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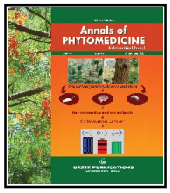

Review Article : Open Access

Medicinal plants for the treatment of erythrasma: A review

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Abstract

Erythrasma is a superficial skin infection that is identified by the brown scaly patches caused by the bacteria, *Corynebacterium minutissimum*. It is typically present in occluded intertriginous areas such the axillae, inframammary areas, interspaces of the toes, intergluteal, and crural folds, and it is more common in diabetics than in other clinical patients. The differential diagnosis of erythrasma includes psoriasis, dermatophytosis, candidiasis and intertrigo, and methods for differentiating include Wood's light examination and bacterial and mycological cultures.Topical antibiotics including fusidin, miconazole cream, clindamycin, and whitfield's ointment, as well as oral antibiotics such clarithromycin, erythromycin, tetracycline, and chloramphenicol, can be used to treat erythrasma. Adverse drug effects, potential drug interactions and cost effectiveness of allopathic medicine need to be considered. Natural treatment is both inexpensive and safe, according to its proponents. In the present study, information on the evidence-base of the plants inhibiting *C. minutissimum*, a causative organism of erythrasma was given with the aim of developing herbal formulations for the management of erythrasma.

1. Introduction

Erythrasma is a common, long lasting superficial skin infection that can develop into a condition if left untreated. The occurrence of erythrasma is reported in literature is around 4%. It is known to occur all over the world and is found more frequently in tropical and subtropical regions. Clinically, it manifests as brownish discoloration of skin usually limited to body folds such as crural region, submammary region, axillae and intergluteal folds (Rao *et al*., 2019). It is a common skin disease caused by the bacterial infection that affects the skin (Wilson *et al*., 2012). The bacteria *Corynebacterium minutissimum*, a lipophilic and filamentous gram-positive, catalase-positive, non-spore forming bacteria, is now widely thought to be the cause of erythrasma (Holdiness, 2003).

Predisposing factors for erythrasma include diabetes mellitus, hyperhydrosis, obesity, warm climate, poor hygiene, and immunocompromised states. However, there were no predisposing factors attributable in the index case. There are two distinct variants of erythrasma: generalized and interdigital. The interdigital is the most common type that presents with fissuring and scaling involving interdigital spaces of toes. The generalized variant is commonly seen in diabetics in whom the skin lesions extend beyond interdigital areas. Pityriasis versicolor can be differentiated from erythrasma by the presence of satellite lesions in the former. Other differential diagnosis includes intertrigo, flexural psoriasis seborrhic dermatitis, and tinea cruris (Rao *et al*., 2019).

Indigenous people use medicinal plants for treating skin diseases based on knowledge accumulated over-time. We compile and emphasize the most important part of ethnodermatology; namely, traditional knowledge of most cited medicinal plants against the microorganism causing skin disease erythrasma.

2. History

Burcliardt was the first to describe the disease in 1859, suggesting that the fine filaments and many granules seen in the scales were caused by a fungal infection. Burchardt's tutor, von Barensprung, invented the term erythrasma in 1862, and called the causal organism *Microsporum minutissimum* (Sarkany *et al*., 1961).

Microsporum minutissimum, Nocardia minutissimum, SporoIrichum minutissimum, Microsporoides minutissimus, Oospora minutissima, Actinomyces nunutissimus, Leptothrix epidermidis, Discomyces minutissimus, and *Microsporum gracile* are the few of the names used to denote the erythrasma-causing micro-organism. Poehlmann (1928) evaluated local elements such as location, humidity, and bodily secretions, as well as individual predisposition, a tendency to sweat, a fragile integument, and systemic illnesses such as diabetes mellitus, may be the etiological aspects of erythrasma.

Lagana was the first to indicate that erythrasma is caused by bacteria (1960). However, Sarkany *et al*. (1961) routinely identified a

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diphtheroid from erythrasma lesions, which they termed *C. minutissimum*, and this gave later investigators a new perspective on the disorder.

