Formulation And Evaluation of Poly-Herbal Antifungal Cream

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***Abstract*—Now a days, fungal infections of skin are one of the most common dermatological problems in world Senghani MK wide. It has been investigated that 40 million people suffer from fungal infections. Fungal diseases are Veerayatan Institute of infections caused by a fungus, a type of microorganism. Most commonly used antifungal drugs such as Pharmacy, Jakhania, Bhuj- amphotericin B and other drugs like ketoconazole, fluconazole and clotrimazole are limited in their Mandvi Highway, Mandvi- spectrum and may produce strain resistances. Neem extract, Tulsi extract, Turmeric extract, Aloe vera Kutch, Gujarat, India extract are well known by its antifungal activity and its uses in skin diseases. The main aim of our research was to develop a novel cream formulation consisting of Neem extract, Tulsi extract, Turmeric extract, Aloe vera extract for the treatment of skin infections. Topical route is most suitable route for skin infections. A novel cream formulation was prepared.**

***Index Terms*—Herbal antifungal cream, fungal disease, herbs, herbal ingredient, skin infection**

I. INTRODUCTION

The body's exterior is covered by the cutaneous membrane, sometimes known as the skin. In terms of weight and surface area, it is the largest organ in the body. Adults' skin weighs 4.5-5 kg (10-11 lb), or roughly 16% of their total body weight, and covers an area of roughly 2 square meters (22 square feet). The thickness of it varies from 4.0 mm (0.16 in.) on the heels to 0.5 mm (0.02 in.) on the eyelids. However, it is 1-2 mm (0.04-0.08 in.) thick over the majority of the body. The skin is composed of two major structural components. The epidermis is the thinner, superficial layer made up of epithelial tissue. The dermis is the thicker, deeper portion of connective tissue.

The subcutaneous layer is located deep within the dermis but is not a part of the skin. This layer, which is made up of adipose and areolar tissues, is also known as the hypodermis. The skin is anchored to the subcutaneous layer by fibers that emerge from the dermis. The subcutaneous layer then connects to the tissues and organs beneath. Large blood arteries that nourish the skin are found in the subcutaneous layer, which also acts as a fat storage facility.

Additionally, this area (and occasionally the dermis) has pressure-sensitive nerve terminals known as lamellated (Pacinian) corpuscles.

1.1. Epidermis

The stratified squamous epithelium within the epidermis is keratinized. Melanocytes, Merkel cells, Langerhans cells, and keratinocytes are its four main cell types. Keratinocytes, consisting of four or five layers, make up approximately 90% of epidermal cells and are responsible for the production of the keratin protein. Protecting the skin and underlying tissues from heat, toxins, and bacteria is aided by fibrous protein. Additionally, lamellar granules-which secrete a water-repellent sealant-are produced by keratinocytes. Melanocytes, which make melanin, make up around 8% of the epidermal cells. The keratinocytes get melanin granules from their long, thin projections that stretch between them.

The brown-black pigment known as melanin absorbs harmful UV rays and adds to skin tone.

After entering keratinocytes, the melanin granules group together to cover the nucleus with a protective layer that faces the skin's surface. They prevent UV radiation from harming the nuclear DNA in this way. Melanocytes are especially vulnerable to UV radiation

damage, even if keratinocytes are somewhat shielded by melanin granules.

1.2. Structure of Skin

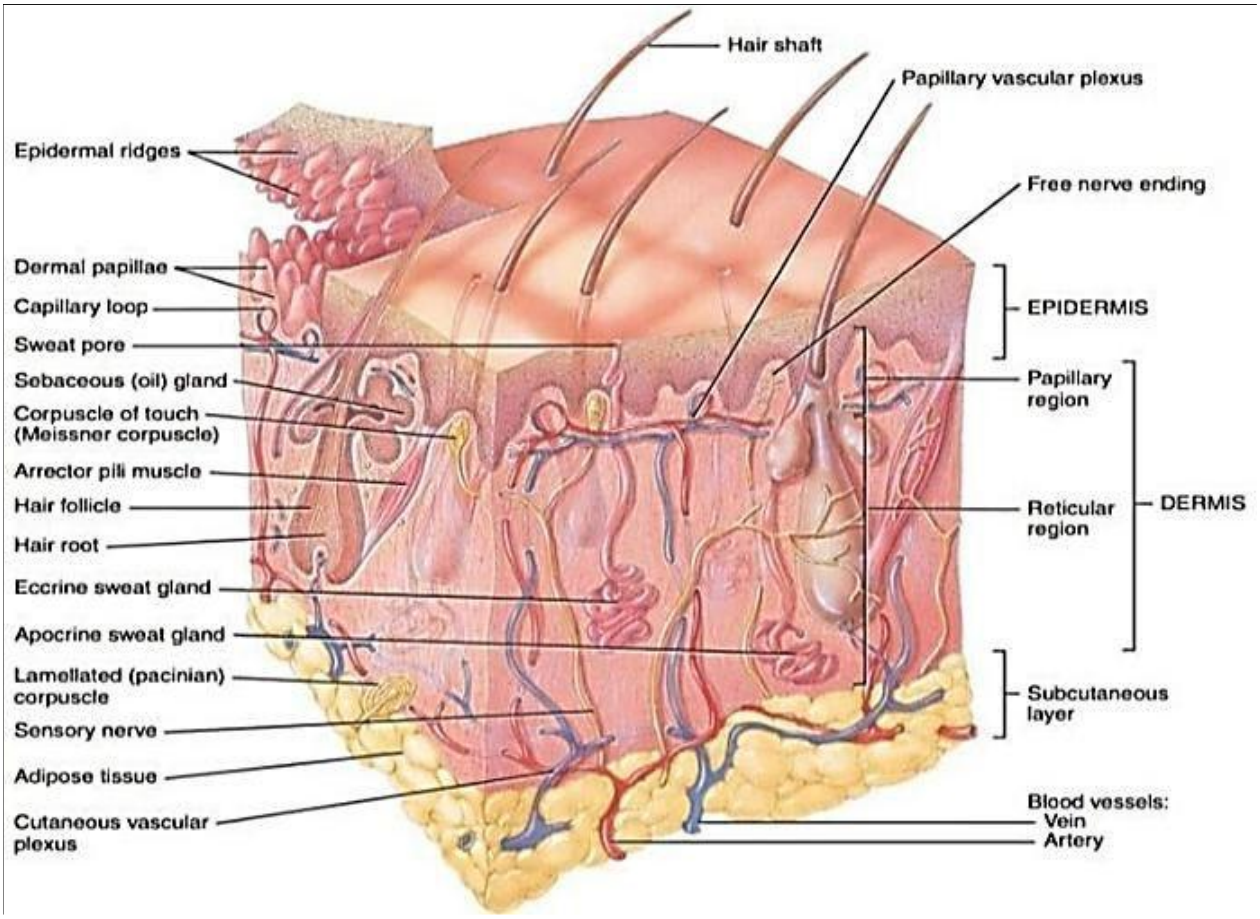


Fig 1.1: Structure of Skin

Red bone marrow gives rise to Langerhans cells, which go to the epidermis and make up a tiny portion of the epidermal cells there. They take part in immune responses aimed at combating skin-invading microorganisms that are susceptible to UV radiation damage.

Merkel cells are the least numerous of the epidermal cells. They are located in the deepest layer of the epidermis, where they contact the flattened process of a sensory neuron (nerve cell), a structure called a tactile (Merkel) disc. Merkel cells and tactile discs detect different aspects of touch sensations.

The epidermis is made up of several different layers of keratinocytes during different phases of development. The stratum basale, stratum spinosum, stratum granulosum, and a thin stratum corneum are the four layers or strata that make up the epidermis in the majority of body parts. The stratum basale, stratum spinosum, stratum granulosum, stratum lucidum, and a thick stratum corneum are the five layers of the epidermis that are exposed to the most friction, such as in the fingertips, palms, and soles.

1.2.1.Stratum Basale

The stratum basale, which is made up of a single row of cuboidal or columnar keratinocytes, is the deepest layer of the epidermis. This layer contains some stem cells, which divide to continuously create new keratinocytes. Keratinocytes in the stratum basale have big nuclei, and their cytoplasm is made up of a tiny Golgi complex, a few mitochondria, a rough endoplasmic reticulum, and several ribosomes.

Tonofilaments are sporadic intermediate filaments found in the cytoskeleton of stratum basale keratinocytes.

The protein that makes up the tonofilaments will eventually transform into keratin in the outermost layers of the epidermis. Tonofilaments adhere to hemidesmosomes, which bind keratinocytes to the basement membrane between the epidermis and the dermis, and to desmosomes, which tie stratuinbasale cells to one another and to the cells of the neighboring stratum spinosum. Deeper layers are also shielded from harm by keratin. The basal layer's keratinocytes are dotted with Merkel cells, Langerhans cells, and melanocytes, along with the tactile discs that go with them. Another name for the stratum basale that highlights its function in cell formation is the stratum germinativum.

