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Research Article

To Formulate And Evaluate Herbal Anti-Inflammatory Cream Containing Betel Leaf Extract, Tulsi Extract, Clove Oil, Menthol Oil, And Aloe Vera For Safe And Effective Topical Application

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ABSTRACT

Inflammation is a protective biological response associated with pain, redness, swelling, and irritation. Conventional anti-inflammatory drugs such as NSAIDs and corticosteroids are effective but may produce adverse effects during prolonged use. Herbal formulations have gained importance due to their natural origin, safety, cost-effectiveness, and better patient compliance. The present study focused on the formulation and evaluation of a herbal anti-inflammatory cream containing betel leaf extract, tulsi extract, clove oil, menthol oil, and aloe vera. The herbal cream was prepared using suitable oil and aqueous phases followed by emulsification. Different formulations (F1–F4) were developed and evaluated for various parameters including physical appearance, pH, homogeneity, spreadability, washability, extrudability, stability, and anti-inflammatory activity. Phytochemical screening of betel leaf extract confirmed the presence of alkaloids, flavonoids, tannins, saponins, phenolic compounds, and terpenoids, which contribute to anti-inflammatory activity. The prepared formulations showed acceptable physical characteristics and pH suitable for topical application. Among all formulations, F1 and F3 demonstrated better stability, homogeneity, and spreadability. Anti-inflammatory activity was evaluated using the protein denaturation method, where the herbal cream exhibited concentration-dependent inhibition. Maximum inhibition of 74.42% was observed at 1000 µg/mL, indicating significant anti-inflammatory potential when compared with standard Diclofenac sodium at 1000 µg/mL

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The study concludes that the formulated herbal anti-inflammatory cream possesses promising therapeutic potential and can serve as a safer alternative to synthetic topical anti-inflammatory preparations. A feedback study was conducted to evaluate the acceptability and user satisfaction of the formulated herbal anti-inflammatory cream.

INTRODUCTION

1.1 Pain

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage and serves as a protective mechanism of the body [1]. It is one of the most common symptoms experienced by individuals suffering from injury, inflammation, infection, or chronic diseases. Pain affects the physical, emotional, and psychological well-being of patients and significantly reduces their quality of life [2].

Pain can be classified into acute pain and chronic pain. Acute pain usually occurs suddenly and lasts for a short duration due to tissue injury, surgery, burns, or inflammation. Chronic pain persists for a prolonged period and is commonly associated with arthritis, cancer, neurological disorders, and musculoskeletal conditions [3]. The sensation of pain is mediated through specialized sensory receptors known as nociceptors, which transmit signals to the central nervous system.

Inflammatory pain occurs due to the release of inflammatory mediators such as prostaglandins, leukotrienes, histamine, serotonin, cytokines, and bradykinin at the site of injury. These mediators stimulate nociceptors and produce redness, swelling, heat, and pain [4]. Excessive inflammation can result in tissue damage and contribute to chronic inflammatory disorders such as rheumatoid arthritis and osteoarthritis.

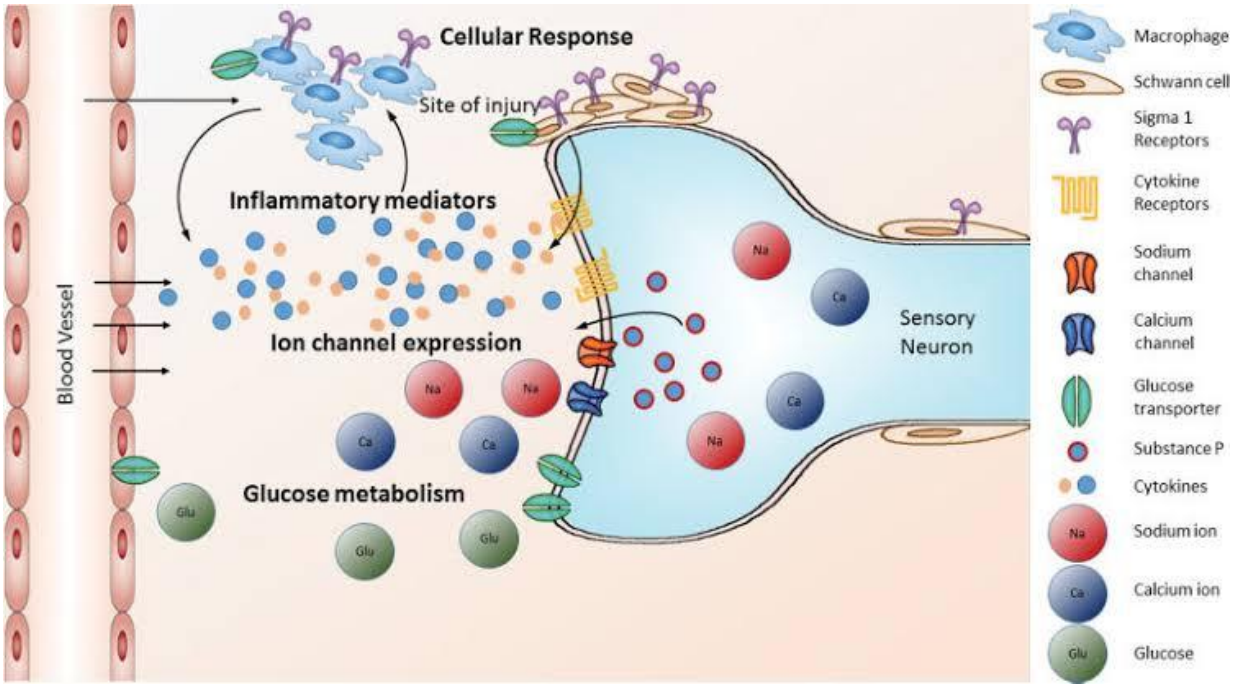


Fig 1.1: Mechanism of pain and inflammatory mediator release.

1.2 Pain Relief Products

Pain management generally involves the use of analgesic and anti-inflammatory agents. Various pharmaceutical dosage forms are available for

relieving pain and inflammation including tablets, capsules, injections, topical gels, creams, ointments, sprays, and transdermal patches [5].

Non-steroidal anti-inflammatory drugs (NSAIDs) such as diclofenac, ibuprofen, ketoprofen, aspirin, and naproxen are widely used for pain relief due to their ability to inhibit cyclooxygenase enzymes responsible for prostaglandin synthesis [6]. Corticosteroids are also used in severe inflammatory conditions because of their strong anti-inflammatory action [7].

In recent years, herbal products have gained considerable attention due to their natural origin, safety, reduced toxicity, and better patient compliance. Herbal formulations containing medicinal plant extracts such as turmeric, aloe vera, ginger, neem, eucalyptus, and menthol are commonly used for pain and inflammation management [8]. These plants contain bioactive constituents such as flavonoids, alkaloids, terpenoids, tannins, and phenolic compounds possessing analgesic and anti-inflammatory activity.

1.3 Disadvantages of Conventional Pain Relief Product

Although conventional pain relief products are effective, they are associated with several disadvantages and adverse effects. Oral administration of NSAIDs may cause gastrointestinal irritation, nausea, vomiting, gastric ulceration, gastrointestinal bleeding, renal toxicity, and cardiovascular complications during prolonged use [9].

Corticosteroids may lead to hormonal imbalance, immunosuppression, osteoporosis, skin thinning, and metabolic disorders upon long-term administration [10]. Injectable formulations may produce pain at the injection site, risk of infection, and require trained healthcare professionals for administration [11].

Topical ointments and gels sometimes exhibit poor patient acceptability because of stickiness, greasiness, unpleasant odour, and staining of clothes. Some formulations may also show poor drug penetration through the skin barrier resulting in reduced therapeutic efficacy [12]. These limitations have encouraged researchers to develop safer and more effective topical herbal formulations.

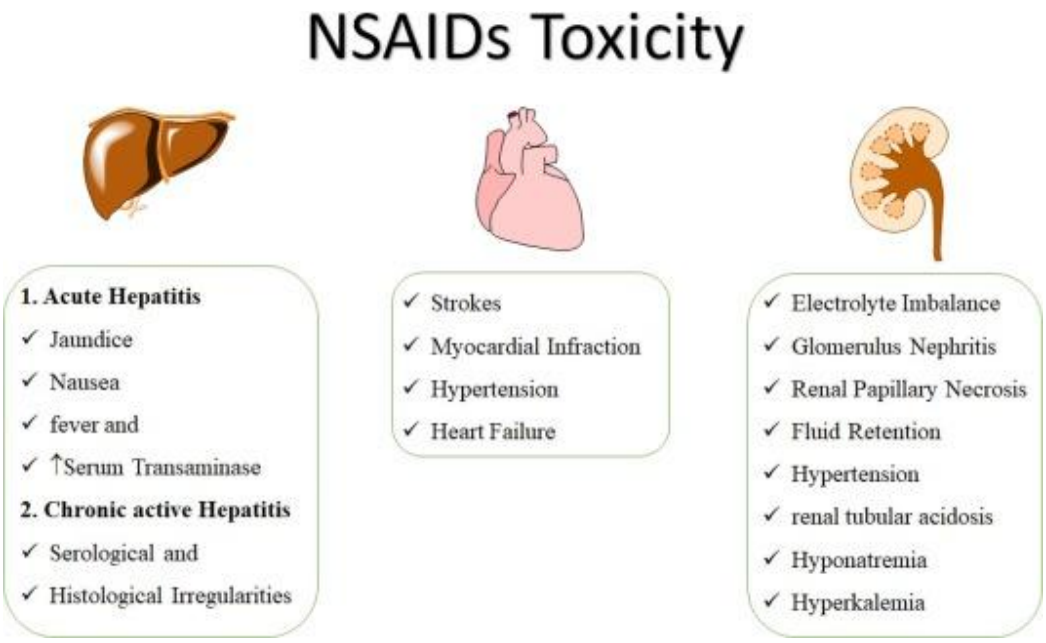


Fig 1.2: Adverse effects associated with conventional NSAIDs.

1.4 Topical Drug Delivery System

Topical drug delivery systems are pharmaceutical preparations applied directly to the skin for localized therapeutic action. The skin acts as a protective barrier against external environmental conditions and microbial invasion. Topical formulations are designed to deliver active ingredients directly to the affected site while minimizing systemic absorption [13].

Topical drug delivery provides several advantages including avoidance of hepatic first-pass metabolism, reduced systemic side effects, targeted drug delivery, prolonged therapeutic effect, and improved patient compliance [14]. Topical formulations are widely used in the treatment of pain, inflammation, fungal infections, psoriasis, eczema, burns, acne, and wound healing conditions.

The effectiveness of topical formulations depends on several factors such as drug solubility, molecular size,skin permeability, hydration of skin, formulation type, and use of penetration enhancers [15]. Penetration enhancers such as propylene glycol, ethanol, and essential oils improve drug permeation through the stratum corneum and enhance therapeutic efficacy.

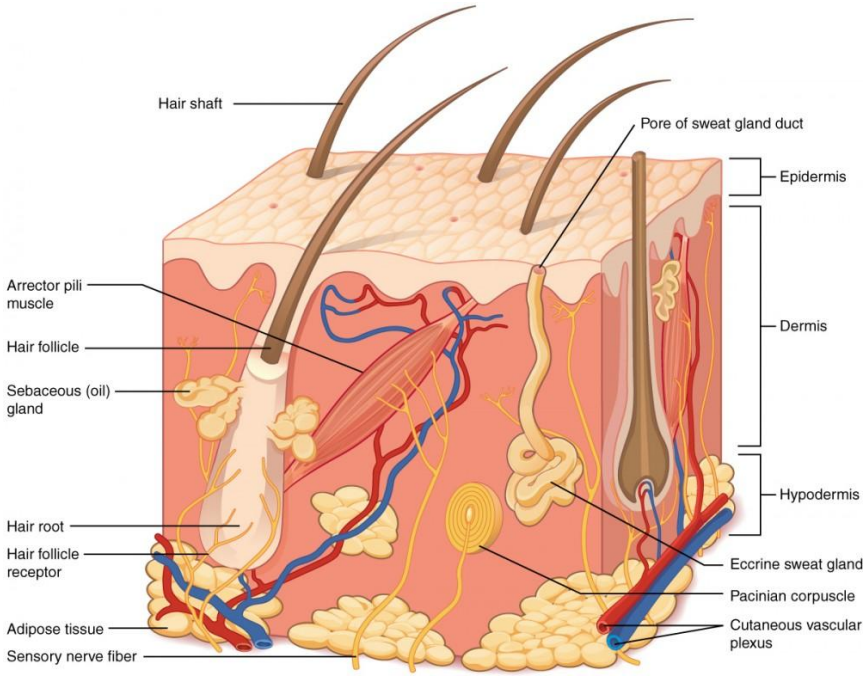


Fig 1.3: Structure of human skin showing layers involved in topical absorption.

