



ANTI-INFLAMMATORY POTENTIALS OF TOPICAL POLY HERBAL CREAM: REVIEW

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ABSTRACT

Creams are the topical preparations which can be applied on the skin. 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 can be ayurvedic, herbal or allopathic which are used by people according to their needs for their skin conditions. Plants generally have varied chemical compositions depending upon species. A good number of plants are known to be of economic and medicinal value. Those that are of medicinal value are often used as herbal remedy for the restoration and maintenance of good health. Some herbs have been considered as drugs and therefore generally safe and effective. According to ayurveda, individual herbs are insufficient to achieve a desired therapeutic effect. When it is optimized as multiple herbs composition in a particular ratio it will give a therapeutic effect in a better way with reduced toxicity. Several plant extracts and their phytoconstituents are known as a promising alternative for wound healing agents due to the presence of diverse active components, ease of access and minimal side effects.

KEYWORDS: Polyherbalisam, Anti-inflammatory, Topical drug delivery.

INTRODUCTION

Medicinal plants have been identified and used throughout human history. Plants have the ability to synthesize a wide variety of chemical compounds that are used to perform important biological functions. The use of plants is as old as mankind and in the coming years, the market will see many new products containing natural oils and herbs. Plants were once the main source and foundation of all cosmetics, before methods were discovered of synthesizing substances with similar properties. Natural molecules derived from plant extracts offer a particularly exciting avenue for further research.^[4]

Plants generally have varied chemical compositions depending upon species. A good number of plants are known to be of economic and medicinal value. Those that are of medicinal value are often used as herbal remedy for the restoration and maintenance of good health. Some herbs have been considered as drugs and therefore generally safe and effective.^[5]

Ever since the birth of mankind of there has been a relationship between life, disease and plants. There is no record that people in prehistoric times used synthetic medicines for their ailments but they tried to make use of the things they could easily procure. The most common

thing they could find was there in environment i.e. the plants and animals. World Health Organization (WHO) has defined herbal medicines are finished, labeled medicinal products that contain active ingredients, aerial or underground parts of the plants or other plant material or combination.^[6]

In India, medicines based on herbal origin have been the basis of treatment and cure for various diseases. Moreover, Indian folk medicine comprises numerous prescriptions for therapeutic purposes such as healing of wounds, inflammation, skin infections, leprosy, diarrhea, scabies, venereal disease, ulcers, snake bite, etc.^[7]

According to Ayurveda, individual herbs are insufficient to achieve a desired therapeutic effect. When it is optimized as multiple herbs composition in a particular ratio it will give a therapeutic effect in a better way with reduced toxicity. Several plant extracts and their phytoconstituents are known as a promising alternative for wound healing agents due to the presence of diverse active components, ease of access and minimal side effects.^[3]

The active phytoconstituents of individual plants have been identified but are generally present in a small

quantities, which is insufficient to produce the desired therapeutic action. Polyherbalism results in cheaper medication by reducing the duration of therapy or individual cost for anti-inflammatory and antimicrobial medications. The incidences of new and relapsing infectious disease and antibiotic resistance has greatly increased the susceptibility of delayed healing. The selected herbs for this study aimed pharmacological targets involved in the wound healing like suppression of the production of inflammatory cytokines and inflammatory transduction cascades, reduction of oxidative factors, enhancement of anti-oxidative enzymes and prevention of the microbial growth at wound site. The development of formulation having anti-inflammatory properties is the need of present times.^[3]

Medicinal plants are source of drugs from many centuries and used extensively as crude materials or as pure compounds for treating various diseases. The chemical diversity of natural products is complementary to the diversity found in synthetic libraries. However, natural products are more complex and have greater ring system diversity because of the long evolutionary selection process. Therefore strategies to exploit natural sources and to develop methodologies for preparation of natural product libraries by combinatorial biosynthesis and related techniques are possible. Mainstream medicine is increasingly receptive to use than plants derived drugs, as current day therapeutic agents are becoming ineffective possibly due to indiscriminate use.^[8]

