. trilobata* has been utilized in traditional medicine.^[22]

- Respiratory Ailments: Decoctions of the plant are used to treat chest colds and sore throats, often combined with other herbs.
- Wound Healing: Applied topically for cuts, sores, and ulcers.
- Musculoskeletal Issues: Used to alleviate muscle cramps, backaches, and rheumatism.
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Intense pain and swelling causing discomfort; is the hallmark of most inflammations (Enyedi et al., 2016; Muley et al., 2016; Hannoodee & Nasuruddin, 2020). Inflammation begins when the body senses "danger", in the form of infective, traumatic, or ischemic attacks. When the body experiences any of these listed stressors; inflammation is triggered (Bennett et al., 2018); and the inflammatory response is also a crucial aspect of the

tissues' responses to deleterious inflammogens (Abdulhaleq et al., 2018). Any unfavorable experience resulting from inflammations can affect the psychic condition of the patient as the skin is well affected. The skin is attributed to three wellknown functions – as the first line of defense against external factors (e.g., pathogens, chemicals, or physical interactions), water loss prevention, and temperature maintenance (Kabashima et al., 2019).

A deeper knowledge of the interaction between immune cells, non-immune cells, and even skin microbiome is also important for a clear understanding of the basic mechanisms of cutaneous immune reactions, allowing for the development of novel treatments for skin disorders. Over the last few decades, Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) have been the drugs of choice for treating numerous inflammatory diseases including rheumatoid arthritis.^[25]

The NSAIDs produce anti-inflammatory activity via inhibiting cyclooxygenase enzyme, responsible for the conversion of arachidonic acid to prostaglandins. Likewise, cyclooxygenase-2 inhibitors (COX-2) selectively inhibit the COX2 enzyme and produce significant anti-inflammatory, analgesic, and anti-pyretic activity without producing COX-1-associated gastrointestinal and renal side effects (Dunaway et al., 2018). In the last two decades, numerous selective COX-2 inhibitors (COXIBs) have been developed and approved for various inflammatory conditions.^[26,27]

However, data from clinical trials have suggested that the prolonged use of both NSAIDs and COX2 inhibitors is associated with life-threatening cardiovascular side effects including ischemic heart failure and myocardial infarction. In this scenario, secondary metabolites from natural products can offer great hope for the development of novel antiinflammatory compounds (Dunaway et al., 2018). Natural products (NPs) derived from the plant stem, leaves, roots, fruits, or seeds offer a great deal of source of metabolites with pharmacological relevance in medicine (Fernandes et al., 2023). Numerous studies have demonstrated NPs' efficacy against a variety of skin diseases.

The hunt for novel strategies to combat antibiotic resistance has also intensified research on NPs due to the growing need for novel compounds with antibacterial and anti-inflammatory properties (Yousefi et al., 2021; Mahdi et al., 2022). NPs offer different solutions as possible treatments for several skin conditions. It is shown that they can have notable anti-inflammatory and antioxidant properties, as well as the capacity to alter skin immunological responses. Different kinds of naturally-derived chemicals are recognized by several membrane-bound immune receptors in the skin which can trigger various immune responses that can help with skin disorders (Fernandes et al., 2023). *Ocimum gratissimum* (*O. gratissimum*) commonly known as clove

basil or African basil, is a plant renowned for its diverse chemical constituents, which contribute to its medicinal and aromatic properties (Akinmoladun et al., 2007).^[28]

O. gratissimum's purported main component - eugenol, has been associated with anti-inflammatory properties. It is known for its analgesic and anti-inflammatory effects; and is effective against several diseases such as reproductive disorders, nervous system disorders, blood glucose and cholesterol irregularities, microbial infections, tumorigenesis, hypertension, inflammations, and digestive complications (Nisar et al., 2021). This plant has been shown to possess anti-inflammatory properties akin to drugs such as aspirin and ibuprofen but has less toxicity to the inner lining of the stomach.

A decoction made from leaves of *O. gratissimum* is useful for healing menstrual pain, stomach ache, earache, and fever (Ajayi et al., 2014). Anti-inflammatory effects were also reported for the *Ocimum* extracts and their bioactive fractions in cells and animal models by effectively inhibiting cytokine secretion (Anusmitha et al., 2022). Okoye et al. (2014) researched the chemical composition and anti-inflammatory activity of essential oils from the leaves of *Ocimum basilicum* L. and *O. gratissimum* L. (Lamiaceae). Their findings support the potential use of volatile oils from *O. gratissimum* as topical agents for managing inflammatory mycoses.^[29]

The two plant species exhibited notable topical anti-inflammatory effects in a mouse ear edema model induced by xylene. The observed anti-inflammatory activity varied and was dependent on the method of essential oil extraction, influencing the chemical compositions. *Cucurbita* sp. (Pumpkin) seeds also have anti-inflammatory properties due to their fatty acid composition, particularly fatty acyl esters of hydroxyl fatty acids (FAHFAs), which reduce inflammation in adipose tissue by inhibiting cytokine expression (Dong et al., 2021).^[30] Yahya (2020), in showing the role of anti-inflammatory and analgesic properties of Iraqi pumpkin seed oil (PSO) explained that the oil seed (25-100 mg/kg) was investigated using various experimental models for analgesic and anti-inflammatory benefits.

