Defence Life Science Journal, Vol. 10, No. 2, April 2025, pp. 154-165, DOI : 10.14429/dlsj.19791

Pathophysiology of Dermatophytes and Potent Phytochemical Sources as Possible Applications against *Trichophyton* Spp.

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ABSTRACT

Trichophyton infections are typically restricted within the epithelial keratinized layer of the skin and therefore grouped among the dermatophytoses. Different species of *Trichophyton* viz., *T. mentagrophytes, T. rubrum* and *T. violaceum* are the important causal agents for the dermatophytic disorders. Azole drugs are extensively employed in the therapeutic practice to treat dermatomycosis. Use of synthetic drugs can cause a number of side effects and may induce drug resistance to the patients. Therefore, plant extracts have been widely investigated as alternative for chemical drugs to solve this problem. Literature data revealed that specific plants showed inhibiting effect against particular species of *Trichophyton* because of their different phytochemical contents. This study is carried out to document different plant species for their antifungal activity against various species of *Trichophyton*. Total of 107 plant species belonging to 50 families have been gathered for their antifungal activity against nine species of *Trichophyton* species viz., *T. asahii, T. erinacei, T. inkin, T. ovoides*, *T. schoenleinii, T. longifusus, T. soudanense, T. tonsurans* and *T. verrucosum.*

Keywords: Antifungal activity; Dermatophytosis; Organic solvents; Plant extracts; *Trichophyton*

NOMENCLATURE

Leaf	:	L
Stem	:	St
Young shoots	:	YS
Root/ Rhizome	:	R
Bark	:	B
Flower/Catkin	:	Fl
Fruit/ Berries/ Pericarp	:	Fr
Seed	:	S
Whole Plant	:	WP
Oil	:	O
Mucilage	:	M
Latex	:	L
Galls	:	G
Bulb	:	B

1. INTRODUCTION

Dermatophytoses represent a significant portion of all cutaneous mycoses around the world. Clinical expression of dermatophytosis depends on the species of pathogen, site of infection, and immunological responses of patients[1]. Dermatophytosis is the most superficial infection over keratinized tissues like skin, nails, and hair, causing chronic or sub-acute infection. Dermatophyte disorders are confined to the epidermis, but in immune-compromised patients, they can be invasive, resulting in severe widespread infections[2]. Three anamorphic genera of dermatophytes are there, viz., *Epidermophyton, Microsporium,* and *Trichophyton.* Amongst these, various *Trichophyton* species like *T. rubrum, T. mentagrophytes, T. terrestre,* and *T. violaceum* are the important causal agents for dermatophytic disorders amongst other genera of dermatophytes. Derm Common anti-mycotic drugs such as azoles, allylamines, polyenes and echinocandins are used to treat dermatomycosis. The allylamines stop ergosterol synthesis by inhibiting another enzyme i.e., squalene epoxidase[3]. Polyene agents like amphotericin B, pimaricin and nystatin react with the sterols of cell membrane (ergosterol and cholesterol in fungal and human cell membranes respectively) and form passages through the membrane, making it leaky. Echinocandins are lipopeptide molecules that damage the cell wall of the dermatophytic fungus by inhibiting (1,3) beta-d-glucan synthase enzyme which is responsible for synthesizing the fungal cell wall component glucan[4]. Azole groups of antifungal drugs viz., fluconazole, itraconazole and ketoconazole arrest cytochrome P_{450}-dependent enzymes especially C14-demethylase. This enzyme is associated with ergosterol synthesis which is an essential constituent of fungal cell membrane. Azole drugs are generally employed in the therapeutic practice for treating dermatomycosis which leads to different side effects and may induce drug resistance. Popping up of drug-resistant strains in all fungal species has been reported.

Received : 23 January 2024, Revised : 30 November 2024
Accepted : 13 January 2025, Online published : 07 April 2025

Common anti-mycotic drugs fail over time and resistance can develop in improper use of these drugs such as either too low dosages or the treatment course is not enough. Therefore, fungi have become resistant to antifungal drugs such as azoles, allylamines, polyenes and echinocandins. Thus, traditional medicines are well-established for practice in dermatology practices[5].

Herbal medicines and herbal preparations have been playing a unique role in treating and cure health disorders from ancient time till date and about 40,000 to 70,000 medicinal herbs are used as traditional medicines across the globe[6]. Medicinal products are currently obtained from the plants directly or indirectly highlighting the plant-based medicines. Plant-based antimicrobial secondary metabolites are effective in treating infectious diseases minimizing many side effects of the synthetic ones[7]. Because of the sessile nature of the plants, they can produce remarkably abundant chemical compounds that are complex consisting multiple chiral centres[8]. These compounds are difficult in synthesizing chemically in a sustainable approach. These natural molecules have proved to have wide range of therapeutic activities[9]. Traditional herbal medicine showed antifungal activity against fungal pathogenic dermatophytic fungi *Trichophyton*[7, 10,11]. In this review article, data regarding antifungal activity of different medicinal plant extracts including the active drug molecules against different species of *Trichophyton* is compiled which will help to find the drug molecules from natural sources.