1.5 Topical Creams

Creams are semisolid pharmaceutical preparations intended for external application to the skin or mucous membrane. They are generally emulsions containing oil phase, aqueous phase, emulsifying agents, preservatives, humectants, and active pharmaceutical ingredients [16].

Creams are classified into oil-in-water (O/W) creams and water-in-oil (W/O) creams depending upon the nature of the continuous phase. Oil-in-water creams are non-greasy, washable, and cosmetically elegant, whereas water-in-oil creams provide better emollient effect and hydration [17].

Herbal topical creams have gained increasing importance in pharmaceutical and cosmetic industries due to the growing demand for natural and safer products. Herbal creams provide localized therapeutic action with reduced systemic toxicity and better patient acceptability [18]. Medicinal plants such as Curcuma longa, Aloe vera, Azadirachta indica, and Zingiber officinale possess significant anti-inflammatory and analgesic properties.

Curcumin present in turmeric inhibits inflammatory pathways and reduces oxidative stress [19]. Aloe vera exhibits soothing and wound healing properties due to polysaccharides and glycoproteins [20]. Neem possesses antimicrobial and anti-inflammatory activity because of compounds such as azadirachtin and nimbidin [21]. Ginger contains gingerols and shogaols which inhibit prostaglandin synthesis and reduce pain and inflammation [22].

1.6 Evaluation of Herbal Cream

Evaluation of herbal cream is essential to ensure quality, safety, efficacy, stability, and patient acceptability of the formulation. Different physicochemical and pharmaceutical evaluation parameters are employed for characterization of cream formulations [23].

1.6.1 Physical Appearance

Physical appearance includes examination of color, odor, texture, consistency, homogeneity, and phase separation. A good cream formulation should possess smooth texture and uniform appearance without grittiness [24].

1.6.2 Ph Determination

The Ph of cream should be compatible with skin Ph to avoid irritation and skin damage. Normal skin Ph ranges from 5 to 7 [25].

1.6.3 Viscosity

Viscosity measurement determines the consistency and flow behavior of cream. Proper viscosity ensures ease of application and stability of formulation [26].

1.6.4 Spreadability

Spreadability determines the ease with which the cream spreads on the skin surface. Good spreadability improves patient compliance and therapeutic effectiveness [27].

1.6.5 Extrudability

Extrudability measures the force required to extrude cream from collapsible tubes. Proper extrudability ensures convenient application by patients [28].

1.6.6 Washability

Washability test determines the ease of removal of cream from skin surface using water [29].

1.6.7 Irritancy Test

Irritancy studies are conducted to determine safety of the formulation and identify any signs of erythema, edema, itching, or allergic reactions [30].

1.6.8 Stability Studies

Stability studies evaluate physical, chemical, and microbial stability of cream under different storage conditions such as temperature and humidity [31]. These studies are important to determine shelf life and quality of the formulation.

1.7 Need for Herbal Anti-Inflammatory Cream

The increasing prevalence of inflammatory disorders and adverse effects associated with synthetic drugs have created a need for safer and more effective herbal topical formulations. Herbal anti-inflammatory creams offer several advantages including natural origin, reduced toxicity, biodegradability, cost-effectiveness, and improved patient compliance [32].

Herbal formulations provide synergistic therapeutic activity due to the presence of multiple phytoconstituents possessing anti-inflammatory, analgesic, antioxidant, antimicrobial, and wound healing properties [33].Scientific formulation and evaluation of herbal creams are essential for establishing their safety, efficacy, stability, and pharmaceutical acceptability.

Therefore, the present study focuses on the formulation and evaluation of herbal anti-inflammatory cream using suitable herbal ingredients and pharmaceutical excipients to achieve effective pain relief with minimal side effects.

2. LITERATURE REVIEW

1. **Herbal Anti-Inflammatory Creams: Brar et al. (2025)** reviewed the therapeutic potential of herbal creams in dermatology and reported that herbal formulations containing Aloe vera, Ocimum sanctum, turmeric, peppermint, and clove possess strong antimicrobial and anti-inflammatory effects. The study also highlighted the importance of standardization, stability testing, and safety evaluation in herbal topical products. Recent studies show increasing interest in herbal topical formulations because they provide anti-inflammatory, antioxidant, antimicrobial, and wound-healing activities with fewer side effects compared to synthetic drugs. Herbal creams containing phytoconstituents such as flavonoids, tannins, alkaloids, terpenoids, and phenolic compounds are widely used for skin disorders and inflammation management.

2. **Aloe vera in Topical Formulations: Bose et al. (2025)** developed a topical hydrogel containing Aloe vera and observed enhanced anti-inflammatory and antioxidant activity with improved skin compatibility. Pawar et al. (2025) formulated a herbal anti-inflammatory cream using Aloe vera and turmeric extracts. The formulation showed good spreadability, stability, and significant reduction in inflammation. Aloe vera is widely used in herbal creams because of its soothing, moisturizing, wound-healing, and anti-inflammatory properties. The polysaccharides and glycoproteins present in Aloe vera help reduce inflammation and improve skin repair.

3. **Betel Leaf in Topical Formulations: George N, Anna CK S, Fathima H, Adithya D. (2024)** reviewed the phytoconstituents, traditional uses, and modern therapeutic potential of Piper betle (betel leaf). The study reported that betel leaf possesses significant anti-inflammatory, antimicrobial, antioxidant, and wound-healing properties due to the presence of bioactive compounds such as hydroxychavicol, eugenol, flavonoids, and phenolic compounds. These phytoconstituents help inhibit microbial growth and reduce inflammation, making betel leaf a promising ingredient in herbal topical formulations and medicinal preparations.

4. **Turmeric and Curcumin-Based Nanoformulations Giri et al. (2024)**: Curcumin from turmeric is an important herbal anti-inflammatory agent. However, poor solubility and low skin penetration limit its effectiveness. Recent studies focused on nanoformulations to improve topical delivery. Prepared a myrrh oil-based nanoemulgel containing curcumin and reported enhanced anti-inflammatory activity and improved skin penetration. Formulated a curcumin nanoemulsion for transdermal delivery and observed better stability and bioavailability. Developed a turmeric- and neem-based nanoemulgel that showed both antimicrobial and anti-inflammatory activity.

5. **Polyherbal Creams and Gels Swamini Bhaskar et al. (2025):** Modern herbal formulations combine multiple plant extracts to achieve synergistic effects. A recent review on herbal gels containing Aloe vera, turmeric, ginger, onion, omega-3 fatty acids, and green tea reported that these ingredients inhibit inflammatory mediators such as COX-2 and NF-κB pathways. The review concluded that polyherbal formulations provide enhanced therapeutic activity compared to single-herb formulations. Optimized a natural anti-inflammatory cream using multiple herbal extracts and found good physical stability, spreadability, and therapeutic activity.

3. DRUG AND EXCIPIENT PROFILE

3.1 Betel leaf

Fig 3.1. Betel Leaf

Synonym:

- Common Name: Betel Leaf, paan leaf
- Botanical Name: piper betel L.
- Marathi Name: Nagvel (*नागवेल*)
- Sanskrit Name : Tambula

Biological source:

Betel leaf consists of the fresh and dried leaves of Piper betle Linn .

Family:

Piperaceae

Active constituents:

- Eugenol
- Safrole
- Hydroxychavicol
- Chavibetol

Chemical Structure:

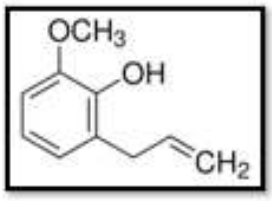


Fig 3.1.1 Eugenol

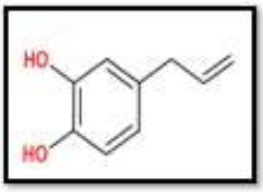


Fig 3.1.2 Hydroxychavicol

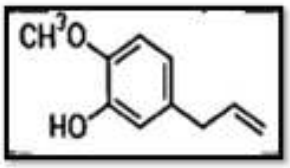


Fig 3.1.3 chavibetol

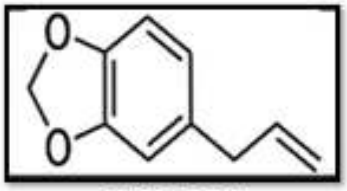


Fig 3.1.4 Safrole

Pharmacological Activity:

1. Anti Inflammation: Help reduce inflammation and soothes skin
2. Antimicrobial: Effective against bacteria and fungi
3. Antioxidant: Protect cell from damage by free radicals
4. Wound Healing: Promote healing and tissue regeneration
5. Analgesic Effect: Provide relief from pain and discomfort

Role / Benefits

- Reduce inflammation and swelling
- Prevent microbial growth and infection
- Provides cooling and soothing effect
- Support skin healing and tissue Repair

Role of Active Constituent :

Eugenol – Acts as an anti-inflammatory, analgesic, and antimicrobial agent, helping to reduce pain, swelling, and microbial growth in the cream.

Hydroxychavicol – Possesses strong antioxidant and antimicrobial properties, which help in wound healing and protection against infections.

Chavibetol – Contributes anti-inflammatory and antiseptic activities, supporting skin soothing and prevention of microbial contamination.

Safrole – Exhibits mild antimicrobial and aromatic properties, enhancing the preservative and soothing effect of the formulation.

Half life :

half-life of dried betel leaf extract was determined as 62 days for the optimised Storage conditions (5 ◦C in dark conditions). [34]

Indications :

Anti-inflammatory properties

Inflammation is a natural defence response of the body against harmful substances, damaged cells, and pathogens, characterized by redness, swelling, pain, heat, and loss of function. Betel leaf contains bioactive compounds such as phenolics, flavonoids, tannins, and terpenoids that possess antioxidant and anti-inflammatory properties, helping to reduce inflammation and protect tissues.

Flavonoids in betel leaf also show anti-allergic, antimicrobial, antidiarrheal, and anticancer activities. Studies have reported that betel leaf extract may help reduce inflammation in conditions like arthritis, asthma, and skin allergies, making it an important medicinal plant in herbal therapy. [35]

Anti microbial properties

Betel leaf possesses several bioactive properties, among which antimicrobial activity is one of the most significant. Its antimicrobial effect also makes it useful as a natural food preservative because it contains bioactive compounds such as chavicol, chavibetol, allyl pyrocatechol, chavibetol acetate, and allyl pyrocatechol diacetate. These compounds help protect food from harmful microorganisms. Betel leaf shows antimicrobial activity against bacteria including E. coli, Streptococcus pyogenes, Pseudomonas aeruginosa, Staphylococcus aureus, and Proteus vulgaris. The presence of sterol compounds in betel leaf extract is mainly responsible for this antimicrobial property.[36]

Anti diabetic properties

Betel leaf extract is known for its significant antidiabetic activity and its ability to regulate

blood glucose levels Studies using glucose tolerance tests have shown that the extract possesses antihyperglycemic effects by reducing external glucose levels Aqueous extracts of betel leaves were also found to lower blood sugar levels in experimental rats. In Streptozotocin (STZ)-induced diabetic rats, treatment with betel leaf extract reduced blood glucose, glycosylated hemoglobin, and liver enzyme activities such as glucose-6-phosphatase and fructose-1,6-bisphosphatase, while increasing hexokinase activity compared to untreated diabetic rats [37]

Dose:

4% - 5% extract: Common for daily antiseptic cream. Best physical stability

10% extract: Common for wound healing + moderate inflammation. Fast healing seen in rat studies

15% extract: Common for burns + strong inflammation. Most effective dose in studies

Adverse Drug Reaction :

- Skin irritation – Burning, tingling, redness
- Allergic contact dermatitis – Rash, itching in sensitive people
- Skin dryness – From ethanol base in extract
- Photosensitivity – Rare, increased sun sensitivity
- Tooth staining – Brown/black discoloration from tannins
- Increased salivation – Excess saliva production
- Mouth irritation – Mild burning if chewed excessively
- Gastric irritation - Nausea, stomach upset at very high doses >300 mg/kg
- Hypoglycemia - May lower blood sugar
- Increased bleeding risk - Antiplatelet effect, caution with blood thinners

Contraindications[38]:

Oral Pathology and Pre-malignancy: Consumption is strictly contraindicated in patients with oral submucous fibrosis (OSF), leukoplakia, or a history of squamous cell carcinoma. Although the leaf itself has shown anti-mutagenic properties in some studies, its synergistic use in "betel quid" (with areca nut and lime) is a primary risk factor for oral and pharyngeal cancers.

