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# TO DESIGN AND FORMULATE HERBAL BASED TOPICAL DRUG DELIVERY SYSTEM

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## ABSTRACT

Over a decade microbial infections of the skin are increasing day by day tremendously. There are a lot treatments for this till now and scientist are working to find out the new treatments. One of these infections is fungal infection of the skin, which generally cause the itching of the skin due to the growth of the fungus. There may be many causes of the fungal infection previously there are many treatments for the fungal infection like clotrimzole, fluconazole, itraconazole, sertaconazole but these are having some side effects so we are working to find out the treatment for the fungal infections from the herbal drugs like coconut oil neem and crcumin extract. These show synergistic action for the treatment of various microbial infections with the lesser side effects.comparitive studies are being done to check whether they show better therapeutic effect or not. Various methods been adopted for the formulation of the ointments like fusion method and emulsification method. Emulsified ointments are the type of ointments which are having better wash ability. Evaluation of the ointment is being done by evaluating various physicochemical and chemical evaluation.

**KEYWORDS:** tremendously, emulsified, synergistic.

## INTRODUCTION

A **topical medication** is a medication that is applied to a particular place on or in the body, as opposed to systemically. Most often this means application to body surfaces such as the skin or mucous membranes to treat ailments via a large range of classes including creams, foams, gels, lotions, and ointments topical effect, in the pharmacodynamic sense, may refer to a local, rather than systemic, target for a medication.

However, many topically administered drugs have systemic effects, because they reach the circulation after being absorbed by the tissues.

Topical medications differ from many other types of drugs because mishandling them can lead to certain complications in a patient or administrator of the drug. With topical therapies, the formulation is as important as the molecule itself because the interaction of the vehicle with the skin can alter the efficacy of the penetrant. The formulation ensures that the drug substance is delivered to the right target site and that it maintains dosage integrity, drug transport, and active duration. The skin is one of the most extensive and readily accessible organs of the human body. The skin of an average adult body covers a surface area of approximately two square meters and receives about one third of the blood circulating through the body. With a thickness of only a few millimeters (2.97 ± 0.28mm), skin separates the underlying blood circulation network from the outside environment and serves as a barrier against physical and chemical attacks.

A medication's potency often is changed with its base. For example, some topical steroids will be classified one or two strengths higher when moving from cream to ointment. As a rule of thumb, an ointment base is more occlusive and will drive the medication into the skin more rapidly than a solution or cream base.

The manufacturer of each topical product has total control over the content of the base of a medication. Although containing the same active ingredients, one manufacturer's cream might be more acidic than the next, which could cause skin irritation or change its absorption rate. For example, a vaginal formulation of miconazole antifungal cream might irritate the skin less than an athlete foot formulation of miconazole cream. These variations can, on occasion, result in different clinical outcomes, even though the active ingredient is the same. No comparative potency labeling exists to ensure equal efficacy between brands of topical steroids (percentage of oil vs water dramatically affect the potency of topical steroid). Studies have confirmed that the potency of some topical steroid products may differ according to manufacturer or brand.

In dermatology, the base of a topical medication is often as important as the medication itself. It is extremely important to receive a medication in the correct base, before applying to the skin. A pharmacist should not substitute an ointment for a cream, or vice versa, as the potency of the medication can change. Some physicians use a thick ointment to replace the

waterproof barrier of the inflamed skin in the treatment of eczema, and a cream might not accomplish the same clinical intention. With topical therapies, the formulation is as important as the molecule itself because the interaction of the vehicle with the skin can alter the efficacy of the penetrant. The formulation ensures that the drug substance is delivered to the right target site and that it maintains dosage integrity, drug transport, and active duration.

For example, the drug substance in a psoriasis treatment may have some efficacy simply from the hydrating or soothing effects of the formulation. Whether the molecule maintains purity, potency, and delivery to the right target site may be masked by the ingredients that surround it. Both the mechanical barrier properties of the top layer of skin, stratum corneum, and the physicochemical properties of the drug affect the transportation of the drug substance from formulation vehicle to the site of action.

