

## Dermatophytosis and Antifungal Therapies in various Systems with Special Emphasis on Homoeopathy: A Narrative Review

### Dermatofitosis y terapias antifúngicas en varios sistemas con énfasis especial en la homeopatía: una revisión narrativa

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#### ABSTRACT

Superficial skin diseases are mainly caused by dermatophytes. Skin affections caused by these dermatophytes are commonly known as ringworm or Tinea or dermatophytosis. Generally, these infections are not that much of serious, but if the infection becomes chronic and resistant to commonly used topical antifungal drugs, it would be very difficult to treat Dermatophytes. *Trichophyton rubrum* is the main causative agent of dermatophyte fungal infections followed by *T. mentagrophyte*. Treatment for these acute and chronic conditions in the conventional system is ineffective. Many studies revealed that Homoeopathic Medicines, Herbals, Siddha Medicines, Ayurvedic Medicines work effectively for these conditions.

The present review reveals the effectiveness of Homoeopathic Medicines, Herbals, Siddha Medicines and Ayurvedic Medicines for superficial fungal infections in clinical and *in-vitro* studies against dermatophytes. Articles published in relevant studies are summarized by different computerized database literature searches (searches were made in PubMed, Google Scholar, Research Gate and Cochrane).

Keywords: Homoeopathy, Dermatophytes, Dermatophytosis, *Trichophyton rubrum*, Antifungal, invitro, Siddha, Ayurveda, Ringworm, Tinea.

#### RESUMEN

Las enfermedades superficiales de la piel son causadas principalmente por dermatofitos. Las afecciones de la piel causadas por estos dermatofitos se conocen comúnmente como tiña o tiña o dermatofitosis. En general, estas infecciones no son tan graves, pero si la infección se vuelve crónica y resistente a los medicamentos antimicóticos tópicos de uso común, sería muy difícil tratar los dermatofitos. *Trichophyton rubrum* es el principal agente causal de las infecciones fúngicas por dermatofitos seguido por *T. mentagrophyte*. El tratamiento de estas condiciones agudas y crónicas en el sistema convencional es ineficaz. Muchos estudios revelaron que los medicamentos homeopáticos, las hierbas, los medicamentos Siddha y los medicamentos ayurvédicos funcionan de manera efectiva para estas afecciones.

La presente revisión revela la eficacia de los medicamentos homeopáticos, las hierbas, los medicamentos Siddha y los medicamentos ayurvédicos para las infecciones fúngicas superficiales en estudios clínicos e in vitro contra dermatofitos. Los artículos publicados en estudios relevantes se resumen mediante

diferentes búsquedas bibliográficas en bases de datos computarizadas (las búsquedas se realizaron en PubMed, Google Scholar, Research Gate y Cochrane).

Palabras clave: Homeopatía, Dermatofitos, Dermatofitosis, *Trichophyton rubrum*, Antifúngico, *in vitro*, Siddha, Ayurveda, Tiña, Tiña.

Key Messages: In this study, the prevalence of ringworm i.e., tinea or dermatophytosis and manifestations of *Trichophyton rubrum* infections, various *in-vivo*, *in-vitro* studies, clinical trial, brief introduction of antifungal treatment with Ayurvedic, Herbal, Siddha and Homoeopathic medicines in the management of dermatophytosis have been discussed under various headings.