Gastrointestinal Disorders: Due to its "sharp" (tikshna) and "hot" (ushna) properties, high oral intake can exacerbate gastric irritation, hyperacidity, or existing peptic ulcers.

Gestational and Lactational Restrictions: Due to a lack of rigorous human safety data and potential effects on fetal development—similar to risks observed with tobacco or alcohol—medicinal use is contraindicated during pregnancy and breastfeeding.

Dermatological Sensitivity: Topical application of concentrated essential oils or extracts is contraindicated for individuals with sensitive skin or established dermatitis, as it may cause chemical burns or irritation.

Pediatric Populations: Use as a medicinal remedy is generally discouraged in children and adolescents due to the absence of established safe dosage guidelines and the risk of accidental exposure to harmful additives like tobacco.

3.2. CLOVE OIL

Fig 3.2. Clove Oil

Synonym:

- Common Name: clove oil
- Botanical Name: Syzygium aromaticum (L.)
- Marathi Name : Lavang Tel (*लवंग तेल*)
- Sanskrit Name : Lavanga Taila (*लवंग तैल*)

Biological source:

Clove oil is derived from the dried flower buds of Syzygium aromaticum (L.) Merrill & Perry.

Family:

Myrtaceae

Active constituents:

- Eugenol
- α humulene
- β caryophyllene
- Eugenol acetate

Chemical structure :

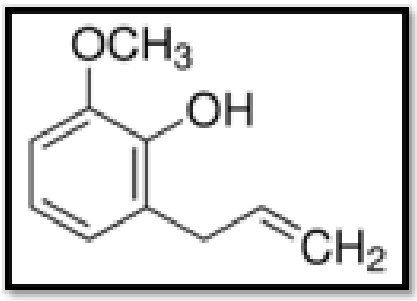


Fig 3.2.1 Eugenol.

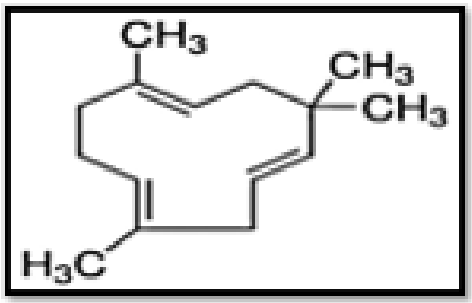
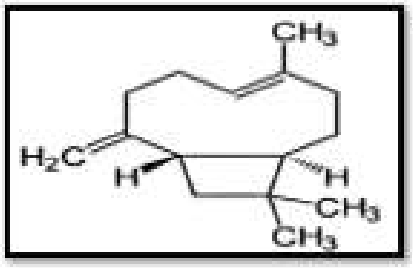
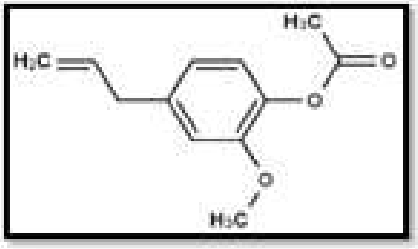


Fig 3.2.2 α humulene





. **Fig 3.2.3 β caryophyllene.** **Fig 3.2.4 Eugenyl acetate**

Role of Active Constituent:

Eugenol – It shows strong anti-inflammatory, analgesic, antimicrobial, and antioxidant activity, which helps reduce pain, inflammation, and microbial growth in herbal cream formulations.

A-Humulene – It possesses anti-inflammatory and antibacterial properties that help in reducing swelling, irritation, and infection at the affected site.

B-Caryophyllene - acts as an anti-inflammatory and analgesic agent by interacting with cannabinoid receptors, thereby helping in pain relief and tissue healing.

Eugenyl acetate - It contributes to antimicrobial and soothing effects, improving the therapeutic action and aroma stability of the cream.

Half life:

Unopened, cool dark place- 3-4 years

Opened, room temp -1-2 years

Opened, fridge 4°C -2-3 years

In cream/lotion - 6-12 months

Indications [39]:

Anti-inflammatory and Wound Healing

Inflammation and oxidative stress are closely linked in disorders such as hypertension, diabetes, cardiovascular, and neurodegenerative diseases. Clove essential oil (CEO) and its major component eugenol show anti-inflammatory effects similar to diclofenac gel, reducing inflammation significantly within 3 hours. In wound models, CEO-treated animals showed over 95% wound contraction within 15 days, with healing effects comparable to neomycin treatment. These findings suggest that CEO may promote wound healing while reducing the adverse effects associated with long-term use of synthetic antibiotics.

Anticancer

The components of CEO, including eugenol, humulene, and caryophyllene, possess anticancer, cytotoxic, and antitumor properties that may help in cancer prevention and supportive therapy. Essential oils may also reduce chemotherapy-related side effects such as nausea, vomiting, appetite loss, and weight reduction. The anticancer activity is mainly linked to their antioxidant and anti-inflammatory actions, which help control ROS-mediated pathways involved in tumor growth, angiogenesis, and metastasis. CEO has shown activity against several cancers, including breast, colon, lung, pancreatic, prostate, cervical cancers, and leukemia. Studies also indicate that eugenol can enhance the cytotoxic and pro-

apoptotic effects of cisplatin in triple-negative breast cancer by suppressing ALDH activity and the NF-κB signaling pathway.

Anesthetic

CEO is considered a safe anesthetic at low concentrations for both vertebrates and invertebrates. It produces rapid anesthesia, quick recovery, and low mortality without affecting responsiveness to external stimuli. Studies have shown that CEO and eugenol reduce corneal sensitivity in rats similarly to lidocaine. In fish species such as Nile tilapia, cardinal tetra, ringed cichlid, and angelfish, CEO effectively induces anesthesia by impairing swimming and balance until complete immobility occurs. The anesthetic effect depends on the concentration and exposure time, and recovery generally occurs without harmful effects.

Dose:

- Adult skin, general -0.5% - 2%
- Acne, wart, fungus- 1%-5%
- Dental pain -1 drop undiluted
- In cream/lotion -0.5% - 1%
- Children >2 years -0.25%-0.5

Adverse Drug Reactions:

- Burning/tingling
- Skin redness
- Contact dermatitis
- Chemical burn
- Skin sensitization
- Photosensitivity

Contraindications [40]

Hypersensitivity and Contact Dermatitis:

Topical use is contraindicated for individuals with known allergies to cloves or eugenol. Research indicates that even low concentrations as low as 0.03% v/v can be cytotoxic to human skin cells like fibroblasts and endothelial cells. This can manifest as contact dermatitis, skin rashes, itching, or blistering.

Application to Broken or Sensitive Skin:

Clove oil should not be applied undiluted to sensitive or damaged skin. It is known to cause oral mucosal burns and skin irritation if applied at high concentrations. Undiluted application can lead to inflammation, rashes, and in extreme cases, permanent skin cell damage.

Bleeding Disorders

Because eugenol is a potent inhibitor of platelet aggregation, clove oil is contraindicated in patients with bleeding disorders such as hemophilia or von Willebrand disease. It may prolong bleeding time and increase hemorrhage risk. Discontinue use at least 2 weeks prior to surgical or dental procedures.

Pediatric Patients

Oral administration is contraindicated in children under 2 years of age. Eugenol toxicity can occur at doses as low as 5-10 mL, leading to hepatotoxicity, seizures, central nervous system depression, and respiratory failure.

Hepatic Impairment:

Oral clove oil is contraindicated in patients with severe liver disease. Eugenol undergoes hepatic metabolism, and doses exceeding 3 mL in adults have been associated with hepatocellular necrosis and liver failure.

Drug Interactions with Anticoagulants:

Concurrent use with warfarin, aspirin, clopidogrel, or NSAIDs is contraindicated. Additive antiplatelet effects may result in prolonged bleeding time, gastrointestinal bleeding, or bruising.

Pharmacological Activity:

1. Anti Inflammatory: Help reduce inflammation and swelling
2. Antimicrobial: Effective against bacteria, fungi and viruses
3. Antioxidant: Protect cells from oxidative stress and damage
4. Analgesic: Provide pain relief and soothing effect
5. Wound healing: Promote healing and tissue regeneration

Role / Benefits:

- Reduce inflammation and pain
- Inhibit microbial growth and infection
- Provide antioxidant protection
- Give pleasant aroma and soothing effect
- Support skin health and healing

3.3. TULSI

Fig 3.3. Tulsi

SYNONYM:

- Common Name: Holy Basil, Sacred Basil
- Botanical Name: Ocimum tenuiflorum
- Marathi Name: Tulas (*तुळस*) or Tulshi (*तुळशी*)
- Sanskrit Name: Tulasi (*तुलसी*)

BIOLOGICAL SOURCE:

Tulsi consists of the fresh and dried leaves, inflorescence (flowering tops), and whole plant parts of Ocimum sanctum Linn.

FAMILY:

Lamiaceae

ACTIVE CONSTITUENTS:

- Linalool
- Orientine
- Ursolic acid
- Vanillin

CHEMICAL STRUCTURE[41] :

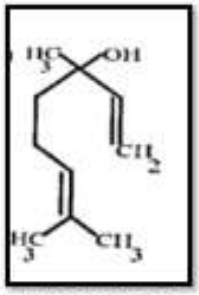


Fig 3.3.1 Linalool

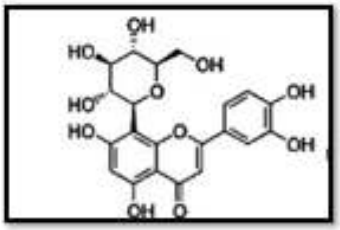


Fig 3.3.2 orientine

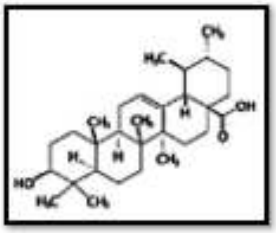


Fig 3.3.3 Ursolic acid

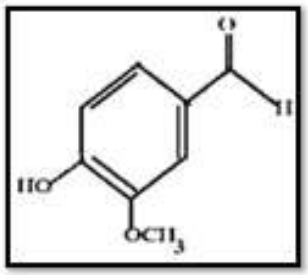


Fig 3.3.4 Vanillin

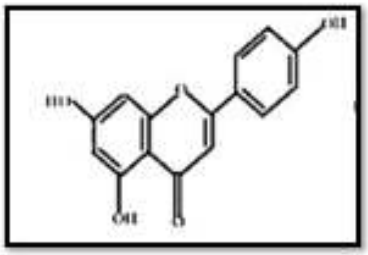


Fig 3.3.5 Apigenin

Role of Active Constituent:

Linalool- **It** possesses anti-inflammatory, analgesic, antimicrobial, and calming activities, which help reduce pain, inflammation, and irritation.

Orientine – It acts as a strong antioxidant and anti-inflammatory flavonoid that protects cells from oxidative stress and supports wound healing.

Ursolic acid- exhibits anti-inflammatory, antimicrobial, antioxidant, and tissue-repair properties, which help in reducing swelling and promoting healing.

Vanillin - It shows antioxidant, anti-inflammatory, antimicrobial, and analgesic activities, helping to protect tissues and reduce inflammation.

Apigenin – It has anti-inflammatory, antioxidant, antimicrobial, and soothing properties that help reduce skin irritation and support healing.

