Formulation and Evaluation of Anti-Inflammatory Cream

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Abstract:

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. ^[1,2,3]

Keywords: Diclofenac sodium, Clove oil, Beeswax, Solvent – Ethanol, Glycerine

Introduction:

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 drugs 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 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 Diclofenac sodium were prepared with base of bees - wax. Therefore, in the next, an optium 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 gastro- intestinal 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. 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's 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 passes 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 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, pharmaceutics, 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 espically 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. 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 ^[4,5,6].

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 loss 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 form 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.

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.

Advantages:

- Localized Action: Diclofenac sodium cream acts locally at the site of application, reducing systemic side effects.
- Effective Pain Relief: Provides significant pain relief for osteoarthritis and soft tissue injuries.
- Improved Physical Function: Enhances physical function and mobility in patients with osteoarthritis.
- Minimal Systemic Absorption: Low systemic absorption reduces the risk of gastrointestinal and other systemic side effects.
- Convenient Application: Easy to apply, making it a convenient treatment option for patients.
- Reduced Risk of Gastrointestinal Complications: Lower risk of gastrointestinal adverse events compared to oral NSAIDs.
- Targeted Delivery: Delivers the medication directly to the affected area, increasing efficacy and reducing side effects.

Ideal properties:

- Easy to apply.
- Spread easily on the skin.
- Pleasant in appearance.
- Less irritation to the skin.
- Melt or liquefy when applied on the skin.^[7,8]

TOPICAL DRUG DELIVERY SYSTEM

Topical drug delivery system is a type of localized drug delivery system used to treat cutaneous disorders by delivering therapeutic chemicals via the skin. Usually, localized skin infection is treated with methods. There are several forms of the treated with these methods. There are several forms of the formulas available, including solids, semisolids and liquid. The skin plays a key role in improving medication absorption when the medicinal ingredients in the solution has a flavourble lipids or water partition coefficient and is not an electrolyte. Although derma treatments come in a variety of formulation and consistency ranges, semisolids dosage forms are the most widely used type.

Advantages of topical drug delivery system:

- Avoiding the metabolism of main passes.
- Easy to apply and very convenient to use.
- Simple way to stop taking the drugs.
- Medication sent at a certain location with preference.
- There will be no gastro- intestinal incompatibility.
- Offers a limited therapeutic window and a short biological half-life for medication use.
- Enhanced adherence form patients.
- Self-care with medicines.
- It offers efficacy at low dosages and with continuous medication administration.
- Reduces the chance of medication level and danger fluctuation.
- Convenient and easy to apply.
- Avoidance of first pass metabolism.
- Avoid of risk.
- Avoid fluctuation of drug levels inter and intra patent variations.

Structure of the skin:

Skin is the largest organ of the body in term of surface area and weight. It has surface area of approximately 16000cm. In adults, skin represent 8% of body weight. It is the outermost layer or tissue of the living body; Skin shows a protective mechanism from external environment. Skin can produce a favorable chemical substance named as vitamin D when skin is exposed in sunlight. The skin helps to regulate the temperature of the human body and also acts as sensory organ. Skin includes various cellular elements like melanocytes, erythrocytes, keratinocytes etc. It has multi-layer structures because of different components like cells and fibers.

The skin consists of skin layers

A. The Epidermis

The outermost layer of the skin is called epidermis which having thickness of about 0.2mm. No veins and capillaries are located in this layer. The thickness of epidermis is depending upon the location of the body. The epidermis mainly consists two types of cells keratinocytes and dendrites cells. It also contains other number of cells like melanocytes, Langerhans cells etc. The epidermis layer is also called as the metabolic active tissue.

The outermost layer is classified into five sub layers and these are

- 1)Stratum corneum
- 2)Stratum lucidium.
- 3)Stratum granulosum
- 4)Stratum spinosum
- 5)Stratum Basale

1) Stratum corneum: The exterior sublayer of the epidermis is called as stratum corneum. It is also referred as the horny cell layer having thickness of about 8-15u m. The layer is of hexagonal shaped and is helpful for prevention of skin from the large amount of dehydration. It contains main component "ceramide", which having important role in water retention.