2. MATERIAL AND METHODS

An extensive literature search was made to investigate the plant sources against dermatophytic infections caused by *Trichophyton* species. To gather the relevant information, scientific databases viz. Google Scholar, Science Direct, PubMed, Scopus, Web of Science and Wiley online data bases were used to search the articles and data was generated from the published articles using the key words such as skin diseases, *Trichophyton,* plant sources, traditional medicines, phyto-chemical compounds and antifungal activity were run separately on these mentioned online search servers. In addition, plant list databases like e-flora of India and Wikipedia were also used to verify the correct names of plant species. Search criteria were restricted to publications in English language. Phytochemical structures are derived from the PubChem database.

3. DIVERSITY OF TRICHOPHYTON SPP. AND PATHOPHYSIOLOGY

Dermatophytes can be classified according to their habitat into three categories such as anthropophilic, geophilic or zoophilic fungal species responsible for dermatophytosis. Geophilic dermatophyte species survive in the soil and depend on the contact with keratinized cells, human beings are infected by anthropophilic dermatophytes only while animals and sometimes humans are infected by zoophilic dermatophytes.

Trichophyton species is one of the causal organisms for dermatophytosis. On the basis of the affected site, dermatophytosis has been classified as tinea corporis (superficial skin infection of the body), tinea barbae (beard), tinea faciei (infection on face), tinea manus (hand infection), tinea cruris (jock itch), tinea capitis (ringworm of scalp and hair shafts), tinea pedis (athlete's foot) and tinea unguium or onchomycosis (nail infection) along with other two dermatophyte genera viz., *Epidermophyton* and *Microsporium*[12].

3.1 Pathophysiology Associated with *Trichophyton* Infections

Trichophyton spores come in contact with the epidermal layer from infected persons or animals or in some cases from the soil. Any change in the natural condition of the stratum corneum and hair follicular ostium like humidity or any injuries provides the nutritional and pH requirements of dermatophytes. Arthrospores can remain alive for several months outside the host and adhere to the keratinocytes within two hours of inoculation[13]. Dermatophytes secrete proteases viz. subtilisins. Proteases are diagnosed as virulence factors that play a crucial role during penetration. Dermatophytes also produce sulfites and reducing agents, which allow proteases to degenerate keratin, which acts as a nutrient source. Proteases have been diagnosed as virulence components. After the adherence to human keratinocytes, which are the significant constituents of hair, nails, and skin, the fungus will degrade the keratinocytes by producing keratinase enzyme, establishing the symptoms of ringworm Fig. 1. Then the dermatophytes invade the stratum corneum[14].

Animal models and clinical studies revealed that, under specific conditions, it can penetrate the dermis, then enter the lymph nodes and infect the internal organs. Subcutaneous injection of *T. mentagrophytes* in mice resulted in spreading into lymph nodes, liver, and spleen[15]. Lymphatic proliferation has been reported concerning proximal white subungual onychomycosis, including deep dermatophytosis in humans[16]. An infection that appears in the surrounding area of the nail lunula may be an indication of auto-reinfection from a deeper region but not a new infection. Dermatophytes can spread to lymph nodes in people who lack CARD9 (caspase recruitment domain-containing protein 9)[17]. Antifungal defense of dermatophytes is influenced by both innate and adaptive immunity.

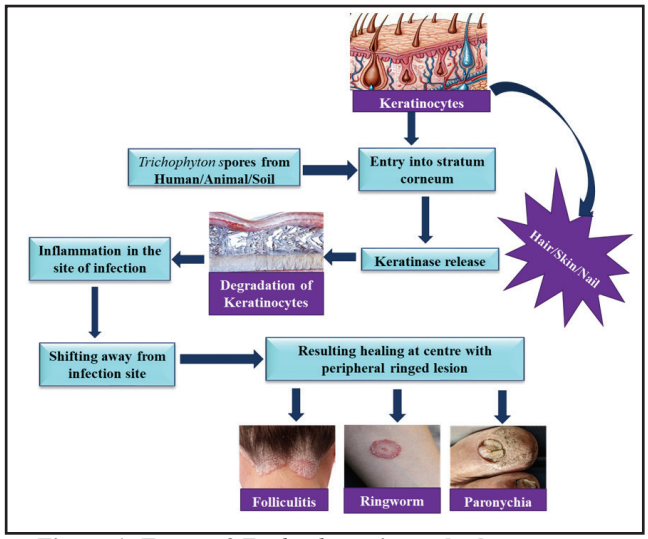

Figure 1. Entry of *Trichophyton* in to the host system.