Various studies are now being conducted relating erythrasma to obesity, diabetes and its association with pityriasis versicolor and dermatophytosis (Parnia Forouzan and Philip, Cohen. 2020).

3. Clinical features

When the outer layers of the skin starts to shed, erythrasma begins as a pinkish patch of skin that turns dark and scaly quickly. The infection is most common in so-called intertriginous areas at the place where two skin patches come into contact or rub together. The armpits, groin, navel, under the breasts, and between the toes are all examples. The patches have regular or uneven boundaries and may cause mild irritation.

Interdigital erythrasma affects the majority of people, primarily in the webbing of the third, fourth, and fifth toes. In a patient with type 2 diabetes, generalised erythrasma is more extensive and generalised erythrasma in a patient with type 2 diabetes is more widespread. Well-defined scaly, lamellar plaques in larger portions of the trunk, proximal parts of limbs, and breast folds may occur in generalised forms. Circular scaling is seen in the discoid form of erythrasma that was mistaken for pityriasis versicolor, psoriasis and pityriasis rotunda.Tropical erythrasma is another name for this condition. Wood's light examination and gram stain were used to detect disciform erythrasma, which was characterised by an atrophic appearance.

The typical type of the lesion is characterised by punctate, well-circumscribed maculopapular lesions. Scales can be oily or furfuraceous in appearance. Fine scaling is associated with older lesions. Serpiginous endings protrude from the advancing ends. There is no tendency for the lesion to vascularize. The colour of the lesion is determined by: (i) the age of the lesion and (ii) the underlying skin pigmentation. It is pink at first, then brown, and there is no central cleansing. In the interdigitoplantar type of erythrasma, vesiculation of the lesion has been seen on occasion. Pruritus preceded vesiculation in the lesions. Vesiculation and erythema were present at first, followed by huge bullae that were initially yellow but gradually became opalescent.

Many of the lesions were asymptomatic, and individuals sought medical help because they were cosmetically impaired. These lesions might be itchy at times. In many cases, chronicity and recurrence are reported. In cases where the pruritus had been present for a long time, erythromycin was used to cure it. Lesions can become eczematous in rare cases. In most cases, an erythrasma infection is self-limiting and will go away without therapy. Erythrasma can occasionally co-occur with contact dermatitis, a fungal infection, or an associated bacterial infection, though consequences are uncommon. In such cases, a *C. minutissimum* infection can spread to deeper layers of skin, causing an abscess or a potentially dangerous skin infection called cellulitis (Greywal and Cohen, 2017).

4. Epidemiology

Erythrasma affects about 4% of the population. It is found all around the globe. In temperate climates, mild types of erythrasma of the axilla, groynes, and toe-webs are rather common. Erythrasma is most common in healthy individuals who live in institutions, such as college dorms, soldiers in barracks, and senior citizens in nursing homes. In children, it is less common. Erythrasma becomes more common as people get older, and it is more common in men. Diabetics appear to have a higher incidence and severity of the condition. Diabetics may be just as prone to erythrasma as they are to candidiasis, which could be due to high amounts of cutaneous free glucose (Morales-Trujillo *et al.*, 2008).

5. Pathophysiology

C. minutissimum infiltrates the stratum corneum and multiplies, causing erythrasma. The bacteria multiplies on the epidermis, develops at the stratum corneum's intracellular level, and penetrates. Keratin fibrils are removed from the bacterium, causing keratolysis. Hyperkeratosis causes erythrasma, which is characterised by reddish brown lesions (Bae and Lee, 2020).

6. Microbiology of *C. minutissimum*

C. minutissimum, which belongs to the aerobic diphtheroids, exhibits diphtheroid-like morphology. The isolates from the skin lesion of luminous scales of erythrasma display rod like organisms, filaments, and coccoid forms when stained with gram stain. The filaments are twisted and range in size from 4 to 10 by 1. The longer filaments appear to be segmented or beaded. The bacillary forms are 1 to 3 inches long and 0.5 inches wide. Subterminal granules can be seen in several of them (Bae and Lee, 2020).