## INTRODUCTION

Dermatophytes are filamentous fungi that mainly affect the superficial keratinized part of skin, hair and nail. <sup>[1, 2]</sup> These are generally transmitted by direct contact from infected people (anthropophilic organisms), animals (zoophilic organisms) and soil (geophilic organisms). <sup>[2, 3, 4]</sup> The most common dermatophyte fungi that cause ringworm belong to three types of genera. They are *Trichophyton*, *Microsporum* and *Epidermophyton*. <sup>[2, 5]</sup> *Trichophyton rubrum* is the most prominent anthropophilic dermatophyte of the phylum Ascomycota. <sup>[6,7]</sup> It infects only superficial keratinized tissue (Skin, Hair and Nails) and moist areas of skin without involving living tissue. These are more common in tropical and subtropical countries. According to World Health Organization (WHO), the prevalence rate of superficial mycotic infection worldwide has been found to be 20-25 %. In rural India overall, the prevalence of superficial fungal infection is 27.6%, among which dermatophytic infection is 75.6% and non-dermatophytic infection is 24.4%. <sup>[8]</sup> The main objective of this review is to explore this crucial subject and will emphasize the different systems with special emphasis on Homoeopathy in the treatment of dermatophytosis.

## METHODOLOGY

Data Synthesis:

Electronic databases such as PubMed, Google Scholar, Research Gate, and Cochrane, as well as published literature, were used to find the literature for this review. Additional relevant studies were found in the reference lists of the papers. The search strategy was created to encompass all *in-vitro* and antifungal studies, Case reports using the descriptors that were published between 2009 to 2021.

Study selection:

The author reviewed the titles, abstracts as well as full articles to remove the duplicates.

Inclusion criteria:

Case reports, case studies, *in-vitro* studies on homoeopathic medicines, Ayurveda and Siddha in the area of tinea/ ringworm published in journals and websites were included. Articles in the English language were only included.

Exclusion criteria:

Only abstracts, letters to editors, conference proceedings and comments were excluded. Articles other than English language were excluded.

Selection of Databases: PubMed, Google Scholar, Research Gate, and Cochrane

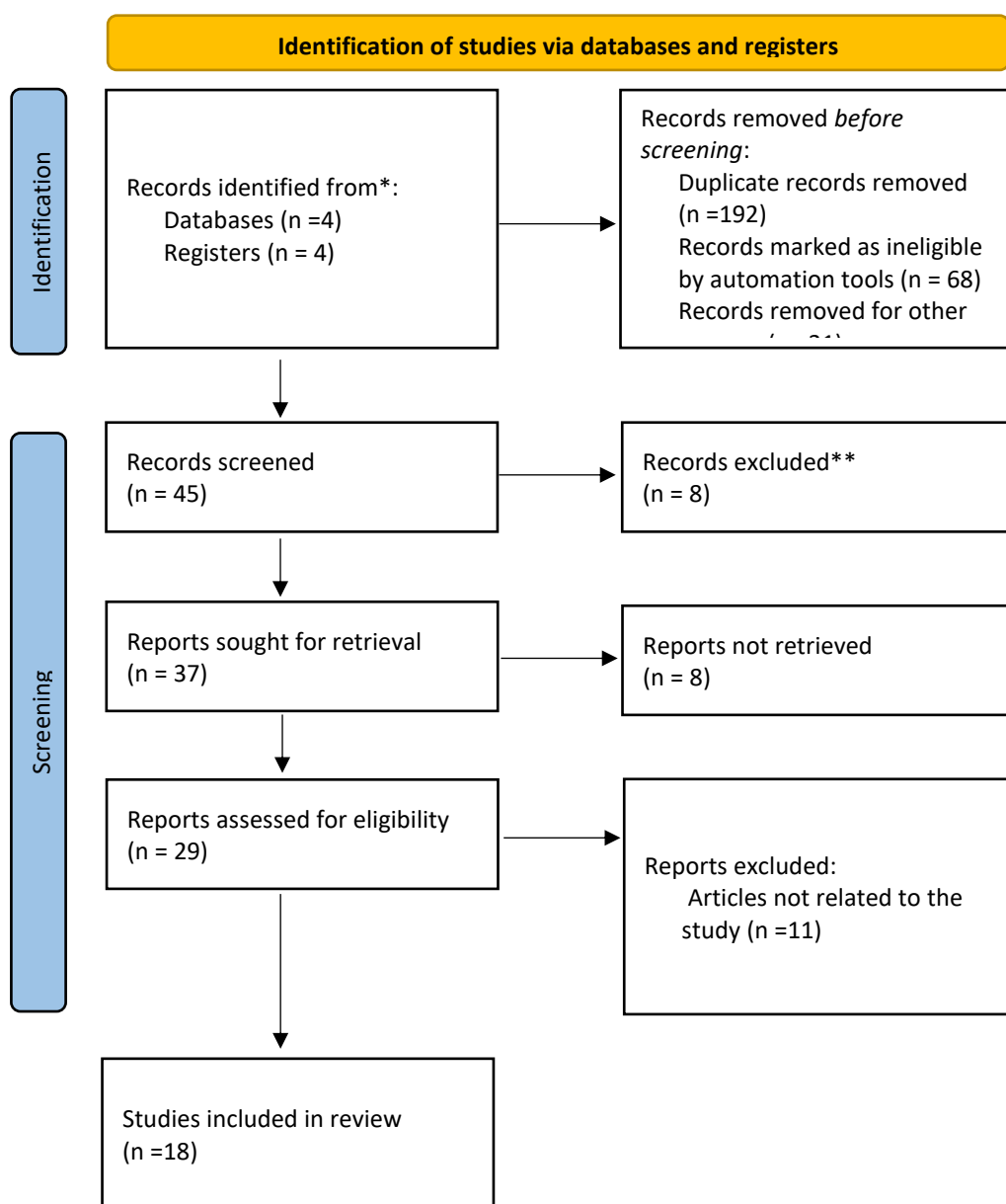
Selection of Keywords:

