SUMMARY
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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. 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. Failure of skin to function correctly because of wounds, infections, cancer or inherited disorder is a major cause of morbidity and disability.

The overall prevalence of skin diseases in population based studies conducted throughout the world varied from 14% to 50%. In rural areas of developing countries, wounds and dermatological conditions constitute one of the five most common reasons for people seeking medical care. 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. Approximately one-third of all traditional medicines are meant for treatment of wounds or skin disorders, compared to only 1-3% of modern drugs.

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. 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.

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.

The evaluation and authentication of traditional remedies can contribute towards the formulation of an integrated healthcare system combining both local and western practices. 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. 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.

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* Forssk. (Euphorbiaceae) and *Dipteracanthus patulus*
(Jacq.) Nees. (syn. *Ruellia patula* Jacq.) (Acanthaceae) have been subjected to systematic pharmacognostical, phytochemical and pharmacological studies.

**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 Taluk, Tirunelveli District, 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 the phytochemicals of the 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 analysis 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 carried out by excision and dead space wound models.
The thesis is organized into FIVE chapters.

Chapter 1 provides the general introduction. It highlights the types of skin diseases, prevalence of skin diseases, herbal remedies for skin diseases, need for evaluation and authentication of traditional remedies. The scientific validation of traditional medicines involving documentation, standardization, and testing of the efficacy and toxicity of the extracts of medicinal plants, and the identification of the active principles. The main objectives of the present investigation are also highlighted in this chapter.

Chapter 2 deals with the documentation of traditional herbal remedies for skin diseases from phytodiversity rich Courtallam region (Tenkasi and Shenkottai taluks of Tirunelveli District, Tamil Nadu, India). The present study has been performed with the aim of producing an inventory of the plants used for various skin diseases in the study area. Information on traditional medicines for skin diseases has been gathered from all possible sources viz. vaidyas, village elders, shepherds, forest dwellers and tribals of Courtallam region. The present study enumerates the uses of 62 plant species belonging to 39 families to treat skin diseases. Of which 23 plants have been used for treating wounds. Comparison of the information received from this study with that of the previously reported literature revealed that the uses of the following plants viz, *Acalypha fruticosa* Forssk. and *Dipteracanthus patulus* (Jacq.) Nees. (syn. *Ruellia patula* Jacq.) have not been mentioned in the Dictionary of Indian folk medicine and Ethnobotany.

Chapter 3 describes the pharmacognostical profiles of the selected medicinal plants, *Acalypha fruticosa* Forssk. and *Dipteracanthus patulus*
Macroscopic and microscopic features of the root, stem and leaf of the two plants, *Acalypha fruticosa* Forssk. and *Dipteracanthus patulus* (Jacq.) Nees. have been described. Physico-chemical parameters like loss of weight on drying, total ash, acid-insoluble ash, water-soluble ash, extractive values of the aerial parts of *Acalypha fruticosa* and the leaves of *Dipteracanthus patulus* have been determined. The fluorescence characteristics of the powder and the extracts of the aerial parts of *Acalypha fruticosa* and the leaves of *Dipteracanthus patulus* are discussed.

Chromatographic fingerprint analyses of the pharmacologically active ethanolic extract of the aerial parts of *Acalypha fruticosa* and methanolic extract of the leaves of *Dipteracanthus patulus* have been presented. The results of the present study provide pharmacognostical reference for the aerial parts of *Acalypha fruticosa* and the leaves of *Dipteracanthus patulus*, which can be used as a diagnostic tool for the correct identification of the drugs and also to test adulteration if any.

Chapter 4 deals with the phytochemical studies on the aerial parts of *Acalypha fruticosa* and the leaves of *Dipteracanthus patulus*. The results on the qualitative analysis of the phytochemicals of the various extracts and the quantitative estimation of elements and the various secondary metabolites like alkaloids, flavonoids, phenols, steroids and tannins present in the two plants, *Acalypha fruticosa* Forssk. and *Dipteracanthus patulus* (Jacq.) are presented. Flavonoids are found to be present in high amount when compared to alkaloids, tannins, phenols and steroids in both the plants. As the ethanolic extract of *Acalypha fruticosa* and the methanolic extract of *Dipteracanthus patulus* are pharmacologically active (exhibited wound healing activity) the
compounds present in the ethanolic extract of *Acalypha fruticosa* and the methanolic extract of *Dipteracanthus patulus* have been identified by GC-MS. Further the selective column chromatographic fractions of the methanolic extract of the leaves of *Dipteracanthus patulus* and the white powdery mass obtained from the petroleum ether extract of the aerial parts of *Acalypha fruticosa* are also subjected to GC-MS analysis and the results are discussed. n-Hexadecanoic acid, 9,12-Octadecadienoic acid (z,z) and 1,2-Benzenedicarboxylic acid diisooctyl ester from the ethanolic extract and α-D-glucopyranoside and Eicosyltrichlorosilane from the white powdery mass obtained from the petroleum ether extract of the aerial parts of *Acalypha fruticosa* have been identified. The compounds identified from the methanolic extract of the leaves of *Dipteracanthus patulus* are: Octane 3, 3-dimethyl, 2, 6-Dimethyl-6-trifluoroacetoxoctane, Tetradecane, 4-Hydroxy-2methylpyrrolidine-2-carboxylic acid, Hexadecane, Octadecane, 1,2-Benzenedicarboxylic acid Bis(2-methylpropyl) ester, Hexadecanoic acid methyl ester, Dibutyl phthalate, n-Hexadecanoic acid, Hexadecanoic acid ethyl ester, 9,12-Octadecadienoic acid (z,z), 9,12,15-Octadecatrienoic acid methyl ester (z,z,z), Linoleic acid ethyl ester, 9,12,15-Octadecatrienoic acid ethyl ester (z,z,z), Octadecanoic acid ethyl ester and 1,2-Benzenedicarboxylic acid diisooctyl ester.