In mice models, the recognition of dermatophytes is mediated by C-type lectin receptors viz., DECTIN-1, DECTIN-2, or MINCLE. DECTIN-1 recognizes *T. rubrum* conidia, and DECTIN-2 recognizes hyphae[18] inducing an intracellular signaling cascade along with CARD9 adaptor protein[17]. This process stimulates pro-inflammatory cytokine production, which is essential for mobilizing immune cells to the infection site. It was discovered that within four hours of infection, conidia of *T. rubrum* are consumed by peritoneal mice macrophages that release TNF- α and IL-10. Conidia produce hyphae inside macrophages after eight hours of infection[19]. Dermatophytes can suppress host defense by developing virulence factors. *T. rubrum* is acclimatized to human skin, resulted in chronic and non-inflammatory lesions[15].

3.1.1 Natural inhibition in Trichophyton infections

Normal human skin and other epithelia can synthesize a number of chemical compounds having antimicrobial properties to protect from the potential cutaneous pathogens. Sweat and sebum contain β defensins such as β defensin-1 and 2 an unsaturated transferrin that inhibits the growth of the dermatophyte in the epidermis. Sebaceous glands produce unsaturated long chain fatty acids which also inhibit the growth of the dermatophyte. β defensin-1 and 2 are cysteine-rich anti-microbial peptides. It has been shown that these two peptides are expressed in the epithelial tissue. Human β defensin-1 is expressed in different sites of human body whereas, β defensin-2 is exhibited in facial and foreskin in comparison with abdominal and breast skin. It has been shown that both β defensin peptides in humans are restricted to the malpighian layer and stratum corneum of the epidermis. This localization of β defensin peptides plays an important role in protecting the skin by building innate immunity[20].

3.1.2 Pharmacological evidence of plant sources against Trichophyton species

An extensive search of the literature revealed that different extracts from various plant sources such as leaves, branches, stem, stem barks, aerial parts, flowers, catkins, essential oil, latex, mucilage, seeds, stem, fruits and fruit peel of 107 plant species have been reported to show antifungal activity against dermatophytic fungus *Trichophyton* (Table 1).

Total of 107 plant species belonging to 50 families revealed antifungal activity against nine species of *Trichophyton* species *viz., T. asahii, T. erinacei, T. inkin, T. ovoides*, *T. schoenleinii, T. longifusus, T. soudanense, T. tonsurans* and *T. verrucosum* (Fig 2).

Leaves of 62 plant species belonging to 33 families have been reported for the antifungal activity against six species of *Trichophyton* viz. *T. mentagrophytes, T. terrestre,T. rubrum, T. simii, T. tonsurans* and *T. violaceum.*Out of these 62 species, 48 species show inhibiting activity against *Trichophyton rubrum*, 19 species against *T. mentagrophytes,* seven species against *T. violaceum,* three species against *T. terrestre* and one species each for *T. simii* and *T. tonsurans*.

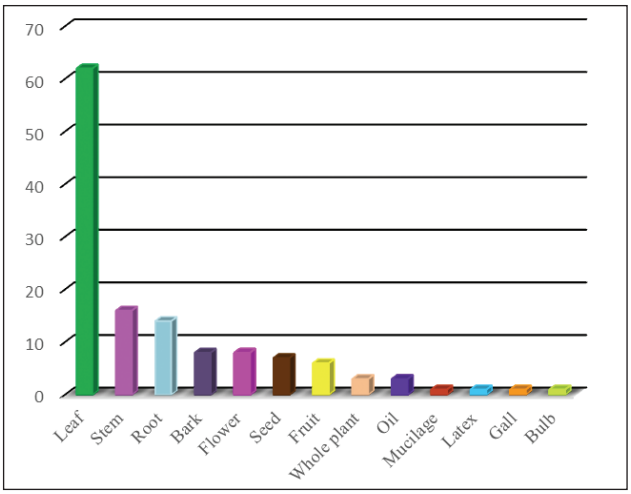

Figure 2. Plant sources showing antifungal activity against *Trichophyton* sps.

Stem extracts of *C. citratus* showedactivity against *T. terrestre* and *T. rubrum* while *P. suberosa* and *T. avicennioides* stem extracts inhibits *T. mentagrophytes* IP 9415. Young branches or shoots of seven plant species like *A. campestris, J. gendarussa, L. inermis, P. lentiscus, P. suberosa, R. raetam* and *S. melongena* shows activity against *Trichophyton* species. *A. lebbek, A. reticulata*, *B. alleghaniensis, S. auriculata, S. anacardium,* and *Z. jujuba* species inhibited the growth of *T. rubrum* and *B. alleghaniensis, P. suberosa, T. avicennioides* showed activity against *T. mentagrophytes* (Table 2).