Inflammation

Inflammation is a complex process, which is frequently associated with pain and involves occurrences such as the increase of vascular permeability, increase of protein denaturation and membrane alteration. When cells in the body are damaged by microbes, physical agents or chemical agents, the injury is in the form of stress. Inflammation of tissue is due to response to stress. It is defensive response that is characterized by redness, pain, heat, and swelling and loss of function in the injured area. Inflammation is one of the body's nonspecific internal systems of defense, the response of a tissue to an accidental cut is similar to response that results from other type of tissue damage, caused by burns due to heat, radiation, bacterial or viral invasion. Inflammation dilutes, destroys, or walls off harmful agents that have entered the body. It activates a sequence of biological events to heal the damage. The most common causes of inflammation are infections, burns and trauma, and many types of immune reactions.^[6]

Classification of inflammation

Inflammation may broadly classify into three categories;

1. Acute inflammation
2. Chronic inflammation
3. Miscellaneous

Lysosomal enzymes released during inflammation produce a variety of disorders which leads to the tissue

injury by damaging the macromolecules and lipid peroxidation of membranes which are assumed to be responsible for certain pathological conditions as heart attacks, septic shocks and rheumatoid arthritis etc. Stabilization of lysosomal membrane is important in limiting the inflammatory response by inhibiting the release of lysosomal constituents of activated neutrophil such as bactericidal enzymes and proteases, which cause further tissue inflammation and damage upon extra cellular release or by stabilizing the lysosomal membrane.^[9]

It is also a defensive attempt by the organism to eradicate the injurious stimuli and initiate the healing process. The cells will undergo activation and release inflammatory mediators at the onset of the inflammation. The inflammatory process involves the release of pro inflammatory cytokines, prostaglandins, and the formation of reactive oxygen species. However, excessive of these inflammatory mediators lead to maintain inflammation and induce a chronic inflammation. Nonsteroidal anti-inflammatory drugs used as an effort to treat inflammation. Nevertheless, the long-term use of this drug will expose consumer or patient to many side effects including gastrointestinal erosion, peptic ulcers, nephrotoxicity, leukopenia, and allergic manifestations.^[10]

In spite of our dependence on local medicine and the tremendous advances in synthetic drugs, a large number of the world populations cannot afford the products of the western pharmaceutical industry and have to rely upon the use of traditional medicines, which are mainly derived from plant material. The main action of anti inflammatory agents is the inhibition of cyclooxygenase enzymes which are responsible for the conversion of arachidonic acid to prostaglandins.^[11]

Nonsteroidal anti-inflammatory drugs (NSAIDs) are the most commonly used drugs to treat pain and inflammatory conditions. These drugs are used dermal or systemically in treatment of various rheumatic diseases, including Rheumatoid arthritis (RA), as well as for Osteoarthritis, low back pain and some joint diseases. Diclofenac sodium is a well tolerated NSAID and topical formulation has excellent permeation and absorption into the skin and is frequently prescribed for the long term treatment of Rheumatoid arthritis, Osteoarthritis and Ankylosing spondylitis.^[14] But they have common side effects like ulcer, bleeding, and renal disorders. Therefore, medicinal plants are the common source of therapeutically active chemical substances with lesser side effects.^[12]

In the last few decades there has been an exponential growth in the field of herbal medicine. It is getting popularized in developing and developed countries owing to its natural origin and lesser side effects. The scientific evidence has brought about the possibility of utilization of herbal plant in the treatment of

inflammatory diseases and the development of anti-inflammatory products.^[13]

Although inflammation helps clear infection, and along with repair, makes wound healing possible, both inflammation and repair have considerable potential to cause harm. Chronic inflammation can result from various inflammatory agents such as virus, bacteria or antigens that stimulate the activation of inflammatory cytokines. Chronic inflammation processes increase oxidative and nitrosative stress and lipid peroxidation by inducing oxidant-generating enzymes such as NADPH oxidase, inducible nitric oxide synthase (iNOS) thereby producing excess of diverse reactive oxygen and nitrogen species (ROS and RNS). ROS, RNS and lipid peroxidation products (LPO) are able to cause damage to cell, protein, mRNA, DNA and lipid in both nucleus and mitochondria. Lipid peroxides (LPO) such as malondialdehyde (MDA), for example, form adducts with DNA bases. This then leads to alterations in the expressions of signaling molecules, and the functions of enzymes and proteins involved in inflammation such as cyclooxygenase-2 (COX-2) and iNOS. Chronic inflammation is abnormal and the excessive ROS, RNS and LPO produced, facilitate carcinogenesis and other chronic diseases. When using edema as an evaluation parameter, it is possible to analyze the anti-inflammatory potential of synthetic compounds, plant extracts and natural products, both topically and systemically. Nowadays, the drugs used for the skin inflammation treatment are corticosteroids and nonsteroidal anti-inflammatory drugs (NSAIDs). However, the routine treatment of inflammatory disease with these agents over long periods of time leads to adverse effects, including pruritus, irritations, skin dryness, folliculitis,