In erythrasma lesions of the toes, shorter bacillary forms are more abundant, but filamentous forms and chains of bacilli are also present. Lesions with a higher proportion of filaments, but always shorter bacillary forms, are more common. Numerous microorganisms can be spotted at various layers of the stratum corneum using an electron microscope. Proliferating freely between the superficial cornified cells on the skin's surface, penetrating these cells from the intercellular space or, less commonly, directly from the skin surface and intracellularly into the keratinized cells. The bacteria in erythrasma can penetrate as deeply as one-half of the thickness of the stratum corneum, according to electron micrographs of the whole layer. Bacteriophages are believed to reside within bacterial cells (Marks and Keio, 2000).

7. Histopathology

For the diagnosis of erythrasma, a biopsy is rarely required. Microscopy of the skin revealed rod-like organisms in the horny layer, thickening of the stratum corneum without parakeratosis, and the highest concentration of *C. minutissimum* in the upper 3rd of the stratum corneum. Reduced electron density around intracellular bacteria and those in direct contact with the cell wall, enlargement of intracellular space, allowing bacterial invasion and separation of horny cells, and devoid of plasma cell membranes at the place of bacterial infiltration (Sebaratnam and Lee, 2017).

8. Causes

C. minutissimum is a generally found to be less harming bacteria that is usually controlled by the immune system. It will only cause infection, if the bacteria are given the correct conditions to thrive in. It could be because a skin fold provides the ideal environment for bacterial colonisation, or it could be because the immune system has been inhibited, making it less capable of controlling an infection.

Reasons includes;

- Live in a humid tropical or subtropical region
- Sweat excessively (hyperhidrosis)
- Poor hygiene
- Old age
- Obesity
- Diabetes
- Taking immune suppressive medicines to treat an autoimmune illness or prevent organ rejection
- HIV or other forms of immune suppression are all causative factors.

Around four per cent of the world's population will be affected with erythrasma at least once in their life, especially for the people living in tropical or subtropical regions. It was considered to be that African Americans are more prone to erythrasma than other racial or ethnic groups in the United States, but the reasons is not clear (Sebaratnam and Lee, 2017).

9. Diagnosis

The appearance of the typical brown patch with fine scaling distinguishes erythrasma from fungal illnesses such as tinea cruris (jock itch), which are more reddish and have thicker scaling along the edges.

Wood's light can be used to diagnose erythrasma. Wood's lamp is a high-pressure mercury lamp with an unique filter that allows a largely monochromatic UV light emitting with a wavelength of 365 nm. It's very beneficial for diagnosing fungal and bacterial infections, as well as assessing pigmentation disorders. The room must be entirely darkened during the examination, and the patient must be completely undressed. *Microsporum audouinii, Microsporum canis,* and *Microsporum ferrugineum* create blue-green fluorescence in their lesions. Golden yellow fluorescence will be given by P*ityriasis versicolor* lesions.

The colonisation of *P. aeruginosa* results in a blue tint. With the help of Wood's lamp, hypopigmentation or depigmen-tation, can be identified more easily. Wood's lamp, which produces a characteristic orange-red glow, can be used to screen urine, stool, and red blood cells of patients suspected of having porphyria. In erythrasma, the suspected lesions are inspected with Wood's light, and coral red fluorescence occurs owing to the bacteria *C. minitissimum* producing porphyrin, and fluorescence may be transiently absent, if the lesions are cleansed with antibiotic soaps before Wood's lamp inspection. If the illness is severe or recurrent, bacterial and fungal cultures may be taken to see if any other infections are present. Erythrasma that is recurrent or extensive may necessitate a random blood glucose test (Klatte *et al*., 2015; Baeand Lee, 2020).