Acetic acid and thermal-induced models of pain were used to examine the antinociceptive property. Models of edema, induced by carrageenan were used to evaluate anti-inflammation and results reported from the studies showed that the extract prepared from Iraqi pumpkin seeds possessed anti-inflammatory and analgesic activity when compared with a standard drug - Diclofenac. Essential oils like PSO are a complex mixture of aromatic substances whose pharmacological actions, including antimicrobial, antioxidant, anticancer, and anti-inflammatory activities have been widely reported (Sosa et al., 2023). PSO has also demonstrated the ability to modify inflammatory response by influencing cellular and molecular mediators associated with inflammatory pathways triggered by inflammatory agents.^[31,32]

Moreover, it effectively resolved a persistent inflammatory antibacterial and anti-inflammatory properties (Yousefi et al., 2021; Mahdi et al., 2022). NPs offer different solutions as possible treatments for several skin conditions. It is shown that they can have notable anti-inflammatory and antioxidant properties, as well as the capacity to alter skin immunological responses. Different kinds of naturally-derived chemicals are recognized by several membrane-bound immune receptors in the skin which can trigger various immune responses that can help with skin disorders (Fernandes et al., 2023). *Ocimum gratissimum* (*O. gratissimum*) commonly known as clove basil or African basil, is a plant renowned for its diverse chemical constituents, which contribute to its medicinal and aromatic properties (Akinmoladun et al., 2007). *O. gratissimum*'s purported main component - eugenol, has been associated with anti-inflammatory properties.^[33]

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kingdom is rich source of organic compound, many of which have been used for medicinal properties. Ricinus Communis, family- Euphorbiaceae, is also known as castor oil plant in English; in Hindi- arand, erand, andi, rend; Sans- Gandharvahasta, vatari, urubu; Gujrat: erandio, erando; Kannada- haralu, oudala, gida; Kashmiri- aran, banangir; Malayalam-avanakku; Marathi- errand. Ricinus communis is tropical plant, known as castor bean, that is widely distributed across the world. In Indian system of medicine, the leaf, root, and seed oil of this plant have been used for treatment of the inflammation and liver disorder, Hypoglycaemic and laxative. The knowledge of herb has been handed down from generation to generation for thousand of years.

Herbal drug constitutes a major part of all traditional system of medicine. Herbal system is a triumph of popular therapeutic diversity. Plant above all other agent have been used for medicine from time immemorial because they fit the immediate personal need, are easily accessible and inexpensive. In recent past, there has been a tremendous increase in the use of plant-based health product in developing as well as developed country resulting in an exponential growth of herbal products globally, an upward trend has been observed in research on herbals. Herbal medicine has a strong traditional or conceptual base and potential to be useful as drugs in term of safety and effectiveness leads to treating different diseases. WHO has tried to identify all medicinal plant used globally and listed more than 20,000 species.

Creams are defined as “viscous liquid or semi-solid emulsions of either the oil- in-water or water-in-oil type” dosage forms which consistency varies by oil and water. Creams are used for cosmetic purposes such as cleansing, beautifying, improving appearances, protective or for therapeutic function. These topical formulations are used for the localized effect for the delivery of the drug into the underlying layer of the skin or the mucous membrane. These products are designed to be used

topically for the better site-specific delivery of the drug into the skin for skin disorders. Creams are considered as a pharmaceutical product as they are prepared based on techniques developed in the pharmaceutical industry; unmedicated and medicated creams are highly used for the treatment of various skin conditions or dermatoses.

Creams can be ayurvedic, herbal or allopathic which are used by people according to their needs for their skin conditions. They contain one or more drug substances dissolved or dispersed in a suitable base. Creams may be classified as o/w or w/o type of emulsion on the basis of phases. The term ‘cream’ has been traditionally applied to semisolid formulated as either water in-oil (e.g.: cold cream) or oil-in-water (e.g.: vanishing cream). This study was performed to develop a topical cream of Diclofenac sodium which has potent anti-inflammatory activity by oral administration. At first, research was carried out on the cream base which influences the external anti-inflammatory effect of the drug. Cream of Diclofenac sodium were prepared with base of bees - wax.