Homoeopathy, Dermatophytes, Dermatophytosis, *Trichophyton rubrum*, Antifungal, *in vitro*, Siddha, Ayurveda, Ringworm, Tinea

## RESULTS

The literature survey was carried out to find the relevant scientific data published between 2009 to 2021 reporting case reports, case studies and *in-vitro* studies on homoeopathic medicines, Ayurveda and Siddha in the area of tinea/ ringworm. This study included 18 full articles for review after excluding the duplicates and non-related data [Table.1].

Table.1 The Study flow diagram



### Dermatophytosis or Ringworm:

Dermatophytosis is a superficial skin condition caused by dermatophytes. [2] It is commonly known as ringworm (because of its round, itchy, and inflammatory patches seen in the common form of the disease) or tinea. [2, 9] General manifestations of ringworm are erythematous, raised, a scaly ring with central clearing. [10] It is contagious and can spread through direct contact from person to person from animals, soil and even from

contaminated things such as clothes or bedclothes. <sup>[4, 8, 11]</sup> Its lesions may sometimes become widespread and have a significant impact on social, psychological, and occupational health-compromising the quality of life. <sup>[9]</sup> It is more prevalent in tropical and subtropical countries like India where the heat and humidity are high for most of the year. <sup>[8]</sup>

Depending upon the body part or area involved in the fungal infection, tinea is classified into various types, they are tinea corporis (infection of extremities and trunk), tinea pedis or athlete's foot (infection of feet), tinea cruris or crotch itch (infection of the groin), tinea unguinum or onychomycosis (infection of nails), tinea capitis (infection of the scalp) and tinea barbae (infection of beard). <sup>[4, 6, 7, 11]</sup> In the recent past, there has been a failure of treatment with available conventional therapy and the emergence of an epidemic of chronic, recurrent dermatophytosis is been found in and around India.