Table 2 also reveals that the roots of 11 plant species belonging to 11 families showed antifungal activity against *Trichophyton* species. Rhizome of three plant species such as *A. nudicaulis, C. longa* and *Z. officinale* shows activity against *Trichophyton* species. Rhizome of *A. nudicaulis* shows activity in defence of *T. mentagrophytes, T. tonsurans* and *T. rubrum*. Rhizome of *C. longa* and *Z. officinale* show activity against *T. rubrum*. Flower extracts of six plant species and catkin extract of two species viz., *P. tremuloides* and *A. viridis* restricted the growth of *T. rubrum, T. mentagrophytes* and *T. tonsurans*. However, fruit extract of four species, fruit peel of *P. granatum* and berries of *J. communis* inhibited the growth of different species of *Trichophyton.* Seed extracts from seven plant species such as *A. indica,C. oleterius, P. nigrum, P. anisum, R. communis, S. foetida* and *S. jambolanum* exhibited inhibitory activities. It has been reported that methanolic seed extracts of *P. anisum* showed a 22 mm Zone of Inhibition (ZOI) against *T. Rubrum*. Whole plant of *A. luteus* and *A. arvensis* against *T. violaceum; P. rupestre* against *T. mentagrophytes* and *T. rubrum*[22]. Other plant sources such as mucilage, latex, galls, crude oils are also proved for having antifungal activity against different species of *Trichophyton*. More research is needed to find out the potent new drug molecule to treat the resistance strains of *Trichophyton*. Bark extracts of eight plant species such as *A. lebbek, Annona reticulata*, *B. alleghaniensis, P. suberosa, Senna auriculata, S.*

Table 1. Quantification of plant parts with respect to family showing activity against *Trichophyton* species.

Family	*L	St	YS	R	B	Fl	Fr	S	WP	O	M	L	G	B
Acanthaceae	#1		1											
Acoraceae				1										
Amaranthaceae	2													
Amaryllidaceae														1
Anacardiaceae	3		1		1									
Annonaceae	2				1									
Apiaceae				1				1						
Apocynaceae	5													
Araliaceae				1										
Asparagaceae	1			1										
Asphodelaceae											1			
Asteraceae	1		4			1			1					
Betulaceae					1	1								
Boraginaceae	1			1										
Capparaceae				1		1								
Caricaceae	1													
Combretaceae	1	2	1	1	2								1	
Cucurbitaceae	3													
Cupressaceae							1							
Euphorbiaceae	2							1				1		
Fabaceae	9	1	1	1	2	2		1						
Geraniaceae							1			1				
Juglandaceae	1						1							
Lamiaceae	6									1				
Liliaceae				1					1					
Lythraceae	1		1				1							
Malvaceae	1							2						
Meliaceae	1									1				
Menispermaceae	1													
Moraceae	1													
Myrtaceae	1							1						
Oleaceae	1													
Onagraceae				1										
Papaveraceae	1													
Phyllanthaceae	1													
Piperaceae	1		1					1						
Plumbaginaceae	1			1										
Poaceae	1													
Primulaceae									1					
Rhamnaceae					1									
Rosaceae	2	1												
Rubiaceae						1								
Rutaceae	2			1										
Salicaceae						1								
Santalaceae	1													
Solanaceae	4		1				2							
Verbenaceae	1					1								
Xanthorrhoeaceae	1													
Zingiberaceae				2										
Zygophyllaceae			1											

(*Leaf: L, Stem: St., Young shoots: YS, Root/ Rhizome: R, Bark: B, Flower/Catkin: Fl, Fruit/ Berries/ Pericarp: Fr., Seed: S, Whole Plant: WP, Oil: O, Mucilage: M, Latex: L, Galls: G, Bulb: B)
(#Numbers indicate the plant species in a particular family and the blank boxes indicates that no data is available for different plant parts having antimicrobial activity against *Trichophyton* species*)*

Table 2. Pharmacologicl/preclinical evidence of leaf extracts of plant species against *Trichophyton* species.