hypertrichosis, hypopigmentation, allergic contact dermatitis, skin maceration, stretch marks and miliary. The adverse effects justify the search for new healings from medicinal plants, that usually present less toxic effects. There are abundant medicinal plants with numerous biological functions in nature. Since 2002, the World Health Organization (WHO) has recognized the importance of the traditional medicine as apart of healthcare. Traditional medicine has a long history of use in health maintenance and in disease prevention and treatment.

Topical drug delivery system

The goal of any drug delivery system is to provide a therapeutic amount of drug to the proper site in the body to promptly achieve and then maintain the desired drug concentrations. The route of administration has a significant impact on the therapeutic outcome of a drug. Skin is one of the most readily accessible organs on human body for topical administration and is main route of topical drug delivery system. Topical delivery can be defined as the application of a drug containing formulation to the skin to directly treat cutaneous disorders (e.g. acne) or the cutaneous manifestations of a general disease (e.g. psoriasis) with the intent of containing the pharmacological or other effect of the drug to the surface of the skin or within the skin. Semi-solid formulation in all their diversity dominate the system for topical delivery, but foams, spray, medicated powders, solutions, as well as medicated adhesive systems are also in use. External topical that are spread, sprayed, or otherwise dispersed on to cutaneous tissues to cover the affected area. Internal topical that are applied to the mucous membrane orally, vaginally or onanorectal tissues for local activity.

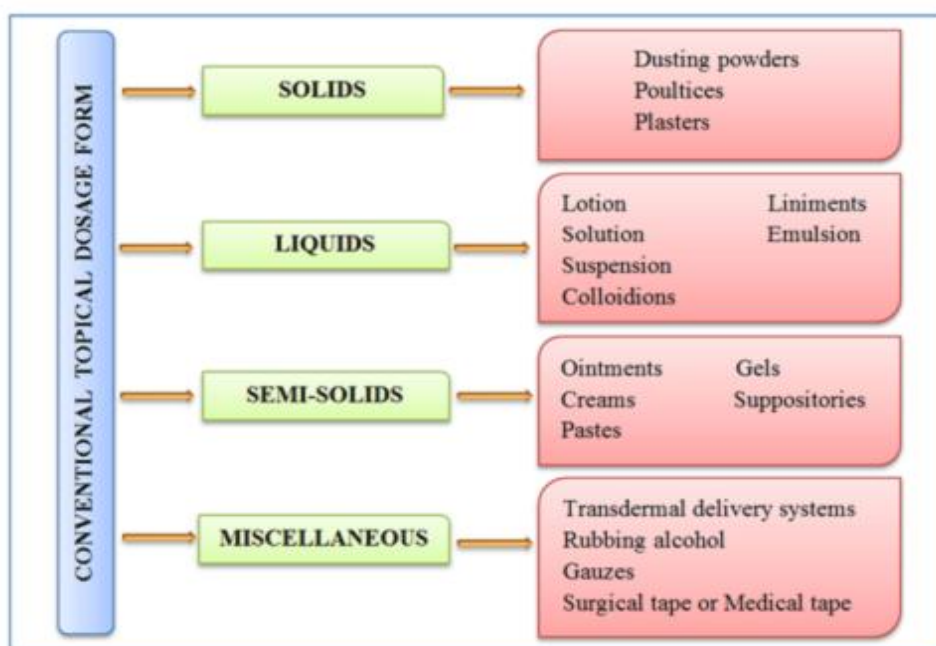


Fig. 1: Classification of conventional topical dosage form.