Skin provides an ideal site for the delivery of drug substances for both local and systemic effects. However, it also acts as a mechanical barrier to the penetration of many drug substances.

**Fungal Infection:** There are various types of microbes, can be divided into six main types: Archae, Bacteria, Fungi, Protista, Viruses and Microbial Mergers. The present invention is directed to dermatological compositions for killing or inhibiting the growth a variety of fungal pathogens known to cause a number of infectious diseases in humans. From this the area of interest will be to formulate the Novel Topical antifungal formulation. Fungal disease is ubiquitous in the world and antifungal medication account for sales of more than US$ 1 billion annually. Most fungal disorder is relatively benign but can become life threatening in immunocompromised or malnourished population. The mainstay of management of fungal infection and dermatophytes associated with skin and nail injuries has been oral and topical antifungal. The delivery of drugs through most commonly used conventional preparations viz. creams, gels, lotions, emulsion, etc. limits the effectiveness of actives due to barrier properties i.e. epidermis of the skin which hinder the drug deposition. Thus selection of proper carrier's extremely important by considering the view in the mind that they should increase drug deposition through topical formulations. [Papps P et al., 2004].

**Fungal infections seen in human can be**

**a) Superficial fungal infections** of skin, hair, nail, mucous membrane. These are due to:

i) Dermatomycoses which causes ring worm or tinea infestation. These dermatophytes are Epidermophyton, Microsporum and Trichophyton, and are classified according to their site of

infestation e.g.; Tinea Capitis (Scalp infection), TInea corporis (body infection), Tinea barbae (infection in the beard), Tinea cruris (infection in groin), Tinea pedis (also called athlete's foot), TInea manum (infection in hands) and Tinea unguium (infection in the hairs).

ii) Candidiasis (or often referred to as thrush) or infection caused by Candida spp affects chiefly the skin, oropharynx and vagina. Seen commonly in immune compromised patients e.g., in patients of AIDS, or with HIV infections, following the use of AMA's over prolonged periods, and in patients of diabetes mellitus.

iii) Pityrosporoum orbiculare causing Ptyriasis versicolor or Tinea versicolor. This is characterized by hyperpigmented macules, which are distinct with fine scaling. Commonly seen on the face, proximal extremities and in the oropharynx. iv) Sporothrix infection of cutaneous region seen as granulomatous lesion. These spread to distant region via the lymphatic system.

**b) Systemic fungal infection** affecting deeper tissues and organs. These include the respiratory tract infection with candidiasis, cryptococcal meningitis and endocarditis, histoplasmosis infection common in the respiratory tract, coccidiomycosis, paracoccidiomycosis, pneumocystis carinii pneumonia all affecting the respiratory system. There has been an increase in the incidence of fungal infection during the past few decades.

**This increase may be attributed to**

**1)** An excessive or irrational use of AMA, which alter the pattern of the commensals in the body, leading to super-infection with the fungal infections, some of which are normally present as commensals.

**2)** A decrease in host defense mechanism as seen in patients of AIDS or patients on cancer chemotherapy, leading to iatrogenic fungal infections.

**3)** An increase in the use of immunosuppresent drugs also causes iatrogenic fungal infections.

**The antifungal agents include**

**1. Antibiotics like a)** polyenes, Amphotericin B, Nystatin, Hamycin, Natamycin and b) Heterocyclic Benzofurans like Griseofulvin