S. No.	Plant name	Family	Extracts/plant parts	Fungal species	Reference
1.	*Achyranthes aspera* L.	Amaranthaceae	Methanol/leaf	Trb	21
			Petroleum ether/leaf	Trb MTCC 1344	21
			Chloroform/leaf	Trb MTCC 1344	21
			Ethyl acetate/leaf	Trb MTCC 1344	21
2.	*Acorus calamus* L.	Acoraceae	Methanol/Root	Ttn, Tmt,Trb	22
3.	*Aegle marmelos* L.	Rutaceae	Methanol/leaf	Trb, Tmt	7, 21
				Trb	24
4.	*Albizia lebbek* (L.)Benth.	Fabaceae	Bark	Trb	25
5.	*Allium cepa* L.	Amaryllidaceae	Bulb	Trb	26
6.	*Aloe arborescens* Miller.	Asphodelaceae	Mucilage from fresh leaf	Tas,Tov, Tin	27
7.	*Alnus viridis* DC.	Betulaceae	Catkins	Ttn, Tmt,Trb	28
8.	*Aloe vera* L.	Xanthorrhoeaceae	Petroleum ether/Leaf	Trb	21
9.	*Amaranthes spinosus* L.	Amaranthaceae	Leaf	Trb	23
10.	*Anacardium occidentale* L.	Anacardiaceae	Ethanol/Leaf	Tmt, Trb	7
11.	*Anagallis arvensis* L.	Primulaceae	Whole plant	Tvl	29
12.	*Anchusa strigosa* L.	Boraginaceae	Methanol/Leaf	Tvl	30
			Aqueous/Root	Tvl	29
13.	*Annona squamosa* L.	Annonaceae	Methanol/Leaf and bark	Trb	25
14.	*A. reticulata L.*	Annonaceae	Methanol/Leaf	Trb	21
15.	*Aralia. nudicaulis* L.	Araliaceae	Aqueous/Rhizome	Ttn,Tmt, Trb	28
16.	*Argemone mexicana* L.	Papaveraceae	Methanol/Leaf	Trb	21
17.	*Artemisia campestris* L.	Asteraceae	Aqueous/Young shoot	Ttn,Tmt, Trb	28
18.	*A. frigida* Willd.	Asteraceae	Aqueous/Aerial parts	Ttn,Tmt, Trb	28
19.	*Asparagus racemosus* L.	Asparagaceae	Ethanol/Leaf(Cladode)	Tmt, Ttr	31
20.	*Asphodelus luteus* L.	Liliaceae	Whole plant	Tvl	32
21.	*A. microcarpus* Salzm. & Viv.	Liliaceae	Aqueous/Root	Tvl	33
22.	*Azadirachta indica* L.	Meliaceae	Ethanol/Leaf	Tmt	7
			Water/leaf	Trb	7
23.	*Betula alleghaniensis* Britt.	Betulaceae	Bark	Ttn,Tmt, Trb	28
24.	*Butea monosperma* L.	Fabaceae	Methanol/Leaf	Trb	21
25.	*Cajanus cajan*	Fabaceae	Chloroform Leaf	Trb	34
26.	*Calotropis gigantean* L.	Apocynaceae	Methanol/Leaf	Trb	35
27.	*Capparis spinosa* L.	Capparaceae	Aqueous/Root	Tvl	27
28.	*Carica papaya L.*	Caricaceae	Ethanol/Leaf	Trb	36

