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Review Article

A Review on Antimicrobial Activity of *Tarunyapidikahara Lepa* Ingredients

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Abstract

Skin is not only a protecting covering of our whole body but also it reflects the physical and mental health. Mukhdushika is the most common skin ailment in the teenage of youngsters, it disfigure the face. Acne vulgaris is chronic inflammatory condition of the pilosebacous follicles and caused by the *Propionibacteriun acnes*. It is correlated with Mukhdushika, a disease mention in Ayurveda. Microbial infections are the leading cause of diseases and disease related mortality. Non–judicious intake of antibiotic is the serious concern for antibiotic resistant strain of bacteria. Antimicrobial resistance (AMR) threatens the ability to successfully treat infectious diseases across the world. Among the most common skin pathogens *Pseudomonas aeruginosa* (gram-negative pathogen) has high antibiotic resistance rate and *Staphylococcus aureus* is another most common human pathogens that leads to many types of local infections such as wound, post-operative infection and also for prosthetic infections. *S. aureus* is also known for its ability to resist antibiotics such as penicillin, methicillin, tetracycline, erythromycin and vancomycin, so there is a need of different treatment to overcome the problem of AMR. Similar problem is also arises in the treatment of acne by antibiotics. Tarunyapidikahara Lepa is an Ayurvedic formulation consisting of equal amount of Lodhra (*Symplocos racemosa* Roxb), Dhanakya (*Coriandrum sativum* Linn.) and Vacha (*Acorus calamus* Linn) prescribed for topical application in Mukhdusika in renowned text Chakradatta, Kshudra Roga Chikitsa. This appraisal summarizes the antimicrobial potential of each ingredient present in the Tarunyapidikhara Lepa.

Keywords: Mukhdushika**,** Acne vulgaris**,** Antibacterial, Antimicrobial resistance Lodhradi Lepa.

INTRODUCTION

In present scenario lifestyle changes like unbalanced diet, pollution, stress, harmonal imbalance directly affect the skin. It causes many skin problems and most common among them is acne vulgaris [1]. Acne vulgaris is considered as an adolescent disorder which is related to the pilosebaceous follicle of the skin and characterized by formation of open and closed comedones, papules, pustules, nodules and cysts [2]. Several remedies are available for acne vulgaris in modern medicament, but treatment must comply with type and severity of the lesions [3]. Modern medicine mainly includes prolonged use of oral and or topical antibiotics (doxycycline, clindamycin and erythromycin), comedolytic (retinoid) and anti- inflammatory agents. Even though these medicines are better treatment options for acne management but with these medications may have some side effects such as increased skin dryness, scaling, erythema, burning, stinging, itching and bacterial resistance are noticeable. Hence, people are seeking for another treatment options for acne vulgaris [3]. According to World Health Organization (WHO) medicinal plants would be the best source to obtain a variety of drugs and 80% of world population is dependent on traditional medicine which involves the use of plant extracts or their active constituents [4]. So as an alternative treatment of acne vulgaris Tarunyapidikhara Lepa can be used. The ingredients present in the Tarunyapidikhara Lepa shows the antimicrobial activities against many bacteria, fungi including *Propionibacterium acne* bacteria which is responsible for the acne vulgaris [5].

Classical Description

In Ayurveda acne vulgaris is correlated with Mukhadushika. Mukhadushika is depicted by Acharya Sushruta under Kshudra Rogas. The “Shalmalikantaka” Silk-cotton tree thorn like eruptions on the face due to

vitiation of Kapha, Vata and Rakta which are found in the adolescents are called as Mukhadushika or Yauvan pidika [6]. In Ayurveda, the treatment of Mukhadushika (Acne vulgaris) are of two types of Chikitsa (Treatment) i.e. Shodhana Chikitsa and Shamana Chikitsa [7]. The Shodhana Chikitsa includes Vamana, Nasya and Shiravedha [7, 8], while the Shamana Chikitsa consists of various types of Lepa and Pralepa, Tarunyapidikahara Lepa, is one of them [8]. Tarunyapidikahara Lepa is an Ayurvedic formulation comprising of equal amount of Lodhra (*Symplocos racemosa* Roxb), Dhanakya (*Coriandrum sativum* Linn.) and Vacha (*Acorus calamus* Linn) given in the management of Mukhdusika for local application [8].

