CHAPTER 1

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1.1. SKIN - THE VITAL ORGAN

Skin is one of the vital organs of the body bestowed with some active and passive physiological actions of protection, sensation, heat regulation, secretion and vitamin D production. Skin is the largest organ in the body in terms of surface area and weight. Skin, being a mirror of different ailments can reflect one’s general health. Skin of infants, children, adults and the elderly with its anatomic and physiologic characteristics acts as a barrier for different environmental insults and undergoes changes in each period during human life (Kocinaj et al., 2009). The spectrum of insults to which skin is susceptible includes disorders caused by chemical and microbial agents, thermal and electromagnetic radiation and mechanical trauma. The most damaging consequence of the skin is invasion by pathogenic microorganisms. As the primary interface between the body and the external environment, the skin provides the first line of defense against broad injury and invasion by microbial pathogens and trauma. In addition skin has many active defense mechanisms (Kupper and Fuhlbrigge, 2004).

Failure of skin to function correctly as a result of wounds, infections, cancer or inherited disorder is a major cause of morbidity and disability. Skin diseases are influenced by various factors like, environment, economy, literacy and occupation and occasionally skin diseases can be manifestations of systemic diseases. Moreover, the skin is an important
target organ for HIV infection. Diseases of the skin pose serious public health problems throughout the world. The social impact of the skin failure is compounded by its visibility, unsightly skin diseases such as eczema or psoriasis, and other conditions such as albinism can lead to social rejection and a lack of confidence in one's appearance. Thus relatively minor skin complaints often cause more anguish to people than other more serious medical conditions. The loss of the so called 'look good and feel good' factor is the greatest disability of all (Burford et al., 2007)

1.2. TYPES OF SKIN DISEASES

The range of skin diseases is wide, spanning inflammatory and infection processes and dire neoplastic disorders such as malignant melanoma. The different skin conditions are far too numerous to list. However, skin conditions tend to fall into following broad categories. Inflammatory skin disorders include dermatitis, eczema, psoriasis, sebaceous cysts and diaper rash. Bacterial skin infections or pyoderma generally arise as primary infections of the skin known as impetigo or as secondary infections of other lesions such as scabies or insect bites. The usual bacterial causes are Group A streptococci or Staphylococcus aureus. Bacterial skin infections include erythrasma, impetigo, ecthyma, folliculitis, erysipelas and cellulitis. Fungal skin infections are broadly referred to as dermatomycoses. Fungi and yeasts are capable of causing many different forms of skin infections. Candida albicans, Trichophyton, Epidermophyton, Microsporum and Malassezia species are the most common fungi. Viral skin infections include chicken pox, Herpes simplex virus (Type 1), Herpes simplex virus (Type 2), measles, and warts. Human
papillomavirus (HPV) causes warts. Skin cancer includes basal cell cancer, squamous cell carcinoma and melanoma. Disorders associated with pigmentary changes range from hereditary defects such as albinism to increased pigmentation or hyper pigmentation. Skin depigmentation is also a feature of leprosy. Tropical ulcer is a common condition found mainly in children and teenagers in well-defined tropical regions which is caused by a combined infection of a number of different bacteria together with a fusiform bacterium, *Fusobacterium ulcerans*. A wide range of skin conditions may develop as a consequence of HIV infection. These include Kaposi's sarcoma and toxic epidermal necrolysis and the itchy papular eruption or papular pruritic eruption of HIV. Disorders of skin can be inherited, for example the syndrome of Ehlers-Danlos and a systemic disorder, the systemic erythematous of lupus (SLE). Ectoparasitic skin diseases or skin infestations include tungiasis, pediculosis, scabies and cutaneous larva migrans.

1.3. PREVALENCE OF SKIN DISEASES

The prevalence of skin diseases in any community depends upon various factors, namely the genetic and racial constitution, the social and hygienic standards, customs and occupations, the nutritional status and age structure of the community, climatic factors and state of industrialization. The pattern of skin diseases varies from one country to another and in various regions within the same country (Devi and Zamzachin, 2006).

The overall prevalence of skin diseases in population based studies conducted throughout the world varied from 14% to 50%. A classic example
of prevalence study was the First US National Health and Nutrition Examination Survey (HANES-1) during 1971-1974 which suggested that nearly one-third had one or more significant skin disorders with an additional 12.5% of the proportion were deemed to have a skin condition that was clinically inactive at the time of examination (Jonson, 1978). Another example in UK was the Lambeth Study in 1975 in which the overall proportion of the population found to have any form of skin diseases was 55% and only 22.5% need medical care (Rea et al., 1976). In rural areas of developing countries, wounds and dermatological conditions constitute one of the five most common reasons for people seeking medical care (Ryan, 1992). Prevalence of skin diseases in developing countries ranges from 20% to 80% (Hay et al., 1984).