Half Life :

Tulsi tea- 6-8 hours

Capsule 300-600mg extract - 12-18 hours

Tincture- 8-12 hours

Essential oil- N/A topical

Indications [42]:

Antilipidemic Activity

Hyperlipidemia and atherosclerosis are increasingly prevalent health concerns. Studies demonstrate that aqueous extract of _O.

basilicum_ effectively reduces total cholesterol, triglycerides, and LDL-cholesterol in rats with triton WR-1339-induced acute hyperlipidemia. Additional research in rabbits showed that dietary supplementation with 1-2% fresh Tulsi leaves for 28 days significantly decreased total lipid levels.

Antibacterial Activity

Aqueous, alcoholic, and chloroform extracts, along with essential oil derived from _Ocimum sanctum_ leaves, have been evaluated against _E. coli, P. aeruginosa, S. typhimurium,_ and _S. aureus_. Extracts of _O. sanctum_ exhibited comparable efficacy against both gram-positive and gram-negative pathogenic bacteria. Essential oil from fresh leaves demonstrated superior antibacterial properties relative to oil from dried leaves, whereas antifungal activity was more pronounced in dried-leaf oil.

Eye Disease

In Ayurvedic practice, fresh leaf juice of _Ocimum sanctum_ combined with triphala is formulated into eye drops for managing glaucoma, chronic conjunctivitis, and other ophthalmic disorders. For routine ocular care, three drops of tulsi oil mixed with honey are traditionally used with the intention of enhancing visual acuity.

Mosquitocidal Activity

The larvicidal potential of Tulsi was assessed using eugenol and triglyceride fractions isolated from its hexane extract against fourth-instar _Aedes aegypti_ larvae. Additionally, when Tulsi seeds are submerged in water, they release a mucilaginous polysaccharide within one hour. Larvae that contact this substance become firmly adhered to it, resulting in mortality due to drowning.

Dose:

Fresh Juice 10-20 ml, Root decoction 50-100 ml, Seed powder 3-6 g.

Adverse Drug Reactions:

- enhanced bleeding risk
- excessive blood sugar lowering (hypoglycemia)
- liver dysfunction,
- potential infertility

Contraindications:

Blood Thinners/Anticoagulants

Tulsi exhibits antiplatelet activity and may inhibit blood coagulation, thereby increasing the risk of ecchymosis and hemorrhage. Concurrent use with anticoagulant or antiplatelet medications is not advised.

Diabetes Medications

Tulsi can potentiate hypoglycemic effects. When used alongside antidiabetic agents, it may cause blood glucose levels to fall below normal range. Close monitoring of blood sugar is recommended.

Surgery

Due to its effect on coagulation and bleeding time, discontinue Tulsi at least 14 days prior to scheduled surgical or dental procedures to reduce perioperative hemorrhage risk

Hypothyroidism

Tulsi may reduce serum thyroxine (T4) concentrations. Use with caution in patients with

hypothyroidism, as it could exacerbate thyroid dysfunction.

Fertility Issues

Research indicates that Tulsi may exert anti-spermatogenic effects by impairing sperm production and motility. Individuals attempting conception or with existing fertility concerns should avoid use.

High Pitta

In Ayurvedic medicine, Tulsi is considered to have "Ushna" or heating properties. It is contraindicated for individuals with Pitta-dominant constitutions or conditions characterized by inflammation, excess heat, or irritation.

Pharmacological Activity:

1. AntiInflammatory : Help reduce inflammation, redness and selling
2. Antimicrobial: Effective against bacteria, fungi and certain viruses
3. Antioxidants: Protect cells from oxidant stress and damage
4. Immunity support: Strengthens immune response and promote wellness
5. Skin soothing and Healing : Soothes irritated skin and support wound healing

Role / Benefits:

- Adaptogenic herb help body adapt to stress
- Natural cleanser purifes skin and environment
- Traditionally used in Ayurvedic for centuries
- Safe natural and suitable for daily used
- Provide aroma with refreshing and caming effect

3.4. ALOE VERA

3.4. ALEO VERA

SYNONYM:

- Common Name: Aleo vera
- Botanical Name: Aloe Barbadians Mill.
- Marathi Name : Korphad (*कोरफड*)
- Sanskrit Name : Ghritkumari (*घृतकुमारी*)

BIOLOGICAL SOURCE:

Aloe vera is derived from the dried latex (juice) of the leaves of Aloe barbadensis Miller.

FAMILY:

Liliaceae

ACTIVE CONSTITUENTS:

- Acemannan
- Aloin
- Aloe emodin
- Aloesin

Chemical structure:

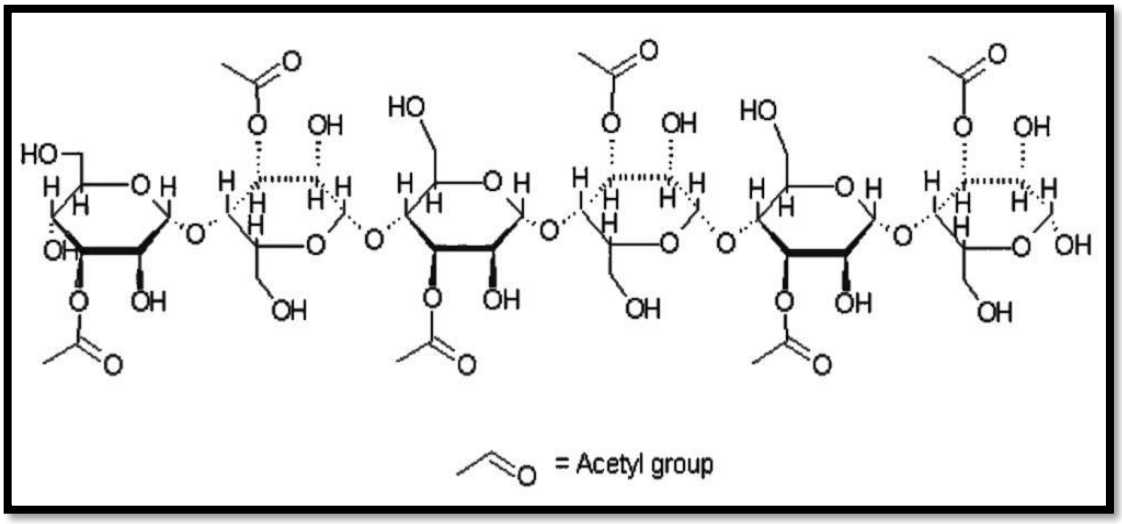


Fig 3.4.1 Acemannan

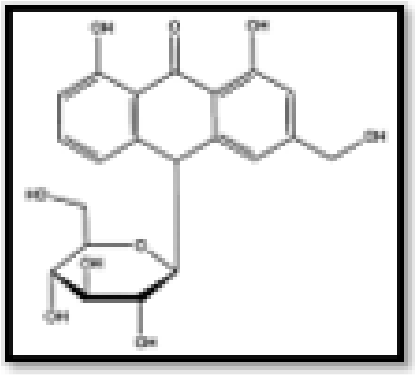


Fig 3.4.2 Aloin

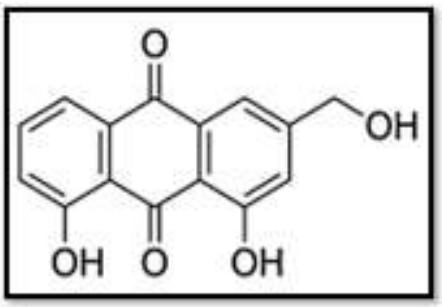


Fig 3.4.3 Aloe-emodin

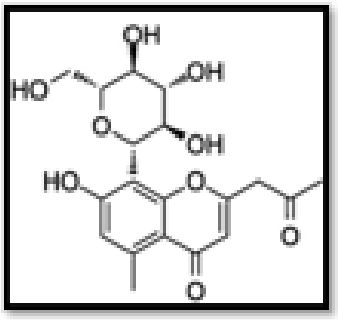


Fig 3.4.4 Aloesin

Role of Active Constituent:

Aloin: Aloin exhibits anti-inflammatory and antimicrobial activity, which helps reduce skin inflammation and prevents microbial growth in the cream formulation.

Acemannan (Polysaccharide): Acemannan promotes wound healing, moisturizes the skin, and enhances immune response, making it useful for soothing irritated skin.

Aloe-emodin: Aloe-emodin possesses antioxidant and anti-inflammatory properties that help protect the skin from oxidative damage and support healing.

Aloesin: Aloesin acts as an antioxidant and skin-soothing agent, helping to reduce irritation and improve skin protection.

Half Life :

Fresh leaf -2-3 days

Fresh gel, fridge-7-10 days

Commercial juice- 2-3 years unopened

Stabilized gel- 2-4 years

Indications[43]:

Burn and Wound Healing

Aloe vera is widely recognized for its ability to soothe and repair burns and wounds. Research indicates that topical application accelerates wound closure and improves wound tensile strength by promoting cellular proliferation, including keratinocytes, hepatocytes, neurons, and endothelial cells.

Aging of the Skin

Dermal aging involves epidermal thinning, wrinkle formation, and the development of fine lines, creases, hyperpigmentation, and facial furrows. Bioactive constituents in Aloe vera have demonstrated the capacity to mitigate age-related skin degeneration by enhancing collagen and elastin biosynthesis, thereby improving skin elasticity and reducing visible signs of aging.

Immune System Restoration

Studies have shown that Aloe vera prevents suppression of cutaneous immune function, which is implicated in photocarcinogenesis. Furthermore, topical administration remains effective when applied up to 24 hours post-UV exposure, maintaining its protective effect against immune suppression.

Moisturizer

Aloe vera's popularity in dermatology and cosmetics is attributed to its exceptional hydrating properties. Evidence suggests it enhances the skin's intrinsic moisture retention, facilitates exfoliation of dead epidermal cells, and exhibits strong penetrative ability to deliver active compounds transdermally. These attributes make it a key component in skincare formulations, with over 95% of dermatologically significant extracts worldwide incorporating Aloe vera.

Arthritis, Joint and Muscle Pain

Aloe vera is reported to alleviate severe musculoskeletal pain related to arthritis, tendonitis, and injury. When applied topically, it penetrates the dermal layers to provide analgesic effects. Research also suggests that daily oral intake may help prevent the onset and promote the regression of adjuvant-induced arthritis.

Anti-Inflammatory

Aloe vera elicits multiple anti-inflammatory pathways, reducing edema associated with trauma and supporting recovery from infections. These actions contribute to pain relief and facilitate the overall wound-healing process.

Biological Vehicle

Aloe vera functions as a biological carrier, enhancing the dermal penetration and absorption of other bioactive compounds into deeper tissues.

Dose :

Topical -Burns/Cuts -Pure gel, thin layer

Topical -Cream - 10-70%

Oral - General wellness - 50-100 ml

Oral -Gastritis/GERD- 30-50 ml

Oral - 100-200 mg

Adverse Drug Reactions [44]:

Dehydration due to frequent stools

Stomach cramping

Irregular heartbeat

Lowered potassium levels

Contraindications :

Gastrointestinal Conditions: Individuals with Crohn's disease, ulcerative colitis, intestinal obstruction, or hemorrhoids should avoid oral ingestion due to the irritating, high-strength laxative effects of aloe latex.

Kidney or Heart Disease: Long-term use of oral aloe can cause potassium depletion and other electrolyte imbalances, which can cause severe issues in those with existing kidney or heart conditions.

Diabetes Medications: Oral aloe may lower blood sugar levels and can cause dangerous fluctuations if you are already taking diabetes medication.

Surgery: Stop taking oral aloe at least 2 weeks before scheduled surgery, as it can increase bleeding risks.

Allergies: Individuals allergic to Liliaceae plants (garlic, onions, tulips) may experience skin irritation or allergic reactions.

Topical Precautions: Do not apply to severe, deep burns or open, severe wounds.