29.	*Cassia alata* L.	Fabaceae	Leaf	Tmt, Trb	7
30.	*C. auriculata* L.	Fabaceae	Ethyl acetate Flower extract	Trb	37
31.	*C. fistula* L.	Fabaceae	Ethyl acetate Leaf	Trb	25
32.	*C. occidentalis* (L.) Rose.	Fabaceae	Seed	Tmt, Ttr	31
33.	*C. oleterius* L.	Malvaceae	Seed	Trb	21
34.	*Catharanthus roseus* L.	Apocynaceae	Methanol/Leaf	Trb	38
35.	*Coccinia indica* L.	Cucurbitaceae	Ethyl acetate/Leaf	Trb	21
36.	*Croton urucurana* Baill.	Euphorbiaceae	Latex	Tmt, Ttn, Trb	39
37.	*Curcuma longa* L.	Zingiberaceae	Methanol/Rhizome	Trb	40
38.	*Cymbopogon citratus* (DC.) Stapf.	Poaceae	Leaf essential oil	Ttr, Trb	41
39.	*Datura metel* L.	Solanaceae	Acetone/Leaf	Trb	42
40.	*Emblica officinalis* L.	Phyllanthaceae	Methanol/Leaf	Trb	21
41.	*Epilobium angustifolium* L.	Onagraceae	Ethanol/Root	Ttn,Tmt, Trb	43
42.	*Euphorbia tirucalli* L.	Euphorbiaceae	Leaf	Trb	21
43.	*Eucalyptus citriodora* Hook.	Myrtaceae	Oil	Tmt, Trb	44
44.	*E. globules* L.	Myrtaceae	Aqueous Leaf	Tmt	45
45.	*Ficus racemosa* L.	Moraceae	Methanol/Leaf	Trb	21
46.	*F. virginiana* L.	Rosaceae	Alcoholic Leaf	Ttn,Tmt, Trb	46
47.	Glycyrrhiza lepidota(Nutt.) Pursh	Fabaceae	Aqueous/Root	Ttn, Trb	28
48.	*Heracleum maximum* W. Bartram	Apiaceae	Aqueous/Root	Ttn,Trb	28
49.	Hyptis suaveolens L.) Poit.	Lamiaceae	Ether Leaf	Trb	47
50.	*Hibiscus rosa-sinensis* L.	Malvaceae	Ethanolic Leaf	Trb	48
51.	*Ixora coccinea* L.	Rubiaceae	Flower	Trb	21
52.	*I. viscosa* L.	Asteraceae	Aqueous/Leaf	Trb,Tmt	49
53.	*Jatropha gossypifolia* L.	Euphorbiaceae	Aqueous/Ethanol/Leaf	Trb,Tmt	7
54.	*Juglans regia* L.	Juglandaceae	Leaf	Tvl	29
			Fruit	Tmt, Tvl	29
55.	*Juniperus communis* L.	Cupressaceae	Berries	TtnTmt, Trb	50
56.	*Justicia gendarussa* Burm.f.	Acanthaceae	Chloroform/Leaf	Tmt	49
			aqueous /Young shoot	Tmt	49
57.	*Lantana camara* L.	Verbenaceae	Leaf	Trb,Ttr, Tmt	41
			Flower (Petroleum ether extract)	Tmt MTCC 7687	52
58.	*Lawsonia inermis* L.	Lythraceae	Acetone/leaf	Tmt,Trb	21
			Methanol: water (70:30)/Leaf	Trb	21
59.	*Luffa cylindrica* (L.) M. Roem.	Cucurbitaceae	Ethyl acetate Leaf extract	Trb	53
60.	*Mangifera indica* L.	Anacardiaceae	aqueous Leaf extract	Trb	54
61.	*Milletia pinnata* (L.) Panigrahi	Fabaceae	Petroleum ether/Leaf	Trb	21
62.	*Momordica charantia* L.	Cucurbitaceae	Aqueous/Leaf	Trb	55
63.	*Nerium oleander* L.	Apocynaceae	Aqueous/Leaf	Trb,Tmt	55
64.	*Ocinum basilicum* L.	Lamiaceae	Crude Leaf	Trb,Tmt	56
65.	*O. gratissimum* L.	Lamiaceae	Ethanol/Leaf	Tmt	56