Pathogenesis of acne

Seborrhea increase androgen concentration due to genetic factors as well as because of attainment of puberty and ultimately leads to the increased sebum production. Androgens synthesis as well as reuptake increases in the sebocyte. These androgens then form androgen-receptor complex within the cytoplasm which enter the nucleus via nucleopore and alter the specific gene sequence and thus affect the reading rate as a result of which sebum production by the sebocyte increases. Thus the produced sebum flow through the pilosebaceous ducts reaches the skin surface. During the flow, this sebum supplies its linoleic acid to the keratinocytes of the hair follicle. This leads to local deficiency of linoleic acid which ultimately leads to the impairment in the follicular barrier. This allows the free fatty acid formed by *P. acnes* by action of its enzyme lipase or by other mechanisms on triglycerides, to enter the follicle. The impairment in the follicular wall can also arise because of oxygen stress or by generation of free radicals by phagocytes in response to invading microorganism. The entered free fatty acids are highly chemotactic and lead to the production of various cytokines such as IL-8 and IL-1α. These cytokines give rise to the inflammation and upward regulation of keratinocyte proliferation. This leads to ductal hypercornification and formation of dense horny lamellae which results into Retention-proliferation hyperkeratosis. Retention-proliferation hyperkeratosis first form microcomedone, which further grow and convert into comedone and this comedone further develop and form acne [9, 10].

Description of ingredients

1 *Symplocos racemosa* Roxb. (Symplocaceae)

The word '*Lodhra*' means 'Propitious'. *Lodhra* is an important Indian traditional herb used in many herbal formulations for management of liver as well as uterine disorders and leucorrhea [11]. The literature indicates utilisation of Lodhra in the management of skin disease, acne, leprosy, eye disease, ear disorders, liver and bowel complaints, tumours, uterine disorders, spongy and bleeding gums, asthma, fever, snakebite, gonorrhoea and arthritis etc [12]. The bark of *Symplocos racemosa* contain antimicrobial activity showed inhibitory effect on the growth of *Micrococcus pyogens* var. *aureus*, *E. coli* and other enteric and dysenteric groups of organisms [12].

Devmurari (2010) evaluated the antibacterial activity spectrum of petroleum ether and ethanolic bark extract against 3 gram positive bacteria, *staphylococcus aureus, Enterococcus faecalis, Bacillus cereus* and three gram negative bacterias *Klebsiella pneumonia, Pseudomonas aeruginosa, Escherichia coli.* Ethanolic extract of *S. racemosa* Roxb. shows better antibacterial activity as compared to pertroleum ether, but it has poor antibacterial activity against gram negative microorganisms like *P. aeruginosa* and *E. Coli* [13].

Kumar GS *et al*. (2007) assessed the antimicrobial activities of *Symplocos racemosa* (Barks) against *Propionibacterium acnes* and *Staphylococcus epidermidis.* The outstanding antimicrobial properties of *Symplocos racemosa* against *Propionibacterium acnes* evaluated based on the disc diffusion assay and dilution method [5].

2 *Coriandrum sativum* Linn. (Apiaceae)

The seeds of Dhanakya are used in the formulations due to carminative, diuretic action along with the preparation of many house-hold medicines to cure acute cold, seasonal fever, nausea, and stomach disorders [14]. Essential oils from commercial samples of *Coriandrum sativum* were analysed by GC-MS and assayed for their antibacterial, antifungal and antioxidant activities. Twenty-five genera of bacteria and one fungal species (*Aspergillus niger*) were used as test organisms and the essential oils showed a high degree of inhibition against all the microorganisms tested [15].

Pietro lo cantore *et al*., (2014) evaluated antibacterial Activity of *Coriandrum sativum* L. and *Foeniculum vulgare* Miller Var. vulgare (Miller) essential oils. The oils exhibited antibacterial activity towards many gram positive strains viz. *Bacillus megaterium* ITM100, *Clavibacter michiganensis* DPP2, DPP3, *C.michiganensis subsp. sepedonicus* NCPPB2137, *Curtobacterium flaccunfaciens pv. flaccunfaciens* ICMP2584, ICMP5370, *C. flaccunfaciens pv. betae* NCPPB372, NCPPB374, *Rhodococcus fascians* and gram negative bacterial strains viz. *Escherichia coli* ITM103, *Pseudomonas syringae pv. phaseolicola* NCPPB2571, IPV-BO1917, USB316, USB320, *P. syringae pv. pisi* NCPPB3496, 895-A, *P. syringae pv. syringae* Y37, NCPPB1910, B366, *P. syringae pv. aptata* NCPPB2664, NCPPB872, *P. syringae pv. apii* NCPPB1626, *P. syringae pv. atrofaciens* NCPPB2612, GSPB1742, *P. syringae pv. lachrymans* USB326, USB327, *P. syringae pv. maculicola* NCPPB2038, NCPPB2704, *P. syringae pv. Tomato* USB328, USB329, *P. syringae pv. glycinea* NCPPB2752, NCPPB2753, *P. cichorii* ICMP5707, *P.*

