

CURRENT PROPOSAL OF HERBS IN SKIN ALIMENTS TREATMENT

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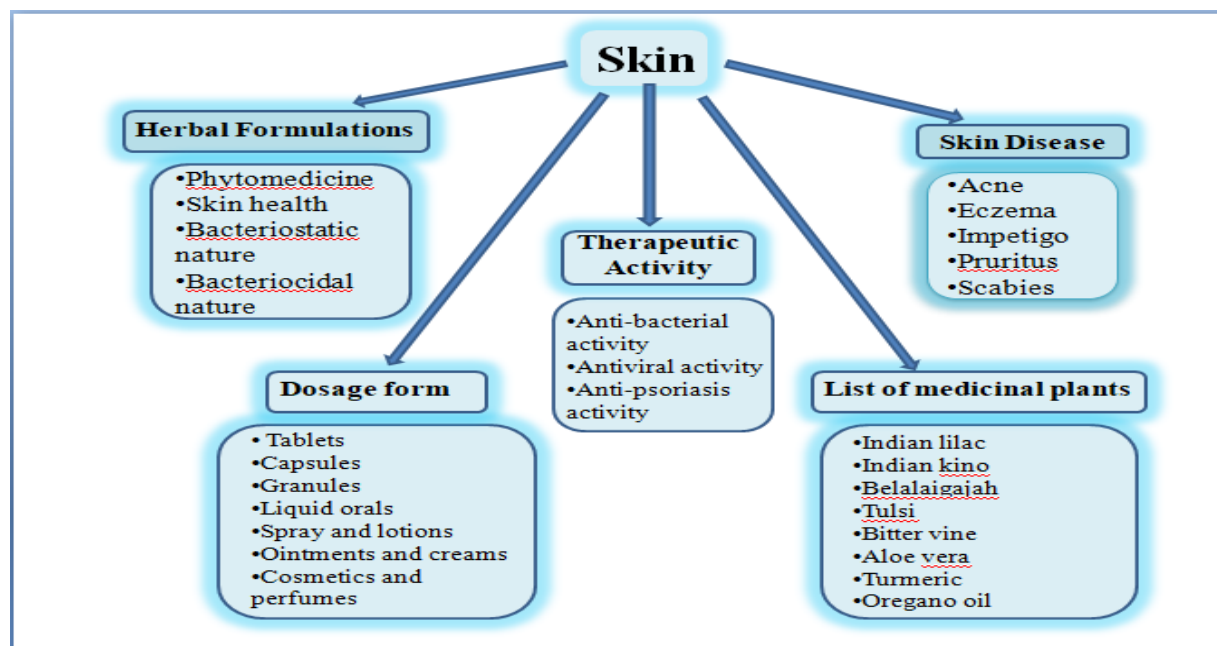
ABSTRACT:

Herbal remedies have been used to heal skin ailments since primitive times. A healthy body depends on having good skin. Skin conditions are widespread today and pose an important risk to everyone's health, including newborns and the elderly. Skin-related illnesses like cancer, herpes, and cellulitis can impact a lot of people. Long-term conventional treatment causes complex diseases in the body's essential organs. Additionally, it places socioeconomic demands on the sufferers. Natural medicine is reportedly safe and inexpensive. Plant use predates the existence of humans. These disorders are routinely treated with a variety of medicinal plants and their parts, which also serve as excellent raw materials for the creation of novel synthetic drugs. Our nearest surviving species, the big apes, also use herbal treatments for self-care. Certain herbs and their applications based on locally available plants were developed as a result of regional commerce in ethnobotanical remedies.

In Europe, the Middle East, Africa, India, China, Japan, Australia, and the Americas, distinct regional herbal use systems have emerged. Two well-known systems that are still in use are the herbal concoctions used in traditional Chinese medicine (TCM) in China and the Ayurvedic herbal remedies in India. The most frequent chemicals from the plant families Fabaceae, Asteraceae, Lamiaceae, etc. that are used to treat skin problems are reviewed, along with in silico studies that compile the most recent information in this field.