Pharmacological Activity :

1. Soothing and calming: Soothes irritated skin and reduce redness
2. Hydrating and moisturizing: Deeply hydrate the skin and improve moisture retention
3. Skin repair and regeneration: Support all regeneration and helping skin repair
4. Wound healing: Promote faster healing of wound and minor burn
5. Protective and balancing: Help maintain healthy skin barrier and balancing ph

Role / Benefits:

- Reduce Inflammation and skin irritation
- Provide deep hydration and softing the skin
- Support tissue Repair and wound healing
- Improve overall skin health and comfort

3.5. PEPPERMINT OIL

Fig 3.5 Peppermint Oil

SYNONYM:

- Common Name : peppermint oil
- Botanical Name: Mentha piperita L.
- Marathi Name: Pudina (*पुदिना*)
- Sanskrit Name: Putiha (*पुतिहा*)

BIOLOGICAL NAME:

Peppermint oil is derived from the fresh or partly dried leaves and flowering tops of *Mentha piperita* L. (family Lamiaceae), a herbaceous perennial plant

FAMILY:

Lamiaceae

ACTIVE CONSTITUENTS:

- Piperitone
- Menthol
- α Pinene
- Pulegone
- 1,8 cineole

Chemical Structure [45]:

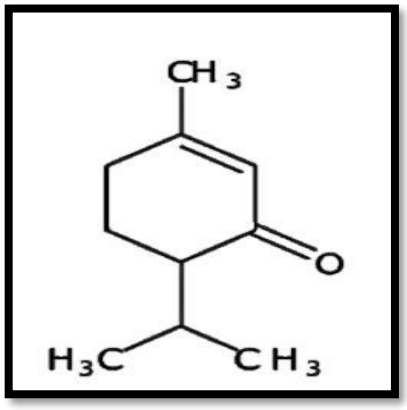


Fig 3.5.1 Piperitone

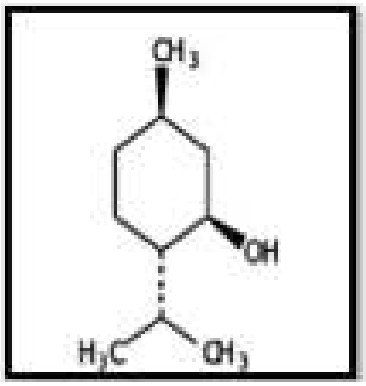


Fig 3.5.2 Menthol

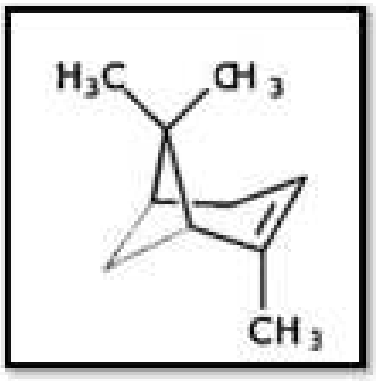


Fig 3.5.3 α Pinene

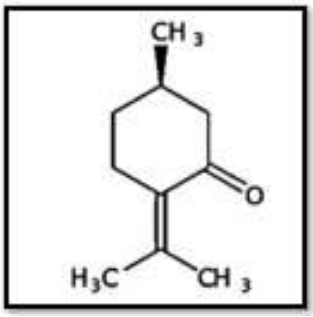


Fig 3.5.4 Pulegone.

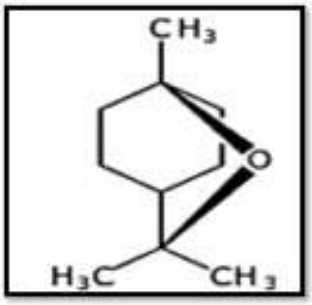


Fig 3.5.5 1,8 cineole

ROLE OF ACTIVE CONSTITUENT:

Piperitone helps to reduce microbial growth and inflammation while providing a refreshing effect in the formulation.

Menthol produces a cooling effect, relieves pain, and soothes irritated skin due to its mild anesthetic and anti-inflammatory action.

α-Pinene helps in reducing inflammation and protects the formulation from microbial contamination through its antimicrobial activity.

Pulegone contributes to antimicrobial activity and provides a pleasant mint-like aroma and soothing effect.

1,8-Cineole helps to relieve pain and inflammation and also exhibits antimicrobial properties that support skin protection.

Indications[46]:

Medications use of perpement oil are

Digestive problems like - Irritable bowel syndrome ,Indigestion, Diarrhea , nausea, vomiting

Respiratory issue – cold, cough,sinus infection

Skin condition like – itching , rashes

Dose

Oral – Capsule- 0.2-0.4 ml TID

Oral – Liquid- 1-2 drops diluted

Topical- 5-10% dilution

Inhalation- 3-5 drops

Adverse Drug Reactions :

- Skin irritation
- contact dermatitis

Contraindications:

Infants and Children

Never apply peppermint oil to the face or nose of infants or young kids. Inhaling it can cause dangerous breathing difficulties, including spasm of the vocal cords or airways.

Pregnancy/Breastfeeding

Do not take peppermint oil orally during pregnancy or while nursing. Safety data is limited, and there's a small risk it could stimulate uterine contractions.

Medical Conditions

Gallbladder/Liver Problems Avoid if you have blocked bile ducts, gallstones, or severe liver disease.

GERD/Heartburn Peppermint oil relaxes the muscle between stomach and esophagus, which can make reflux and heartburn worse.

3.6 Glycerin [47]:

Nonproperity Name :

Glycerin or Glycerol

Synonyms :

Croderol; E422, glicerol, glycerine; glycerolum; Glycon G-100, Kemstrene; Optim; Pricerine; 1,2,3-propanetriol; trihydroxypropane glycerol

Chemical Name :

Propane -1,2,3- triole

Molecular weight :

92.09 g/mol

Molecular formula:

C3H8O3

CAS No :

56-81-5

STRUCTURE:

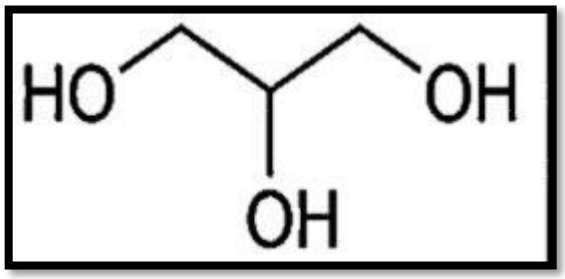


Fig 3.5.6 Glycerin

Description :

Glycerin is a clear, colorless, odorless, viscous, hygroscopic liquid, it has a sweet taste approximately 0.6 times as sweet as sucrose.

PH:

6.0

Solubility:

Table 3.5.1 solubility of Glycerin

Solvent	Solubility
Acetone	Slightly soluble
Benzone	Partially insoluble
Chloroform (95%)	Partially Soluble
Ethanol	Soluble
Ether	1 in 500
Ethyl acetate	1 in 11
Menthanol	Soluble
Oil	Partially Soluble
Water	Soluble

Uses:

Glycerin was incorporated as a humectant to maintain skin moisture, improve spreadability, and provide a smooth and moisturizing effect to the herbal cream.

Density:

1.26 g/cm³

Melting point :

17.8 °C (64.0 °F; 290.9 K)

Application:

In topical pharmaceutical formulations and cosmetics, glycerin is used primarily for its humectant and emollient properties. Glycerin is used as a solvent or cosolvent in creams and emulsions .Glycerin is additionally used in aqueous and nonaqueous gels and also as an additive in patch applications, In parenteral formulations, glycerin is used mainly as solvent and co solvent., In oral solutions, glycerin is used as a solvent, sweetening agent, antimicrobial preservative, and viscosity-increasing agent. It is

also used a plasticizer and in film coatings Glycerin is used as a plasticizer of gelatin in the production of soft-gelatin capsules and gelatin suppositories. Glycerin is employed as a therapeutic agent in a variety of clinical applications and is also used as a food additive.

3.7 Steric Acid [48]:

Nonproperity Name :

Stearic Acid

Synonyms:

Octadecanoic acid; Stearin acid; 1-Heptadecanecarboxylic acid; Emersol 120;Hydrofol Acid 150; C18 fatty acid

Chemical Name:

Octadecanoic acid

Molecular Weight:

284.48 g/mol

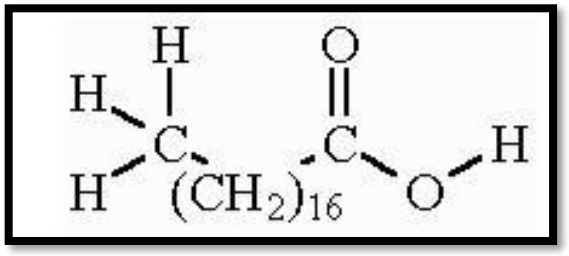
Molecular Formula :

C18H3602

CAS No:

57-11-4

Structure:



3.5.7 Steric acid

Description:

Stearic acid is a white, waxy, hard solid with a faint odor. It is a saturated long-chain fatty acid commonly used in pharmaceutical and cosmetic formulations as an emulsifying agent, thickening agent, and stabilizer.

pH:

Approximately 5.5-7.0 (in dispersion)

Solubility:

Table 3.5.2 solubility of Steric acid

Solvent	Solubility
Acetone	Slightly soluble
Benzone	Soluble
Chloroform	Slightly soluble
Ethanol	Slightly soluble
Ether	Soluble
Oil	Freely soluble

Water	Soluble

Uses:

Stearic acid is incorporated as an emulsifying and thickening agent to improve the consistency, stability, texture, and spreadability of herbal cream formulations.

Density

0.94 g/cm³

Melting Point :

69.369.6 °C

Application:

In topical pharmaceutical and cosmetic formulations, stearic acid is mainly used as an emulsifier, viscosity-enhancing agent, and stabilizer in creams, lotions, ointments, and emulsions.

3.8 Cetyle Alcohol [49]:

Nonproprietary Name :
Cetyl Alcohol

Synonyms :
1-Hexadecanol; Palmityl alcohol; Cetanol; Hexadecyl alcohol

Chemical Name :
Hexadecan-1-ol

Molecular Weight :
242.44 g/mol

Molecular Formula :
$C_{16}H_{34}O$

CAS No :
36653-82-4

Structure :

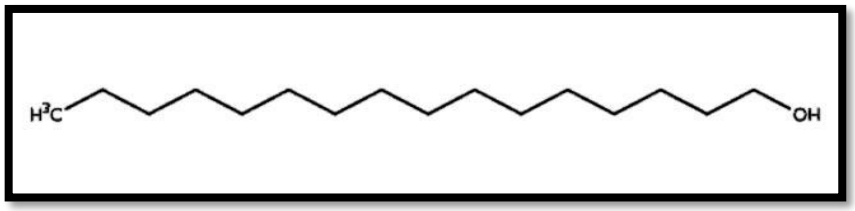


Fig 3.5.8 cetyl alcohol

Description:

Cetyl alcohol is a white, waxy, flaky solid with a mild characteristic odor. It is a fatty alcohol widely used in pharmaceutical and cosmetic preparations as an emollient, thickening agent, emulsifier, and stabilizer.

pH :

Neutral (approximately 6 – 7 in dispersion)

Solubility:

Table 3.5.3 solubility of cetyl alcohol

Solvent	Solubility

Acetone	Slightly soluble
Chloroform	Soluble
Ethanol	Soluble
Ether	Freely soluble
Oil	Freely soluble
Water	Insoluble

Uses:

Cetyl alcohol is used as an emulsifying agent, emollient, viscosity enhancer, and stabilizer in creams, lotions, ointments, and topical pharmaceutical formulations.

Density:

0.81 g/cm³

Melting Point:

49-52 °C

Application:

In pharmaceutical and cosmetic formulations, cetyl alcohol improves texture, consistency, spreadability, and stability of creams and lotions. It also provides a softening and moisturizing effect on the skin.