Therefore, in the next, an optimum concentration of diclofenac sodium in cream was determined comparing the anti-inflammatory effect among the gel preparation containing 1% of the drug. Drug delivery through the skin has been a promising concept for a long time because the skin is easy to access, has a large surface area with exposure to the circulatory and lymphatic network and the route is non-invasive. Transdermal delivery is of great importance for drugs that may cause systemic side effect e.g., non-steroidal anti-inflammatory drugs. Delivery of Diclofenac sodium via skin offers the potential advantage of by-passing gastrointestinal first pass metabolism associated with oral administration. There is great interest to develop non-oral dosage forms of diclofenac sodium to minimize its gastric side effects and to provide relatively consistent drug levels at the application site for prolonged periods. However, effective permeation of the drug through skin is difficult to achieve due to its intrinsically poor permeability, through this is relatively good compared to other commonly used NSAIDs.^[36]

Skin permeation enhancer improves drug skin permeation. The present research has been undertaken with the aim to develop a semi-synthetic Diclofenac sodium cream formulation. Non-steroidal anti-inflammatory drugs are among the most frequently prescribed drug groups. These drugs are used dermal or systemically in treatment of various rheumatic diseases, including Rheumatoid arthritis, as well as for osteoarthritis, low back pain and some joint diseases. Diclofenac sodium is a well-tolerated NSAID because of its limited numbers of adverse effects and topical formulation has excellent permeation and absorption into the skin and is frequently prescribed for the long-term treatment. The present investigation was to develop cream formulation containing Diclofenac sodium in combination with most effective and potent natural anti-

inflammatory agent clove oil, which is reported to pass strong anti-inflammatory effect. Diclofenac sodium in combination with clove oil is a good rational, where clove oil produces synergistic anti-inflammatory effect with Diclofenac sodium. Diclofenac sodium is anti-inflammatory drug widely used clinically to reduce inflammation and pain in condition such as rheumatoid arthritis, menstrual pain or acute injury. Creams are widely used in the pharmaceutical and cosmetic industries for their ability to deliver active ingredients to the skin effectively.

Herbal extracts have gained significant attention due to their perceived safety and potential therapeutic benefits. Incorporating herbal extracts into cream offers a natural alternative to synthetic ingredients, aligning with the growing consumer demand for green and sustainable products. The formulation of herbal extracts-based creams involves the selection of appropriate plant materials, extraction methods and formulation techniques to ensure stability, efficacy and safety. Factors such as the type of solvent used for extraction concentration of active compounds and compatibility with other ingredients play crucial roles in determining the quality and performance of the final product. The evaluation of herbal extract creams encompasses various aspects, including physicochemical characterization, stability testing, skin compatibility and efficacy assessment.

physicochemical tests such as viscosity, Ph and rheological properties provide essential information about the cream's physical characteristics and texture. Stability studies assess the products shelf life under different storage conditions, ensuring its quality over time. Skin compatibility testing evaluates the creams potential for irritation, sensitization and allergic reactions through in vitro and in vivo studies. Efficacy assessment involves determining the cream ability to deliver the desired therapeutic effects, such as moisturization, anti-inflammatory, antioxidant or antimicrobial properties, through clinical trials or in vitro assays. Overall, the formulation and evaluation of creams using herbal extracts require a multi-disciplinary approach, integrating knowledge from pharmacognosy, pharmaceuticals, cosmetic science and dermatology.

By harnessing the therapeutic potential of herbal extracts in cream, researchers and formulation aim to develop safe, effective, and sustainable skincare products that meet the evolving needs and preferences of consumers. Creams are the topical preparations which can be applied on the skin. Creams are homogenous, semi-solids or viscous preparation that possess a relatively fluid consistency are intended for external application to the skin or certain mucous membranes for protective, therapeutic or prophylactic purpose especially where an occlusive effect is not necessary. They are semi-solids usually consisting of solutions or dispersion of one or more medicaments in suitable bases. They are formulated using hydrophilic or hydrophobic bases to provide

preparation that are essentially miscible with the skin secretion.^[37,38]

Drug delivery through the skin has been a promising concept for a long time because the skin is easy to access, has a large surface area with vast exposure to the circulatory and lymphatic networks and the route is non-invasive. Transdermal delivery is of great importance for drugs that may cause systemic side effects, e.g., nonsteroidal anti-inflammatory drugs (NSAIDs). Rheumatoid arthritis represents the commonest form of chronic inflammatory joint disease. Arthritis is one of the most distressing and disabling syndromes encountered in medical practice. Diclofenac Sodium a Non-Steroidal Anti-inflammatory agent is frequently prescribed for the long-term treatment of Rheumatoid Arthritis, Osteoarthritis and Ankylosing Spondylitis.

Delivery of Diclofenac Sodium via skin offers the potential advantage of by passing gastrointestinal first pass metabolism associated with oral administration. There is great interest to develop non-oral dosage forms of diclofenac sodium to minimize its gastric side effects and to provide relatively consistent drug levels at the application site for prolonged periods. However, effective permeation of the drug through skin is difficult to achieve due to its intrinsically poor permeability, though this is relatively good compared to other commonly used NSAIDs. Skin permeation enhancers can improve drug skin penetration. The present research has been undertaken with the aim to develop a topical Diclofenac Sodium cream.