KEYWORDS: Ayurveda, Cancer, Disease, Herbs, Skin, Species, Remedies.

GRAPHICAL ABSTRACT:



INTRODUCTION

Transdermal and dermal drug delivery are promising alternatives to traditional drug delivery techniques. Drugs can have local or systemic effects when applied topically. The success of a topical dermatological formulation depends on how readily the medicine is absorbed by the target organ, the skin may be the primary site. For the drug to have the appropriate therapeutic effect with the least amount of systemic exposure, the medication must reach the target area at the necessary concentration. When it comes to the transport of active chemicals to and through skin, the barrier characteristics and resulting impermeability of the skin provide significant challenges. The pharmaceutical companies are investing more money to create breakthrough medicines that can get around the skin's natural barrier functions(1). The skin is considered as a complex organ similar to brain and has a greater range of cell types. Some characteristics of transdermal drug infiltrations remain unexplained despite how easily the skin can be accessed for drug delivery and research. There is still more research needed to determine the precise route by which chemicals enter the body and how formulations can change this. Many potential medicinal products are now being produced as a result of modern technology's use of combinatorial chemistry and parallel synthesis.

Thus, in the early phases of drug discovery, the pharmaceutical industry needs reliable rapid methods to evaluate a drug lead's potential for tissue permeability. In vivo human skin research is not always feasible due to the invasiveness of biopsies and their high expense. These algorithms can be used to choose the best transdermal drugs even if they are now unaware of how to predict skin permeability (2). One would want to analyze drug absorption using human skin rather than animal skin since in-vitro investigations that rely on human skin to assess drug diffusion and metabolism generate more accurate data on absorption. Some may opt to use human skin instead of animal skin in in vitro tests to assess medication dispersion and metabolism because studies employing human skin provides more accurate absorption data than those using animal skin. (3).

SKIN

The outermost layer that offers shielding of the body is the skin that functions as an insulation to ensure safety to internal organs from transcending influence of environment.. Immune system of the skin gets altered when it challenged by the (bacteria, fungus, etc.), otherwise it's undisturbed and in an inactive state. When the immune system is altered, skin inflammation & hyperproliferation taken place, which are symptoms of the psoriasis (4).

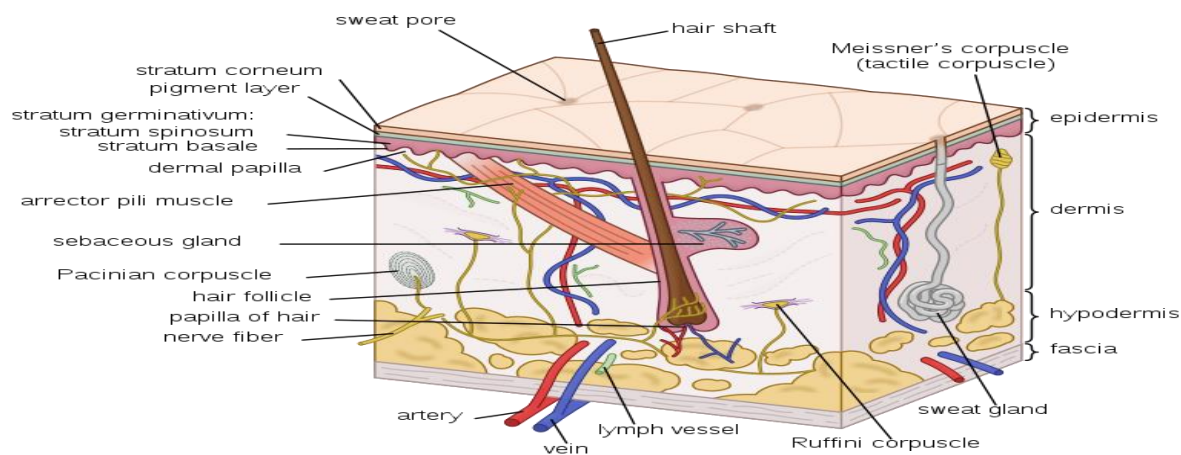


Figure 1 Skin Structure (Human skin-Wikipedia 2020)