Survey of two village communities in Tanzania, revealed that 27% of patients had a treatable skin disease (Gibbs, 1996). In western Ethiopia between 47% and 53% of the members of two rural communities claimed to have skin disease (Figueroa et al., 1998).

The prevalence of skin diseases amongst children, in various parts of India has ranged from 8.7% to 49.1% in school based surveys (Sharma and Sharma, 1990 and Kumar et al., 1988). Infections and infestations were the main group of dermatoses in all institution and community based prevalence studies (Sharma and Mendiratta, 1999 and Negi et al., 2001). Dermatological problems constitute at least 30% of all outpatient visits to pediatrician and 30% of all visits to a dermatologist involve children (Federman et al., 2001 and Thappa, 2002). Studies on the point prevalence of skin conditions in 12,586 Indian school children indicated that the overall point prevalence of
one or more identifiable/apparent skin conditions was 38.8%. Of those studied, 3786 children (30%) had only one skin disease, 765 (6%) had two, and 336 (2.7%) had three skin pathologies. The most common skin conditions and their respective point prevalence were skin infections (11.4%), pityriasis alba (8.4%), dermatitis/nonspecific eczemas (5.2%), infestations (5.0%), disorders of pigmentation (2.6%) and keratinization disorders (mostly keratosis pilaris) (1.3%) (Dogra and Kumar, 2003).

Rural people sustain injuries while working in the fields; burns from cooking and sleeping near fires; leg ulcers resulting from untreated wounds, diabetes, and leprosy; injuries incurred in conflicts and increasingly, injuries resulting from traffic accidents (Bodeker et al., 1999). Community based epidemiological study of wounds in India revealed the prevalence of acute and chronic wounds as 10.55 and 4.48 per 1000 population respectively (Gupta et al., 2004). The healing of wounds caused by accident, assault, warfare and surgical operations has always been a central consideration in surgical practice because any breach in continuity of skin exposes the deeper tissues to the danger of infections.

1.4. MANAGEMENT OF SKIN DISEASES

Current therapies focus on treating symptoms of skin disorders with a combination of moisturizers, antihistamines, antibiotics and corticosteroids, with the aims of repairing barrier function and reducing itch, secondary infections and inflammation. However, steroids can disrupt a number of cytokine networks involved in lymphocyte function, resulting in immune-suppression and their long-term topical use can decrease collagen
synthesis, leading to skin atrophy (Oikarinen et al., 1998). Although there have been revolutionary changes in the management and treatment of dermatologic disorders with topical therapies, these potent remedies do not always work in recalcitrant and intractable cases. When all the modern preparations have been exhausted, falling back on some old remedies often proves curative (Litt, 1989). There has been a growing trend towards natural medicines and the use of dietary supplements for modern healthcare, as people throughout the world are becoming increasingly dissatisfied with the possible side-effects, lack of noticeable long-term results and high cost associated with allopathic drugs. Herbal products have provided a more natural and often more effective alternative.

1.4.1. Herbal remedies for skin diseases

shown good anecdotal results. Plant based therapeutic preparations are cyclically returning to complement the dermatologic therapy. They serve as therapeutic alternatives, safer choices or in some cases as the only effective treatment (Dattner, 2003). In the recent years there has been increasing interest in the use of herbal therapy for dermatologic disorders (Berk and Kanzler, 2004 and Meyer et al., 2005).

The traditional practice of topically treating dermatologic conditions with plant-derived medicines predates the cultures of ancient Egypt and remains vital today in the industrialized cultures of both the United States and Europe. Recent scientific studies lend support to some of the claims of herbal practitioners for the safety and efficacy of many herbs like, lemon balm (Melissa officinalis), chamomile (Matricaria recutita) calendula (Calendula officinalis), witch hazel (Hamamelis virginiana) licorice root (Glycyrrhiza glabra and Glycyrrhiza uralensis) and Aloe vera (Brown and Dattner, 1998). Neem (Azadirachta indica) is indigenous to India, and every part of the plant has been used medicinally. In a report of more than 800 villagers in India, a paste of neem and turmeric applied topically appeared to treat chronic ulcers and scabies (Peirce, 1999).