1.2.2.Stratum Spinosum

Eight to ten layers of many-sided keratinocytes fit tightly together in the stratum spinosum, which is located superficially to the stratum basale. The cells in this layer's outermost regions flatten out a little. Some of the cells in the stratum basale may still be able to divide, and these keratinocytes share the same organelles as those cells. Despite being rounder and bigger in living tissue, stratum spinosum cells shrink and separate when prepared for microscopic inspection, giving the impression that they are coated in thorn-like spines. Bundles of tonofilaments insert into a desmosome at each spiny protrusion in a prepared tissue segment, firmly binding the cells together.

1.2.3.Stratum Granulosum

At the middle of the epidermis, the stratum granulosum consists of three to five layers of flattened keratinocytes that are undergoing apoptosis. The nuclei and other organelles of these cells begin to degenerate, and tonofilaments become more apparent. A distinctive feature of cells in this layer is the presence of darkly staining granules of a protein called keratohyalin, which converts the tonofilaments into keratin. Also present in the keratinocytes are membrane- enclosed lamellar granules, which release a lipid-rich secretion. This secretion fills the spaces between cells of the stratum granulosum, stratum lucidum, and stratum corneum. The lipid-rich secretion acts as a water-repellent sealant, retarding loss of body fluids and entry of foreign materials. As their nuclei break down during apoptosis, the keratinocytes of the stratum granulosum can no longer carry on vital metabolic reactions, and they die. Thus, the stratum granulosum marks the transition between the deeper, metabolically active strata and the dead cells of the more superficial strata.

1.2.4.Stratum Lucidum

The stratum lucidum is present only in the thick skin of the fingertips, palms, and soles. It consists of three to five layers of flattened clear, dead keratinocytes that contain large amounts of keratin and thickened plasma membranes.

1.2.5.Stratum Corneum

The stratum corneum consists of 25 to 30 layers of flattened dead keratinocytes. These cells are continuously shed and replaced by cells from the deeper strata. The interior of the cells contains mostly keratin. Between the cells are lipids from lamellar granules that help make this layer an effective water-repellent barrier. Its multiple layers of dead cells also help to protect deeper layers from injury and microbial invasion. Constant exposure of skin to friction stimulates the formation of a callus, an abnormal thickening of the stratum corneum.

1.3. Dermis

The second, deeper part of the skin, the dermis, is composed mainly of connective tissue containing collagen and elastic fibers. The few cells present in the dermis include fibroblasts, macrophages, and some adipocytes. Blood vessels, nerves, glands, and hair follicles are embedded in dermal tissue. Based on its tissue structure, the dermis can be divided into a papillary region and a reticular region. The papillary region is the superficial part of the dermis. About one-fifth of the thickness of the total layer. It consists of areolar connective tissue containing fine elastic fibers. Its surface area is greatly increased by small, fingerlike projections called dermal papillae. These nippleshaped structures indent the epidermis and some contain capillary loops. Other dermal papillae also contain tactile receptors called corpuscles of touch or Meissner corpuscles, nerve endings that are sensitive to touch. Also present in the dermal papillae are free nerve endings, dendrites that lack any apparent structural specialization. Different free nerve endings initiate

signals that give rise to sensations of warmth, coolness, pain, tickling, and itching. The deeper part of the dermis is called the reticular region. It consists of dense irregular connective tissue containing bundles of collagen and some coarse elastic fibers. The bundles of collagen fibers in the reticular region interlace in a netlike manner. A few adipose cells, hair follicles, nerves, sebaceous (oil) glands, and sudoriferous (sweat) glands occupy the spaces between fibers. The combination of collagen and elastic fibers in the reticular region provides the skin with strength, extensibility and elasticity. The extensibility of skin can readily be seen in pregnancy and obesity. Extreme stretching, however, may produce small tears in the dermis, causing striae or stretch marks that are visible as red or silvery white streaks on the skin surface.

The surfaces of the palms, fingers, soles, and toes have a series of ridges and grooves. They appear either as straight lines or as a pattern of loops and whorls, as on the tips of the digits. These epidermal ridges develop during the third and fourth fetal months as the epidermis conforms to the contours of the underlying dermal papillae of the papillary region. The ridges increase the surface area of the epidermis and thus increase the grip of the hand or foot by increasing friction. Because the ducts of sweat glands open on the tops of the epidermal ridges as sweat pores, the sweat and ridges form fingerprints upon touching a smooth object. The epidermal ridge pat tern is genetically determined and is unique for each individual. Normally, the ridge pattern does not change during life, except to enlarge, and thus can serve as the basis for identification through fingerprints or footprints. The study of the pattern of epidermal ridges is called dermatoglyphics [1].

1.3.1.Subcutaneous

The hypodermis is sometimes called the subcutaneous layer, or superficial fascia. It is not part of the skin, but lies deep to the dermis and thus forms a connection between the skin and the underlying structures of the body. Thus, the hypodermis is often discussed along with the skin because of the close structural and functional association of these two superficial body structures.

The hypodermis is mostly loose fibrous and adipose tissue. The fat content of the hypodermis varies with the state of nutrition and in obese individuals may exceed 10 cm in thickness in certain areas. The density and arrangement of fat cells and collagen fibers in this area determine the relative mobility of the skin. Bands of fibers running through the hypodermis help hold the skin to underlying structures such as deep fascia and muscles. When skin is removed from an animal by blunt dissection, separation occurs in the "cleavage plane" that exists between the superficial fascia and the underlying structures [2].

1.4. Type Of Skin

Although the skin over the entire body is similar in structure, there are quite a few local variations related to thickness of the epidermis, strength, flexibility, degree of keratinization, distribution and type of hair, density and types of glands, pigmentation, vascularity (blood supply) and innervation (nerve supply). Based on structural and functional properties, we recognize two major types of skin: thin (hairy) and thick (hairless).

1.4.1.Thin Skin:

Covers all parts of the body except for the palms, palmar surfaces of the digits and the soles. Its epidermis is thin, just 0.10-0.15 mm. A distinct stratum lucidum is lacking and the strataspinosum and corneum are relatively thin. Thin skin has lower, broader and fewer dermal papillae and thus lacks epidermal ridges. Additionally, even though thin skin has hair follicles, arrectorpili muscles and sebaceous (oil) glands, it has fewer sweat glands than thick skin. Finally, thin skin has a sparser distribution of sensory receptors than thick skin.

1.4.2.Thick Skin

Covers the palms, palmar surfaces of the fingers and soles. Its epidermis is relatively thick, 0.6-4.5 mm and features a distinct stratum lucidum as well as thicker strata spinosum and corneum. The dermal papillae of thick skin are higher, narrower and more numerous than those in thin skin and thus thick skin has epidermal ridges. Thick skin lacks hair follicles, arrectorpili muscles and sebaceous glands and has more sweat glands than thin skin.

Sensory receptors are more densely clustered in thick skin

[1].

1.5. Function of Skin

1.5.1.Protection:

The skin forms a relatively waterproof layer that protects the deeper and more delicate structures. As an important non-specific defence mechanism it acts as a barrier against: Invasion by microbes

- Chemicals
- Physical agents, e.g., mild trauma, ultraviolet light Dehydration.

The dermis contains specialised immune cells called Langerhans cells. They phagocytose intruding antigens and travel to lymphoid tissue, where they present antigen to Tlymphocytes, thus stimulating an immune response.

Due to the presence of the sensory nerve endings in the skin the body reacts by reflex action to unpleasant or painful stimuli, protecting it from further injury.

1.5.2.Regulation of body temperature:

The temperature of the body remains fairly constant at about 36.8 °C (98.4 °F) across a wide range of environmental temperatures. In health, variations are usually limited to between 0.5 and 0.75 °C, although it is raised slightly in the evening, during exercise and in women just after ovulation. When metabolic rate increases body temperature rises and when it decreases body temperature falls.

To ensure this constant temperature a balance is maintained between heat produced in the body and heat lost to the environment.

1.5.3.Heat production

- Some of the energy released in the cells during metabolic activity is in the form of heat and the most active organs, chemically and physically, produce the most heat. The principal organs involved are as follows.
- The muscles: Contraction of skeletal muscles produces a large amount of heat and the more strenuous the muscular exercise the greater the heat produced. Shivering involves muscle contraction and produces heat when there is the risk of the body temperature falling below normal.
- The liver: Is very chemically active, and heat is produced as a by-product. Metabolic rate and heat production are increased after eating.
- The digestive organs: Produce heat during peristalsis and by the chemical reactions involved in digestion.

1.5.4.Heat loss

Most of the heat loss from the body occurs through the skin. Small amounts are lost in expired air, urine and faeces.

Only the heat lost through the skin can be regulated to maintain a constant body temperature. There is no control over heat lost by the other routes.