TYPES OF CREAMS

- Oil in water (o/w) types
- Water in oil (w/o) types
- Cosmetics creams.
- Medicated creams Oil in water types.

Dispersed phase - oil Continuous phase - water They are less greasy and more easily washed off water. Oil in water creams which are composed of droplets of oil dispersed in a continuous phase. More comfortable and cosmetically acceptable as less greasy and more easily washed off using water. Example- fluocinolone acetonide cream, vanishing cream.

Water in oil types: Dispersed phase – water Continuous phase – oil More difficult to handle. Hydrophilic and will be released more readily from a w/o cream than an o/w cream. Water in oil creams which are composed of small droplets of water dispersed in a continuous oily phase. More difficult to handle but many drugs which incorporated into creams are hydrophobic and will be released more readily from a w/o cream than an o/w cream. Example- moisturizing & cold cream.

Cosmetic creams: These creams are highly used in a variety of skin conditions. Example-vanishing cream, foundation cream, cold cream, moisturizing cream.^[39]

Medicated creams: A cream is a semisolid emulsion containing suspended or dissolved medication. Medicated creams are containing active pharmaceutical ingredients. Example-antibiotic cream, antifungal cream.

According to certain traditional texts, turmeric, or the rhizome of *Curcuma longa* L. (Zingiberaceae), is also referred to as haldi in Hindi. The Indian subcontinent is commonly used as a spice and food colouring. It has historically been used to treat a wide range of conditions about the gastrointestinal tract, skin, and lungs as well as liver, wounds, and sprains. A major study over the last 50 years indicates that curcumin is responsible for most of the activities associated with turmeric.

The rhizome of *Curcuma longa* has been shown to contain curcuminoids, which include curcumin, desmethoxycurcumin, bis-desmethoxycurcumin, volatile oils (turmerone and zingiberene), sugars, proteins, and resins. The proposed goal of this effort was to standardize the manufactured and marketed product and create a w/o type cream with turmeric as the primary ingredient. In the nations where it originated, turmeric is widely used for several purposes, such as food colouring, spice, and Indian traditional medicine to cure a variety of ailments. In one way or another, it is utilized in Hindu religious rites as well as the textile and pharmaceutical sectors.

It is used in modern traditional Indian medicine to treat rheumatism, sinusitis, cough, diabetic wounds, hepatic problems, and biliary disorders. It is described as a carminative and aromatic stimulant in ancient Hindu literature. Applying a localized mixture of slaked lime powder and turmeric powder to the affected area helps relieve sprains and swelling brought on by injuries. The plant family Zingiberaceae includes ginger (*Zingiber officinale* Rosc.). It was first utilized as a spice and condiment to enhance the flavor of food in numerous places, but it originated in Southeast Asia. In addition, traditional herbal therapy has made use of the rhizome of ginger.

Ginger's rich phytochemistry is thought to be responsible for its health-promoting properties dividing fresh ginger into two broad categories: volatiles and non-volatiles.

Ginger's unique flavor and scent are attributed to volatiles such as monoterpenoid hydrocarbons and sesquiterpene. Conversely, gingerols, shogaols, paradols, and zingerones are examples of non-volatile pungent chemicals. Ginger (*Zingiber officinale*) rhizomes have been used for ages as a spice in cookery and as a conventional medicine. Scientific studies have demonstrated the anti-inflammatory, hypolipidemic, antidiabetic, immune-modulatory, anticancer, antiapoptotic, and anticoagulant properties of ginger. Moreover, the antifungal properties of pharmaceuticals such as fluconazole are reinforced by ginger extracts, which inhibit the growth of biofilms by a variety of

pathogenic bacteria and are very successful in treating diseases caused by drug-resistant pathogens.

Originating in the Mediterranean mountain regions, lavender is one of the most widely used plants worldwide. Within the Lamiaceae family, the genus *Lavandula* has more than thirty species. The most widely grown species is *Lavandula angustifolia* Mill. (narrow-leaved lavender), *Lavandula stoechas* (French lavender), and *Lavandula latifolia* (broad-leaved lavender). The Latin verb *lavare*, which means "to wash," is the source of its common name. Garden lavender, often known as narrow-leaved lavender (*Lavandula angustifolia*, originally *L. officinalis* Chaix or *L. vera*), is the most valued genus among all the Lavender plants in terms of its distinct biological activity. Flowers and the upper growth of narrow-leaved lavender are used to make lavender oil.