Bedi and Shenefelt (2002) reviewed the herbal medications that show scientific evidence of clinical efficacy in the treatment of dermatologic disorders. Peirce (1999) reported that several herbs like witch hazel (Hamamelis virginiana), lady's mantle (Alchemilla vulgaris), mullein (Verbascum thapsus) and St John's wort (Hypericum perforatum) contain tannins which act as astringents. Tannins used topically are thought to be beneficial in treating dermatitis by coagulating surface proteins of cells,
thereby reducing permeability and secretion. The precipitated proteins also form a protective layer on the skin. Witch hazel (*Hamamelis virginiana*) bark extract is commonly used by making a decoction from 5 to 10 g of herb in 1 cup (0.24 L) of water. Witch hazel is considered very safe to use topically. Essential oil extracted from the leaves of *Melaleuca alternifolia* (Tea tree) play a role in topical acne treatment and has been widely used topically for the treatment of bacterial and fungal infections. Tea tree oil has shown in vitro activity against a wide variety of microorganisms, including *Propionibacterium acnes*, *Staphylococcus aureus*, *Escherichia coli*, *Candida albicans*, *Trichophyton mentagrophytes* and *Trichophyton rubrum* (Williams *et al.*, 1988). Fruit acids, such as citric, gluconic, gluconolactone, glycolic, malic and tartaric acids have been used topically and have shown promise in treating acne because of their exfoliative properties (Hunt and Barnetson, 1992). *Aloe vera* gel is obtained from the leaf and has been used topically for centuries for the treatment of wounds and burns (Syed *et al.*, 1996). Several case reports and animal studies have demonstrated that *Aloe vera* reduces burning, itching and scarring associated with radiation dermatitis (Klein and Penneys, 1988). It can be effective for genital herpes, psoriasis, human papilloma virus, seborrheic dermatitis, aphthous stomatitis, xerosis, lichen planus, frostbite, burn, wound healing and inflammation. *Calendula officinalis*, commonly known as marigold, has been used topically since ancient times and is currently approved by the German commission as an antiseptic and to heal wounds. Contemporary herbalists continue to recommend a topical preparation for the treatment of wounds, ulcers, burns, boils, rashes, chapped hands, herpes
zoster and varicose veins. Pentacyclic triterpenes, trihydroxyalcohols, flavonoids, and saponins have been isolated and may contribute to *Calendula*'s anti-inflammatory and wound-healing actions (Leung and Foster, 1996). Topical uses of *Melissa officinalis* (lemon balm) include treating herpes simplex and minor wounds. Water extracts of the leaves of *M. officinalis* have noted antiviral properties *in vitro* and have been shown to have a viricidal effect against herpes simplex virus type 1 (Dimitrova et al., 1993). Studies have demonstrated the efficacy of topical preparation of dried lemon balm extract 1% cream (Lomaherpan) (Wöbling and Leonhardt, 1994). Herpes zoster and post herpetic neuralgia have been treated with a topical licorice (*Glycyrrhiza glabra, Glycyrrhiza uralensis*) gel preparation. Glycyrrhizin, one of the active components of licorice, has been shown to inhibit replication of varicella zoster (Baba and Shigeta, 1987). Anise (*Pimpinella anisum*) seeds are a source of an essential oil that has displayed antibacterial and insecticidal activity *in vitro* and has been used topically to treat scabies and head lice (Bedi and Shenefelt, 2002). Calotropis (*Calotropis procera*) has been used in India and greater celandine (*Chelidonium majus*) has been used in China for the treatment of warts. In traditional Chinese medicine a mixture of 10 herbs (*Potentilla chinensis, Tribulus terrestris, Rehmannia glutinosa, Lophatherum gracile, Clematis armandii, Ledebouriella saseloides, Dictamnus dasycarpus, Paeonia lactiflora, Schizonepeta tenuifolia, and Glycyrrhiza glabra*) has been used in treating atopic dermatitis.
Psoriasis has been treated for centuries with herbal preparations, both topical and oral. One common Chinese herbal medicine, known as Radix Angelicae dahuricae (*Angelica dahurica*), which contains the furocoumarins imperatorin, isoimperatorin and alloimperatorin has been taken for psoriasis. The main ingredient in cayenne pepper, *Capsicum frutescens* or capsaicin, has also been studied for the treatment of psoriasis. Two clinical trials have demonstrated the efficacy of 0.025% capsaicin cream (Zostrix) in the treatment of psoriasis. The first study of 44 patients with moderate and severe psoriasis vulgaris found that application of capsaicin cream led to a significant reduction in scaling and erythema over a 6-week period (Bernstein *et al.*, 1986).