Heat loss through the skin is affected by the difference between body and environmental temperatures, the amount of the body surface exposed to the air and the type of clothes worn. Air is a poor conductor of heat and when layers of air are trapped in clothing and between the skin and clothing they act as effective insulators against excessive heat loss. For this reason, several layers of lightweight clothes provide more effective insulation against a low environmental temperature than one heavy garment. A balance is maintained between heat production and heat loss. Control is achieved mainly by thermoreceptors in the hypothalamus.

II. MECHANISMS OF HEAT LOSS

In evaporation, the body is cooled when heat is used to convert the water in sweat to water vapour. In radiation, exposed parts of the body radiate heat away from the body. In conduction, clothes and other objects in contact with the skin take up heat. In convection, air passing over the exposed parts of the body is heated and rises, cool air replaces it and convection currents are set up. Heat is also lost from the clothes by convection.

2.1. Control Of Body Temperature

Nervous control:

The temperature regulating centre in the hypothalamus is responsive to the temperature of circulating blood. This centre controls body temperature through autonomic nerve stimulation of the sweat glands when body temperature rises. The vasomotor centre in the medulla oblongata controls the diameter of the small arteries and arterioles, and therefore the amount of blood which circulates in the capillaries in the dermis. The vasomotor centre is influenced by the temperature of its blood supply and by nerve impulses from the hypothalamus. When body temperature rises the skin capillaries dilate and the extra blood near the surface increases heat loss by radiation, conduction and convection. The skin is warm and pink in colour. When

body temperature falls arteriolar constriction conserves heat and the skin is whiter and feels cool.

Activity of the sweat glands:
When the temperature of the body is increased by 0.25 to 0.5 °C the sweat glands are stimulated to secrete sweat, which is conveyed to the surface of the body by ducts. When sweat droplets can be seen on the skin the rate of production is exceeding the rate of evaporation. This is most likely to happen when the environmental air is humid and the temperature high. Loss of heat from the body by unnoticeable evaporation of water through the skin and expired air occurs even when the environmental temperature is low. This is called insensible water loss (around 500 ml per day) and is accompanied by insensible heat loss.

Effects of vasodilatation:
The amount of heat lost from the skin depends to a great extent on the amount of blood in the vessels in the dermis. As heat production increases, the arterioles become dilated and more blood pours into the capillary network in the skin. In addition to increasing the amount of sweat produced the temperature of the skin is raised and there is an increase in the amount of heat lost by radiation, conduction and convection. If the external environmental temperature is low or if heat production is decreased, vasoconstriction is stimulated by sympathetic nerves. This decreases the blood flow near the body surface, conserving heat.

Fever:
This is often the result of infection and is caused by release of chemicals (pyrogens) from damaged tissue and the cells involved in inflammation. Pyrogens act on the hypothalamus, which releases prostaglandins that reset the hypothalamic thermostat to a higher temperature. The body responds by activating heat-promoting mechanisms, e.g., shivering and vasoconstriction until the new higher temperature is reached. When the thermostat is reset to the normal level, heat-loss mechanisms are activated. There is profuse sweating and vasodilatation accompanied by warm, pink (flushed) skin until body temperature falls to the normal range again.

Hypothermia:
This is present when core temperature, e.g., the rectal temperature, is below 35 °C (95 °F). At a rectal temperature below 32 °C (89.6 °F), compensatory mechanisms to restore body temperature usually fail, e.g., shivering is replaced by muscle rigidity and cramp vasoconstriction fails to occur and there is lowered blood pressure, pulse and respiration rates. Mental confusion and disorientation occur. Death usually occurs when the temperature falls below 25 °C (77°F). Individuals at the extremes of age are prone to hypothermia.

2.2. Formation of vitamin D
7-dehydrocholesterol is a lipid-based substance in the skin and ultraviolet light from the sun converts it to vitamin D. This circulates in the blood and is used, with calcium and phosphate, in the formation and maintenance of bone. Any vitamin D in excess of immediate requirements is stored in the liver.

2.3. Sensation
Sensory receptors consist of nerve endings in the dermis that are sensitive to touch, pressure, temperature or pain. Stimulation generates nerve impulses in sensory nerves that are transmitted to the cerebral cortex. Some areas have more sensory receptors than others causing them to be especially sensitive, e.g., the lips and fingertips.

2.4. Absorption
This property is limited but substances that can be absorbed include: some drugs, in transdermal patches, e.g., hormones used as replacement therapy in postmenopausal women, nicotine as an aid to stopping smoking. Some toxic chemicals, e.g., mercury.

2.5. Excretion
- The skin is a minor excretory organ for some substances including:
- Sodium chloride in sweat and excess sweating may lead to abnormally low blood sodium levels
- Urea, especially when kidney function is impaired
- Aromatic substances, e.g., garlic and other spices.

III. INTRODUCTION OF FUNGI AND VARIOUS FUNGAL INFECTION

3.1. Fungi
“Fungi are a kingdom of usually multi-cellular eukaryotic organism that are heterotrops and have important role in nutrient cycling in an ecosystem” [4].

3.2. Characteristics of fungi

Some fungi are single-celled, while others are multi-cellular. Single-celled fungi are called yeast. Some fungi alternate between single celled yeast and multi-cellular forms depending on what stage of the life cycle they are in. Fungi cells have a nucleus and organelles, like plant and animal cells do.

The cell walls of fungi contain chitin, which is hard substance also found in the exoskeletons of insects and arthropods such as crustaceans. They do not contain cellulose, which commonly makes up plant cell walls. Multi-cellular fungi have many hyphae, which are braching filaments. Hyphae have tubular shape and are split into cell- like compartments by walls that are known as septa. These cells can have more than one nucleus, and nuclei and other organelles can move in between them. A fungus network of hyphae is called a mycelium [4].

3.3. Types of Fungi

- Chytridiomycota:

Chytrids, the organisms found in Chytridiomycota, are usually asexual, and produce spores that no around using flagella, small tail like appendages. It can cause fungal infection in frogs by burrowing under their skin.

- Zygomycota:

These are mainly terrestrial. They cause problem by growing on human few sources. Ex: Rhizopus stolonifer a bread mold.

- Glomeromycota:

They are found in soil. The fungi obtain sugar from plant and in return, dissolves, minerals in the soil to provide the plant with nutrients. These fungi also reproduce asexually.

- Ascomycota:

These are the pathogens of plant and animals, including humans in which they are responsible for infection like Athelete's Foot, Ringworm, and ergotism, which causes vomiting, convulsions, hallucination and sometimes even death [4].

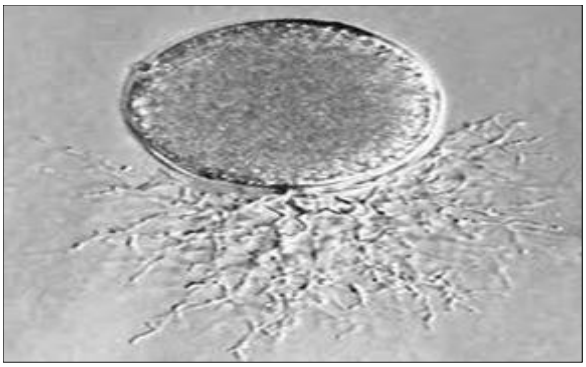


Fig 2: Chytridiomycota

Fig 3: Zygomycota

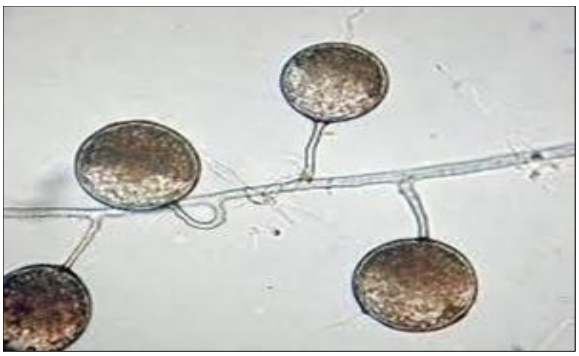


Fig 4: Glomeromycota

Fig 5: Ascomycota

3.4. Fungal infection

Fungal infections are one of the deadliest infections accounting in excess of 1.5 million deaths annually worldwide. The main reason for fungal infection is neglected by the society. Over the past two decades, fungal infections have increased significantly in frequency and as causes of morbidity and mortality [6, 7].

Fungal infections are also called mycosis, is a skin disease caused by a fungus and a type of microorganisms. There are millions of species of fungi, fungi can live in the air, soil, water, plants and also live-in human body. They can also lead to skin problems like rashes or bumps. Fungal infections come in different forms like ringworm, athletes' foot, yeast infections and jock itch. Some fungi like aspergillus can be dangerous and leads to life threatening disease. Fungal infections can be contagious and can be spread from one person to another person [8, 9].