Ringworm can be diagnosed by thorough case taking, history, proper physical examination, and through microscopy method by Potassium hydroxide (KOH) stain. (It is inexpensive, easy to perform and has high sensitivity). <sup>[10]</sup>

Homoeopathy is the second most popular system of medicine which is being used in the world. Homoeopathy is mainly based on the principle '*Similia Similibus Curentur*'. This came into light after repeated experiments done on himself, his family members and friends by Dr. C. F. S. Hahnemann the founder of homoeopathy. <sup>[12]</sup> Ringworm can be treated homoeopathically when prescribed constitutionally based on totality of symptoms by highly diluted homoeopathic medicines which are prepared by potentization. <sup>[12, 13]</sup>

#### Studies on Dermatophytes collected from Animals:

In domestic animals and pets, dermatophytosis is the commonly seen condition. The prevalence of dermatophyte infection in different animals is 45%-53.3%. *Begum et al*, in 2021, conducted a study by collecting 157 samples from animals with microscopy and *in-vitro* studies. Among all the agents, *T. Mentagrophyte* is more common followed by *M. canis* in animals. The author concludes that for diagnosis of dermatophytosis direct microscopy and *in-vitro* culture studies plays an important role. The most effective antifungal drug is clotrimazole and fluconazole shows the least antifungal activity. <sup>[14]</sup> *Meenakshi et al*, in 2012, presents *in vitro* study of dermatophyte samples found in dogs in Jaipur. The results show that *Psoralea corylifolia* Essential Oil possesses inhibitory actions against various fungi. The author concluded that these plants extracts could be used as antiseptic and anti-fungal agents with a suggestion of further studies are required to establish it as a topical agent. <sup>[15]</sup> *Paryuni et al*, in 2020, demonstrates that dermatophytosis is a zoonotic fungal infection seen in animals that is mainly caused by three genera of fungi namely *Microsporum*, *Trichophyton* and *Epidermophyton*. In animals localized alopecia, erythema and crust are the clinical manifestations of ringworm. Cortisol and pro-inflammatory cytokines with increased levels play an important role in ringworm infection. Concludes that factors like the type of dermatophyte species infecting; virulence of the agent; and the immune status, age, and gender of the host plays an important role in dermatophyte infections. <sup>[16]</sup>

#### Dermatophytosis in Paediatric Group:

*Gandhi et al*, in 2019, demonstrates that among the skin complaints, most commonly dermatophyte infections were seen in 10-14 years of age group children with 19% prevalence including male and female infection rate as 1.27:1. In people living in rural areas with 72% prevalence and 64% in low socioeconomic background. Among all the dermatophyte manifestations tinea corporis possesses the highest incidence rate. Overcrowding and lack of awareness about fungal infections and hygiene, poor knowledge about treatment for these dermatophyte infections among the common public are the major contributing factors for these fungal infections. <sup>[17]</sup>

#### Antifungal studies in Various systems

#### Studies with Allopathic medicines

The treatment of superficial fungal infections should have attention regarding precipitating factors of the disease like skin moisture in choosing a proper antifungal therapy. Systemic therapy must be given to the cases that develop resistance. The steroids should be used with caution, as these potentially causes atrophy and complications to the patient. <sup>[18]</sup> In allopathy for the treatment of ringworm, many antifungal agents are commonly available in the form of topical or oral medications. The commonly used drugs for dermatophytosis or ringworm are Terbinafine, Naftifine, Griseofulvin, Itraconazole, Ketoconazole, Fluconazole and Clotrimazole. Clotrimazole is the best antimycotic agent against dermatophytes followed by Terbinafine and Griseofulvin. <sup>[19, 20, 21]</sup> More research gaps in dermatophytosis management as well as lack of updates in national and international guidelines for it, increase difficulties in the management of dermatophytosis. <sup>[22]</sup>