The skin, which weighs between 2 and 6 kg, is the biggest organ in the body. (16 percent of total body weight), and covering an area of around 1.7 m². It act as a hindrance from the deleterious external factors, provides shield against bacteria and other microorganisms, UV radiation, mechanistic pressures to the tissues. However, skin is important because it is responsible for the various body functions which includes sense, touch, and body temperature regulation, provides vitamin D and waste product elimination through sweating (5).

SKIN ANATOMY

Since the outermost layer of skin cells is constantly being shed and changed by interior cells that move to the top surface, the skin is thought of as a dynamic organ that is always changing. There are numerous derivatives of skin which includes nails, hairs, sebaceous gland, apocrine glands etc. (6). Skin thickness varies according to the location where it is situated such as sole of feet and hands palm have comparatively thicker skin. Skin has three essential layers showed in Figure 1.1, which protect various different organs of the body. They are Epidermis, Dermis and Subcutis (hypodermis).

a. Epidermis and their layers

The epidermis, the skin's outermost layer, is between 0.1 and 1.4 mm thick, and keratinocytes are the primary cells in this layer that produce keratin proteins. It also comprises other cells for instance Langerhans, Melanocyte and Merkel cells. It's also anticipated that skin shed millions of cells at every 40 min which approximately around 18 kg of dead cell over a lifespan and this whole skin shedding process termed as desquamation. According to observations, the epidermis layer's stratum basale to stratum corneum transition takes place over the course of 28 to 30 days (7).

Stratum basale

The epidermis' basal cell layer consists of keratinocytes that are dividing or non-dividing. These cells are fibril keratin and melanocytes (in order to synthesize melanin). Also in the basal cell layer are the Merkel cells (to convey a sense like touch in the skin) (Montagna 2012).

Spinosum stratum layer (Malpighian)

Desmosoma connects the polyhedral cell layer, which is created by daughter basal cells migrating upward. This layer contains mostly langerhan cells (immunologically active cells).

Stratum granulomatous

The cells in these layers flatten and lose their nuclei. In actuality, keratohyalin granules are prevalent in membrane vesicles and cells, and there is extensive lysosomal activity (in the breakdown of cell components and the fragmentation of cells). 40 percent of the lipids are made up of ceramides, fatty acids, phosphate, and protein.

Stratum lucidum

In the palm and sole, where the skin is extremely dense, the nucleation of their cells takes place between the stratum granulosum and the stratum corneum.

Corneum stratum

The horny layer, which overlays sheets of polyhedral cornified cells without nuclei, is where keratinocytes mature to their full potential (corneocytes).

b. Dermis

The dermis is a thick connective tissue matrix that supports and nourishes the epidermis physically. The field substance known as connective tissue is composed of large organic molecules, protein fibres, and water (combination of the polysaccharides as complex carbohydrates and proteins). The most common type of polysaccharide in this tissue is a glycosaminoglycan (GAGS) that contains hyaluronic acid. However, this matrix of tissue is called the extracellular matrix.

c. Hypodermis or subcutaneous tissue

This layer serves to protect the dermis underneath it. Fat cells and connective tissue make up the majority of the hypodermis, which protects the interior structure. This layer can shield against trauma and act as an insulator against heat.

DRUGS ROUTES OF SKIN PENETRATION

Transepidermal route

The intercellular passage is however known as the transepidermal route, primarily used via the skin, particularly when reaching the steady state of the stratum corneum. The drug moves through narrow spaces amid the skin in this kind of permeation route (8).

Transcellular route

Transcellular route is sometimes considered an intracellular route, includes penetration by corneocytes and intercellular lipids. Compounds permeating via this route usage the inadequacies in the corneocytes that make water-based openings. Hydrophilic compounds are therefore meant to be favoured for delivery through this route (9).