3.9 Triethanolamie [50]:

Nonproprietary Name :

Triethanolamine

Synonyms :

TEA; Trolamine; 2,2′,2″-Nitrilotriethanol; Tris(2-hydroxyethyl)amine

Chemical Name :

2,2′,2″-Nitrilotriethanol

Molecular Weight :

149.19 g/mol

Molecular Formula :

$C_6H_{15}NO_3$

CAS No :

102-71-6

Structure:

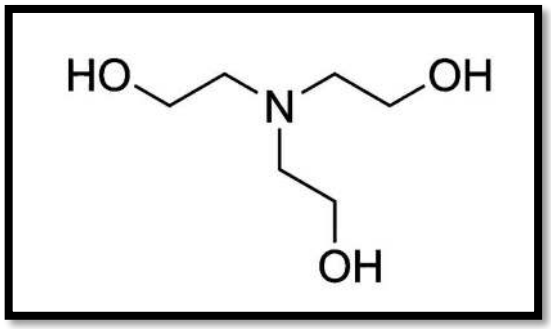


Fig 3.5.9 Triethanolamie

Description:

Triethanolamine is a clear, colorless to pale yellow, viscous liquid with a slight ammonia-like odor. It is widely used in pharmaceutical and cosmetic formulations as a pH-adjusting agent, emulsifier, and surfactant.

pH:

10.0 11.5 (1% aqueous solution)

Solubility:

Table 3.5.4 solubility of Triethanolamine

Solvent	Solubility
Acetone	Miscible
Chloroform	Slightly soluble
Ethanol	Miscible
Ether	Slightly soluble
Water	Miscible

Uses:

Triethanolamine is used as an emulsifying agent, alkalizing agent, pH adjuster, and surfactant in creams, lotions, gels, emulsions, and topical pharmaceutical preparations.

Density:

1.12 g/cm³

Melting Point :

20-21 °C

Application:

In pharmaceutical and cosmetic formulations, triethanolamine is commonly used to stabilize emulsions and adjust pH. It reacts with fatty acids such as stearic acid to form stable emulsifying

3.10 methyl paraben [51]:

Nonproprietary Name :

Methyl Paraben

Synonyms :

Methyl p-hydroxybenzoate; Nipagin; Methyl 4-hydroxybenzoate

Chemical Name :

Methyl 4-hydroxybenzoate

Molecular Weight :

152.15 g/mol

Molecular Formula :

$C_8H_8O_3$

CAS No :

99-76-3

Structure:

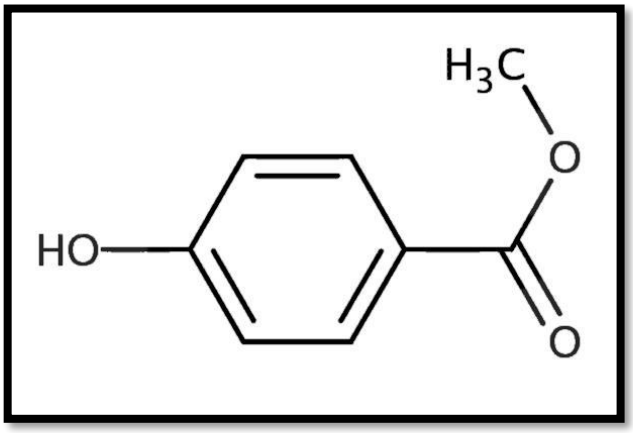


Fig 3.5.10 methyl paraben

Description:

Methyl paraben is a white crystalline powder or colorless crystals with a faint odor. It is widely used as an antimicrobial preservative in pharmaceutical, cosmetic, and food preparations.

pH:

Approximately 4 – 8 (stable range)

Solubility:

Table 3.5.5 solubility of methyl paraben

Solvent	Solubility
Acetone	Freely soluble
Ethanol	Freely soluble
Ether	Soluble
Propylene glycol	Soluble
Water	Slightly soluble

Uses:

Methyl paraben is used as a preservative to prevent microbial growth and increase the shelf life of creams, lotions, gels, ointments, and pharmaceutical formulations.

Density:

1.46 g/cm³

Melting Point:

125-128 °C

APPLICATION:

In pharmaceutical and cosmetic formulations, methyl paraben is commonly used as an antifungal and antibacterial preservative. It helps maintain formulation stability and prevents contamination during storage.

4. AIM, NEED AND OBJECTIVE

4.1. AIM OF THE STUDY:

To formulate and evaluate herbal anti-inflammatory cream containing Betel Leaf

extract, Tulsi extract, clove oil, menthol oil, and Aloe Vera for safe and effective topical application.

4.2. NEED OF STUDY:

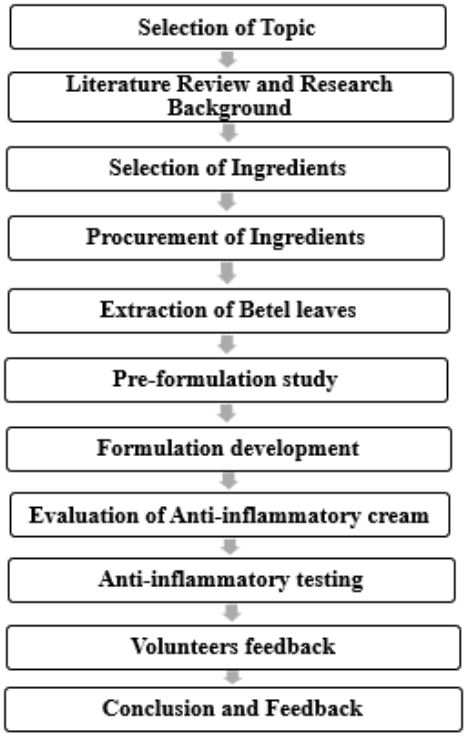
- Inflammation causes pain, redness, swelling, and irritation.
- Synthetic creams may produce side effects on prolonged use.
- Herbal formulations are safer and more economical.
- Herbal ingredients possess anti-inflammatory and soothing properties.
- Combination of Betel Leaf, Tulsi, Clove, Aloe Vera, and menthol may provide effective topical relief.
- Aim to develop a safe and effective herbal anti-inflammatory cream.

4.3. OBJECTIVE

- To formulate a herbal anti-inflammatory cream.
- To use betel leaf extract, tulsi extract, clove oil, menthol oil, and aloe vera in the formulation.
- To evaluate physical parameters of the cream.
- To perform phytochemical screening of herbal extracts.
- To evaluate anti-inflammatory activity by protein denaturation method.
- To compare activity with standard drug.
- To develop a stable, safe, and effective herbal formulation.

To promote herbal ingredients in topical preparations.

5.PLAN OF WORK



6. MATERIALS AND METHODS

a. INGREDIENTS

Table 6.1 Materials and equipment used for formulation of herbal pain relief cream

Sr No.	Active ingredients	Excipients	Equipment
1	Betel leaf extract	Stearic acid	Water bath
2	Clove oil	Cetyl alcohol	pH meter
3	Peppermint Oil	White soft paraffin	Beakers
4	Aloe Vera	Liquid paraffin	Mortar Pestel
5	Tulsi Extract	Propyl Paraben	
6		Glycerin	
7		Propylene glycol	
8		Methyl paraben	
9		Water	
10		Triethanolamine	

b. METHODS

6.2.1. Extraction of Piper betel (Betel leaf)

6.2.2. Pre-formulation studies of Piper Betel leaf

6.2.2.1. Preliminary tests for Piper betel leaf

- Organoleptic Parameters
- Phytochemical studies
- pH test

6.2.3. Formulation of Anti-inflammatory cream

6.2.4. Evaluation of Anti-inflammatory cream

6.2.4.1. Organoleptic Evaluation

6.2.4.2. pH

6.2.4.3. Homogeneity

6.2.4.4. Spreadability

6.2.4.5. Washability

6.2.4.6. Skin Irritation Test

6.2.4.7. Stability study

6.2.5. Anti-inflammatory testing by protein denaturation method

6.2.1.EXTRACTION OF BETEL LEAF

1) Collection and cleaning of leaves

Fresh and healthy betel leaves were collected and washes properly with tap water and followed by distilled water to remove dust and impurities.

2) Drying

Leaves were dried at room temperature for 2-3 days.

3) Powder preparation

Coarse powder of leaves was prepared using grinder and and stored in air tight container.

4) Maceration process

Accurately weighed 10g of powder was transferred in glass container and 70 ml of

ethanol and 30 ml of water was added. Mixture was kept aside for 72 hours at room temperature with occasionally shaking.

5) Filtration

After maceration, mixture was filtered and extract was collected.

6) Concentration

Solvent evaporated using water bath and thick semisolid extract was obtained.

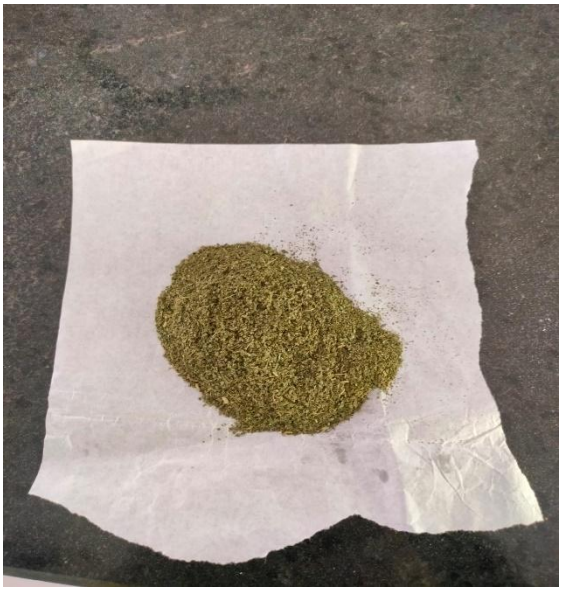


Fig 6.2.1.1 Coarse powder of betel leaves

Fig 6.2.1.2 Maceration process (Mixture)

Fig 6.2.1.3. Filtration process

Fig 6.2.1.4. Extract obtained

6.2.2PREFORMULATION STUDIES OF BETEL LEAF

6.2.2.1. PRELIMINARY TESTS FOR BETEL LEAF

1. Organoleptic Parameters

The extracts appearance, color, odor, and taste were evaluated.

2. Phytochemical Studies

The aqueous extract was analyzed through phytochemical screening to determine the presence or absence of various constituents.

- **Tests for Alkaloids:**

Principle

Alkaloids react with Mayer's reagent to produce cream colored precipitate.

Procedure

1. Take 2 mL of ethanolic extract in a test tube.
2. Add 2–3 drops of dilute hydrochloric acid and mix well.
3. Filter the solution.
4. Add few drops of Mayer's reagent to the filtrate.

Observation

Formation of cream or white precipitate indicates presence of alkaloids.

- **Tests for Flavonoids (Shinoda Test):**

Principle

Flavonoids react with magnesium and hydrochloric acid to produce pink or red coloration.

Procedure

1. Take 2 mL extract in a test tube.
2. Add small pieces of magnesium ribbon.
3. Add few drops of concentrated hydrochloric acid carefully.

Observation

Appearance of pink, orange, or red color indicates presence of flavonoids.

- **Test for Saponins (Foam Test)**

Principle

Saponins have soap-like property and produce stable foam in water.

Procedure

1. Mix 2 mL extract with 5 mL distilled water.
2. Shake vigorously for 2–3 minutes.

Observation

Persistent foam formation for 10–15 minutes indicates presence of saponins.

- **Test for Glycosides (Keller–Killiani Test)**

Principle

Cardiac glycosides react with ferric chloride and sulfuric acid to form brown ring.

Procedure

1. Take 2 mL extract.
2. Add 1 mL glacial acetic acid containing traces of ferric chloride.
3. Carefully add concentrated sulfuric acid along the side of test tube.

Observation

Formation of brown ring at junction indicates presence of glycosides.

- **Test for Phenolic Compounds**

Principle

Phenolic compounds react with ferric chloride to produce blue or black color.

Procedure

1. Take 2 mL extract.
2. Add few drops of ferric chloride solution.

Observation

Deep blue, green, or black coloration indicates phenolic compounds.

- **Test for Terpenoids (Salkowski Test)**

Principle

Terpenoids react with sulfuric acid producing reddish brown coloration.

Procedure

1. Mix 2 mL extract with 2 mL chloroform.
2. Carefully add concentrated sulfuric acid along the wall of test tube.

Observation

Reddish-brown layer at interface confirms terpenoids.