3.5. Type of fungal infection:

- Superficial:

Affect skin - mucous membrane. e.g.: tinea versicolor dermatophytes: Fungi that affect keratin layer of skin, hair, nail. e.g.: tinea pedis, ring worm infection Candidiasis: Yeast- like, oral thrush, vulvovaginitis, nail infections.

- Deep infections:

Affect internal organs as: lung, heart, brain leading to pneumonia, endocarditis, meningitis [4].

3.6. Various infection includes

Dermatophytosis

Dermatophyte fungi are organisms that digest keratin. Dermatophytes infect the stratum corneum of the epidermis and keratinized tissues derived from it, such as hair or nail. *Trichophyton* spp., *Microsporum* spp., and *Epidermophyton* spp. are responsible for most of the superficial fungal infections, although the causative agents can be some yeast and some non-dermatophyte molds [10].

Tinea pedis

Also known as Foot Ringworm, Athlete's foot. Tinea pedis or foot ringworm is the term designated for dermatophytosis of the feet. It is thought to be the most common dermatophytosis with prevalence rate of 30-70%. The typical sites of infection are inter-digital spaces and soles. If infection involves entire foot, then the term used is moccasin foot. The infection varies from mild to severe, acute to chronic and may have inflammation, vesicles and pustules. Tinea pedis is successfully treated with combination of topical and oral antifungal agents [11].

Tinea corporis

Also known as Ringworm of the body. Tinea corporis refers to the colonization of arthroconidia of dermatophytes on glabrous skin. It is superficial fungal infection and limit itself in the superficial layer radially without involving the viable tissues. It excludes the hand, feet, face, scalp, nails and groin region. All species of *Epidermatophyton*, *Trichophyton* and *Microsporum* are able to produce lesions of tinea corporis, however, most prevalent etiological species are *M. canis*, *T. rubrum* and *T. mentagophytes*. Lesions produced by these species are ringshaped and may be single, multiple or confluent [12].

Tinea unguium or onychomycosis

Also known as Nail's Ringworm, Onychomycosis, Dermatophytic onychomycosis. Fungal infection of nail is called tinea unguium associated with dermatophytes.

The other term which makes a confusion is onychomycosis which is refers to infection caused by any nondermatophytic fungus. However, onychomycosis is the term that commonly used to describe all fungal infections of the nail. *T. rubrum* and *T. mentagrophytes* dermatophytes are the principal causes of onychomycosis [11].

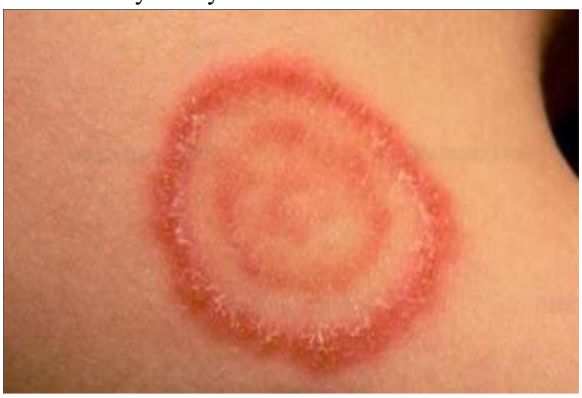


Fig 6: Dermatophytosis

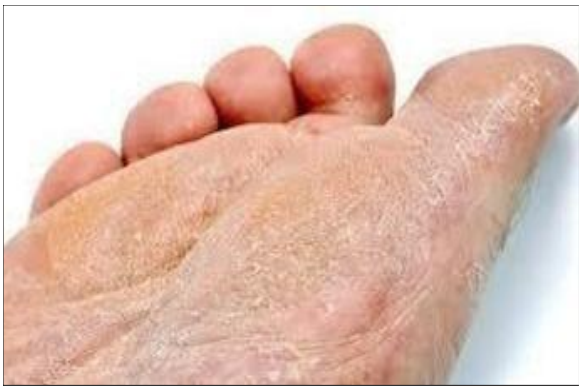


Fig 7: Tinea pedis

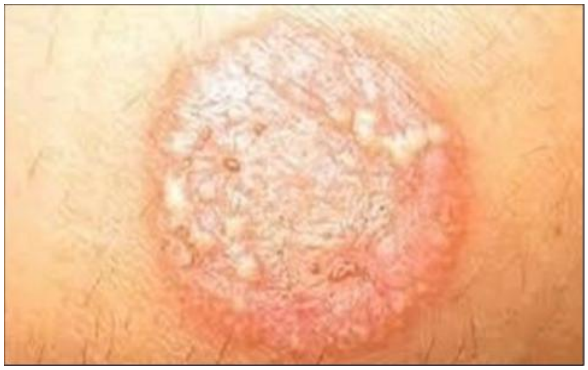


Fig 8: Tinea corporis

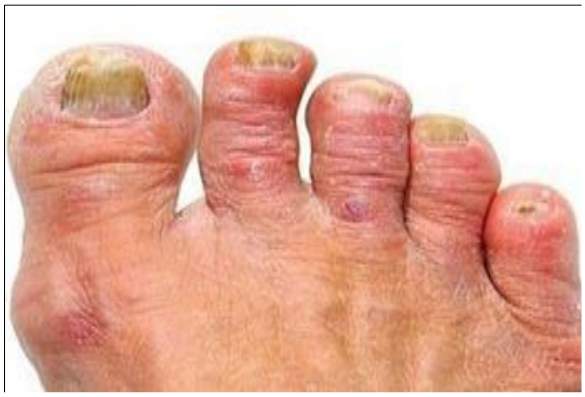


Fig 9: Tinea unguium or onchomycosis

Causes of Fungal Skin Infection

- Due to antibiotics.
- Poor eating habits.
- Hormone imbalance.

3.7. Diagnosis

Doctors may suspect a fungal infection when they see a red, irritated, or scaly rash in one of the commonly affected areas. They can usually confirm the diagnosis of a fungal skin infection by scraping off a small amount of skin and having it examined under a microscope or placed in a culture medium where the specific fungus can grow and be identified.

3.8. Fungal Treatment

Treatment with fungi to treat different types of fungal infections, a variety of preparations for fungal treatments are available. They are available as injectables, tablets meant to be inserted into the vagina (pessaries), sprays, solutions, lotions, and pills for oral use. Fungal Treatment: What is it 03 the kind and severity of your fungal infection, together with any other medical conditions, will determine how long your therapy will take. Certain treatment regimens, like those for vaginal thrush, can be completed in a matter of days. Some regimens (like those for scalp ringworm infections) might last up to eight weeks. Most function by causing damage to the fungus's cell wall, which results in the fungal cell dying. How to handle fungal infections. Topical antifungals, such as creams, liquids, or sprays these are applied to the skin, scalp, and nails to treat fungal infections. Clotrimazole, terbinafine, amorolfine, miconazole, ketoconazole, econazole, and miconazole are a few of them. They are available under a variety of brand names.

IV. INTRODUCTION OF POLYHERBAL CREAM

4.1. Defination

- Polyherbal: It is the formulation in which two or more than two herb or its extracts are used.
- Cream: It is semi-solid dosage form of a medication for a topical use.
- Polyherbal Cream: It is the semi-solid dosage form in which two or more than two herb or its extracts are used.

- Anti-fungal Cream: Cream which are used either to inhibit the growth or to kill the fungi.

4.2. Introduction of cream

Creams are the topical preparations which can be applied on the skin. Creams are defined as "viscous liquid or Semisolid emulsions of either the oil-in-water or water-in-oil type" dosage forms which consistency varies by Oil and water.

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).

Advantages

- It is the easiest way to deliver a drug.
- It does not show the side effect on the other body organ.
- Convenient and easy to apply.
- It does not show the side effect on the other body organ.
- It can slow down the signs of aging.
- Less greasy compared to ointment.

Disadvantages

- Skin irritation.
- Some drugs show low penetrable through the skin.
- Possibility of allergic reactions.
- Stability is not as good as ointment.
- They are less hydrophobic than other semisolid preparation, so risk of contamination is high than others.

4.3. Types of Skin Creams

They are divided into two types

- Oil-in-Water (O/W) creams:

Which are composed of small droplets of oil dispersed in a continuous phase, and an emulsion in which the oil is dispersed as droplets throughout the aqueous phase is termed an oilin-water (O/W) emulsion.

- Water-in-Oil (W/O) creams:

Which are composed of small droplets of water dispersed in a continuous oily phase. When water is the Dispersed phase and an oil the dispersion medium, the emulsion is of the water-in-oil (W/O) type.

4.4. General ingredients used in skin creams

The raw materials which are used in a manufacturing of skin creams include:

Water:

This is the most important and widely used raw material in any cream formulation. These are the Cheapest and easily available. In skin creams, water is used as solvent to dissolve other ingredients of creams. Water can also form emulsions; it depends upon how much quantity of water is used in the formulation and sometimes referred to as oil-inwater emulsions and sometimes water-in-oil emulsions depending upon the Quantities of oil phase and water phase used.