Transappendageal route

Molecular movement through the sweat glands, hair follicles and sebaceous glands.

TOPICAL DRUG DELIVERY SYSTEM

Topical medication delivery systems have garnered increased attention in the previous several years for the treatment of numerous skin-related illnesses. Topical delivery is intended to limit the pharmacological effects of a medicine to the skin's surface or interior when the formulation is applied topically to treat cutaneous illnesses or the cutaneous manifestations of a systemic disease. For the delivery of any medication to the skin, drug delivery systems such as foams, sprays, medicated powders, solutions, and even medicated adhesive systems in the form of semi-solid formulations are good options. (10).

Benefits

1. First-pass metabolism prevention.
2. Easy to use and convenient.
3. Steer clear of the risks and disadvantages associated with intravenous therapy and the different factors (pH variations, enzyme levels, stomach emptying rate, etc.) that can impact absorption.
4. One can attain efficacy with a reduced daily dosage of medication by implementing continuous drug input. Prevent drug levels from changing between and within patents.

Drawbacks

1. Skin irritation or contact dermatitis may be brought on by the medication and/or excipients.
2. Some medications don't pass through the skin very well.
3. The potential for allergic reactions
4. Only those medications that need a very low plasma concentration to work can be utilised; otherwise, an enzyme in the skin may denature the medication.
5. Greater difficulty is associated with skin absorption of larger particle size medications (11).

SKIN DISEASES AND ITS TREATMENT

Skin illnesses, which impact almost 900 million people globally, are one of the most common complaints in human health. Pruritus, acne, eczema, impetigo, *Molluscum contagiosum*/warts, and scabies are all common skin illnesses (12). Other skin diseases caused by an excess of opportunistic bacteria, such as atopic dermatitis and acne vulgaris, also require intense therapy and provide a significant impact (13).

Impetigo is a contagious skin infection that causes superficial skin pustules around the nose and mouth. A bacterial illness that affects the inner layers of the skin is known as cellulitis. It affects specially the dermis and subcutaneous fat. It is a skin and subcutaneous tissue infection that is widespread. Acne vulgaris is a common adolescent skin condition believed to be caused by an increase in male sex hormones following puberty. Hair sebaceous glands get clogged and infected, resulting in irritation and pustule production. Acne is the most frequent skin disorder among teenagers and young adults aged 12 to 35 years old. (14). Other most common cause of nonfatal disease burden was skin illnesses.

As a result, skin conditions have an influence on patients' quality of life due to the emotional and social stigma they carry. Climate, cleanliness, food, and hormone fluctuations are some of the internal and external elements that affect skin disorders specifically.

Although, autonomous microorganisms are important regulators of immune retaliation and cutis defence systems. (Yu et al. 2020). A variety of skin infections have been linked to long-term deformity, stigma, and incapacity. The skin microbiota is a diverse collection of microbes that includes commensal bacteria (Clebak and Malone 2018). The makeup of these bacterial communities is influenced by the properties of the skin, which are produced by variations in follicle-to-follicle in temperature, pH, moisture, and sebum concentration. Skin illness is caused by imbalances in microbial populations that permit the establishment and colonisation of opportunistic species (15).

There is currently no treatment for these illnesses, and there is still much to learn about their causes and the function of the skin microbiome (16). Numerous allopathic antibiotics like mupirocin, dicloxacillin, cephalixin, clindamycin, trimethoprim sulfamethoxazole, penicillin, amoxicillin, ceftriaxone, clindamycin oxacillin, nafcillin, tedizolid, doxycycline, minocycline, linezolid, vancomycin and many more (17) or retinoic acids, as well as topical corticosteroids for acne and atopic dermatitis, are among the traditional treatments for skin infections (18).