Advantages of topical drug delivery system

- Avoidance of first pass metabolism.
- Convenient and easy to apply.
- Avoidance of the risks and inconveniences of intravenous therapy and of the varied conditions of absorption, like pH changes, presence of enzymes,
- Achievement of efficacy with lower total daily dosage of drug by continuous drug input.
- Avoids fluctuation in drug levels, inter- and inpatient variations.
- Ability to easily terminate the medications, when needed.
- A relatively large area of application in comparison with buccal or nasal cavity
- Ability to deliver drug more selectively to a specific site.
- Providing utilization of drugs with short biological half-life,
- Improving physiological and pharmacological response.
- Improve patient compliance.
- Provide suitability for self-medication.

Disadvantages of topical drug delivery system

- Skin irritation of contact dermatitis may occur due to the drug and/or excipients.
- Poor permeability of some drugs through the skin.
- Possibility of allergenic reactions.
- Can be used only for drugs which require very small plasma concentration for action
- Enzyme in epidermis may denature the drugs
- Drugs of larger particle size not easy to absorb through the skin.^[6]

Topical drug delivery is an interesting approach to treat skin diseases and to avoid pain and low patient compliance in cases where a systemic delivery is required. However, the stratum corneum, which is the outermost skin layer, strongly protects the body from the entrance of substances, especially those hydrophilic. In this context, different physical methods have been studied to overcome the stratum corneum barrier and facilitate penetration of drugs into or through the skin. Among them, iontophoresis, low-frequency ultrasound and microneedles have been widely employed for transdermal drug delivery. More recently, they are also studied to aid in the treatment of dermatological disorders, such as skin tumors and inflammation. Basically, iontophoresis refers to the movement of charged and non-charged hydrophilic molecules through the skin due to the application of a low constant electric current and the contributions of electro migration and electro osmosis. In low-frequency ultrasound, cavitation is the main mechanism for skin permeabilization that consists on the formation of microbubbles that disorganize the stratum corneum. Microneedles are microprojections, minimally invasive, that can be designed with different lengths, materials and geometry to increase skin permeability. In this review, concepts, mechanisms and applications of these three physical methods will be presented and discussed with focus on their use in dermatological treatments. Moreover, comparative studies using different physical methods will be presented and also some clinical perspectives will be addressed.

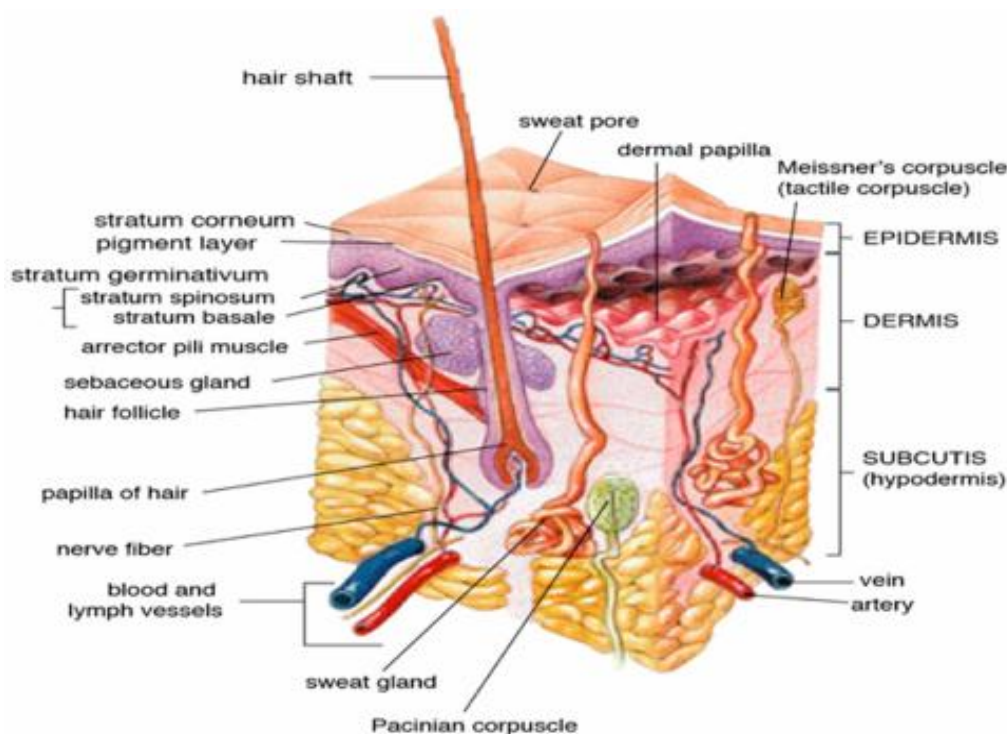


Fig. 2: Structure of human skin.