66.	*Olea europaea* L.	Oleaceae	Ethanol/Leaf	Tmt, Trb	56
67.	*Pelargonium graveolens* L. Her.	Geraniaceae	Fruit	Tsc, Ter, Tsd	57
68.	*Pimpinella anisum* L.	Apiaceae	Seed	Trb	24
69.	*Piper nigrum* L.	Piperaceae	Seed	Ttr, Ttn	59
70.	*P. regnellii* (Miq.) C. DC.	Piperaceae	Leaf (super critical CO_2 extraction)	Tmt	60
71.	*P. umbellatum* L.	Piperaceae	Ethanol/Aerial part	Trb	61
72.	*Pistacia lentiscus* L.	Anacardiaceae	Methanol:water(70:30)/ Leaf	Tmt, Tvl	62
73.	*P. europaea* L.	Plumbaginaceae	Leaf	Tvl	62, 29
74.	*Phagnalon rupestre* (L.) DC.	Asteraceae	Ether/Aerial part	Tmt, Trb	63
75.	*Plumbago zeylanica* L.	Plumbaginaceae	Ethanol/Root	Tmt, Trb	64
76.	*Populus tremuloides* Michx.	Salicaceae	Catkins	Ttn,Tmt, Trb	28
77.	*Potentilla simplex* Michx.	Rosaceae	Aqueous/Leaf Aqueous/Stem	Trb Trb	28 29
78.	*Psoralea corylifolia* L.	Fabaceae	Methanol/Seed	Trb,Tmt	11
79.	*Pteleopsis suberosa* Engl. et Diels.	Combretaceae	Methanol /Ethanol Stem	Tmt IP 9415	65
80.	*Punica granatum* L.	Lythraceae	Peel of fruit	Tmt ATCC 1481, Trb ATCC 28189	66
81.	*Retama raetam* (Forssk.) Webb & Berthel.	Fabaceae	Ethanol/Leaf	Tvl	36
82.	*Ricinus communis* L.	Euphorbiaceae	Seed	Trb	21
83.	*Ruscus aculeatus* L.	Asparagaceae	Root	Tvl	29
84.	*S. fruticosa* Mill.	Lamiaceae	Ethanol/Leaf	Tvl	67
85.	*Santalum album* L.	Santalaceae	n-hexane/Leaf	Trb	10
86.	*Solanum melongena* L.	Solanaceae	Chloroform/Leaf	Tmt	51
87.	*Solanum nigrum* L.	Solanaceae	Methanol/Leaf	Tmt, Trb, Tvl	21
88.	*Sterculia foetida* L.	Malvaceae	Seed	Trb	21
89.	*Semecarpus anacardium* L.	Anacardiaceae	Bark	Trb	21
90.	*Senna alata* (L.) Roxb.	Fabaceae	Flower	Tmt, Tvr	7
91.	*Senna auriculata* (L.) Roxb.	Fabaceae	Aqueous/Stem	Trb	68
92.	*S. tora* (L.) Roxb.	Fabaceae	Ethyl acetate/Leaf	Trb	21
93.	*Solidago gigantean* Ait.	Asteraceae	Flower	Ttn, Tmt, Trb	28
94.	*Syzygium jambolanum* DC.	Myrtaceae	Seed	Tmt, TrbMTCC7859	69
95.	*Tamarindus indica* L.	Fabaceae	Chloroform/Leaf	Trb	21
96.	*Tectona grandis* L.	Lamiaceae	Ethyl acetate/Leaf	Trb	21
97.	*Terminalia avicennioides* Guill. & Perr.	Combretaceae	Ethanol/Leaf/Root	Tmt IP 9415	70
98.	*T. chebula* L.	Combretaceae	Methanolic extract Galls	Tmt, Trb, Tsd	71
99.	*Thevetia nerrifolia* Juss. Ex A. DC.	Apocynaceae	Ethyl acetate/Leaf	Trb	21
100.	*Tinospora cordifolia* (Willd.) Hook. F. & Thoms.	Menispermaceae	Ethyl acetate/Leaf	Trb	21
101.	*Toddalia asiatica* (L.) Lam.	Rutaceae	Ethyl acetate/Leaf /Root	Tmt, Tsm	72
102.	*Tribulus terrestris* L.	Zygophyllaceae	Ethyl Acetate/Methanol/ Aerial parts	Trb	21
103.	*Tridax procumbens* L.	Asteraceae	Aerial parts	Trb	21
104.	*Vitex negundo* L.	Lamiaceae	Methanol/Leaf	Trb	21
105.	*Wrightia tinctoria* R. Br.	Apocynaceae	Leaf with coconut oil	Trb	73
106.	*Zingiber officinale* L.	Zingiberaceae	Methanol/Rhizome	Trb	21
107.	*Ziziphus jujuba* Mill.	Rhamnaceae	Bark	Trb	74

(*T. asahii*: Tas; *T. erinacei*: Ter; *T. inkin*: Tin; *T. longifusus*: Tlg; *T. mentagrophytes: Tmt; T. ovoides*: Tov; *T. rubrum*: Trb; *T. schoenleinii:* Tsc; *T. simii*: Tsm; *T. soudanense*: Tsd; *T. terrestre:* Ttr, *T. tonsurans:*Ttn; *T. verrucosum*:Tvr; *T. violaceaum*: Tvl)

anacardium, T. avicennioides and *Z. jujuba* reported to show anti-mycotic activity against *Trichophyton* species. Amongst these species *B. alleghaniensis* bark extracts reported to show inhibiting activity against *T. tonsurans, T. rubrum,* and *T. mentagrophytes*[28].

It was previously reported in the literature that, out of 64 evergreen woody species, extracts of 56 species showed antimycotic activity of *T. mentagrophytes* against Athlete's foot[75]. *Toddalia asiatica* leaf extracts show activity against *T. simii* and *F. virginiana* leaf extracts show activity against *T. tonsurans*. Methanolic extract obtained from the leaf of *A. marmelos* showed a 16mm zone of inhibition against *T. rubrum*[22]. Nine plants from the family Fabaceae have shown activity against different species of *Trichophyton* followed by six species from Lamiaceae, five from Apocynaceae, four from Solanaceae, three each from Anacardiaceae and Cucurbitaceae and two each from Amaranthaceae, Annonaceae, Euphorbiaceae, Rosaceae and Rutaceae(Fig. 3).