Allopathy refers to the treatment of diseases with medicines that have effects that differ from those of the disease being treated. However, there are significant shortcomings with allopathic therapy, such as inefficiency in curing some chronic diseases and a wide variety of unavoidable bad effects, which must be addressed carefully in order to create an efficient and safe healthcare system (19). Allopathic treatment produces quick results, but it may not completely heal an illness, and it also has negative effects (20).

For new and re-emerging infectious diseases, a novel technology or antibacterial agent with distinct chemical structures and cutting-edge mechanisms of action is urgently needed. However, the use of allopathic drugs has been associated with a range of minor to severe adverse effects. Acne vulgaris has been related to changes in the skin's microbiome, systemic inflammation, and antibiotic resistance. On the other hand, corticosteroids gradually lose their therapeutic benefits and thin the skin, induce rosacea, and suppress melanocytes. (21). Probiotic and postbiotic-derived bioactives applied topically have shown promising results in

treating this skin disease while reducing adverse effects related by the usage of conventional treatment methods (22).

For a very long time, botanicals were considered an excellent provider of natural ingredients which have been utilized to maintain human health; in recent years, more thorough research has been done on natural cures(23).

Thus, oils and extracts made from plants were examined as an attempt for alternative therapy since they contain non-phytotoxic chemicals and have antibacterial and anti-dermatophyte characteristics. Several research groups from all around the world looked into the biological functions of therapeutic plants. These researches concentrated on the typical applications of many species, as well as public knowledge and empirical investigations explaining the usage of medicinal plants, with a focus on how these plants could help the pharmaceutical sector (24).

HERBAL FORMULATION CURRENT AND FUTURE SCENARIO

Herbal formulations or herbal medication are formed by using plant ingredients. Plants have a mixture of molecular products with varying levels of bioactivity. These molecules result in novel drugs and new approaches for the creation of drugs to treat a range of disorders.. “According to World Health Organization (WHO) in 2005, "herbal medicine," "traditional herbal medicine," or "phytomedicine" consists of plant parts having medicinal properties such as roots, stems, leaves, bark, fruits, berries, or seeds”. Only 1-2 percent of tropical genus has been discovered as therapeutic plants, despite the information that the world's flowering plant variety is 2.5 lakh species (25). Natural prescriptions, frequently known as plant materials or herbalism, are utilized to fix wounds and diseases by utilizing entire plants or divides of plants (26). Herbal drugs are therapeutic plants that are utilized to forestall and treat infections and difficulties, just as to advance well being and healing (27). Natural drugs are the world's most seasoned strategy for wellbeing care (28). Herbal medicines are widely used in health-care and as nutritional supplements (29). Many herbal preparations are utilised for various illnesses, including those of the skin. Herbal therapy is becoming increasingly popular among patients and clinicians. The practice of treating dermatologic problems topically with plant-derived medications stretches back to ancient Egypt's cultures and is still important in today's industrialised world. Herbal remedies, which have been utilised for generations, are now being researched scientifically (30). Despite the growing global popularity of herbal medicine, medicinal plant production is fraught with difficulties. In other words, the herbal medicine industry's infrastructure has not been adequately considered. The toxicity of the drug has poor quality control and medical monitoring. There is no international standard specifying the process and dosage of herbal medications, nor is there any monitoring of their side effects. Furthermore, people's knowledge of the dangers of self-medication and the potential combinations of herbal medicines with chemical pharmaceuticals is lacking, and the proper and timely use of herbal medicines has not been prioritised. These are only a few of the issues that could have an impact on herbal medicine's impact on health care (31).

Herbal medications are very effective, have fewer adverse effects, and are compatible with human physiology; but, unlike current synthetic drugs, they are not widely used in medicine. The entire revenue market for herbal drugs is 50.9 billion dollars, which is significantly smaller than the synthetic drug industry, which was 934.8 billion dollars (32).