Mechanism of action

Transepidermal absorption

It is now generally believed that the transepidermal pathway is principally responsible for diffusion across the skin. The resistance encountered along this pathway arises in the stratum corneum. Permeation by the transepidermal route first involves partitioning into the stratum corneum. Diffusion then takes place across this tissue. The current popular belief is that most substances diffuse across the stratum corneum via the intercellular lipid route. This is a tortuous pathway of limited fractional volume and even more limited productive fractional area in the plane of diffusion. However, there appears to be another microscopic path through the stratum corneum for extremely polar compounds and ions. Otherwise, these would not permeate at rates that are measurable considering their o/w distributing tendencies. When a permeating drug exits at the stratum corneum, it enters the wet cell mass of the epidermis and since the epidermis has no direct blood supply, drug is forced to diffuse across it to reach the vasculature immediately space for ions and polar non electrolyte molecules to diffusionally squeeze through. Thus, permeation requires frequent crossings of cell membranes, each crossing being a thermodynamically prohibitive event for such water-soluble species extremely lipophilic molecules on the other hand, are thermodynamically constrained from dissolving in the watery regime of the cell (cytoplasm). Thus the viable tissue is rate determining when non polar compounds are involved. Passage through the dermal region represents a final hurdle to systemic entry. This is so regardless of whether permeation is transepidermal or by a shunt route. Permeation through the dermis is through the interlocking channels of the ground substance. Diffusion through the dermis is facile and without molecules since gaps between the collagen fibers are far too wide to filter large molecules. Since the viable epidermis and dermis lack measure physicochemical distinction, they are generally considered as a single shield of diffusion, except when penetrates of extreme polarity are involved, as the epidermis offers measurable resistance to such species.

Transfollicular (Shunt pathway) absorption

The skin's appendages offer only secondary avenues for permeation. Sebaceous and eccrine glands are the only appendages, which are seriously considered as shunts by passing the stratum corneum since these are distributed over the entire body, though eccrine glands are numerous, their orifices are tiny and add up to a minuscule fraction of the body's surface. Moreover, they are either vacuolated or so profusely active that molecule cannot diffuse inwardly against the glands output. For these reasons, they are not considered as a serious route for percutaneous absorption.

However, the follicular route remains an important avenue for percutaneous absorption since the opening of the follicular pore, where the hair shaft exists the skin, is

relatively large and sebum aids in diffusion of penetrates. Partitioning into sebum, followed by diffusion through the sebum to the depths of the epidermis is the envisioned mechanism of permeation by this route. Vasculature subserving the hair follicle located in the dermis is the likely point of systemic entry. Absorption across a membrane, the current or flux is and the terms of matter or molecules rather than electrons, and the driving force is a concentration gradient (technically, a chemical potential gradient) rather than a voltage drop. A membrane acts as a "diffusion resistor". Resistance is proportional to thickness (h), inversely proportional to the diffusive mobility of matter within the membrane or to the diffusion coefficient (D), inversely proportional to the fractional area of route where there is more than one (F), and inversely proportional to the carrying capacity of a phase.

Factor affecting topical permeation

Physicochemical properties of drug substances

- Partition coefficient
- pH-condition
- Drug solubility
- Concentration
- Particle size
- Polymorphism
- Molecular weight

Penetration enhancer

Percutaneous absorption can be enhanced in two ways either by chemical enhancer or by physical method.

Chemical penetration enhancer

By definition, a chemical skin penetration enhancer increases skin permeability by reversibly damaging or by altering the physicochemical nature of the stratum corneum to reduce its diffusion resistance. Among the alterations are increased hydration of stratum corneum and / or a change in the structure of the lipids and lipoproteins in the intercellular channels through solvent action or denaturation.