10. Prevention

Erythrasma can be prevented by the following measures such as:

- Skin has to be kept dry and clean.
- Skin has to be dried completely after bathing.
- Excessive sweating needs to be avoided.
- Clean and dry clothes are to be worn.
- Should avoid hot or humid areas.

11. Treatment

- The most common therapy for erythrasma is to use antibacterial soap to clear up a slight infection (Holdiness, 2002).
- If the infection is more severe, a topical antibiotic such as fusidin, miconazole cream, clindamycin, or whitfield's ointment (benzoic acid and salicylic acid) is applied twice daily for one to two weeks (Piergiorgio 2013; Avci *et al*., 2013).
- Oral antibiotics such as clarithromycin, erythromycin, tetracycline, and chloramphenicol may be required for serious infections (Prabhakar and Prathyusha, 2016). Septicaemia, a dangerous blood infection that can develop when erythrasma persists, is only an uncommon complication of erythrasma (Chodkiewicz and Cohen, 2013).

12. Herbal remedies for treating erythrasma

Because of their numerous applications, plant-derived compounds have recently attracted a lot of attention (Mary Grace Jinukuti and Archana Giri, 2013). Herbs are becoming more popular as part of a trend to modify one's lifestyle. Apart from having minimal or no adverse effects, plant-based bioactive chemicals have been shown to have a significant impact on human health (Tamanna Malik *et al*., 2020). Due to shifting consumer preferences for herbal medicine, there has been a trend toward plant-based medications in recent years. The ayurvedic medical method has been used in India for ages. In developing nations like India, herbal medications are used to treat 80 per cent of the population for a variety of ailments (Karishma Joshi *et al*., 2017). Approximately, a third of all traditional medicines are used to treat wounds or infections (Manoharachary and Nagaraju, 2016). Information on plants inhibiting *C. minutissimum* was given as these plants are the easily available source for the development of new drugs.

12.1 *Murraya koenigii* (L.)

Murraya koenigii (L.) Spreng (Rutaceae) is used as a stimulant, stomachic, febrifuge, analgesic, and to cure diarrhoea, dysentery, insect bites, and to relieve body heat. At varied doses of 50-500 mg/ml, an ethanolic extract of curry leaves was found to have substantial antibacterial activity against *C. minutissimum* (Vaibhav Khandare and Satish Sakhawade, 2017).

12.2 *Salvia officinalis* (L.)

Using an agar microdilution antimicrobial assay in humans, different fractions of methanolic extract of *Salvia officinalis* (L.) (sage) were tested against two main bacteria responsible for axillary odour (*S. epidermidis* and *Corynebacterium* spp.). In healthy subjects, a single treatment with a stick deodorant containing dichloromethane sage extract at concentrations of 200, 400, or 600 g/ml was effective in reducing axillary malodor compared to the control (Mohammad Ali Shahtalebi *et al*., 2013).

12.3 *Amaranthus viridis* (L.) and *Malvastrum coromandelianum* (L.)

Amaranthus viridis (L.) (Amaranthaceae) is a widely distributed plant that grows in a variety of climates and has been used as an

antipyretic in ancient ayurvedic medicine, as well as for the treatment of inflammation, ulcers, diabetes, asthma, and hyperlipidemia. *Malvastrum coromandelianum* (L.) Garcke, an annual to perennial herb belonging to the Malvaceae family, has been shown to have hypoglycemic, antipyretic, smooth muscle activity, and ulceroprotective properties (Sima Kumari *et al*., 2018; ChaiyasitSittiwet *et al*., 2008).

The antimicrobial activity of chloroform and aqueous leaf extracts from three common weeds, *Amaranthus viridis*, *Lantana camara*, and *Malvastrumcor omandelianum*, against four bacterial species, *Xanthomonas axonopodis*, *Pseudomonas syringae* (gram-negative bacteria), *C. minutissium*, *Clostridium difficile* (gram-positive bacteria), and major the chloroform extracts of *A. viridis* and *M. coromandalianum* had the highest activity against gram-positive *C. minutissium* of all the extracts examined (Mushatq *et al*., 2012).