viridiflava DPP5, DPP18, *P. corrugata* NCPPB2445, *P. tolaasii* NCPPB2192, *P. reactans* NCPPB1311, *P. agarici* NCPPB2289, *Erwinia carotovora subsp. carotovora* ICMP5702, *E. carotovora subsp. atroseptica* ICMP1526, *Agrobacterium tumefaciens* USB1001, USB1005, *Burkholderia gladioli pv. agaricicola* ICMP 11096, *Xanthomonas campestris pv. phaseoli* NCPPB3035, GSPB1217, ICMP238, *X. campestris pv. phaseoli var. fuscans* ICMP239, ICMP3403, GSPB275, XCPFu4487, *X. campestris pv. vesicatoria* NCPPB422, DAPP-PG95, DAPP-PG32,
DAPP-PG35, *X. campestris pv. campestris* , but in general, the bactericidal activity of *Coriandrum sativum* oil was higher than that of *F. vulgare* var. Vulgare. Particularly, coriander oil inhibited the growth of *E. coli* and *B. megaterium*. Moreover, the above oil inhibited the growth of strains of important plant pathogenic bacteria belonging to either Gram-negative genera such as *Pseudomonas, Erwinia, Xanthomonas*, and *Agrobacterium* or Gram-positive genera such as *Clavibacter, Curtobacterium, and Rhodococcus* except *Pseudomonas syringae pv. lachrymans, Pseudomonas viridiflava, and Pseudomonas reactans* strains [16].

Oudah IM *et al*., (2010) evaluated the antibacterial effect of aqueous and ethanolic extracts of different parts of coriander against nine different pathogenic bacteria isolated from urine, stool, blood and CSF of different patients (*Burkhella capacia, Escherichia coli, Enterobacter cloacae, Gamella morbillorum, α-Haemolytic streptococci, Klebsiella pneumonia, Proteus mirabilis, Streptococcus pneumonia, and Salmonella typhi*). The ethanolic extracts of seeds, leaves and stems showed wide range of antibacterial activity and the highest values for inhibition zone was recorded against *Klebsiella pneumoniae* and *Proteus mirabilis.* On the other hand, the cold aqueous extract of Coriander seeds had inhibitory effect against only some tested bacteria [17].

Ratha bai V *et al*., (2012) investigated the antimicrobial activity of ethanol, methanol, chloroform, acetone, hexane and petroleum ether extracts of *Coriandrum sativum* against infectious pathogenic bacteria such as *Staphylococcus aureus, Klebsiella Pneumonia, E. coli and Pseudomonas aeruginosa*; and various fungi including *Candida kefyr, Candida tropicalis Candida albicans* and *Aspergillus niger*, using agar well diffusion method. The methanol extract of *Coriandrum sativum* showed better antibacterial and antifungal activity against *Staphylococcus aureus, Klebsiella pneumonia, Candida albicans* and *Aspergillus niger* with zone of diameter 12.17±0.29mm and 12.17±0.15mm, 14.20±0.20mm and 10.10±0.10mm respectively. This study explained that the antibacterial and antifungal effects of methanol extract showed a varying degree which was more than ethanol, acetone, chloroform, hexane and petroleum ether extracts [18].

Reddy LH *et al*., (2012) evaluated the antibacterial potential of the leaf essential oil, methanol, chloroform, petroleum ether and ethyl acetate extracts of the leaves of Coriander against human pathogenic bacteria such as *Salmonella paratyphi, Staphylococcus aureus, Bacillus cereus, Enterobacter faecalis, Escherichia coli, Proteus vulgaris, Klebsiella pneumoniae, Pseudomonas aeruginosa and Serratia marcescens* by agar well diffusion method. Leaf essential oil as well as leaf ethyl acetate, chloroform and methanol extracts of *Coriandrum sativum* (Dhanyak) exhibited marked activity against Gram- positive and Gram-negative bacteria and their activity was quite comparable with the standard antibiotics such as gentamicin, tobramycin sulphate, ofloxacin and ciprofloxacin screened under similar conditions [19].