Few studies like, *Chen et al*, in 2009, showed the direct inhibition of hyphal growth activity of Acidic mammalian chitinase (AMCase) in *in-vitro* against *Candida albicans*, *Aspergillus fumigatus* and *Trichophyton rubrum* strains by the disc diffusion susceptibility test, macro-dilution method and MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide] method. According to the author natural AM Case inhibits the growth of the dermatophytes. <sup>[23]</sup> *T. rubrum* is susceptible to Terbinafine and Luliconazole. <sup>[21, 24]</sup> *Pakshir et al*, in 2009, shows the antifungal activity of six antifungal drugs against several fresh clinical dermatophyte Iranian isolates. The anti-fungal drugs studied by the author were Terbinafine, Griseofulvin, Clotrimazole, Miconazole, Fluconazole and Ketoconazole with the isolates belonging to three genera and eight species like *Trichophyton mentagrophytes*, *T. rubrum*, *Epidermophyton floccosum*, *T. violaceum*, *Microsporum gypseum*, *T. tonsurans*, *T. verrucosum*, *T. schoenleinii*, including an unknown dermatophyte. Demonstrates that all the above drugs are the most ideal antifungal drugs for the treatment of dermatophytosis and Clotrimazole is the best antimycotic agent against dermatophytes followed by Terbinafine and Griseofulvin. <sup>[19]</sup> As the Fungi are becoming resistant and as there are many side effects a need of developing safer therapies for the treatment of dermatophytosis or ringworm or tinea is there.

#### Studies with Herbals and Siddha medicines

Siddha is one of the AYUSH systems of medicines. <sup>[25]</sup> In Siddha, skin diseases are classified into 18 Kuttas. Pundareega kuttam is one and can be correlated to dermatophytosis. <sup>[26]</sup> Medicinal plants and some formulations in Siddha system are helpful in the treatment of dermatophytosis. <sup>[26, 27]</sup> All the medicinal plants possess valuable medicinal properties with phytochemical components like glycosides, tannins, alcohols, aldehydes etc. Old traditional medicines prepared by Siddha showing relevance in today's *in-vitro* studies which are carried out with appropriate parameters. <sup>[27]</sup> *Rajarethinam et al*, in 2019, in a clinical case study of dermatophytosis or tinea which is analogous to Padarthamarai kuttam, was treated with Kandhaga Rasayanam, a Siddha herbo-mineral formulation having Sulphur (mineral ingredient) showed positive results. After treatment patient improved and scrapings of lesions showed negative results for the infection. Further evaluation studies are needed to validate the Kandhaga Rasayanam and other herbal plants in the treatment of Padarthamarai kuttam. <sup>[25]</sup>

#### Studies with Ayurvedic medicines

Skin disorders in Ayurveda are known by word 'Kushtha'. Most of the medicines in Ayurveda are not tested for their efficacy and toxicity as sufficient clinical studies are lacking. For the treatment of skin ailments, Dadrughna Lepa oil & cream formulations are potential as antifungal therapy against common fungi *Microsporum canis*, *Trichophyton rubrum* & *Epidermophyton floccosum* <sup>[28]</sup>. As well Virechana karma, a procedure in Panchakarma gives very promising results when it is followed by internal medicines for the treatment of tinea cruris. <sup>[29]</sup> *Gomes et al*, in 2013, in an *in-vitro* study, where 28 Ayurvedic preparations were tested for antimicrobial activities which were used to treat superficial skin infections. Pathogens selected for the study were *Trichophyton rubrum*, *Microsporum gypseum*, *Candida albicans*, *Malassezia furfur*, *Staphylococcus*

*aureus* and *Streptococcus pyogenes*. Among 28 preparations only two Ayurvedic preparations (Mixture of *Terminella chebula*, *Terminella bellerica* and *Embllica officinalis* and other with *Terminella chebula* only) have the antimicrobial activity against all the microorganisms tested. So, Ayurvedic decoctions prepared from *T. chebula*, *T. bellerica*, *E. officinalis* mixture and *T. chebula* could be used as universal treatment for superficial infections caused by microorganisms. <sup>[30]</sup> *Rajalekshmi et al*, in 2020, in a study reported that, single drug for specific dermatophyte species to encourage, diagnose specific treatment by explaining the action of *Tvakchurna* an extract of *Dinesavalli* which showed the significance for both chloroform and ethanol extracts. Among all extracts, chloroform extracts showed the highest significance. Methanol extracts showed only minimal inhibition zone and were statistically insignificant, whereas ethanol extracts showed the highest result. <sup>[31]</sup>