12.4 *Tamarindus indica* (L.)

Tamarindus indica (L.), also known as Amlika, Amli, Imli, Ambli, Puliyan, and Ambala, belongs to the Leguminosae/Fabaceae family and has been used as a refrigerant in fevers, as well as laxatives and carminatives. In a concentration-dependent manner, tamarind bark crude extract was found to have antibacterial activity against three bacteria: *S. aureus*, *C. minutissimum*, and *Streptococcus* spp. (Anna Muriel *et al*., 2018).

12.5 *Lanata camara* (L.)

Lantana camara (L.), sometimes known as wild or red sage, belongs to the Verbenaceae family and grows as an evergreen weed in most parts of the world. *L. camara* plant extracts and essential oil have a variety of bioactivities, including antibacterial activity. *In vitro* studies were conducted on the efficiency of aqueous and chloroform extracts of *L. camara* against four bacterial species: *Xanthomonas axonopodis*, *Pseudomonas syringae* (gram-negative bacteria), *C. minutissimum*, and *Clostridium difficile* (gram-positive bacteria). Both extracts had equivalent (moderate) antibacterial activity against all microorganisms tested (Mushatq *et al*., 2012).

12.6 *Citrus* peel essential oil

Citrus peel essential oils from *Citrus sinensis* (L.) var. Malta and Mousami, *Citrus reticulate* (L.) var. Tangerine and Mandarin, and *Citrus paradise* (L.) grape fruit were tested for antimicrobial activity against five bacterial strains: *Listeria monocytogenes*, *C. minutissimum*, *E. coli*, *Yersinia* spp., and *Klebsi* against the five bacterial strains, the essential oils demonstrated varying degrees of inhibitory potential. Mandarin essential oil had the second highest inhibitory potential against *E. coli* and *C. minutissimum* (4.7 cm and 2.8 cm, respectively) among the oils evaluated (Shabnam Javed *et al*., 2014).

12.7 *Calophyllu minophyllum* oil (L.)

Calophyllu minophyllum (L.) (Calophyllaceae), known in French Polynesia as “tamanu,” is an evergreen pantropical tree that grows predominantly along the seashores. Traditional medicine still uses its barks, leaves, and fruits. The oil extracted from the nuts has also been used in the past. Tamanu oil is utilised topically on skin and mucous membrane diseases. This oil is extremely useful for treating a variety of skin conditions. *C. minophyllum* oil (CIO) has been proven to have strong antibacterial properties against germs that cause skin infections. Antibacterial activity on aerobic gram+ bacteria strains such *S. aureus*, *Bacillus cereus*, *S. epidermidis*, *Staphylococcus haemolyticus*, and *C. minutissimum* were found to be quite noteworthy. All of the *C. minophyllum* oil (CIO) strains tested against gram+ bacteria had MIC values that were similar to or lesser than the standard ofloxacin (Leguillier *et al*., 2015).

13. Conclusion

Complementary therapy for dermatological problems and treatment remains the main option for millions of people in the Indian subcontinent herbal therapy has increased in popularity in the past two decades among patients seeking alternative treatments to conventional western allopathic medicine. Herbs have a lot of potential for treating a variety of skin conditions. In India, more than 80% of people rely on traditional medicine and employ a variety of plant-based medicines to treat skin disorders. Herbals are a rich source of active ingredients and can be safer and cost effective treatment for skin diseases ranging from rashes to dreadful skin cancer.They are relatively inexpensive when compared to conventional allopathic drugs and can be of tremendous help to the Indian population in general, and the impoverished in particular. We hope this article will further accelerate the development of this area to identify a new generation of natural human skin treatments that will help meet the growing consumer demand for safe, sustainable, and natural treatmentsfor the management of erythrasma.

Conflict of interest

The authors declare no conflicts of interest relevant to this article.

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