6.2.3. FORMULATION OF ANTI-INFLAMMATORY CREAM

Table 6.2 Formulation of Anti-inflammatory cream

Ingredients	F1	F2	F3	F4
Active ingredients				
Betel leaf extract	0.5ml	1ml	1.5ml	2ml
Clove oil	0.2ml	0.3ml	0.4ml	0.5ml
Menthol oil	0.2ml	0.3ml	0.4ml	0.5ml
Tulsi extract	0.5ml	1ml	1.5ml	2ml
Aloe vera gel	1g	1.5g	1.5g	2g
Aqueous phase				
Purified water	Q.S.	Q.S.	Q.S.	Q.S.
Glycerin	2.0ml	2.0ml	2.0ml	2.0ml
Propylene glycol	2.0ml	2.0ml	2.0ml	2.0ml
Methyl paraben	0.15g	0.15g	0.15g	0.15g
Oil phase				
Stearic acid	4.0g	4.0g	4.0g	4.0g
Cetyl alcohol	1.5g	1.5g	1.5g	1.5g
White soft paraffin	3.0g	3.0g	3.0g	3.0g
Liquid paraffin	2.5ml	2.5ml	2.5ml	2.5ml
Propyl paraben	0.05g	0.05g	0.05g	0.05g
Triethanol amine	0.5ml	0.5ml	0.5ml	0.5ml

Procedure for preparation of Anti-inflammatory herbal cream

Step 1: Preparation of Aqueous Phase

1. Take a clean beaker and add the required quantity of purified water.
2. Add glycerin and propylene glycol into the water.

3. Dissolve methyl paraben in the aqueous phase with continuous stirring.

4. Add aloe vera gel and tulsi extract slowly while stirring.

5. Heat the aqueous phase to about 70–75°C.

Step 2: Preparation of Oil Phase

1. In another beaker, add stearic acid, cetyl alcohol, white soft paraffin, and liquid paraffin.

2. Add propyl paraben to the oil phase.

3. Heat the mixture to 70–75°C until all ingredients melt completely.

4. Add triethanolamine and mix properly.

Step 3: Emulsification

1. Slowly add the hot oil phase into the hot aqueous phase with continuous stirring.
2. Stir continuously using a mechanical stirrer or homogenizer until a smooth cream is formed.
3. Continue stirring during cooling to obtain proper consistency and uniformity.

Step 4: Addition of Active Ingredients

1. When the temperature falls below 40°C, add:

- Betel leaf extract
- Clove oil
- Menthol oil

2. Mix thoroughly to ensure uniform distribution of active ingredients.

6.2.4. Evaluation of Anti-inflammatory cream

6.2.4.1. Organoleptic Evaluation

The prepared cream was evaluated for its physical appearance by simple visual observation. Parameters such as color, odor, texture, and overall appearance were examined to ensure the acceptability of the formulation.

Procedure:

A small quantity of the cream was placed in a clean watch glass and observed under normal daylight. The color, smell, smoothness, and presence of any lumps or phase separation were carefully checked.

6.2.4.2. pH Determination

The pH of the cream was determined to ensure that the formulation was compatible with the skin and would not cause irritation during application.

Procedure:

About 1 g of the cream was weighed accurately and dispersed in 10 mL of distilled water.

The mixture was allowed to stand for approximately 2 hours at room temperature. The pH was then measured using a calibrated digital pH meter.

6.2.4.3. Homogeneity Test

The homogeneity test was performed to check the uniform distribution of ingredients throughout the formulation.

Procedure:

A small amount of cream was pressed between the thumb and index finger and also spread on a clean glass slide. The formulation was observed for uniformity and the presence of coarse particles.

6.2.4.4.Spreadability Test

Spreadability of the cream was evaluated to determine how easily the formulation could be spread on the skin surface.

Formula Used

S = ML/T

Where:

S = Spreadability

M= Weight tied to upper slide

L = Length moved by the slide

T = Time taken to separate the slides

Procedure

Approximately 1 g of cream was placed between two glass slides. A known weight was placed on the upper slide, and the time required for the upper slide to move a certain distance was noted.

6.2.4.5. Washability Test

The washability test was carried out to determine how easily the cream could be removed from the skin surface.

Procedure:

A small quantity of cream was applied on the skin and washed with normal tap water.

6.2.4.6. Extrudability Test

The extrudability test was performed to evaluate the ease with which the cream could be expelled from the collapsible tube.

Procedure:

The cream-filled tube was pressed manually, and the amount of cream extruded under constant pressure was observed.

6.2.4.6. Skin Irritation Test

The skin irritation test was performed to assess the safety of the cream for topical use.

Procedure:

A small amount of cream was applied to a specific area of skin and observed for 24 hours for any signs of redness, itching, swelling, or irritation.

6.2.4.7. Stability study

The stability study was conducted to evaluate the physical stability of the formulation under different storage conditions.

Procedure:

The formulated cream was stored at room temperature, refrigerated condition, and accelerated temperature condition (40°C ± 2°C). The formulation was observed periodically for any changes in color, odor, pH, consistency, and phase separation.

6.2.5. Anti-inflammatory testing by protein denaturation method

Procedure for In Vitro Anti-Inflammatory Activity by Protein Denaturation Method

The anti-inflammatory activity of the prepared cream was evaluated using the protein denaturation method. This method is commonly used to determine the ability of a sample to prevent protein denaturation, which is one of the major causes of inflammation in the body. Bovine Serum Albumin (BSA) was used as the

protein source, and Diclofenac sodium was used as the standard anti-inflammatory drug.

Materials Required

- Bovine Serum Albumin (BSA)
- Phosphate buffer saline (PBS) of pH 6.4
- Diclofenac sodium
- Test cream sample
- Distilled water
- Test tubes
- Water bath
- UV-Visible spectrophotometer

Preparation of Solutions:

Preparation of BSA Solution:

A 1% BSA solution was prepared by dissolving 1 g of bovine serum albumin in 100 mL of phosphate buffer solution (pH 6.4)

Preparation of Standard Solution:

Different concentrations of Diclofenac sodium (200, 400, 600, 800, and 1000 µg/mL) were prepared using distilled water.

Preparation of Test Sample:

The cream sample was prepared in different concentrations ranging from 200–1000 µg/mL using a suitable solvent.

Procedure:

In clean test tubes, 0.5 mL of the test sample was mixed with 0.5 mL of 1% BSA solution.

Similarly, standard drug solutions were prepared by mixing 0.5 mL of Diclofenac sodium solution with 0.5 mL of BSA solution.

For the control, 0.5 mL of phosphate buffer was mixed with 0.5 mL of BSA solution.

All the test tubes were incubated at 37°C for about 15–20 minutes to allow interaction between the protein and the sample.

After incubation, the mixtures were heated at 70°C in a water bath for 5–10 minutes to induce protein denaturation.

The samples were then cooled to room temperature.

The absorbance of all samples was measured at 660 nm using a UV-Visible spectrophotometer.

Calculation

The percentage inhibition of protein denaturation was calculated using the following formula:

% Inhibition= Absorbance of control – Absorbance of test × 100 Absorbance of test

7. RESULTS AND DISCUSSION

7.1 Preformulation studies Results

7.1.1. Betel leaf extract

7.1.1.1. Organoleptic studies:

Table 7.1: Organoleptic properties of betel leaf extract

Organoleptic	Observations
Color	Dark green to greenish brown
Odor	Characteristic odor and pungent odor of betel leaf
Appearance	Concentrated extract with smooth consistency

7.1.1.2. Physiochemical studies:

	Name of test	Results
Alkaloids	Mayer's test	Present
Flavonoids	Shinoda test	Present
Tannins	Ferric chloride test	Present
Saponins	Foam test	Present
Glycosides	Keller – killani test	Present
Phenols	Ferric chloride test	Present
Terpenoids	Salkowski test	Present

7.2 Evaluation of Anti-inflammatory cream

7.2.1. Organoleptic test

Organoleptic test	F1	F2	F3	F4	Inference
Color	Dull-off white	Light brown	Creamish white	Light yellow	Colors indicated proper incorporation of ingredients and acceptable appearance.
Odor	Weak herbal	Strong herbal	Minty herbal	Faint herbal	Odor of F1, F4 is more acceptable for topical application.
Appearance	Smooth and dense	Thick and uneven	Creamy and thick	Smooth, semi soft	Appearance indicated good consistency and texture.

7.2.2. pH

pH	F1	F2	F3	F4	inference
	5.5	6	6.5	5.8	pH and indicates that the creams are suitable for topical application without causing irritation.

7.2.3. Homogenesity

homogenesity	F1	F2	F3	F4	Inference
	good	poor	Good	moderate	F1, F3 and F4 showed good homogeneity indicating uniform distribution of ingredients

7.2.4. Spreadability

spreadability	F1	F2	F3	F4	Inference
	6.66cm	5cm	5.6cm	5.8cm	F1, F2 and F4 showed good spreadability indicating easy aaplication.

7.2.5. Washability

Washability	F1	F2	F3	F4	Inference
	Good	Moderate	Good	Good	F1, F2 and F3were easily washable with water indicating good patient compliance.

7.2.6. Extrudability

Extrudability	F1	F2	F3	F4	Inference
	Good with uniform flow	Poor	Good	Good	F1,F2 and F3 showed good extrudability with smooth and uniform flow from container.

7.2.7. Stability

stability	F1	F2	F3	F4	Inference
	stable	Unstable , phase separation	stable	Moderately stable	F1 and F3 were found to be stable. F4 was moderately stable and.

7.3. Results of Anti-inflammatory testing by protein denaturation method

The cream showed noticeable anti-inflammatory activity in the protein denaturation assay. The percentage inhibition increased gradually with increase in concentration, indicating a dose-dependent effect. Diclofenac sodium showed higher inhibition values compared to the test sample at all concentrations. However, the BLT cream demonstrated good anti-inflammatory potential, especially at higher concentrations.

Concentration	Diclofenac sodium (% inhibition)	Herbal cream (% inhibition)
200	72.87	37.60

400	78.29	46.51
600	81.40	55.04
800	84.88	65.50
1000	85.27	74.42

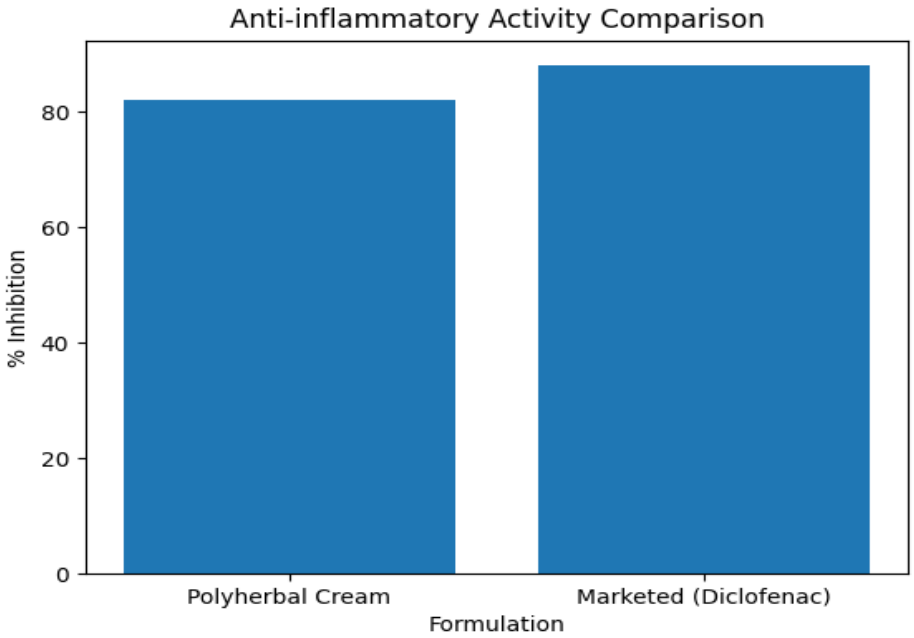


Fig7.3.1 Anti-inflammatory Activity Comparison (Vertical Bar Chart)

8. SUMMARY AND CONCLUSION

The present thesis entitled "Formulation and Evaluation of Herbal Pain Relief Cream" focused on the development of a safe, effective, and economical herbal topical formulation for the management of pain and inflammation. Inflammation is a common physiological response associated with redness, swelling, irritation, and pain. Although synthetic anti-inflammatory drugs such as NSAIDs and corticosteroids are widely used, prolonged use may lead to adverse effects including gastric irritation, skin reactions, and systemic complications. Therefore, herbal formulations have emerged as a promising alternative because of their natural origin, reduced side effects, affordability, and better patient compliance.