From the selective column chromatographic fraction of the methanolic extract of the leaves of *Dipteracanthus patulus*, L-alanine 1,1-dimethylethyl ester hydrochloride, Clivorine-(12-acetylxyloxy)-14,15,20,21-tetradehydro-15,20-dihydro-8-n, 5H-Cyclopropa[3,4]benz[1,2-e]azulen-5-one, 2-Methyl-4-benzyl-(n-benzyltrifluoroacatamido)oxazole and Methyl12-N-hexyl-octadecanote are identified.
Quantitative determination of elements in *Acalypha fruticosa* indicated that the concentration of macroelements (K, Na, Ca, Mg and S) ranges from 0.01% to 4.23% and that of the microelements (Zn, Cu, Fe, Mn, Bo and Mo) ranges from 0.02 ppm to 87.62 ppm. In *Dipteracanthus patulus* the concentration of macroelements ranges from 0.16% to 4.16% and the microelements ranges from 0.02 ppm to 84.59 ppm. Of the macroelements analyzed, calcium is present in high amount followed by magnesium and potassium in *Acalypha fruticosa*. In *Dipteracanthus patulus*, the concentration of magnesium is high followed by calcium and potassium. Among the minor elements, iron and manganese are present in higher quantity in both the plants. The concentration of copper is more in *Dipteracanthus patulus* when compared to *Acalypha fruticosa*. Substantial amount of Zinc is present in both the plants.

Chapter 5 deals with the validation of the traditional claims of *Acalypha fruticosa* Forssk. and *Dipteracanthus patulus* (Jacq.) Nees. (syn. *Ruellia patula* Jacq.) as they are being used in the study area for skin diseases and in particular to the treatment of wounds. The ethanolic extract of aerial parts of *Acalypha fruticosa* and the methanolic extract of the leaves of *Dipteracanthus patulus* are investigated for their wound healing activity by excision and dead space wound models in rats. Excision wound inflicted by cutting away approximately 500 mm², full thickness of skin from the depilated area on the back under light ether anaesthesia. Two types of formulations of extract ointment (5% w/w) and (10% w/w) are prepared by incorporating 5 g and 10 g of extract in 100 g of simple ointment base as per British Pharmacopoeia for topical administration. The ointments (0.5 g each) are
applied topically with a fine brush once daily till the wound is completely healed. Excision wound model is used to monitor wound contraction. Wound contraction which contributes for wound closure or reduction in the wound area is expressed as percentage reduction of the original wound area (500 mm$^2$).

Dead space wounds are made by implanting subcutaneously a polypropylene tube (2.5 x 0.5 cm) beneath the dorsal para-vertebral lumbar skin, under light ether anaesthesia. On the 11$^{th}$ day, the granulation tissues formed on the implanted tubes have been dissected out carefully. The wet weight of the granulation tissue is noted. Tensile strength of the granulation tissue has been measured. The granulation tissue is dried in a hot air oven at 60°C for 12 hours and the dry weight is recorded. The granulation tissues have been subjected to histological study. Dead space wound provides an opportunity to study the effect of wound agents on granulation and collagenation of the healing process.

The results of the present study demonstrated that the ethanolic extract of *Acalypha fruticosa* and the methanolic extract of *Dipteracanthus patulus* promote wound healing. The results of the present study provide pharmacological evidence on the traditional use of the plants, *Acalypha fruticosa* and *Dipteracanthus patulus* as wound healing agents as well as indicate that these plants satisfy the criteria of the wound healing agents by increasing the rate of contraction of wound, weight of granulation tissue, tensile strength of granulation tissue and formation of collagen.
FUTURE PROSPECTS

The use of these herbal drugs over the years by the traditional healers is indicative of their safety for the claimed uses. However, toxicity and skin sensitivity studies have to be carried out for all the plants enumerated in this study.

All the standardization parameters determined in this study are conducted on plants collected from the same locality. Therefore, similar work is recommended on the same species collected from different localities in the country, for reproducibility of results.

Further investigation on the isolation and characterization of the bioactive compound(s) by modern chromatographic and spectroscopic techniques will lead to the development of new drugs.