2) Stratum lucidum: Stratum lucidum is composed as thin clear layer of dead skin cells. It is found only in areas of thick skin on the palms of the hands and soles of the feet.

3) Stratum granulosum: The layer is also called as granular cell layer having thickness of 3pm. It contains 2-4 layers of granular cell. The shape of the cells is flatter because the keratin fibers are increasingly filled up into the cells.

4) Stratum spinosum: It is also called prickle cell layer having thickness ranges from 50-150um. It consists of number of cells, which may differ in shape and structure.

5) Stratum basale: Stratum Basale is composed as single layer and is the deepest and sublayer of epidermis. In stratum basale, keratinocytes are produced and shows their movement upward to the outer surface. The process of movement of keratinocytes is known as turnover. For one cycle of this process takes days and keratinocytes also changes their functions and structure. This is also called as basal cell layer and holds 8% of water in epidermis

B. The Dermis

1) Most of the magic happens in the dermis at least in the skin. Most of the dermis is made up of collagen and elastin as well as fibroblasts. This layer has several functions.

2) In the dermis there are blood vessels and the lymphatic vessels that nourish the skin and eliminate waste products or toxins.

3) Sweat glands are present in the dermis. They create sweat through your pores, removing impurities as cool your body.

4) The hair follicles (where your hair attaches) and the sebaceous glands, which produce the oils that make the skin soft and smooth the skin sometimes overzealously resulting in rashes and oily skin are also found in the dermis.

C. The Subcutaneous layer

1) The deepest layer of skin is the layer of fat that connects your bones to your muscles and bones. It goes deep that the active ingredients in your skincare products can never reach.

2) The subcutaneous layer is like a thermostat. It protects the body and can also be used as a source of energy in a pinch.

3) Fat also acts as a filter, protecting your muscles, bones and organs from damage.

4) Finally, the subcutaneous layer contains additional blood vessels, nerve endings, hair follicular roots and the deepest oil producing sebaceous gland.^[9,10]



Figure 1: Structure of the skin

DRUGS AND EXCIPIENT

1.DICLOFENAC SODIUM:

This medication is used to relieve joint pain from arthritis.

Diclofenac belongs to a class of drugs known as nonsteroidal anti-inflammatory drugs (NSAIDs).

Diclofenac falls under the NSAIDS class of drug.

Some benefits in of NSAIDS in the pharma world are as follows:

- 1.) They are a class of medicines available by prescription and OTC.
- 2.) They are some of the most commonly used medicines for pain and fever.
- 3.) used to treat medical conditions such as arthritis, menstrual cramps, headaches, colds, and the flu.
- 4.) work by blocking the production of certain chemicals in the body.



Figure 2: Diclofenac Sodium

Mechanism of action:

Diclofenac inhibits cyclo-oxygenase enzyme, which are responsible for producing prostaglandins that contribute to pain and inflammation.

Diclofenac sodium is a non-selective, reversible, and competitive inhibitor of cyclooxygenase (COX). It inhibits both COX-1 and COX-2 enzymes, which are responsible for producing prostaglandins. Prostaglandins contribute to inflammation and pain signalling.

Molecular formula: C14H10Cl2NNaO2.

Iupac name: 2-[(2,6-dichlorophenyl) amino] benzene acetic acid sodium salt.

Physical state: Solid at room temperature.

Melting point: 295.2-295.6°C.

Solubility: It's soluble in water, methanol, and other organic solvents.