Oil, fates and waxes:

Oil, fats and waxes and derivatives their form comprise an essential portion of creams. Waxes act as an emulsifier, fats act as a thickener and oil act as a perfuming agent, preservative, etc. according To its function. Oil may be two types' mineral and glyceride.

Mineral oil:

Mineral oil consists of hydrocarbons derived from petroleum oil. Mineral oil is clear, odorless, and heavily refined oil and it is widely used in cosmetics. It is light weight and inexpensive, it helps to reduce water Loss from the body and keeps body moisturized. A number of mineral oils are used in cream formulation. Examples: Light liquid paraffin, Heavy liquid Paraffin, Liquid petroleum.

Vegetable oil:

Form a barrier on the surface of the skin and slow down the loss of water, helping to maintain Plumpness of skin. Vegetable oils may also be used to increase the thickness of the lipid or oil portion of cream or personal care products. E.g., Almond oil, germ oil, avocado oil, sunflower oil etc.

Waxes:

Which are used in preparation of cream includes beeswax, carnauba wax, ceresin, spermaceti, etc. Waxes are used in cosmetics because it helps to keep an emulsion from separation of oil and liquid components. These waxes also increase the thickness

of the lipid portion and sticks on the surface of the skin.

Fats:
Different types of fats are used in the preparation of creams. These materials can be obtained from Animals, plants or mineral origin. Glyceride oils and fats may be of animals or vegetable origin. They consist of Combinations of higher fatty acids and glycerin. When saponified they form soap, or fatty acid and glycerin, depending upon process used. The most common of these fatty acids are lauric, margaric, plamitic, stearic, saturated group. Oleic acid is liquid and most popular unsaturated fatty acid. More specially the oil most Commonly used in other cosmetics are olive oil, almond oil, seasame oil, peanut oil, cocoa butter fat, mutton Tallow, lard and beef stearine.

Lanolin:
It is derived from wool fat of a sheep. Lanolin is of two types- the hydrous lanolin contains between 25%-30% water. Anhydrous lanolin has point of 38 °C-42 °C and has a slight odour. These ingredients act as a Lubricant on the skin surface, which gives the skin soft and smooth appearance. Lanolin helps to form emulsion and blends well with other substances used in cosmetic and personal care products.

Colours:
Before the development of the modern technology, colours primarily came from substances found in Nature such as turmeric, saffron, indigo, etc. They also could be produced without using plants harvested in the wild.

Emollients:
Emollients, also commonly referred to as moisturizers, are products that help to soften skin or to treat skin that has become dry. Most emollients are forms of oil or grease, such as mineral oil, squalene, and Lanolin

Humectants:
These are important multi-functional ingredients found in most skin care formulations. Humectants are hydroscopic organic compounds. These are the materials that can absorb or retain moisture these has many benefits such as moisturization, exfoliation, etc. Examples of humectant are glycerin, Hydroxyethyl urea, betaine, sodium PCA, Sodium-L-Lactate, etc.

Perfumes:
Perfume is a substance that imparts a scent or order, including a sweet and pleasant smell. Examples Of natural perfumes used in creams are- White Blossoms, Rosy Dreams, Orange Blossom.

Vitamins:
Vitamins plays an important role in maintaining the physiological function of whole body and the Skin. Vitamin A, B, C, E etc. are generally used.

Preservatives:
The use of preservatives in cosmetics is essential to prevent alteration caused by microorganism and contamination during formulation, shipment, storage and consumer use. Antioxidants can also be used to protect alteration caused by exposure to oxygen. Synthetic preservatives when used in low concentration effectively preserve the products [5].

Polyherbal Cream
The basic idea of skin care cosmetics or herbal creams lies deep in the Rig-Veda, Yajurveda, Ayurveda, Unani, and Homeopathic system of medicine. So before use of synthetic creams for various disesase and infection herbal creams (lepa) are used in most of the countries. These creams are the products in which herbs are used in crude or in extract form. These herbs should have varieties of properties like antioxidant, anti-inflammatory, antiseptic, emollient, antibacterial, and antifungal activities etc.
Herbal formulations always have attracted considerable attention because of their good activity and comparatively lesser or nil side effects with synthetic formulation. An herbal cream that can give effective protection to skin and free from any toxicity or toxic residue or any irritation when regularly used and should also be cosmetically acceptable. Herbal medicine is one the most universal system of health care system [4].

Advantages of herbal system of medicines
Lower risk of side effects.
- Widespread availability.
- Effectives with chronic medicine.

- Low-cost effectiveness makes them all the more alluring.
- Natural detoxification process of the body is effectively enhanced by herbal medicine.

Disadvantages of herbal system of medicines
Bulk dosing.

- Poor stability in higher acidic pH, liver metabolism etc.
- Large molecular size limiting the absorption via passive diffusion.
- High amount of raw material is required for processing the medicine.
- Isolation and purification of individual components from whole herbal extract led to partial or total loss of therapeutic activity [4].

4.5. Pharmacognosy of Plants

1. Neem

Synonyms: Azadirachta indica, commonly known as neem, margosa, nimtree of Indian lilac.

- Biological Sources: Neem consists of the fresh or dried leaves and seed oil of Azadirachta indica Juss (Melia Indica or M. azadirachta Linn.) Family: Meliaceae.
- Chemical Constituents: The chemical constituents are found in the leaves of neem as nimbin, nimbanene, 6desacetyl nimbinene, nimbandiol, nimbolide, ascorbic acid, n- hexacosanol and amino acid, 7-desacetyl-7benzoyl azadiradione, 7-desacetyl-7-benzoyl gedunin, 17-hydroxy azadiradione and nimbiol.
- Uses: efficacious against a variety of skin diseases, septic sores, and infected burns. The leaves, applied in the form of poultices or decoctions, are also recommended for boils, ulcers, and eczema. The oil is used for skin diseases such as scrofula, indolent ulcers, and ringworm.

2. Tulsi

Fig 12: Tulsi

Synonyms: Sacred basil, Kali-Tulsi, Veranda

- Biological Source:

Tulsi consists of the fresh and dried leaves of Ocimum species like Ocimum sanctum L. and Ocimum basilicum L.

- Family: Lamiaceae
- Chemical Constituents:

The leaves of ocimum sanctum contain 0.7%volatile oil comprising about 71% eugenol and20% methyl eugenol. The oil also contains carvacrol and sesquiterpene hydrocarbon caryophyllene. Two flavonoids orientin andandvicen in from aqueous leaf extract of ocimumsanctum have been isolated.

Uses

- Lowers stress and anxiety.
- Stimulates and vitalises your body.
- Lower your blood sugar.

3. Aloe Vera

Fig 13: Aloe Vera

Synonyms: "Burn Aloe," "Indian Aloe," "True Aloe," "First Aid Plant," "Aloe barbadensis," and "Barbados aloe".

- Biological Source:

Aloe is the dried juice collected by incision, from the bases of the leaves of various species of Aloe. Active components with its properties: Aloe vera contain 75 potentially active constituents: vitamins, enzymes, minerals, sugars, lignin, saponins, salicylic acids and amino acids.

- Family: Asphodelaceae (Liliaceae)
- Chemical Constituents:

Aloe vera contains many chemical constituents, including water, polysaccharides, anthraquinones, vitamins, minerals, enzymes, and amino acids.

Uses

- It contains healthful plant compounds.
- It has antibacterial properties.
- It may benefit the skin.

4. Turmeric

Fig 14: Turmeric

Synonyms: Haldi (Hindi); Curcuma;

- Biological Source:

Turmeric's biological source is the dried rhizome of the plant Curcuma longa.

- Family: Zingiberaceae
- Chemical Constituents:

Turmeric primarily contains curcuminoids, including curcumin, demethoxycurcumin, and bisdemethoxycurcumin, which are responsible for its golden color and various biological activities. In addition to curcuminoids, turmeric also contains essential oils with aromatic compounds like turmerone, and various other phenolic compounds and terpenoids.

Uses

- Flavor and Color
- Natural Coloring Agent
- It is widely used in cooking

V. INTRODUCTION OF EXTRACTION

5.1. Extraction and its types

Extraction is the first step to separate the desired natural products from the raw materials.

Extraction methods include solvent extraction, distillation method, pressing and sublimation according to the extraction principle.

In general, extraction procedures include maceration, digestion, decoction, infusion, percolation, Soxhlet extraction, superficial extraction, ultrasound- assisted, and microwave-assisted extractions.

5.2. Solvent extraction

It is the most widely used method. The extraction of natural products progresses through the following stages The solvent penetrates into the solid matrix

- The solute dissolves in the solvents
- The solute is diffused out of the solid matrix
- The extracted solutes are collected. Any factor enhancing the diffusivity and solubility in the above steps will facilitate the extraction.

The properties of the extraction solvent, the particle size of the raw materials, the solvent-to-solid ration, the extraction temperature and the extraction duration will affect the extraction efficiency.