Arnica comes from the dried flowers of *Arnica montana*. Arnica has been used for centuries as an anti-inflammatory aid to rub into sore muscles and joints, bruises, insect bites, boils, inflamed gums, acne eruptions, and hemorrhoids (Peirce, 1999). German chamomile (*Matricaria recutita*), a member of the daisy family, has been used for centuries, internally and externally, for almost all ailments, most notably gastrointestinal tract symptoms, oral or skin inflammation and dermatitis.

Several herbs, flax (*Linum usitatissimum*), fenugreek (*Trigonella foenum-graecum*), English plantain (*Plantago major*), heartseases (*Viola tricolor*), marshmallow (*Althaea officinalis*), mullein (*Verbascum thapsus*) and slippery elm (*Ulmus rubra*) contain mucilage, which is useful topically to soothe and act as an emollient on skin. Mucilage quickly swells into a gooey mass when it comes in contact with water,
thereby aiding in dry or mildly inflamed skin (Peirce, 1999). Chinese herbal formula, Dabao is used for the treatment of androgenic alopecia (Kessels et al., 1991). The components of Dabao include 50% ethanol, 42% water, and 8% Chinese herbal extracts, including saffron flowers (*Crocus sativus*), mulberry leaves (*Morus alba*), stemona root (*Stemona tuberosa*), fruits of the pepper plant (*Capsicum annuum*), sesame leaves (*Sesamum indicum*), the skin of the Szechuan pepper fruit (*Pericarpium zanthoxyli*), ginger root (*Zingiber officinale*), Chinese angelica root (*Angelica sinensis*), bark of the pseudolarix (*Pseudolarix amabilis*) and fruit of the hawthorn (*Crataegus pinnatifida*). There is also evidence that black tea (*Camellia sinensis*) may play a role in the prevention of skin tumors (Javed et al., 1998). It appears that the theaflavins are the active components in chemoprevention. Red ginseng (*Panax ginseng*) is a classic traditional Chinese medicine thought to enhance immune function of the body. In a recent study, red ginseng extracts used topically appeared to inhibit chemically induced skin tumors in mice (Xiaoguang et al., 1998). Topically applied silymarin (*Silybum marianum*) appeared to possess high protective effects against chemically induced skin tumor promotion in mice (Lahiri-Chatterjee et al., 1999).

Medicinal plants continue to play a central role in the healthcare system of large proportions of the world's population. This is particularly true in developing countries, where herbal medicine has a long and uninterrupted history of use (Akerele, 1984). Interest in natural healing grows and more and more people are turning to traditional herbal remedies for relief from
pain and disease. The past may indeed become our future as experts predict that this back to nature movement is not just a fad but a sound source of valid alternative medicine which is likely to gain momentum in the years to come (Tyler, 1999). In Germany, a regulatory authority known as Commission E has performed an extensive review of common botanicals and has evaluated the quality of evidence, clinical efficacy, and uses of 300 herbal preparations (Blumenthal et al., 1998 and Bisset and Wichtl, 2001). In developed countries such as United States of America, majority of people (55%) combine alternative treatments with conventional medicine and about one-fifth of the Americans use natural supplement such as herbs for maintaining health (Stein, 2004).

The World Health Organization estimates that 80% of the people in developing countries of the world rely on traditional medicine for their primary health care needs and about 85% of traditional medicine involves the use of plant extracts. This means that about 3.5 to 4 billion people in the world rely on plants as sources of drugs (Farnsworth et al., 1985). Modern medicine or allopathy has gradually developed over the years by the scientific and observational efforts of scientists. However the basis of its development remains in the roots of traditional medicine and therapies. Nevertheless, the ancient wisdom has been the basis of modern medicine and will remain as one important source of future medicine and therapeutics. Traditional knowledge can serve as a powerful search engine which will greatly facilitate intentional, focused and safe natural product drug discovery. Traditional knowledge and experiential database can provide new functional leads to reduce time, money and toxicity, the three main hurdles in the drug
development (Patwardhan, 1992). The history of drug discovery implies that the ethnobotanical approach is the most productive of the plant-surveying methods and recent findings confirm that impression. Approximately, 119 pure chemical substances extracted from higher plants are used in medicine throughout the world and 74% of the 119 chemical compounds used as drugs have the same or related use as reported in medicinal folkloric information. Therefore documentation of folk uses of medicinal plants offers opportunities for medical research before the knowledge disappears (Farnsworth et al., 1985).