Solvents

These compounds increase penetration possibly by swelling the polar pathway and/or by fluidizing lipids. Examples include water, alcohols, methanol and ethanol; alkyl methyl sulfoxide, dimethyl sulfoxide, alkyl homologs of methyl sulfoxide, dimethyl acetamide and dimethyl formamide; pyrrolidones-2-pyrrolidone, N-methyl, 2-pyrrolidone; laurocapram (Azone), miscellaneous solvents- propylene glycol, glycerol, silicone fluids, isopropyl palmitate.

Surfactant

These compounds are proposed to enhance polar pathway transport, especially of hydrophilic drug. The ability of the surfactant to alter penetration is a function of polar head group and the hydrocarbon chain length. Commonly used surfactants are as follow,

- **Anionic surfactant:** It can penetrant and interact strong with skin. Examples include are Dioctyl sulphosuccinate, Sodium lauryl sulphate, Decodecyl methyl sulphoxide etc.
- **Cationic surfactant:** Cationic surfactants are reportedly more irritating than anionic surfactants and they have not been widely studied as skin permeation enhancer.
- **Nonionic surfactant:** Nonionic surfactants have last potential for irritation. Example includes are Pluronic F127, Pluronic F68 etc.
- **Bile salts:** Sodium taurocholate, Sodium deoxycholate, and Sodium tauroglycocholate.
- **Binary system:** These apparently open the heterogeneous multi laminated pathway as well as the continuous pathways. Examples include are Propylene glycol-oleic acid and 1,4-butanediol-linoleic acid.
- **Miscellaneous chemicals:** These includes urea, N,N-dimethyl-mtoluamide, calcium thioglycolate etc.^[14]

Creams

Creams are the topical preparations which can be applied on the skin. 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.¹ 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 disorders². 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)

Classification of creams

All the skin creams can be classified on different basis:

1. According to function, e.g. cleansing, foundation, massage, etc.
2. According to characteristics properties, e.g. cold creams, vanishing creams, etc.
3. According to the nature or type of emulsion.

Types of creams according to function, characteristic properties and type of emulsion:

1. Make-up cream (o/w emulsion):
 - a) Vanishing creams.
 - b) Foundation creams.
2. Cleansing cream, Cleansing milk, Cleansing lotion (w/o emulsion)
3. Winter cream (w/o emulsion):
 - a) Cold cream or moisturizing creams.
 4. All-purpose cream and general creams.
 5. Night cream and massage creams.
 6. Skin protective cream.
 7. Hand and body creams.

Advantages and Disadvantages of creams as a drug delivery system

Advantages of topical drug delivery system:

- It is the easiest way to deliver a drug.
- It avoids first pass metabolism.
- Topical formulation is very useful for delivery of rectal, vaginal drug delivery.
- It is non-invasive.
- It gives a high level of patient satisfaction.
- Easily medicaments can be terminated when required.
- Avoidance of gastro-intestinal incompatibility.
- It is safe and effective delivery of drug molecules with lower doses as compared to conventional system.

Disadvantages of topical drug delivery system

- Skin irritation or dermatitis may occur due to the drug or excipients.
- Most drugs have a high molecular weight and are poorly lipid soluble, so are not absorbed via skin or mucous membranes.
- Very slow absorption.
- It can be used only for those drugs which need very small plasma concentration for action.^[1]

General method of preparation of creams

Preparation of o/w emulsion cream

The oil soluble components and the emulsifier are taken in one beaker and melted in a water bath at 75°C. And in another beaker water, preservatives and water-soluble components are taken and melted at 75°C. After heating, the oil phase was taken in a mortar and pestle and slowly the water phase was added and triturated till clicking sound was heard. Finally, when the temperature cools down, perfuming agents and/or preservatives are added. In this preparation, water content will be more than the oil.