Studies with Homoeopathic medicines:

#### Case studies and Case reports in Homoeopathy

Homoeopathic medicines are cost-effective and with less or no side effects, works well for infectious diseases and also has significant effects as antifungal or antidermatophytic activity. <sup>[32, 33]</sup>

*Singh et al*, in 2020, demonstrate the activity of Homoeopathic drugs for dermatophyte fungal infections by treating a case series of 5 fungal infected cases with selected homoeopathic drugs. The drugs selected were *Sanicula aqua* (30C, 200C); *Sepia succus* (30C, 200C), *Mercurius solubilis* (30C, 200C) and *Sulphur* (30C, 200C) showed significance against dermatophyte infections with the importance of hygiene management. <sup>[32]</sup> *Uttamchandani et al*, in 2019, explains the effectiveness of ultrahigh diluted Homoeopathic drugs as antifungal agents against the dermatophytes. Homoeopathic medicines *Rhus toxicodendron* (30C, 200C), *Arsenic album* 30C and *Apis mellifica* (30C, 200C) showed significant result against dermatophytes. Author concludes that, case report study needs further studies of phase 1 clinical trials to have more considerable evidence for mechanism of action of ultrahigh diluted homoeopathic medicines. <sup>[33]</sup> *Bala et al*, in 2019, reported a case of 'Ringworm' in a 65 years old female, which was treated with individualized constitutional Homoeopathic medicine based on the totality of symptoms that cured the patient. The author concluded the importance of anti-miasmatic prescription in cases of suppressed symptoms with other therapies. <sup>[34]</sup> *Dixit et al*, in 2020, presented a case of 40 years old male presented with complaints of several coin-like eruptions on chest, shoulder and back. He prescribed the drug *Sepia* based on totality of symptoms and proper repertorization. After follow-ups up to 17 weeks patient showed marked improvement. This study concludes that homoeopathic medicine works significantly when selected based on individualization in tinea infections. However, results from a single case study won't be conclusive and there is a need for large, designed studies which gives evidence that homeopathy plays a major role in tinea corporis. <sup>[35]</sup> *Gupta et al*, in 2019, presents a case of 40years old female suffering with Tinea corporis which was successfully treated by Homoeopathy with drug *Rumex crispus* selected based on individualization. The author used 'keynote prescription' on the basis of PQRS symptoms for the selection of drug. This study concludes that homoeopathic drugs selected based on PQRS symptoms have the affinity to cure the Tinea corporis. This shows that keynote prescription will play important role in the effective selection and better prescription of drugs homoeopathically. <sup>[36]</sup> *Waheed et al*, in 2021, presents a case of dermatophyte infection treated by homoeopathic medicines *Sepia officinalis* and *Sulphur* after proper case taking and showed marked improvement with reduction of complaints. The prescription was based on Kent's repertorization and totality of symptoms. The author suggests that further scientific validation studies are required to have the evidence of the mechanism of action of medicines. <sup>[37]</sup>

#### In-vitro studies in Homoeopathy

*Shinde et al*, in 2018, in an in-vitro study, aimed to screen the ability of homoeopathic medicines to inhibit *Candida albicans*. From the study, the author showed that selected homoeopathic medicines could inhibit the *Candida albicans* at various potencies and indicates that homeopathic medicines have activity even at lower potencies. <sup>[38]</sup> *Patil et al*, in 2019, in a review article, demonstrated the effectiveness of different homoeopathic medicines in multiple in-vitro studies. The studies revealed that homoeopathic medicines have evidence based

medicinal effects against the pathogens that cause infections of humans and plants. Thus, ultrahigh diluted Homoeopathic medicines are effective in *in-vitro* studies. [39]