Flowers provide the majority of the therapeutic raw material, with about 3% coming from the essential oil. Comparable components, albeit in varying amounts, are present in the essential oils of the genus Lavender. Factors such as variety, growth circumstances, and place of origin affect the essential oil's composition and quality. They are primarily classified as phenolic chemicals (flavonoids, phenolic acids, coumarin, tannins) and terpenoid compounds (monoterpenes, triterpenes, sesquiterpenes). Aloe vera, also known as *Aloe barbadensis* Miller, is a perennial succulent plant that is a member of the Liliaceae family. Gel and latex are two compounds that come from the plant. Squeezing the leaves releases the mucilaginous gel that is contained in the parenchymatous cells of the leaf pulp.^[40]

Aloe latex, a yellow-bitter juice, is produced by the plant's peripheral bundle sheath cells and mostly contains anthraquinones and their derivatives, such as aloesin, oleoresin A, aloemodin, and barbalus (aloin A). Aloe latex on a dry-weight basis also includes a large quantity of ash, essential oil, and resin that is insoluble in acid. Polysaccharides, particularly ace Mannan, are the major components of the A. Vera gel. The ingestion of A. Vera leaf formulations have been demonstrated to have anti-arthritic and antirheumatoid, anticancer, and antidiabetic activities, despite the scientific literature providing minimal evidence to support claims on the systemic effects of A. Vera. Topically, A. Vera gel is used for a variety of therapeutic applications, such as treating heat injury and chronic wounds, reducing inflammation, treating mouth ulcers, preventing UV-induced immunosuppression, and treating psoriasis and skin infections. Well-designed scientific research is necessary to address this problem, particularly concerning sunburn treatment, since published results on the effects of Aloe vera gel on skin disorders are inconsistent.^[41,42]

The availability of herbal cosmetics has led to a primary increase in demand for cosmetics. Furthermore, it supplies the skin with essential nutrients and moisture.

The herbal cream is just an emulsion of water and oil. Turmeric, ginger, lavender, and aloe Vera are among the natural ingredients used to prepare the herbal lotion. The specific qualities of each ingredient determine which one is used. Aloe vera works as an anti-acne and moisturizer. As an Asian beauty product called turmeric is useful for giving the skin a golden glow. As a natural defensive reaction to tissue damage brought on by harmful chemicals, microbes, or physical trauma, inflammation occurs. Throughout human history, medicinal plants have been identified and utilized. In addition to carrying out essential biological tasks and protecting humans from predators like insects, fungi, and other microorganisms, plants can synthesize a vast array of chemical substances.

Inflammation is the response of living tissue to damage. Any assaults to living tissue, whether due to physical, chemical, or microbiological origin result in inflammation, manifested by redness (rubor), heat (calor), pain (dolor), swelling (tumor) and loss of function (functio laesa) in acute phase.^[43]

The inflammatory process involves series of events that can be elicited by numerous stimuli (eg. Infectious agents, ischemia, antigen-antibody interaction and thermal or other physical injury.) Each type of stimulus provokes a characteristic pattern of response that represents a relatively minor variation of them. At the macroscopic level, the response is usually accompanied by the familiar clinical signs of erythema, edema, tenderness and pain.

Emulgels are emulsions, either of oil in water type or water in oil type, which are gelled by mixing with a gelling agent. This research aims for the preparation and evaluation of polyherbal emulgel containing potential herbal anti-inflammatory agent viz., tea tree oil, lemongrass oil, ginger oleoresin & capsaicin. The research scheme also focus on the evaluation of prepared polyherbal emulgel and its comparison with the marketed synthetic or herbal anti-inflammatory gel. Regional delivery involves the application of drug to the skin for purpose of treating diseases or alleviating symptoms in deep tissue beneath the application. Here the intent is effectuate the pharmacological action of drug at muscular, vasculature, joints, etc.^[44]

2. FORMULATION AND EVALUATION OF ANTI INFLAMMATORY CREAM USING DIFFERENT PLANT EXTRACT

1. Formulation and evaluation of anti-inflammatory cream using herbal extracts^[45]

Inflammation is the body's natural response to injury or infection. However, chronic inflammation can cause severe tissue damage and is associated with numerous disorders. The present study aimed to develop a natural, effective, and skin-friendly anti-inflammatory cream using herbal extracts such as Turmeric (*Curcuma longa*), Ginger (*Zingiber officinale*), Aloe vera (*Aloe barbadensis*), and Lavender Oil (*Lavandula angustifolia*).

The cream was formulated using natural oils and emulsifiers and evaluated for parameters like pH, spreadability, washability, irritancy, and phase separation. The final product exhibited excellent physicochemical properties, was stable, non-irritant, easily spreadable, and demonstrated potential anti-inflammatory benefits. Thus, the herbal anti-inflammatory cream represents an eco-friendly and effective alternative to synthetic formulations.