Preparation of w/o emulsion creams

The oil soluble components and the emulsifier are taken in one beaker and melted at 75°C. And in another beaker water and water-soluble components are taken and melted at 75°C. After melting, water phase are taken in mortar and pestle and slowly oil phase was added and

trituated till clicking sound was heard. And when the temperature of the cream will get cooled, then the perfuming agents are added. In this preparation, water phase will be less and oil phase will be more.^[16]

Creams are semisolid formulations widely acceptable by the society. The formulations should be subjected to stability study as per I.P. guidelines for the period of minimum one month. Creams are meant for wider applications in the skin like beautification, regeneration, treatment and maintenance. The use and type of cream depends on the need of person. Now a days herbal creams are more acceptable as compared to synthetic marketed products. In future, herbal based creams will acquire the entire market.^[1]

Polyherbal formulation

The active phytoconstituents of individual plants have been identified but are generally present in a small quantities, which is insufficient to produce the desired therapeutic action. Polyherbalism results in cheaper medication by reducing the duration of therapy or individual cost for anti-inflammatory and antimicrobial medications. The incidences of new and relapsing infectious disease and antibiotic resistance has greatly

increased the susceptibility of delayed healing. The selected herbs for this study aimed pharmacological targets involved in the wound healing like suppression of the production of inflammatory cytokines and inflammatory transduction cascades, reduction of oxidative factors, enhancement of anti-oxidative enzymes and prevention of the microbial growth at wound site.^[3]

Key traditional therapeutic herbal strategy exploits the combination of several medicinal herbs

To achieve extra therapeutic effectiveness. This is known as polyherbalism. Polyherbal formulations are mixture of herbs, prepared in a number of formulations such as decoctions, elixirs, infusions, creams, gels, ointments and paste etc, in order to achieve maximum therapeutic efficacy. Polyherbal formulations have plant-based pharmacological agents which may exert synergistic, potentiate, agonistic or antagonistic actions by virtue of its diverse active principles within themselves. These pharmacological principles work together in a dynamic way to produce maximum therapeutic efficacy with minimum side effects.^[15]

Table 1: Applications of polyherbal creams with Anti-inflammatory activity.

Formulation	Jurnal and year of publication	Advantages	Outcome of the study
<i>Cardiospermum halicacabum</i> , <i>Vitex negundo</i>	Brazilian Journal of Pharmaceutical Sciences - 2016	It has long residence time on the skin, high viscosity, moisturizing effect on flaky skin due to their occlusive properties, more bio adhesiveness, less irritation, independent of water solubility of active ingredient, ease of application and better release characters.	Anti-arthritis activity of the developed topical herbal cream formulation may be due to the presence of luteolin and apigenin in methanol leaf extracts of <i>Cardiospermum halicacabum</i> and <i>Vitex negundo</i>
<i>Plumbago zeylanica</i> Linn, <i>Datura stramonium</i> Linn and <i>Argemone mexicana</i> Linn	Biomedicine & Pharmacotherapy-2019	The antimicrobial and anti-inflammatory effect of Polyherbal drug provoked and promoted the wound healing process through accelerated remodelling of damaged tissue.	The antioxidant, anti-inflammatory and antimicrobial activities of polyherbal composition might be among the contributing factors that showed remarkable improvement in collagen synthesis, wound contraction, WBS and reduced microbial load that could be involved in the enhancement of wound healing process.
<i>Kalanchoe brasiliensis</i> and <i>Kalanchoe pinnata</i>	Biomedicine & Pharmacotherapy -2019	Showed a better result in both edematogenic models since it had activity in the lowest concentration.	Treatments with K. brasiliensis and K. pinnata leaf aqueous extracts incorporated in a topical administration formulation can decrease the local inflammatory

<i>Aloe vera</i> , <i>Brassica oleracea</i> , <i>Curcuma longa</i> , <i>Daucus carota</i> , <i>Emblica officinalis</i> , <i>Glycyrrhiza glabra</i> , <i>Solanum lycopersicum</i>	Internationale Pharmaceutica Scientia - 2013	These formulations are safe to use for skin.	process improve as well synergize the cosmetic properties of prepared products compare to individual extracts.
<i>zadirachta indica</i> and <i>Curcuma longa</i>	Journal of Scientific and Innovative Research- 2016	This cream could become a media to use these medicinal properties effectively and easily as a simple dosage form.	Neem and Turmeric is used for their various medicinal properties like antibacterial, antifungal, anti-inflammatory etc.

CONCLUSION

Topical drug delivery system is to provide a therapeutic amount of drug to the proper site in the body to promptly achieve and then maintain the desired drug concentrations. The better activity of polyherbal formulation may be due to the synergistic action of the plants constituents present in the formulation. Thus, the prepared topical cream possess good therapeutic action.

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