Dosage forms of herbal formulation

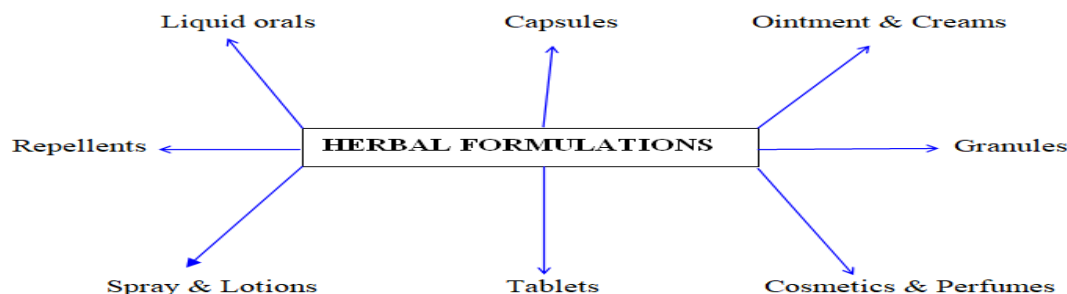


Figure 1.2 Different herbal formulations (33).

Advantages and disadvantages of herbal formulations (34)

Various advantages and disadvantages of herbal formulations are as follows

A. Herbal Medicine's Benefits

The various advantages of herbs are low or no cost, universal accessibility, increased toleration, added security, fewer adverse effects and high potency with efficiency.

B. Herbal Drugs' Negative Effect

The disadvantages of herbs are unable to treat illnesses and injuries in a timely manner, complexity in standardizations and Self-dosing risk (35).

Important medicinal plants with therapeutic values

Traditional claims have already demonstrated their promise; nevertheless, further scientific study and use in the form of a suitable formulation can validate the claim and thereby improve the therapeutic success by a factor of ten (36). All plants are commonly used in traditional medicine to treat skin disorders topically, and they are affordable and readily available, with no evidence of bacterial resistance to the whole-plant extracts. (37)

Table 1.1 Lists some of the most important plant species with therapeutic use are as follows

S. No.	Medicinal Plants	Therapeutics Activity
	Indian lilac, GawarPatha, RaktaChandana, Indian Kino,Haldi, Clove of garlic, Lemon, Aam, Belalaigajah, Seven golden candlesticks, Maddar, Bitter cucumber, Yacon, Tulsi, Samadera, Sweetwood, Anar, Mouse-ear cress,IndianAcalypha, Devil's horsehip, Malabar nut, Usnakntaka, Blumeamembranacea, The apple of sodom, White weed, Jack in the bush, Bitter vine,East Indian globe thistle and Tridax	Anti-bacterial Activity (38)

	daisy.	
	Achilleafragrantissimasima whole, Indian bael, Aloe vera, Breadfruit, Desert date, Turmeric, nut grass, Tea plant, caper bush, Wild calabash, pink rock-rose, Flax-leaved daphne, Japanese persimmon, False yellowhead, Asthma plant, Weeping fig, Fig, liquorice, Chinese liquorice, Hyssop, Spring snowflake, Msdonna lily, Houpu magnolia, Lemon balm, Pennyroyal, Horseradish tree, Nutmeg, Olive and Panax ginseng.	Antiviral Activities (39)
	Pot marigold, Oregano oil, milk thistle, neem, Sickle Senna and Sweet indrajao	Anti-psoriasis Activity (40)

Topical ointment is a new trend in delivering antibacterial agents more effectively. Because of their many advantages, topically applied medicine products are recommended for the treatment of cutaneous disorders over their systemic counterparts. Topical treatments have no adverse effects on the system because there is no systemic absorption. Additionally, they are easy to make, administer, and utilize, and they improve patient compliance. (41).

CONCLUSION

In current, various topical aliment treatments are available that developed from allopathic drugs produced moderate to severe side effects with antibiotics resistance. Considering the harmful side effects and antibiotic resistance of synthetic allopathic medicines, attention has been given towards to find an alternative approach that is much safer and efficient than allopathic medicines. Traditionally used herbal drugs showed good potential for various medicinal activities as reported in various scientific literatures.

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