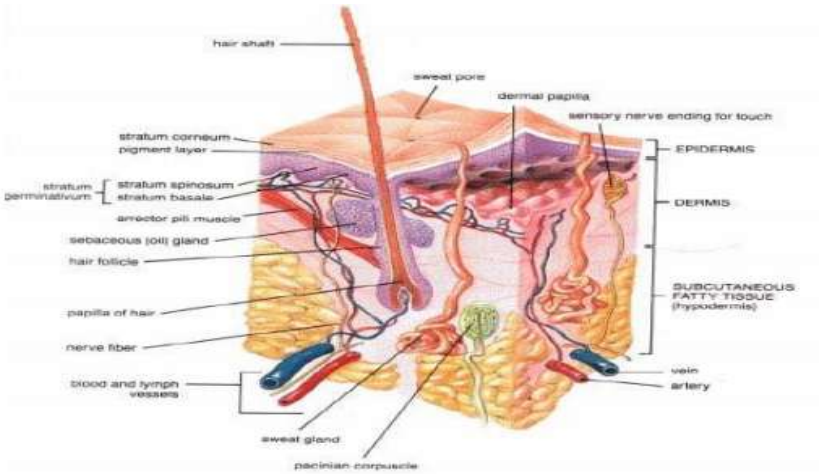
**2. Antimetabolites:** flucytosine

**3. Azoles:** Imidazoles, Clotrimazole, Miconazole, Econazole, Ketoconazole, Triazoles, Fluconazole iatraconazole.

**4. Topical agents:** Tolnaftate, Benzoic acid, undecyclenic acid, Quiniodochlor, Buclosamide, Haloprogin, Cyclopiroxolamine, Sodium thiosulphate.

**Anatomy of skin:** The skin is multilayered organ composed of many histological layers. It is generally described in terms of three tissue layers (Figure 1). Skin is an anatomical barrier between the body and its environment and contributes to 16-18 % of normal body weight.

**i. Epidermis**




Epidermis, the outermost skin layer comprises of stratified squamous epithelial cells. The epithelial cells are held together mainly by highly convoluted interlocking bridges, which are responsible for the unique integrity of the skin. Microscopic sections of the epidermis show two main parts: the stratum corneum and the stratum germinativum. The stratum corneum forms the outermost layer of the epidermis and consists of many layers of compacted flattened, dehydrated, keratinized cells in stratified layer. These cells loose their nuclei and are physiologically rather inactive. They are formed and continuously replenished by the slow upward migration of cells produced by basal cell layer of the stratum germinativum, which is regenerative layer of the epidermis. In the thicker part of the skin, the transition from the living cells of the germinativum to the zone of the dead, cornified cells of the stratum corneum is made prominent by three layers: the stratum spinosum (prickly layer), stratum granulosum (granular layer) and stratum lucidum (clear layer) Stratum corneum, also called as horny layer which consists of compacted, dead, keratinized cells with a density of 1.55. Because of the dense nature of stratum corneum, values of diffusion coefficient in this tissue are very much smaller than any other skin tissue, which results in higher resistance and greater impenetrability. Hence, stratum corneum is responsible for the barrier function of the skin. It also behaves as the primary barrier to percutaneous absorption.

**ii. Dermis**: The dermis (or corneum) essentially consists of 80 % of protein in the matrix of mucopolysaccharides (ground substance). Protein including collagen and elastin fibres are oriented parallel to the epidermis. The dermis supports and interacts with the epidermis facilitating its conformation to the underlying muscles and bones. Blood vessels, lymphatic, nerves as well as the epidermal appendages such as the hair follicles, sebaceous glands and sweat glands are mainly contained and supported within the dermis. Beneath the dermis, the fibrous tissue opens out and merges with the fat-containing subcutaneous tissue.

**iii. Subcutaneous fat layer Subcutaneous**

fat layer serves as a cushion for the dermis and epidermis. It also provides a thermal barrier. Collagenous fibres form the dermis thread between the superficial skin layer and subcutaneous layer. Combined, these layers form the skin which is pierced at various places by two types of potential diffusion shunts: hair follicles and sweat glands. These skin appendages however, actually occupy only 0.1 % of the human skin surface. This transappendageal route of percutaneous absorption, however, provides a very limited contribution to the transdermal permeation of most neutral molecules at a steady state

## ADVANTAGES OF TOPICAL DRUG DELIVERY SYSTEM

- Ability to deliver drug more selectively.
- Site specific.
- Avoiding fluctuations in drug levels.
- Inter and intra patient variations.