Results: Table.1 The Study flow diagram

## DISCUSSION

The present review shows all the AYUSH systems especially Homoeopathy is effective in treating the dermatophytes that cause superficial fungal diseases. In order to combat this menace, dermatologists have been compelled to think outside the box when it comes to the treatment of superficial dermatophytosis, which has grown increasingly challenging. [22] In this review *in-vitro* studies, case studies and case reports are included. These superficial dermatophytes infect animals and the paediatric age group to the geriatric age group in human beings. Due to the lack of awareness about the disease as well as management of dermatophytosis among the population and gaps in the updates of guidelines, it is becoming difficult to treat these infections. [22]

In the modern system of medicine treatment for these fungal infections, many antifungal therapeutics are available in the form of topical or oral formulations. Sometimes these formulations are used along with steroids that may harm patients in cases of overdose. Terbinafine, Naftifine, Griseofulvin, Itraconazole, Ketoconazole, Fluconazole and Clotrimazole are the generally used drugs for the treatment. Among these Clotrimazole acts as the best antifungal agent. [19,20,21] For the treatment of tinea, ringworm, and dermatophytosis, safer medicines must be developed since the fungi are growing more resistant.

In the Siddha system of medicine, skin affections known as Pundareega Kuttam which is correlated to dermatophytosis can be treated effectively with formulations. A Siddha herbo-mineral formulation namely Kandhaga Rasayanam showed positive results in a clinical study. In this way, the Siddha system of medicine has a good outcome in the treatment of skin affections. [25]

In the Ayurveda skin disorders known as Kushtha, can be treated effectively. Cream formulations and oil of Dadrugna Lepa along with Virechana karma, a procedure in Panchakarma give better results. This shows the importance of panchakarma in treating skin disease along with internal medicines. [28] It is reported that few ayurvedic preparations showed *in-vitro* antifungal effects against the skin microbes. But these can be used as a universal treatment for skin infections caused by microorganisms. [30] Further studies are required to evaluate the mechanism of action of these medicines.

Homoeopathy is a system that works based on a holistic principle '*Similia Similibus Curentur*', has a good reputation in treating skin affections. [32,33]

From the different case reports and case studies, Homoeopathic medicines that showed good results in superficial skin infections or ringworm are *Sanicula aqua*, *Sepia*, *Mercurius solubilis*, and *Sulphur*, *Rhus toxicodendron*, *Arsenic album* and *Apis mellifica*, *Rumex*. These medicines were selected based on the PQRS approach, anti-miasmatic approach or with repertorization and totality of symptoms. Different modes of approach in treating the patients but got good results. And there are many other Homoeopathic medicines are there that work on the skin so further research studies should be done. [32-37]

From the studies, it is evident that Homoeopathic medicines have *in-vitro* antimicrobial activities even at lower potencies. But exact mechanism of action of these medicines is not known. So further extreme research studies are required to know the exact mechanism of action of these ultra-high diluted Homoeopathic medicines in the era of evidence-based medicine. [38, 39] This can help in the development of preclinical Homoeopathic Materia medica. To offer conclusive data, substantial evidence on these serially diluted pharmaceutical results must be reproduced using a systematic process. [39]

## CONCLUSION

The treatment for dermatophytosis in conventional system with topical agents, antifungal drugs mixed with steroids will have harmful effects on patients, who were already suffering from skin affections, like adding fuel to the fire. Whereas treatment in alternative system of medicines AYUSH has very minimal or no side effects which give permanent relief to the patient and are also cost-effective. Homoeopathy is the second largest

system of medicine which is being practised worldwide. Homoeopathy provides treatment based on nature's law of cure (Similia Similibus Curentur). There is an immediate urge for the exploration of the efficacy of the alternative system of medicine for the treatment of skin diseases and preclinical and clinical studies to know the efficacy and mechanism of action of these alternative or complementary systems of medicine as these are cost-effective and with less or no side effects.

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