The study involved the formulation of a herbal cream using natural ingredients such as betel leaf extract, tulsi extract, clove oil, menthol oil, and aloe vera, all of which possess significant anti-inflammatory, analgesic, antimicrobial, and soothing properties. The cream was prepared using oil and aqueous phases followed by emulsification to obtain a stable oil-in-water emulsion suitable for topical application. Different formulations (F1–F4) were developed by varying the concentration of ingredients and excipients.

The prepared formulations were evaluated for various physicochemical and pharmaceutical parameters including colour, odour, consistency, pH, homogeneity, spreadability, washability, extrudability, viscosity, stability, and skin compatibility. The pH of all formulations was

found to be within the acceptable range for skin application, indicating minimal chances of irritation. The creams also exhibited good homogeneity, smooth texture, satisfactory spreadability, and ease of removal with water, making them suitable for patient use.

Phytochemical screening of betel leaf extract confirmed the presence of important bioactive constituents such as alkaloids, flavonoids, tannins, saponins, phenolic compounds, and terpenoids. These phytoconstituents are known to contribute significantly to anti-inflammatory and antioxidant activity. Anti-inflammatory activity of the formulations was evaluated using the protein denaturation method. The formulations demonstrated concentration-dependent inhibition, with maximum inhibition observed at higher concentrations. Among the developed formulations, F1 and F3 showed better physical stability, spreadability, homogeneity, and anti-inflammatory activity compared to the other formulations.

The overall findings of the study suggest that the developed herbal pain relief cream possesses effective anti-inflammatory potential along with desirable pharmaceutical characteristics. The formulation provides a natural and safer alternative to conventional topical preparations and may be beneficial for the treatment of pain, inflammation, and minor skin-related discomforts.

The present research successfully formulated and evaluated a herbal pain relief cream using natural ingredients possessing anti-inflammatory and analgesic properties. The study confirmed that herbal ingredients such as betel leaf extract, tulsi extract, clove oil, menthol oil, and aloe vera can be effectively incorporated into a stable topical cream formulation. The prepared formulations exhibited satisfactory physicochemical properties including appropriate pH, good homogeneity, smooth consistency, spreadability, washability, and stability, making them suitable for topical application.

The phytochemical analysis indicated the presence of various bioactive compounds responsible for therapeutic activity. Evaluation of anti-inflammatory activity demonstrated that the herbal formulations produced significant inhibition of protein denaturation in a concentration-dependent manner, thereby confirming their potential effectiveness in reducing inflammation and pain. Among all the formulations, F1 and F3 were found to be the most stable and effective formulations.

The study concludes that herbal topical formulations can serve as a safe, economical, and effective alternative to synthetic anti-inflammatory preparations with reduced risk of adverse effects. The developed herbal pain relief cream showed promising therapeutic potential and good patient acceptability. Further clinical studies and large-scale stability studies may help in establishing the formulation for commercial pharmaceutical applications in the future.

9. FUTURE PROSPECTS

- Further studies can be carried out for long-term stability testing of the herbal cream.
- Clinical studies on human volunteers can be performed to confirm safety and efficacy.
- Advanced studies can be conducted to determine the exact mechanism of anti-inflammatory action.
- The formulation can be modified into gels, ointments, sprays, or transdermal preparations for improved delivery.
- Additional herbal ingredients with analgesic and wound-healing properties may be incorporated for enhanced therapeutic effect.

- Large-scale manufacturing and commercialization of the herbal cream can be explored.
- Skin permeation and bioavailability studies can be performed for better formulation optimization.
- The formulation may be evaluated for other dermatological applications such as muscle pain, arthritis, burns, and skin irritation.
- Nanotechnology-based herbal topical systems can be developed to improve penetration and effectiveness.

Further research may help establish herbal anti-inflammatory creams as safer alternatives to conventional synthetic products

REFERENCES

1. Raja SN, Carr DB, Cohen M, et al. The revised International Association for the Study of Pain definition of pain. Pain. 2020;161(9):1976-1982.
2. Cohen SP, Vase L, Hooten WM. Chronic pain: an update on burden and best practices. Lancet. 2021;397(10289):2082-2097.
3. Treede RD, Rief W, Barke A, et al. Chronic pain as a symptom or a disease. Pain. 2019;160(1):19-27.
4. Chen L, Deng H, Cui H, et al. Inflammatory responses and inflammation-associated diseases. Oncotarget. 2018;9(6):7204-7218.
5. Kumar V, Abbas AK, Aster JC. Robbins Basic Pathology. 10th ed. Elsevier; 2020.
6. Ghlichloo I, Gerriets V. Nonsteroidal Anti-inflammatory Drugs (NSAIDs). StatPearls Publishing. 2023.
7. Barnes PJ. Anti-inflammatory actions of glucocorticoids. Clinical Science. 2019;94(6):557-572.
8. Salehi B, Ata A, Kumar NVA, et al. Antiinflammatory and antioxidant effects of herbal medicines. Biomolecules. 2019;9(11):641.
9. Sostres C, Gargallo CJ, Lanas A. NSAIDs and gastrointestinal damage. Arthritis Research & Therapy. 2013;15(Suppl 3):S3.
10. Barnes PJ. Corticosteroid effects in inflammatory diseases. Clinical Science. 2019;94(6):557-572.
11. Paudel KS, Milewski M, Swadley CL, et al. Challenges in dermal/transdermal delivery. Therapeutic Delivery. 2010;1(1):109-131.
12. Brown MB, Martin GP, Jones SA, Akomeah FK. Dermal and transdermal drug delivery systems. Drug Delivery. 2006;13(3):175-187.
13. Benson HAE, Watkinson AC. Topical and Transdermal Drug Delivery. Wiley; 2019.
14. Prausnitz MR, Langer R. Transdermal drug delivery. Nature Biotechnology. 2008;26(11):1261-1268.
15. Williams AC, Barry BW. Penetration enhancers. Advanced Drug Delivery Reviews. 2012;64:128-137.
16. Aulton ME, Taylor KMG. Aulton's Pharmaceutics. 5th ed. Elsevier; 2018.
17. Lachman L, Lieberman HA, Kanig JL. Industrial Pharmacy. 4th ed. CBS Publishers; 2019.
18. Draelos ZD. Herbal skin care products. Dermatologic Clinics. 2019;18(4):597-607.
19. Hewlings SJ, Kalman DS. Curcumin and human health. Foods. 2017;6(10):92.
20. Surjushe A, Vasani R, Saple DG. Aloe vera review. Indian Journal of Dermatology. 2008;53(4):163-166.
21. Alzohairy MA. Therapeutic role of Neem. Evidence-Based Complementary and Alternative Medicine. 2016;2016:7382506.
22. Mashhadi NS, Ghiasvand R, Askari G, et al. Anti-inflammatory effects of ginger. International Journal of Preventive Medicine. 2013;4(Suppl 1):S36-S42.

23. Mukherjee PK. Quality Control and Evaluation of Herbal Drugs. Elsevier; 2019.
24. Sharma PP. Cosmetics: Formulation and Quality Control. 5th ed. Vandana Publications; 2020.
25. Sinko PJ. Martin's Physical Pharmacy and Pharmaceutical Sciences. 7th ed. Wolters Kluwer; 2017.
26. Swarbrick J. Encyclopedia of Pharmaceutical Technology. 4th ed. Informa Healthcare; 2019.
27. Kale SN, Deore SL. Emulsion and nanoemulsion review. Systematic Reviews in Pharmacy. 2017;8(1):39-47.
28. Ansel HC, Popovich NG, Allen LV. Pharmaceutical Dosage Forms and Drug Delivery Systems. 10th ed. Lippincott Williams & Wilkins; 2020.
29. OECD Guidelines for Skin Irritation Testing. OECD Publishing; 2021.
30. ICH Harmonised Guideline Q1A(R2). Stability Testing of New Drug Substances and Products. 2003.
31. Yuan H, Ma Q, Ye L, Piao G. Traditional and herbal medicines. Molecules. 2016;21(5):559.
32. Ekor M. Growing use of herbal medicines. Frontiers in Pharmacology. 2014;4:177.
33. Mukherjee PK. Herbal Drug Evaluation. Elsevier; 2019.
34. Ali A, Chong CH, Mah SH, Abdullah LC, Choong TSY, Chua BL. Impact of storage conditions on the stability of predominant phenolic constituents and antioxidant activity of dried _Piper betle_ extracts. Molecules. 2018;23(2):484.
35. Kirve DC. An overview of betel leaf: Green gold of India. Journal of Pharmacognosy and Phytochemistry. 2024;13(2):240-248.
36. George N, Anna CK S, Fathima H, Adithya D. Betel leaf: An integrative review of its phytoconstituents, traditional uses and modern therapeutic potential. Journal of Pharmacognosy and Phytochemistry. 2024;13(6):124-135.
37. Baviskar HP, Dhake GT, Kasai MA, Chaudhari NB, Deshmukh TA. Review of _Piper betle_. Research Journal of Pharmacognosy and Phytochemistry. 2017;9(2):128-134.
38. Gavade A, Fakir S, Shedbale S, Jadage DR. An overview on betel leaf. Int J Pharm Sci. 2025;3(4):Article IJPS/250304088.
39. Linán-Atero R, Aghababaei F, Rodriguez Garcia S, Hasiri Z, Ziogkas D, Moreno A, Hadidi M. Clove essential oil: Chemical profile, biological activities, encapsulation strategies, and food applications. Antioxidants. 2024;13(4):488.
40. Pandey VK, Shams R, Singh R, Dar AH, Pandiselvam R, Rusu AV, Trif M. A comprehensive review on clove (_Syzygium aromaticum_ L.) essential oil and its significance in the formulation of edible coatings for potential food applications. Front Nutr. 2022;9:987674.
41. Verma S. Chemical constituents and pharmacological action of _Ocimum sanctum_ (Indian holy basil-Tulsi). J Phytopharmacol. 2016;5(5):205-207.
42. Samanth M. The chemical constituents of _Ocimum sanctum_ and its pharmacological applications: A review. In: Recent Developments in Chemistry and Biochemistry Research. Vol 11. B P International; 2025. P. 119-152.
43. Saleem A, Naureen I, Naeem M, Murad HS, Maqsood S, Tasleem G. _Aloe vera_ gel effect on skin and pharmacological properties. Sch Int J Anat Physiol. 2022;5(1):1-8.
44. Sampath Kumar KP, Bhowmik D, Chiranjib, Biswajit. _Aloe vera_: A potential herb and its medicinal importance. J Chem Pharm Res. 2010;2(1):21-29.

45. Shrivastava A. A review on peppermint oil. Asian J Pharm Clin Res. 2009;2(2):87-91.
46. Carlson RE, Buch RM, von Fraunhofer JA. Peppermint (_Mentha piperita_ L.) essential oil in systemic and oral health. EC Dent Sci. 2021;20(7):43-55.
47. Cosmetic Ingredient Review Expert Panel. Safety assessment of glycerin as used in cosmetics. Draft final report for panel review. Washington, DC: Cosmetic Ingredient Review; 2014 Nov 14.
48. Jain CP, Naruka PS. Formulation and evaluation of herbal tablets containing stearic acid as lubricant. Int J Pharm Sci. 2012;4(1):237-240.
49. Fiume MM, Heldreth B, Bergfeld WF, Belsito DV, Hill RA, Klaassen CD, et al. Safety assessment of cetyl alcohol, isostearyl alcohol, myristyl alcohol, and behenyl alcohol as used in cosmetics. Int J Toxicol. 2022;41(1_suppl):5S-36S.
50. Cosmetic Ingredient Review Expert Panel. Amended final safety assessment: Triethanolamine and triethanolamine-containing ingredients as used in cosmetics. Washington, DC: Cosmetic Ingredient Review; 2011 Oct 17.
51. Scientific Committee on Consumer Safety (SCCS). Opinion on methylparaben (CAS No. 99-76-3, EC No. 202-785-7). SCCS/1652/23 Final Opinion. Brussels: European Commission; 2023 Dec 14. Corrigendum adopted 2024 Feb 28.

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