The selection of the solvent is crucial for solvent extraction. Selectivity, solubility, cost and safety should be considered in selection of solvents. Based on the law of similarity and intermiscibility (like dissolves like), solvents with a polarity value near to the polarity of the solute are likely to perform better and vice versa. Alcohols (Ethanol and Methanol) are universal solvents in solvent extraction for phytochemical investigation.

Generally, the finer the particle size is, the better result the extraction achieves. The extraction efficiency will be enhanced by the small particle penetration of solvent and diffusion of solutes.

High temperatures increase the solubility and diffusion. Temperatures that too high, however, may cause solvents to be lost, leading to extracts of

undesirable impurities and the decomposition of thermolabile components.

The extraction efficiency increases with the increase in extraction duration in a certain time range. Increasing time will not affect the extraction after the equilibrium of the solute is reached inside and outside the solid material. The solvent used for the extraction of medicinal plants is also known as the menstruum. The choice of solvent depends on the type of plant, part of plant to be extracted, nature of the bioactive compounds, and the availability of solvent. In general, polar solvents such as water, methanol, and ethanol are used in extraction of polar compound, whereas nonpolar solvents such as hexane and dichloromethane are used in extraction of nonpolar compounds.

Solvent used in extraction is classified according to their polarity, from n-hexane which is the least polar to water the most polar.

5.3. Maceration

This is an extraction procedure in which coarsely powdered drug material, either leaves or stem bark or root bark, is placed inside a container; the menstruum is poured on top until completely covered the drug material. The container is then closed and kept for at least three days. The content is stirred periodically, and if placed inside bottle it should be shaken time to time to ensure complete extraction. At the end of extraction, the micelle is separated from marc by filtration or decantation. Subsequently, the micelle is then separated from the menstruum by evaporation in an oven or on top of water bath. This method is convenient and very suitable for thermolabile plant material.

5.4. Infusion

This is an extraction process such as maceration. The drug material is grinded into fine powder, and then placed inside a clean container. The extraction solvent hot or cold is then poured on top of the drug material, soaked, and kept for a short period of time. This method is suitable for extraction bioactive constituents that are readily soluble. In addition, it is an appropriate method for preparation of fresh extract before use. The solvent to sample ratio is usually 4:1 or 16:1 depending on the intended use.

5.5. Digestion

This is an extraction method that involves the use of moderate heat during extraction process. The solvent of extraction is poured into a clean container followed by powdered drug material. The mixture is placed over water bath or in an oven at a temperature about 50○C. Heat was applied throughout the extraction process to decrease the viscosity of extraction solvent and enhance the removal of secondary metabolites. This method is suitable for plant materials that are readily soluble.

5.6. Decoction

This is a process that involves continuous hot extraction using specified volume of water as a solvent. A dried, grinded, and powdered plant material is placed into a clean container. Water is then poured and stirred. Heat is then applied throughout the process to hasten the extraction. The process is lasted for a short duration usually about 15min. The ratio of solvent to crude drug is usually 4:1 or 16:1. It is used for extraction of water soluble and heat stable plant material.

5.7. Percolation

The apparatus used in this process is called percolator. It is a narrow-cone- shaped glass vessel with opening at both ends. A dried, grinded, and finely powdered plant material is moistened with the solvent of extraction in a clean container. More quantity of solvent is added, and the mixture is kept for a period of 4h. Subsequently, the content is then transferred into percolator with the lower end closed and allow to stand for a period of 24h.The solvent of extraction is then poured from the top until the drug material is completely saturated. The lower part of the percolator is then opened, and the liquid allowed to drip slowly. Some quantity of solvent was added continuously, and the extraction taken place by gravitational force, pushing the solvent through the drug material downward. The addition of solvent stopped when the volume of solvent added reached 75% of the intended quantity of the entire preparations. The extract is separated by filtration followed by decantation. The marc is then expressed and final amount of solvent added to get required volume.

5.8. Soxhlet extraction

This process is otherwise known as continuous hot extraction. The apparatus is called Soxhlet extractor made up of glass. It consists of a round bottom flask, extraction chamber, siphon tube, and condenser at the top. A dried, grinded, and finely powdered plant material is placed inside porous bag (thimble) made up of a clean cloth or strong filter paper and tightly closed. The extraction solvent is poured into the bottom flask, followed by the thimble into the extraction chamber. The solvent is then heated from the bottom flask, evaporates, and passes through the condenser where it condenses and flow down to the extraction chamber and extracts the drug by coming in contact. Consequently, when the level of solvent in the extraction chamber reaches the top of the siphon, the solvent and the extracted plant material flow back to the flask. The entire process continues repeatedly until the drug is completely extracted, a point when a solvent flowing from extraction chamber does not leave any residue behind. This method is suitable for plant material that is partially soluble in the chosen solvent and for plant materials with insoluble impurities. However, it is not a suitable method for thermolabile plant materials.

Advantages

Large amount of drug can be extracted with smaller amount of solvent. It is also applicable to plant materials that are heat stable.

No filtration is required, and high amount of heat could be applied.

Disadvantages

Regular shaking is not possible, and the method is not suitable for thermolabile materials [13].

VI. MATERIAL AND METHODOLOGY

Selection of the plants/its part for poly-herbal antifungal cream:

There are many herbal antifungal plants in world but amongst them five plants are selected named as: Neem, Tulsi, Aloe vera, Turmeric.

Authentication

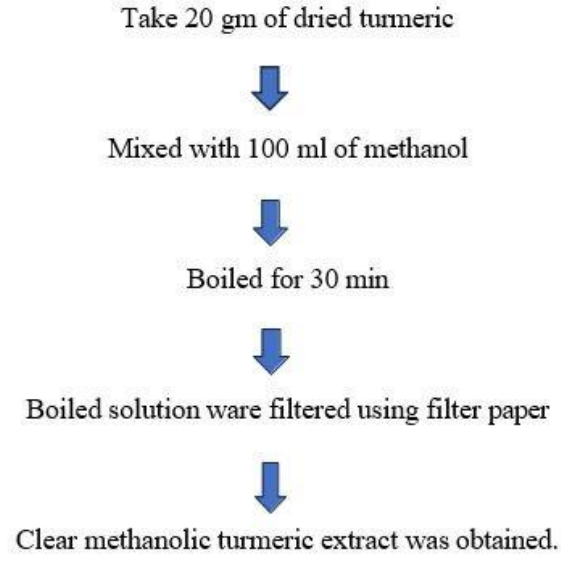
- After collecting all required amount of the part of plant, then herbarium is prepared which contains all the required information of plants with its selected part attached to the herbarium.
- This herbarium is presented at Lalan College in Bhuj, in front of the botanist, where they verify and authenticated the plant's part.
- On getting proper authentication, we started extraction process of part by using specific methods.

Extraction process

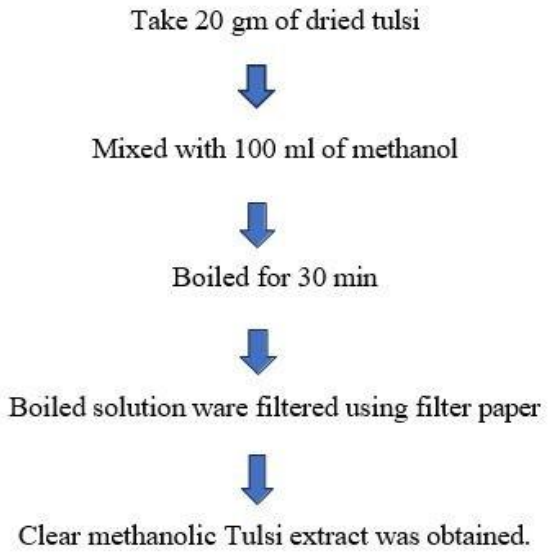
There is specific extraction process for specific parts of plants

Neem extract

Turmeric Extract



Tulsi Extract



Chromatographic Evaluation

Chromatography: One technique used in labs to break down a mixture into its parts is chromatography. The mixture passes through a system on which fluid solvent known as the mobile phase dissolves it. The stationary phase material is fixed [14].

The various forms of chromatography are as follows:

- Paper chromatography,
- Thin layer chromatography (TLC),
- Gel electrophoresis,
- Chromatography in columns,
- Chromatography with ion exchange,
- Chromatography with gel filtration,
- Gas-liquid chromatography & Affinity chromatography [15].

Thin Layer Chromatography (TLC)

To separate components in non-volatile mixtures, chromatography techniques such as thin-layer chromatography are applied [16].

It is carried out on a TLC plate composed of an adsorbent material thinly coated over a non-reactive solid [17]. This is called the stationary phase [18]. The sample is eluted using the mobile phase, which is a solvent or solvent mixture, once it has been put on the plate [19].