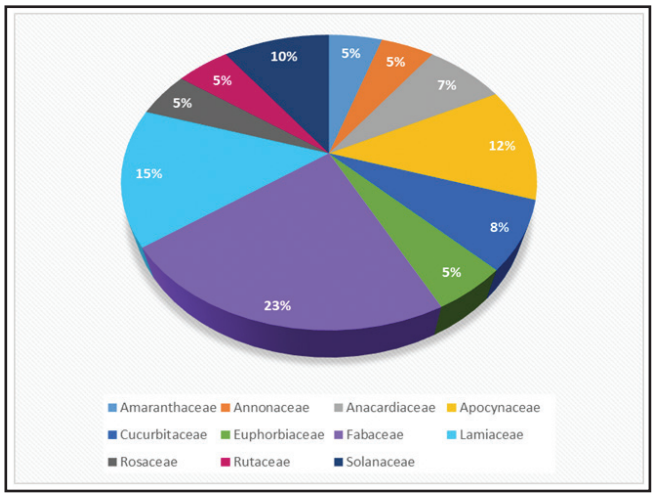

Figure 3. Leaf extracts from plants belonging to various families.

The phylogenic tree is drawn to identify a close relation between reported plant families based on the inhibiting activity against *Trichophyton* species causing dermatophytosis. In the dendrogram cluster. Some families are very closely related to each other and some are far from different (Fig. 4). Among these 50 families, Acorcaceae has been reported to have the longest recitation gap from Xanthorrhoeaceae.

3.2 Phyto-Compounds against *Trichophyton* Species

Phytochemical constituents of specific plant extracts depend upon the solvents used in the extraction process. The amount of active constituents relies on a number of components like collection time of the plant material, season of collection, climatic conditions and the soil types including the solvents. It was reported that geographical location also plays an important role and it was shown that *P. aduncum* leaf extract contains high sesquiterpene in Panama samples and the presence of monoterpenes in samples collected from Bolivia[76]. Furthermore, phenylpropanoid dillapiol has been detected in *P. aduncum* leaves in Amazonian species, but it has not been identified in the specimens collected from the southern region of Brazil[77]. Plant extract contains complex compounds, and biological activity depends on the combined effects of the constituents. Therefore, it is tough to assign its activity to a specific compound.

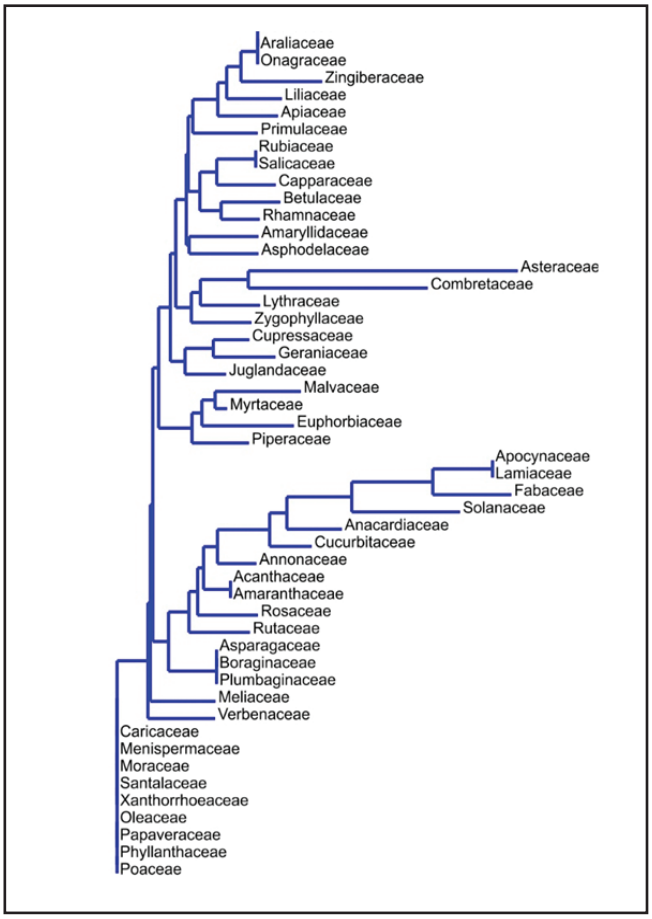

Figure 4. Dendrogram cluster in identifying relations and similarities between different plant families against Trichophyton species.

5. CONCLUSION

Scientific evidence is essential for the future utilisation of these plants in finding the drug molecules in the treatment of dermatophytic infections resulting by *Trichophyton* species. Aggregated data indicates the use of different plant sources such as leaves, roots, aerial parts, stems, bark, flower, catkins, fruits, fruit peel, seeds, essential oil, whole plants, gums, mucilage, and galls in *Trychophyton* infection. It is evident that organic solvents are better extraction solvents than water, and the response of *Trychophyton* species varied with

solvents used for extraction as well as with the plant parts. The use of these sources will help to reduce the dependence on synthesized drugs. This may also reduce the emergence of resistant strains to various synthetic antifungal medicines. Proper treatment depends on the species involved, the infection area, and the extent of the infection, including the efficacy, safety measures, and pharmacokinetics of the available drugs.

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