Uses: Diclofenac is a nonsteroidal anti-inflammatory drug (NSAID) used to treat mild-to-moderate pain, and helps to relieve symptoms of arthritis (e.g., osteoarthritis or rheumatoid arthritis), such as inflammation, swelling, stiffness, and joint. ^[24,25,26]

2.BEES WAX:

Beeswax is an excellent addition to cosmetic products for many reasons. When used in lotions and creams, beeswax creates a barrier which helps to seal moisture into the skin. This barrier also helps to thicken homemade cosmetics and lotions because it is solid at room temperature and has a relatively high melting point of 147 degrees Fahrenheit. This is espically helpful in recepies that include high amounts of coconut oil, which has a low melting point or other oils that are liquids at room temperature. Beeswax also has vitamin A, which improves hydration to the skin and promotes cell regeneration.

Bees need wax as construction material for their combs. They produce it their wax glands, which are fully developed in 12 to 18 days old workers. In older bees the wax glands diminish their activity. How ever in emergency situation wax-synthesis can be reactivated. Greatest quantities the of wax are produced during

the growth of phase of bee colonies, under moderate climate conditions during April to June. A bibliography on the synthesis of beeswax is given in the monograph of Hepburn.

The main raw materials for wax formation are carbohydrates, i.e. the honey sugars fructose, glucose and sucrose. The ratio of sugar to wax can vary from 3 to 30:1, a ratio of around 20:1 being typical for central Europe.

The stronger the colony, the smaller the ratio, the more economical the wax production for the Colony. One Langstroth frame, containing only 100 g of wax can hold 2-4 kg of honey.

Wax production and comb construction activity in the bee colony are determined by following factors

Nector flow: the greater the flow, the more combs are needed for storage.

Brood rearing (egg laying): the more eggs are layered, the more comb cells are needed

The presence of a queen: only colonies with a queen build combs.

Temperature: temperatures higher than 15° C favour comb building activity. The presence of pollen as a Protein source.



Figure 3: Beeswax

Biological source: Obtained from honey comb of the bees apis mellifera.

Family: Apidae

Molecular weight: 300 – 550

Melting point: 61 – 65

Chemical constituents: Myricin (myricyl palmitate)

Physical properties: Acids, but soluble in most organic solvents. The melting point of beeswax ranges from 62 to 65 degree Celsius.

Solubility: Insoluble in water partially soluble in hot water ethanol soluble in fatty and essential oils.

Biological properties:

In general, hydro carbons (15%), esters (71%), free acids (8%) and other chemicals (6%) are present in un hydrolysed beeswax.

Uses:

- Beeswax, both yellow and white, is utilized in cosmetic manufacture as thickeners, emulsifiers, and stiffening agents.
- Beeswax absolute is added to soaps and perfumes to provide aroma.
- Additionally, tablets can be polished with beeswax absolute or white.
- Preparation of ointment. ^[14,15,16]

3.CLOVE OIL:

Clove oil contains eugenol, which is the primary bioactive compound responsible for its anti – inflammatory properties. Clove oil contains around 80% eugenol.

Clove oil has antibacterial, antibacterial, antifungal & anti-cancerous qualities.

Clove oil has been used as a bioactive ingredient in coating fresh fruits & vegetables. Clove oil has been used to treat gastritis symptoms.

Clove oil is used in cosmetics, medicine & food.

Its well established as an analgesic & anti – inflammatory agent.

Clove oil, derived from the buds of the clove tree, is a pale yellow to dark brown liquid with a distinct aroma and is primarily composed of eugenol. It exhibits morphological characteristics like high oil content in the flower buds, followed by flower stalks and leaves and is known for its antimicrobial and antioxidant properties.





Biological source: Clove oil, obtained from the flower buds of the Syzygium aromaticum tree.

Kingdom: Plantae (plants)

Family: Myrtaceae

Colour: Clove oil typically ranges from pale yellow to dark brown.

Aroma: It has a characteristic, pungent and aromatic smell.

Main constituents: The primary compent of clove oil is eugenol, a phenylpropanoid.

Other constituents: Besides eugenol, clove oil also contains other compounds like caryophyllene, eugenol acetate and minor components.