TLC of Curcumin Preparation of stationary phase

Take few grams of silica gel G in a beaker then add some amount of distilled water to make slurry. And stir the solution properly to attain uniform viscosity. Next step is Pour the slurry on a glass slide. Keep the glass slide in hot air oven for 30 minutes at 100C.then Dried TLC plate is obtained and handled properly.

Preparation of mobile phase:

A mixture of 10 volumes of chloroform, 1.0 volume of methanol, 0.5 volume of glacial acetic acid. Cover the beaker with the lead and keep it for 15 mins for saturation.

Spotting of TLC plate:

Mark the TLC plate 1 cm from the top and 1 cm from bottom. Next step is application of spot of curcumin extract with the help of Capillary tubes which is obsolete and gives circular spotting.

TLC of Neem Preparation of stationary phase

Take few grams of silica gel G in a beaker then add some amount of distilled water to make slurry. And Stir the solution properly to attain uniform viscosity. Next step is Pour the slurry on a glass slide. Keep the glass slide in hot air oven for 30 minutes at 100C.then Dried TLC plate is obtained and handled properly.

Preparation of mobile phase:

A mixture of Methanol: Toluene (8:2) Cover the beaker with the lead and keep it for 15 mins for saturation.

Spotting of TLC plate:

Mark the TLC plate 1 cm from the top and 1 cm from bottom. Next step is application of spot of neem extract with the help of Capillary tubes which is obsolete and gives circular spotting.

Rf values:

The positions of each molecule in the mixture can be ascertained by calculating the ratio between the solute and solvent travel times [20].

Value serves as a qualitative means of characterizing the molecules.

$$= \frac{\text{The Solute's travel distance } R_f}{\text{The Solvent's travel distance}}$$

The Rf value of Turmeric extract

- Distance travelled by the solute: 5.3 cm
- Distance travelled by the solute: 6.4 cm
- From the formula it is obtained that

- Rf value: 0.82 (Yellow colour)

The Rf value of Neem extract
- Distance travelled by the solute: 3 cm
- Distance travelled by the solute: 4.2 cm
- From the formula it is obtained that
- Rf value: 0.71(Green / Yellow)

Phytochemical screening
It is the qualitative test to identify the chemical components present in the sample of interest.
We perform specific phytochemical screening of specific extract.

Formulation and Evaluation
Ingredient [21, 22]

Formulation

Table 1: Ingredient Quantity Roles

Sl. No.	Ingredient	Quantity	Roles
01	Neem	1 gm	Antifungal agent
02	Turmeric	2.5 gm	Antifungal agent
03	Tulsi	1 gm	Antifungal agent
04	Aloe vera gel	7 ml	Soothing agent, moisturizer
05	Glycerin	10 ml	Lubricant
06	Tween- 20	10 ml	Emulsifier
07	Beeswax	1.5 gm	Emollient
08	Borax	0.2 gm	Buffer
09	Silica gel	0.1 gm	Adsorbent
10	Bentonite	4 gm	Thickening agent
11	Methylparaben	0.2 gm	Preservative
12	Rose oil	q. s.	Fragrance

Material
Neem:
Neem, scientifically known as Azadirachta indica, is a versatile tree native to the Indian subcontinent. It holds significant cultural, medicinal, and agricultural importance. Neem has been used in traditional medicine for centuries. Its extracts contain compounds with antibacterial, antifungal, antiviral, and anti-inflammatory properties. Neem oil, derived from its seeds, is used topically to treat skin conditions like acne, eczema, and psoriasis. It's also used in oral care products for its ability to combat bacteria. Neembased products are widely available in the market, including soaps, shampoos, lotions, toothpaste, and herbal supplements. These products capitalize on neem's antimicrobial and skin-nourishing properties [23, 24].

Turmeric
Turmeric, scientifically known as Curcuma longa, is a flowering plant of the ginger family, native to the Indian subcontinent and Southeast Asia. It has been used for thousands of years in traditional medicine and cooking, particularly in India and other parts of Asia [24].

Tulsi
Tulsi (Ocimum sanctum), also known as holy basil, exhibits antifungal activity, with studies showing its extracts and essential oil inhibit the growth of various fungal pathogens, including dermatophytes and Candida species.

Aloe vera
The Aloe vera gel is made up of water, amino acids, vitamins, lipids, sterols, tannins, and enzymes and also contains phenol, saponin, anthraquinones components, which have antiviral, antibacterial, and antifungal properties. Aloe vera is a plant species that has been used for centuries for its medicinal and healing properties. Aloe vera, a succulent plant species native to North Africa, is renowned for its multifaceted uses in traditional medicine and various industries. The plant's gel-like substance, found in its fleshy leaves, has been extensively studied for its
potential health benefits and therapeutic properties [24, 25].

Other excipients Glycerine
Glycerine, also known as glycerol, is a colorless, odorless, viscous liquid that is sweet-tasting. It's commonly used in pharmaceuticals, cosmetics, food, and even explosives. Studies on glycerine cover its various applications, including its use as a moisturizer, its role in pharmaceutical formulations, and its potential health effects when ingested or applied topically. It is a trihydroxy sugar alcohol, meaning it contains three hydroxyl groups, which contribute to its solubility in both water and alcohol [26].

Tween-20

The Tween-20 study investigates the properties and applications of a surfactant known as Tween-20, which is commonly used in various industries including pharmaceuticals, food, and cosmetics. Tween-20 is a nonionic surfactant belonging to the Tween series, produced by ethoxylation of sorbitan monolaurate. Twin-20 exhibits amphiphilic properties, meaning it has both hydrophilic and hydrophobic regions. This characteristic allows it to reduce surface tension and form stable emulsions by interacting with both water and oil molecules. As a result, Tween-20 is frequently employed as an emulsifier, stabilizer, and solubilizing agent in various formulations [26].

Beeswax

Beeswax, a natural substance secreted by honeybees, plays a vital role in the hive's construction and maintenance. It is composed primarily of esters, fatty acids, and hydrocarbons, making it a complex mixture with various applications. Beeswax has a unique combination of properties that make it valuable in numerous industries. Its main components include palmitic, oleic, and linoleic acids, along with various alcohols like triacontanol and melissyl alcohol. These compounds give beeswax its characteristic odor and consistency [27].

Borax

Borax, also known as sodium borate, is a versatile compound with various applications across industries and households. Its chemical formula is Na2B4O7•10H2O.

Borax is primarily mined from natural deposits in countries like Turkey, the United States, and Chile. In terms of its properties, borax is a white, odourless powder that dissolves easily in water. One of its most notable characteristics is its ability to act as a buffering agent, helping to stabilize pH levels in solutions. This property makes it valuable in cleaning products, cosmetics, and even as a food additive
[28].

Silica gel

Silica gel is a porous form of silica dioxide, synthetically manufactured from sodium silicate. It appears as small, translucent beads or granules and is known for its high adsorption capacity. Silica gel has a wide range of applications due to its ability to absorb and hold moisture, odor, and other substances without reacting chemically with
them [24, 25].

Bentonite

Bentonite is a versatile clay mineral renowned for its unique properties and wide-ranging applications across various industries. It is primarily composed of montmorillonite, a swelling clay mineral, along with other minerals such as quartz, feldspar, and gypsum. This composition gives bentonite remarkable characteristics including high water absorption capacity, plasticity, swelling ability, and thixotropy [29].

Methyl paraben

Methyl paraben is a commonly used preservative in cosmetics, pharmaceuticals, and food products due to its ability to inhibit microbial growth and extend product shelf life. Chemically, it belongs to the paraben family, which are esters of para-hydroxybenzoic acid. Methyl paraben is typically synthesized from para-hydroxybenzoic acid and methanol. Its antimicrobial properties make it effective against a wide range of bacteria and fungi, enhancing product stability and safety. However, there has been some controversy surrounding its safety, particularly its potential to disrupt endocrine function as it can mimic estrogen, though scientific consensus suggests that at typical exposure levels, it poses minimal risk to human health [30].

Rose oil

Rose oil, also known as rose otto or rose essential oil, is extracted from the petals of various types of roses, primarily Rosa damascena or Rosa centifolia. The extraction process typically involves steam distillation or solvent extraction, yielding a concentrated oil with a strong, floral scent. Rose oil is often used in aromatherapy for its calming and moodenhancing effects. Some studies suggest that inhaling the scent of rose oil may reduce anxiety and promote relaxation.