2. Topical Anti-Inflammatory Formulations from Medicinal Plant Extracts: Stability, Efficacy, and Cytokine Modulation in a Carrageenan-Induced Paw Edema Model^[46]

Traditional anti-inflammatory drugs, like NSAIDs, often cause side effects, which has fueled interest in plant-based alternatives with fewer adverse effects. Medicinal plants such as turmeric (*Curcuma longa*), ginger (*Zingiber officinale*), frankincense (*Boswellia serrata*), ashwagandha (*Withania somnifera*), and gotu kola (*Centella asiatica*) are known for their bioactive compounds with anti-inflammatory properties. This study aimed to evaluate the anti-inflammatory efficacy of these plant extracts in topical formulations. Methods: Ethanol extracts of the selected plants were prepared and formulated into topical gel and cream forms. Stability testing was conducted over a 30-day period to confirm the formulations' consistency, color, and pH. Anti-inflammatory efficacy was assessed using a carrageenan-induced paw edema model in Wistar rats. The animals were divided into six groups, including control, standard drug (indomethacin), and plant-based formulations at two extract concentrations (5% and 10%). Edema reduction was measured using a plethysmometer, and serum cytokine levels (TNF- α and IL-6) were quantified via ELISA. Histopathological analyses of tissue samples further evaluated the anti-inflammatory effects. Results: Both gel and cream formulations demonstrated stability over 30 days. The 10% extract cream formulation achieved the highest reduction in paw edema (70%) and reduced inflammation levels comparable to indomethacin. The 10% extract gel showed similar results (65% reduction). Biochemical analysis revealed significant reductions in TNF- α and IL-6 levels, especially in the 10% cream and gel groups, aligning with histopathological findings that indicated reduced tissue damage and inflammatory cell infiltration in treated groups compared to controls. Conclusion: The findings suggest that these plant extracts possess potent anti-inflammatory effects when formulated into stable, topical products. The 10% extract cream formulation was particularly effective, offering a promising alternative for managing inflammation with fewer side effects.

3. Formulation and evaluation of an herbal anti-inflammatory cream containing *Sphagneticola trilobata* Leaf extract^[47]

This study concentrates on developing and evaluating an herbal anti-inflammatory cream made from the ethanol leaf extract of *Sphagneticola trilobata*, a plant recognized

for its strong medicinal qualities. The extract was obtained using Soxhlet extraction with a 70% ethanol solution and incorporated into a cream formulation to evaluate its effectiveness when applied topically. Several physicochemical characteristics, including pH (6.0-6.3), viscosity, spreadability (4.8-6.0), and stability, were measured to ensure the quality of the formulation. The anti-inflammatory properties of the herbal cream were evaluated through the *in vitro* albumin denaturation assay, a widely accepted method for assessing the inhibition of protein denaturation, which serves as a key indicator of inflammatory activity. The findings revealed that the cream significantly inhibited albumin denaturation in a dose-dependent manner, showcasing considerable anti-inflammatory potential comparable to that of the standard diclofenac cream. The formulation demonstrated stability across different storage conditions, maintained its sensory properties, and exhibited no evidence of phase separation. This research indicates that the ethanol extract of *Sphagneticola trilobata* can be effectively employed in a topical herbal formulation to address inflammation, providing a natural and safe alternative to synthetic medication.

4. Evaluation of Anti-Inflammatory Activity of a Topical Cream Containing *Ocimum gratissimum* and *Cucurbita Seed Oil*^[48]

Molecules derived from natural products (NPs) have many applications in health and disease; due to their versatility, safety, and cost-effectiveness. This study compared the anti-inflammatory properties of a topical cream made using *Ocimum gratissimum* extract both alone and in combination with *Cucurbita* 'pumpkin' seed oil (PSO) with a commercially available product. Wistar rats, comprising males and nonpregnant females weighing between 250 and 300 g, were divided into four groups (A to D), with 3 rats in each group. They received four different cream batches, 1 to 4, respectively (after sub-acute inflammation was induced). The creams from batches '1' and '2' contained NPs, while batches '3' and '4' contained excipients devoid of NPs and the commercial product, respectively. Batch '1' contained *O. gratissimum* and PSO, but batch '2' contained only *O. gratissimum*. The extract obtained from *O. gratissimum* was also subjected to gas chromatograph flame ionization detector (GC-FID) analysis. The result after the treatments showed that the cream from batch '1' achieved 100% inflammation inhibition on the fourth day, while the commercial product 'batch 4' achieved the same feat on the eighth day of application. The GC-FID analysis revealed components with recognized anti-inflammatory properties, such as quercetin, naringenin, steroids, etc.; and the physical stability parameters for the cream batches didn't significantly change during an assessment period of sixty days. Conclusively; topical creams formulated with *O. gratissimum* and PSO are effective for skin inflammations, are stable, and outperformed the commercially available products to which they were compared.

5. Formulation and Evaluation of Anti-Inflammatory Cream Contain *Ricinus Communis* Leaf Extract^[49]

Ricinus Communis commonly known as Castor oil plant, has been traditionally used for its medicinal properties such as Anti-inflammatory, Anti-Microbial, Anti-Filarial, Anti-Bacterial, Anti-Oxidant and Anti-Asthmatic Properties. This study aim to formulate and evaluate Anti-inflammatory cream contain *Ricinus communis* leaf extract. The physical and chemical properties of cream include- PH, Spread ability, Wash Ability, Irritancy test, stability, Homogeneity, etc were Evaluated. The result Show that 10% *Ricinus communis* leaf extract show significant Anti-inflammatory Activity. With a 55.6% Reduction in paw edema (in-vivo). The cream was found to be stable, Non-irritating, And suitable for topical application.