## MATERIALS AND METHODS

### MATERIALS

**1.NEEM**

**Family**: Meliaceae

**Botanical name**: Azadirachta Indica.

**Chemical composition of neem**

Neem tree has numerous medicinal properties by virtue of its chemical compounds. Seeds of the Neem tree contain the highest concentration of Azadirachtin. Apart from Azadirachtin, salannin, gedunin, azadirone, nimbin, nimbidine, nimbicidine, nimbinol, etc are other important liminoids.

**Medicinal properties of Neem:** The Neem tree has many medicinal uses. The chemical compounds present in neem have anti-inflammatory, antiarthritic, antipyretic, hypoglycaemic, Antifungal, spermicidal, antimalarial, antibacterial and Diuretic properties. Flower, leaves, bark and seeds of neem are used in home remedies and in preparation of medicines. Bark of neem acts as antipyretic and helps to reduce fever. Flowers are used in intestinal disorders. Juice from fresh leaves is very helpful in treating skin diseases, wounds and obesity. Oil from neem seeds is used in arthritis, skin diseases and muscular sprains. Neem is very effective in treating gum diseases.

The neem is proved to be beneficial in treating skin diseases because of its antibiotic, antifungal and blood purifying properties.

**2.CURCUMIN**

Curcumin is a bright yellow chemical produced by some plants. It is the principal curcuminoid of turmeric (Curcuma longa), a member of the ginger family (Zingiberaceae). It is sold as an herbal supplement, cosmetics ingredient, food flavoringand food coloring. As a food additive, its E number is E100.

It was isolated in 1815 when Vogel and Pelletier reported the isolation of a "yellow coloring-matter" from the rhizomes of turmeric and named it curcumin. Although curcumin has been used historically in Ayurvedic medicine, its potential medicinal properties remain unproven and are an area of active investigation.

Chemically, curcumin is a diarylheptanoid, belonging to the group of curcuminoids, which are natural phenols responsible for turmeric's' yellow color. It is a tautomeric compound existing in enolic form in organic solvents and as a keto form in water.

**3. COCONUT OIL**

**FAMILY-** Palmaceae

**PART USED-**Oil of the seed

**CHEMICAL CONSTITUENT**

It generally contains triglycerides. 95% saturated fatty acids. Caprylic acid 2% ,capric acid 50-80%, Lauric acid 3%, Myristic acid 1%.

**USES**

- Hydrate the skin
- Softening of skin.
- Psoriasis
- Antifungal
- Dry skin
- Acne
- Antioxidant

**METHODS**

**FUSION METHOD**

➢ Medicated ointments and ointment bases containing components such as BEESWAX, PARAFIN, STERYL ALCOHOL are prepared by fusion.

➢ Ointments containing ingredients which are quite solid at room temperature are prepared by melting ingredients in a porcelain dish over water bath.

➢ The usual method is to melt the substance with highest melting point first and then add ingredients in order of their melting points.

➢ Stirring should be continuous until ointment is homogenous and reaches to congealing point.

**EMULSIFICATION METHOD**

This method of preparation is generally used for preparation of emulsified systems such as emulsified ointments or creams. In this method the oil soluble and water soluble constituents are dissolved separately in the appropriate phases. A suitable emulsifying agent is selected for the type of emulsion is required, and this is also dissolved in either aqueous or oil phase. The two phases are then heated to an appropriate temperature and mixed together with continuous agitation until a homogenious emulsion is obtained.

**CONCLUSION**

By concluding current review it shows that new and alternative drug delivery systems are currently focusing in various research activities. The research is based on the concept that synergistic action of the antifungal activity of neem is expected to enhance by using oils like coconut oil, Tea tree oil. They generally act like fluid mosaic model which increase the pore size of the skin cells and enhance the penetration of the drug to the fungus**.** Emulsified ointment is the type of ointment which have better wash ability and better therapeutic effect

therefore emulsified ointment bases are selected for the formulation of ointment by emulsification method.

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