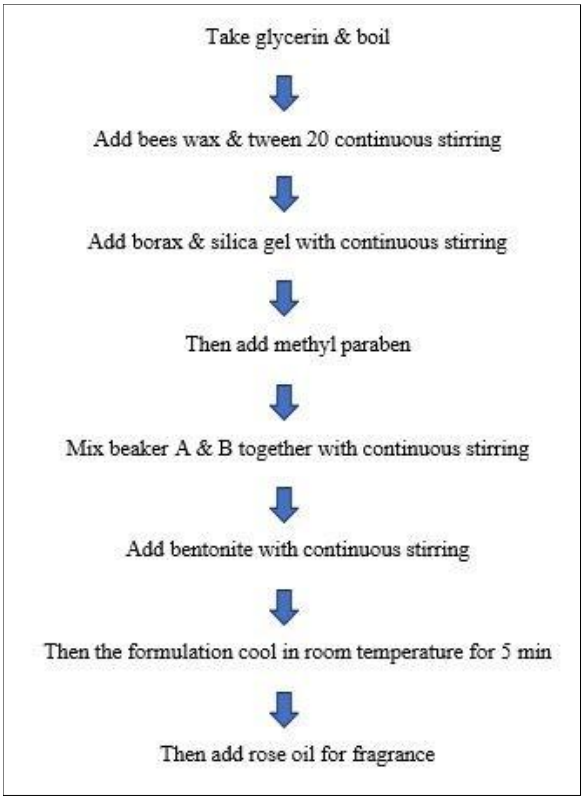
Method of Preparation

Take two beaker A & B, wash and clean properly.

In Beaker A

- Take aloe vera gel & boil on water bath.
- Add neem extract, tulsi extract and turmeric extract with continuous stirring.

In Beaker B



Evaluation parameter

Physical properties (Organoleptic characteristics)

The physical properties of antifungal cream play a significant role in its usability, efficacy, and overall user experience. The cream was observed for colour, odour, appearance and texture [31].

Table 2: Properties Observation

Sl. No.	Properties	Observation
1	Colour	Pale yellow
2	Odour	Characteristic
3	Appearance	Semi-solid
4	Texture	Smooth

pH determination:

The pH of various semi-solid (cream) formulation were determined by using digital pH meter. Weight 2.5g of cream and dispersed in 25ml of distilled water and stored for 2 hours. Then measurement of pH by using digital pH meter [32]. Result the pH values are 6.33.

Patch Test:

A patch test for an herbal antifungal cream involves applying a small amount of the product onto a small area of the skin, typically on the forearm or behind the ear. The purpose of this test is to evaluate the cream's potential for causing irritation or allergic reactions in sensitive individuals. After application, the area is observed for any signs of redness, swelling, itching, or other adverse reactions over a period of 24 to 48 hours. This test helps to assess the cream's safety profile and determine if it is suitable for use on larger areas of the skin without causing harm or discomfort [32].

Result:

No any inflammation or irritation to the skin.

Spreadability Test

The spreadability test for a herbal antifungal cream assesses its ability to evenly distribute and cover a given surface area upon application. This test typically involves placing a fixed quantity of the cream onto a standardized surface, such as glass or a skin mimic substrate, and measuring the diameter of the spread after a specified time period. Factors like viscosity, texture, and formulation components influence the cream's spreadability. A cream with good spreadability ensures uniform coverage, easy application, and enhanced efficacy. This test helps in optimizing formulation parameters to achieve desired spreading characteristics for better consumer experience and therapeutic outcomes.

Result:

Good spreadability ensures uniform coverage, easy application, and enhanced efficacy.

Homogeneity

The homogeneity of herbal antifungal cream is crucial for consistent effectiveness and application. Ensuring uniform distribution of active ingredients throughout the product is essential to guarantee each application delivers the intended benefits. Achieving homogeneity involves meticulous formulation and manufacturing processes, including thorough mixing of ingredients and quality control measures. Manufacturers utilize techniques like blending, emulsification, and particle size reduction to achieve desired consistency. Additionally, analytical methods such as visual inspection, microscopy, and spectroscopy are

employed to assess homogeneity. By maintaining homogeneity.

Result:
Cream is uniform distribute on skin.

Determination of type of emulsion Dilution test
In this test the emulsion is diluted either with oil or water. If the emulsion iso/w type and it is diluted with water, it will remain stable as water is the dispersion medium" but if it is diluted with oil, the emulsion will break as oil and water are not miscible with each other. Oil in water emulsion can easily be diluted with anaqueous solvent, whereas water in oil emulsion can be diluted with an oily liquid.

VII. RESULTS & DISCUSSION

7.1. Phytochemical Screening of Tulsi Extract and Aloe Vera Extract

Table 3: Phytochemical test for Tulsi and Aloe Vera

Sl. No.	Chemical test	Procedure	Observation	Inference
1	Test for Alkaloids Wagner's test	1 ml extract + 1 ml of Wagner's reagent	The appearance of brown flocculent and precipitation reveals	Alkaloids present
2	Test for Tannins	1ml extract + 1 ml of 0.1% Ferric chloride-+ 0.1N HCL was added	blue-black coloration	Tannins present
3	Test for saponins Foam test	1ml extract+ 1ml distilled water and shake vigorously	Formation of foam	Saponins present
4	Test for flavonoids	1 ml extract+ 1 ml of dilute ammonia solution +concentrated H2SO4 dropwise.	A yellow coloration observed	Flavonoids present
5.	Test for glycosides (keller-kiliani test)	1ml extract+1ml glacial acetic acid+ 1drop of ferric chloride Solution+1 ml conc H2SO4	Formation of brown ring at the interface	Cardiac glycosides present

Phytochemical screening of Tulsi (Ocimum sanctum) and bioactive compounds, including alkaloids, flavonoids, Aloe vera (Aloe barbadensis) reveals a presence of several tannins, saponins, and glycosides, in both plants.

7.2. Phytochemical Screening of Turmeric Extract

Table 4: Phytochemical test for Turmeric

Sl. no.	Chemical test	Procedure	Observation	Inference
1	Test for Tannins Lead test	10 mg turmeric + 1ml distilled water+ 1-3 drops of Ferric chloride	Observed blue or green colour	Tannins present
2	Test for Saponins Foam test	10 mg turmeric+ 1ml distilled water and shake vigorously	Formation of foam	Saponins present
3	Test for Terpenoids Salkowski's test	20 mg of turmeric + 1ml of chloroform + 1ml of con H2SO4	reddish brown discolouration at the interface	Terpenoids present
4	Test for Proteins Biuret's test	2ml of Biuret reagent + 2ml of extract, Shake well and warm it on water bath	Appearance of red or violet colour	Proteins present

Turmeric exhibits a variety of phytochemicals including alkaloids, triterpenes, saponins, flavonoids, tannins, phenols, and vitamin C. Qualitative phytochemical screening methods can be used to identify the presence of these compounds.

7.3. Phytochemical Screening of Neem Extract

Table 5: Phytochemical test for Neem

Sr. no.	Chemical test	Procedure	Observation	Inference
1	Test for Alkaloids Mayer's test	To 3 ml of filtrate + few drops of Mayer's reagent	Formation of creamy precipitate	Alkaloids present
2	Test for saponins	0.5 g of sample + s boiled with 50 ml of distilled water and filtered + 5 ml of each filtrate and shake vigorously	Formation of foam	Saponins present
3	Test For Flavonoids	3 ml of Neem leaf extract + 10 ml of Distilled water and mix it well.	Yellow colour was observed.	Flavonoids present
4	Test For Glycosides	To the 5 ml of filtrate /extract + add 0.3ml of Fehling's solution A and B.	Red litmus paper turns to blue.	Glycosides present

Phytochemical screening of Neem reveals the presence of flavonoids, saponins, terpenoids, and tannins various secondary metabolites, including alkaloids,

7.4. Evaluation parameters of cream

Table 6: Evaluation parameters of cream

Sl. No.	Test	Result
1	Physical Evaluation (Organoleptic characteristics)	
	A. Colour	Pale yellow
	B. Odour	Characteristic
	C. Appearance	Semi-solid
	D. Texture	Smooth
2	pH	6.33
3	Patch Test	No irritation on the skin.
4	Spreadability Test	Good spreadability ensures uniform coverage, easy application, and enhanced efficacy
5	Homogeneity	Cream is uniform distribute on skin

The prepared cream was evaluated for physical appearance, pH, skin irritation to observed side effect. It was inferred from the result that cream formulation were good in appearance and homogeneity. The overall result of the research the prepared cream formulation shows significant anti- fungal activity.

VIII. CONCLUSION

The Polyherbal cream are prepared from natural extracts. There is an increasing demand for herbal cosmetics because of fewer Side effects and is safe to use. In the present work, it was performed to extract and formulate polyherbal antifungal cream from Neem extract, Tulsi extract, Aloe vera extract, and Turmeric Extract. The present study demonstrates that the plant materials were collected from local areas of Bhuj-Kutch, Gujarat. The Phytochemical screening of various herbal extracts and thin layer chromatography studies were performed successfully which indicates the presence of active chemical constituents in respective plants and are responsible for anti-fungal activity. The evaluation tests like pH, odor, color, homogeneity, spreadability test was performed. The prepared formulation has no evidence of phase separation and good consistency during the study period. The prepared formulations showed pH range that is approximately 6.33 and supposed to have good anti-fungal activity. The cream is expected to produce protection to the skin from fungal infections.

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