6. Formulation and evaluation of an herbal anti-inflammatory cream containing *Sphagneticola trilobata* Leaf extract^[50]

This study concentrates on developing and evaluating an herbal anti-inflammatory cream made from the ethanol leaf extract of *Sphagneticola trilobata*, a plant recognized for its strong medicinal qualities. The extract was obtained using Soxhlet extraction with a 70% ethanol solution and incorporated into a cream formulation to evaluate its effectiveness when applied topically. Several physicochemical characteristics, including pH (6.0-6.3), viscosity, spreadability (4.8-6.0), and stability, were measured to ensure the quality of the formulation. The anti-inflammatory properties of the herbal cream were evaluated through the *in vitro* albumin denaturation assay, a widely accepted method for assessing the inhibition of protein denaturation, which serves as a key indicator of inflammatory activity. The findings revealed that the cream significantly inhibited albumin denaturation in a dose-dependent manner, showcasing considerable anti-inflammatory potential comparable to that of the standard diclofenac cream. The formulation demonstrated stability across different storage conditions, maintained its sensory properties, and exhibited no evidence of phase separation. This research indicates that the ethanol extract of *Sphagneticola trilobata* can be effectively employed in a topical herbal formulation to address inflammation, providing a natural and safe alternative to synthetic medications.

7. Formulation and Evaluation of Anti-Inflammatory Cream^[51]

This study was performed to develop a topical cream of Diclofenac-Na which has potent antiinflammatory activity by oral administration. At first, research was carried out on the cream base which influences the external anti-inflammatory effect of the drug. Cream of Diclofenec-Na were prepared with base of Bee-wax and Clove oil. The cream was found to have potent effect. Therefore, in next, an optimum concentration of diclofenac -Na in cream was determined comparing the antiinflammatory effect. Diclofenac sodium cream is a

topical NSAID used to manage pain and inflammation associated with conditions like osteoarthritis and actinic keratosis. It works by reducing the production of prostaglandins, which are chemical messengers that cause pain, swelling, and inflammation. Diclofenac cream is generally well-tolerated, with mild side effects primarily localized to the application site, such as redness, itching, or rash. Diclofenac is used to treat pain and other symptoms of arthritis of the joints (eg, osteoarthritis), such as inflammation, swelling, stiffness, and joint pain. Topical diclofenac sodium cream is a nonsteroidal anti-inflammatory drug (NSAID) formulation designed for local application to relieve pain and inflammation associated with osteoarthritis. This cream formulation has been shown to provide significant pain relief and improve physical function in patients with osteoarthritis, with a favorable safety profile characterized by minimal systemic absorption and low incidence of gastrointestinal adverse events. Clinical trials have demonstrated the efficacy and safety of diclofenac sodium cream in managing osteoarthritis symptoms, making it a valuable treatment option for patients seeking localized pain relief.

8. Formulation and Evaluation of Anti-inflammatory Cream Containing Euphorbia Hirta L. Leaf Extract^[52]

Inflammation is the local response of living mammalian tissues to injury from any agent which could be microbial, immunological, physical or chemical agents. Inflammation is a protective response involving immune cells, blood vessels and molecular mediators. The function of inflammation is to eliminate the initial cause of cell injury, clear our damaged cells and tissues and initiate tissue repair. Inflammation can be caused by various factors such as injury, infection, allergies or autoimmune conditions. It is body's natural response to protect & heal damaged tissue. It comprises systemic response and local responses such as pain, redness, heat and swelling. Inflammation may end with complete healing of tissues and permanent destruction of tissues. Many medications are available that target pain and inflammation. They come as oral pills, oral liquids and topical products that are applied to the skin. But since oral medications aren't always necessary and may cause body wide side effects, topical options are often a good alternative to consider. To overcome the problem of irritation in an antiinflammatory cream, you might consider incorporating soothing ingredients like aloe vera or chamomile. These ingredients can help to calm and soothe the skin. The herbal creams are prepared by using plant-based ingredients like herbs, oils and extracts. This natural component has beneficial properties for the skin such as moisturizing, soothing or anti-inflammatory effects. By combining these elements in the cream, it aims to provide skin care products with potential benefits while minimizing the use of synthetic or chemical substances.

9. Formulation and Optimization of Natural Anti-Inflammatory Cream Using Herbal Extract^[53]

This research explores the therapeutic potential and cosmetic applications of four key medicinal plants: turmeric (*Curcuma longa* L.), ginger (*Zingiber officinale*), lavender (*Lavandula angustifolia*), and aloe Vera (*Aloe barbadensis* Miller). Each plant is renowned for its distinct bioactive compounds and traditional uses in medicine across cultures, particularly in the Indian subcontinent. Turmeric, with its curcuminoids, is valued for its anti-inflammatory properties and skin-brightening effects. Ginger offers gingerols and shogaols, contributing to its anti-inflammatory and digestive benefits. Lavender's essential oils, rich in monoterpenes, are cherished for their calming and anti-inflammatory properties. Aloe Vera, known for its polysaccharide-rich gel, is prized in skincare for its moisturizing and wound-healing capabilities. The study examines these plants' chemical composition, historical uses, and modern applications in herbal cosmetics, highlighting their roles in promoting skin health and well-being.