Physical properties:

Specific garvity: 0.9559 - 1.101 g ml

Refractive index: 1.5075 – 1.5467

Solubility: Not fully soluble in 70% ethanol.

Biological activities: Clove oil is known for its antifungal, insecticidal, antibacterial and antioxidants properties.

Uses:

- Clove oil, rich in eugenol is used for pain relief.
- Here's a more detailed breakdown of the uses of clove oil:
- Pain Relief and Dental Applications:
- Toothache: Clove oil is traditionally used for toothache pain due to its analgesic and anesthetic properties.
- Dental Care: It can be used in dental preparations (pastes, gels, solutions) to relieve pain and combat bacterial infections.
- Sore Gums and Mouth Ulcers: Clove oil can help soothe and heal mouth sores, ulcers, and sore gums.
- Acne Treatment: Clove oil's antibacterial and anti-inflammatory properties can help treat acne and reduce inflammation.
- Anti-aging: It can help prevent the appearance of fine lines and wrinkles.
- Hair Care: Clove oil can improve blood circulation to the scalp, promoting better nutrient delivery to hair follicles and potentially reducing scalp itchiness and dandruff.
- Skin Infections: Clove oil can help prevent the formation of infections. ^[17,18,19]

4.PROPYLPARABEN:

Propylparaben is a preservative commonly used in cosmetics, pharmaceuticals, and food. Here are detailed aspectsof propylparaben.

1.Chemical structure: propylparaben is the propyl ester of p-hydroxybenzoic acid. Its chemical formula is C10H12O3, and its IUPAC name is propyl 4 – hydroxybenzoate.

2.Function: propylparaben is primarily used as a preservative to prevent the growth of bacteria and fungi in products. It helps extend the shelf life of cosmetics, pharmaceuticals, and food by inhibiting microbial growth.

3.Soloubility: propylparaben is soluble in alcohol and oils but only slightly soluble in water. Its solubility in water can be increased by the addition of alkaline substances.

4.Safety: propylparaben has been extensively studied for its safety and is generally recognized as safe (GRAS) by regulatory agencies when used in accordance with good manufacturing practices.

Propylparaben is generally considered safe for use in low concentration but some individuals may experience allergic reaction.

5.Comoatibility:

propylparaben is compatible with a wide range of cosmetic ingredients and is often used in combination with other preservatives to provide broad spectrum antimicrobial protection.

6.Other parabens: Propylparaben is one of a series of parabens, including methylparaben, ethyl paraben and butylparaben, which are also used as preservatives.



Figure 5: Propylparaben

Mechanism of action:

Propylparaben works by inhibiting the growth of micro- organisms, including bacteria, fungi, and molds, which are responsible for spoilage and contamination.

Molecular formula: C10H12O

Iupac name: Propyl 4-hydroxybenzoate

Physical state: Solid at room temperature

Melting point: 96 to 99 °C

Solubility: It's soluble in water and organic solvents.

Uses:

- Propylparaben is primarily used as an antimicrobial preservative in various products, including cosmetics, pharmaceuticals and food to prevent the growth of bacteria, fungi and molds.
- This extending shelf life and ensuring product safety. ^[20,21]

5.GLYCERINE:

Common name: Glycerol, Glycerine, Glycerine, Propanetriol, 1,2,3-Trihydroxypropane, 1,2,3-Propanetriol,

Molecular formula: C3H8O3

Iupac name: Propane-1,2,3-triol

Melting point: 17.8 °C (64.0 °F)

Boiling point: 290 °C (554 °F)

Physical state: at Room Temperature (20 °C): Liquid

Solubility: Miscible in water

Physiological characteristics: Colourless, odourless, viscous liquid

Pharmacological aspects:

Pharmacodynamic Property: Glycerine attracts water into the outer layer of the skin, keeping it hydrated and soft.

Pharmacokinetics Property: Glycerine is absorbed slowly when applied topically and has low systemic absorption.