It is estimated that 265,000 flowering species inhabit the earth. Of these, less than half of one per cent has been studied exhaustively for their chemical compositions and medicinal values. In a world with limited financial resources, it is impossible to screen each of the remaining species for biological activity. In the late 1970s and early 1980s, several groups of scientists independently set off to different corners of the world for the express purpose of finding innovative drugs through ethnobotanical research. Ethnobotanists interested in drug discovery often rely on healers to identify plants that are likely to contain potent bioactive chemicals. Many healers are elderly and lack apprentices. As they die, much of their knowledge of local vegetation dies, too. Plant knowledge seems to be disappearing even faster than the forests themselves. Ethnobotanists choose the societies located in a floristically diverse area such as, a tropical rain forest. Such diversity dramatically increases the number of plants available. It therefore enhances the likelihood that plants with pharmacologically active molecules will be pressed into service (Cox and Balick, 1994).
1.5. SCIENTIFIC VALIDATION OF TRADITIONAL MEDICINES

The evaluation and authentication of traditional remedies can contribute towards the formulation of an integrated healthcare system combining both local and western practices (Cotton, 1996). This involves the documentation, standardization, and testing of the efficacy and toxicity of the extracts of medicinal plants, and the identification of the active principles. WHO (1993) has formulated research guidelines for evaluating the safety and efficacy of herbal medicines. Thus pharmacological screening of traditional medicinal plants is of vital importance both to provide a scientific basis for the continued use of the plants, thereby validating their historical utilization by traditional healers and to provide society with sources of new, effective and safe drugs (Taylor et al., 2001). Drug discovery strategies based on natural products and traditional medicines are re-emerging as attractive options. Drug discovery and development need not always be confined to new molecular entities. Rationally designed, carefully standardized, synergistic traditional herbal formulations and botanical drug products with robust scientific evidence can also be alternatives (Patwardhan and Mashelkar, 2009). The traditional uses of many medicinal plants have been scientifically validated (Villegas et al., 1997; Jaswanth et al., 2001; Bedi and Shenefelt, 2002; Biswas and Mukherjee, 2003; Samy et al., 2006; Duraipandiyan et al., 2006 and Khalil et al., 2007).

In view of these facts, that the ethnobotanical approach is actually one of several methods that can be applied in choosing plants for
pharmacological studies, the present investigation is undertaken to gather information on traditional medicines for skin diseases from all possible sources viz. vaidyas, village elders, shepherds, forest dwellers and tribals of Courtallam region and to validate the ethnotherapeutic claims of the selected medicinal plants of Courtallam region used for skin diseases. The selected medicinal plants, *Acalypha fruticosa* Forrsk. (Euphorbiaceae) and *Dipteracanthus patulus* (Jacq.) Nees. (syn. *Ruellia patula* Jacq.) (Acanthaceae) have been subjected to systematic pharmacognostical, phytochemical and pharmacological studies.
1.6. MAIN OBJECTIVES

The main objectives of the present investigation are:

1. To gather information on traditional medicines for skin diseases from all possible sources viz. vaidyas, village elders, shepherds, forest dwellers and tribals of Courtallam region (Tenkasi and Shenkottai taluks of Tirunelveli District of Tamil Nadu, India).

2. To evaluate the Pharmacognostical profiles of the two selected medicinal plants, *Acalypha fruticosa* Forssk. and *Dipteracanthus patulus* (Jacq.) Nees. (syn. *Ruellia patula* Jacq.)

3. To perform qualitative analysis of phytochemicals in various extracts. To estimate quantitatively the percentage of elements and the various secondary metabolites present in the two plants *Acalypha fruticosa* Forssk. and *Dipteracanthus patulus* (Jacq.) Nees (syn. *Ruellia patula* Jacq.).

4. To perform the GC-MS studies of the extracts of *Acalypha fruticosa* Forssk. and *Dipteracanthus patulus* (Jacq.) Nees (syn. *Ruellia patula* Jacq.).

5. To validate the ethnotherapeutic claims of the selected plants used in skin diseases, wound healing activity of the extracts of the plants, *Acalypha fruticosa* Forssk. and *Dipteracanthus patulus* (Jacq.) Nees (syn. *Ruellia patula* Jacq.) has been studied.
1.7. REFERENCES