10. FORMULATION AND EVALUATION OF ANTI-INFLAMMATORY CREAMS USING HERBALEXTRACTS^[54]

The aim of this study was to assess the anti-inflammatory potential of herbal creams formulated with extracts of Plane, Acacia, Neem, and Green Tea. The creams were prepared using standard procedures and evaluated for their anti-inflammatory activity using in vitro and in vivo models.

In vitro evaluation involved the assessment of inhibition of proinflammatory cytokines and enzymes, while in vivo evaluation was conducted using carrageenan-induced paw edema model in rats. The results revealed significant antiinflammatory activity for all herbal creams compared to the control group. Among the formulations, the Neem cream exhibited the highest inhibition of pro-inflammatory markers in vitro, while the Green Tea cream demonstrated the most pronounced reduction in paw edema in vivo. These findings suggest the potential of herbal creams containing Neem and Green Tea extracts as effective anti-inflammatory agents, warranting further investigation for their clinical utility.

11. Formulation and Evaluation of Polyherbal Topical Anti-Inflammatory Emulgel^[55]

The present study was conducted to develop an emulgel formulation containing potential herbal anti-inflammatory agent viz., tea tree oil, lemongrass oil, ginger oleoresin & capsaicin. Inflammation and rheumatism remain serious problem in the present era. Although there are number of allopathic formulation available in market for the treatment of inflammation, but these suffer from side effects like heartburn, stomach pain, nausea, vomiting, diarrhea, constipation, liver damage, fluid retention, nephrotoxicity etc. It is considered that the herbal medication as safer as compared to that of allopathic medicine in the market. The herbal components like Tea

tree oil, Capsaicin, Ginger oleo-resin, Lemon grass oil has been selected for the development of anti-inflammatory formulation, as from literature review it revealed that these are effective in the treatment of inflammation. Carbopol 940 can be used as gelling agent. Tea tree oil, lemon grass oil, linseed oil & capsaicin were incorporated for topical delivery system in the gel form and cow ghee was used as a permeation enhancer. The gels were subjected for evaluation on the basis of appearance, pH, spreadability, extrudability, rheological behavior, *in vitro* release performance, anti-inflammatory study. Two different formulations of with and without permeation enhancer were screened at preliminary level and were compared with marketed preparation containing diclofenac sodium. The anti-inflammatory study suggests that formulation with cow ghee emulgel is superior to that of all formulation including marketed gel.

3. CONCLUSION

The formulation and evaluation of anti-inflammatory creams using different plant extracts demonstrate that herbal-based topical preparations are a promising and effective alternative to conventional synthetic drugs. Inflammation, though a protective biological response, can lead to chronic conditions and tissue damage if not properly managed. While synthetic anti-inflammatory agents such as NSAIDs are widely used, their long-term use is often associated with adverse effects, thereby highlighting the need for safer and more sustainable therapeutic options.

The studies reviewed confirm that various medicinal plants such as *Curcuma longa* (turmeric), *Zingiber officinale* (ginger), *Aloe vera*, *Lavandula angustifolia* (lavender), *Ocimum gratissimum*, *Sphagneticola trilobata*, and *Ricinus communis* possess significant anti-inflammatory properties due to the presence of bioactive compounds like curcuminoids, gingerols, flavonoids, terpenoids, and essential oils. These phytoconstituents act by inhibiting inflammatory mediators, reducing cytokine production, and preventing protein denaturation.

The formulation of herbal creams involves careful selection of suitable bases, emulsifiers, and extraction methods to ensure stability, compatibility, and optimal drug delivery. Evaluation parameters such as pH, viscosity, spreadability, homogeneity, stability, irritancy, and washability play a crucial role in determining the quality and effectiveness of the final product. Most formulations reviewed exhibited good physicochemical properties, stability over time, non-irritancy, and satisfactory spreadability, making them suitable for topical application.

Furthermore, *in vitro* and *in vivo* studies, including albumin denaturation assays and carrageenan-induced edema models, have demonstrated that herbal creams can produce significant anti-inflammatory effects comparable

to standard drugs like diclofenac. Polyherbal formulations, in particular, showed enhanced efficacy due to synergistic interactions among plant constituents. In conclusion, herbal anti-inflammatory creams offer a safe, effective, and eco-friendly approach for managing inflammation-related skin conditions. They align with the growing demand for natural and sustainable healthcare products. However, further research, including clinical trials and standardization of formulations, is necessary to validate their therapeutic efficacy, ensure quality control, and promote their widespread acceptance in modern medicine.

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