Mechanism of action: Glycerine words by drawing moisture from the air into the skin outer layer, thereby keeping the skin hydrated and preventing dryness.



Figure 6: Glycerine

Uses: Moisturizing agent, solvent, humectant.^[22]

6.DISTILLED WATER:

Common name: Distilled water

Physiological characteristics: Clear, Colourless, Odourless Liquid

Pharmacological aspect:

Pharmacodynamic Property: Hydrates the skin, acts as a solvent for other ingredients.

Pharmacokinetic Property: Not absorbed systemically, acts locally on the skin.

Mechanism of action: Distilled water acts as a carrier for the other ingredients, enusuring they are evently distributed in the formulation and providing hydration to the skin.

Uses:Solvent^[23]

INGREDIENTS AND THEIR CATEGORY

Sr.no.	Ingredients	Category
1	Diclofenac sodium	Anti-inflammatory
2	Methanol	Solvent
3	Beeswax	Cream base
4	Propylparaben	Preservatives
5	Clove oil	Anti-oxidants
6	Glycerine	Moisturizer

PREPERATION OF CREAM

1.Weing and Dispensing:

Weigh and accurately 1% w/w diclofenac sodium and 99% cream base (Beeswax).

2. Dissolution of Diclofenac Sodium:

Dissolve diclofenac sodium in methanol (10-20 % of the total weight) with gently heating (40-50 degree Celsius) and stirring.

3. Mixing with Cream Base:

Gradually add the diclofenac sodium methanol solution to the cream base and crude drug extract while stirring.

4. Addition of Distilled Water and Glycerine:

Add distilled water (10-20% of the total weight) and glycerine (5-10% of the total weight) to the mixture and stir well.

5.Add Preservation and pH Adjustment:

Add preservatives to the cream to prevent microbial growth.

Adjust the pH of the cream to a suitable range (e.g. pH 5.5-6.5) using pH adjusters.

6. Packaging:

Fill the cream into suitable containers. [27,28,29,30]

FORMULATION TABLE:

Sr.No.	Ingredients	Batch F1 (10gm)	Batch F2 (10gm)	Batch F3 (10gm)	Batch F4 (10gm)	Batch F5 (10gm)
1	Diclofenac	1gm	1gm	1gm	2gm	2gm

	sodium					
2	Beeswax	1.25gm	1.69gm	1.70gm	1.15gm	1.15gm
3	Methanol	2ml	2ml	2ml	2ml	2ml
4	Clove oil	1.50ml	1.50ml	1.20ml	1.20ml	1.20ml
5	Glycerine	2.5ml	2.50ml	3ml	3ml	3ml
6	Propylparaben	0.29gm	0.30gm	0.50gm	0.50gm	0.50gm
7	Distilled water	qs	qs	qs	qs	qs

FORMULATION PARAMETERS TEST FOR CREAM

1.Organoleptic Evaluation: An organoleptic examination seeks to determine the outward appearance. Cream formulated was taken. This evaluation ware examined by the visual examination.

Colour: The colour of formulation is white off.

Texture: Formulation having smooth texture.

Odour: The odour of formulation is unpleasant.

2.Determination of Spreadability:

About 1g of each sample was weighed and placed at the centre of glass plate and another glass plate was placed over it carefully. Above the glass plates, 2kg weight was placed at the centre of plate, avoid sliding of plate. The diameter of the paste in cm was measured after 30 minutes. The experiment was repeated 3 times and the average was reported for all the samples.

Spreadability was calculated using the following formula

 $S = M \setminus L |T|$

Were,

S= Spreadability

M= Weight in the pan (tied to the upper slide)

L= Length moved by the glass slide

T= Time

3.Skin Irritation Test:

Apply cream on dorsal side of your non dominant hand and check for edam, erythema or irritability on your hand for twenty – four hours.

4.Homogeneity:

All developed creams were packed in containers and then tested for homogeneity by visual inspection. They were tested for their appearance and presence of any aggregates.

5.Measurement of pH:

pH of cream formulated were determined by using pH meter. Take 1 gm of cream and dissolved in 10 ml distilled water and keep apart for two hours. Then the measurement of pH formulation was done by dipping the glass electrode completely into the cream and average values are reported.

6.Phase Separation:

•Prepared cream was kept in a closed container at a temperature of 25-100 degree Celsius.

•Then phase separation was checked for 24th for 30 days.

•Any change in the result no phase was observed in formulation.

7.Washability:

We tested how easy it is to wash off soap from our hands using tap water. Soap was easy to wash off.

8.Greaisness: Heare the cream was applied on the skin surface in the form of smear and checked if the smear was oily or grease like.

9.Stability: The stability of cream refers to its ability to maintain its properties, such as texture, appearance and composition over time and under various condition. It involves assessing factors like phase separation, viscosity, microbial growth and oxidation. Stability testing helps determine the shelf life and quality of the cream product.

RESULT AND DISSUCATION

EVALUATION PARAMETER OF CREAM

1.Organoleptic Evaluation:

Formulation	Colour	Texture	Odour
F1	White	Smooth	Pleasent
F2	White	Smooth	Pleasent
F3	White	Smooth	Pleasent
F4	White	Smooth	Pleasent
F5	White	Smooth	Pleasent

2. Determination of Spreadability:

		Parameter	F1	F2	F3	F4	F5
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Evaluated					
Spreadability	14.10	14.00	15.15	15.50	16.61

3.Skin Irritation Test: There is no skin of irritancy on skin after an applicant of cream

4.Measurement of pH:

Sr.No.	Formulation Batches	Observation
1	F1	5.00
2	F2	5.47
3	F3	6.1
4	F4	6.25
5	F5	6.25



Figure7: Digital pH meter

(standard batch)

5. Result of Phase Separation:

•Prepared cream was kept in a container at a temperature of 25-100 degree Celsius

•Then phase separation was checked for 24 - 30 days.

•Any change in the result no phase separation was observed in formulation.



Figure 7: Phase Separation

DISCUSSION AND CONCLUSION

DISCUSSION:

The stability of anti-inflammatory creams was observing changes in parameters like colour, odour, pH, under extreme condition and all anti-inflammatory creams were found to be substantially stable.

The prepared creams were homogenous and in good appearance consistency. The pH values of all formulations were in close range. The spreadibility of formulation indicates that the cream formulation is easy to apply. The formulation was found to be more consistent. The diclofenac sodium cream is found to be effective to pain and inflammation. This reserch provide a foundation for the development of pain relief and to reduce the inflammation and further improvement for better formulation is required. Common side effects include redness, itching, rash, dry skin, scaling or peeling where you use it. Diclofenac is a nonsteroidal anti-inflammatory drug used to treat mild to moderate pain and helps to relive symptoms of arthritis, such as inflammation, swelling, stiffness and joint pain.

CONCLUSION:

The final produts are evulauted for its appearance, odour, pH and stability to ensure that it meet the desired cosmetic and is safe and effective for use on the topically on body. With carefully formulation and evaluation of semi-synthetic anti-inflammatory cream with diclofenac sodium, clove oil, methanol, glycerine, propylparaben can provide effective and natural option for promating healthyand painless filling. Herbal product can be a good substitute for chemical-based skin care product. Further market studies and continuous refinement of the formulation may enhance its commerical viability and contribute to its widespread adoption in promoting skin healthcare and well-being. From the above project we can conclude by using clove oil, glycerine cream showed a multi-purpose effect and all the herbal ingredients showed significant different activities.Based on result and discussion, the F1 formulation were stable at room temperature and can be safety used on skin. The present study concludes that the formulationdeveloped showsits physiochemical properties like spreadability, homogeneity, viscosity, and consistency are good. The present cream formulation was developed by taking into consideration that in cream formulations there is present no direct contact of active drug. The Diclofenac sodium cream is found to be effective to mimic the pain and inflammation.

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