Bogavac M. *et al*.,(2015) investigated the antibacterial potential of two commercial essential oils (EOs) from *Coriandrum sativum* against vaginal clinical strains of bacteria and yeast. Antimicrobial activities were determined using macro-diffusion (disc, well) and micro-dilution method against twelve clinical strains of bacteria: *Escherichia coli, Proteus mirabilis, S. aureus and Enterococcus sp., S. aureus* ATCC 25923, ATCC 6538 and *Escherichia coli* 25922 and two clinical *Candida albicans* ATTC 10231 strains. The antimicrobial effect of *Coriandrum sativum* EOs was strain specific and the antibacterial activity was higher against almost all tested bacteria, except multiple resistant strains of *Eneterococcus sp.* and *Proteus sp* but it showed low fungicidal activity [20]. Sourmaghi MH *et al*., (2015) evaluated antimicrobial activities of essential oils against *Staphylococcus aureus, Pseudomonas aeruginosa, Escherichia coli and Candida albicans* by micro-dilution method. The essential oils of *Coriandrum sativum* fruits obtained by hydro-distillation (HD EO) exhibited greater activity against *Staphylococcus aureus* and *Candida albicans* than that obtained by microwave-assisted hydro- distillation (MAHD EO). Furthermore, their activities against *E. coli* and *P. aeruginosa* were the equal with minimum inhibitory concentration, MIC 0.781 and 6.25 µl/ml, for HD EO and MAHD EO respectively [21]. Casetti F *et al*., (2012) investigated the antibacterial activity of essential coriander oil (ECO) on bacteria with dermatological relevance and skin tolerance of antimicrobial effective ECO concentrations. Essential coriander oil (ECO) showed good antibacterial activity towards most of the bacterial strains tested, including *Streptococcus pyogenes* (Lancefield group A) and methicillin resistant *Staphylococcus aureus* (MRSA), with mean minimal inhibitory concentrations of 0.04% v/v and 0.25% v/v, respectively [22].

Khan DA *et al*., (2013) screened the hydro-alcoholic extract of the crude *Coriandrum sativum* for antibacterial activity against various bacterial species by disk diffusion method against B. *cereus, S. aureus, P. aeruginosa* and *E.coli*. The result showed that the extract of *Coriandrum sativum* was effective only against

Bacillus cereus [23].

Soares BV *et al.,* (2012) evaluated the antifungal activity of essential oil from *Coriandrum sativum* fruits against *Microsporum canis* and *Candida spp*. by the agar-well diffusion method. The minimum inhibitory concentration (MIC) and the minimum fungicidal concentration (MFC) were evaluated by the broth micro-dilution method. The study showed that the essential oil induced growth inhibition zones of 28 ± 5.42 and 9.25 ± 0.5mm for *M. canis* and *Candida spp*. respectively. The MICs for *M. canis* and *Candida* spp strains ranged from 78 to 620 and310 to 620 respectively. The MFCs for *M. canis* and *Candida* spp strains ranged from 150 to 1.250 µg/ml and 620 to 1.250 µg/ml, respectively [24].

3 *Acorus calamus* Linn. (Acoraceae)

Acorus species have long been considered to have medicinal properties in Asia, Europe and North America. They have been used as a folk remedy for the management of arthritis, neuralgia, diarrhoea, dyspepsia, hair loss and other disorders [25-27]. According to an anti-microbial study, the leaf and rhizome part of *Acorus calamus* are found to have the antibacterial activity. The methanolic extract of *Acorus calamus* exhibited the inhibitory action against the bacterial strains of *Salmonella typhi, P. aeruginosa, Klebsiella pneumoniae, and Staphylococcus aureus* [28]. An in-vitro study on β-asarone compound fraction extracted from the crude methanolic extract of *Acorus Calamus* rhizomes has been found to possess the antifungal activity against the yeast strain of *Candida Albicans, Saccharomyces Cerevisae, Cryptococcus Neoformans* [29], and also against *Aspergillus Niger* [30].

Asha Devi S. *et al.,* (2009) evaluated antimicrobial activity of *Acorus calamus* rhizome and leaf extracts obtained with different solvents viz., petroleum ether, chloroform, hexane and ethyl acetate. Ethyl acetate extracts among others were found to be highly effective. Both rhizome and leaf extracts demonstrated substantial antifungal activities, but they did not show any antibacterial activity except that of *E. coli* [31].

De M *et al*., (1999) reported *A. calamus* has lack of antibacterial activity [32] while recently Phongpaichit *et al*., (2005) have observed very less antibacterial activity in his study on antimicrobial properties of *A. calamus* rhizome [33]. Even though, there are several published reports available on antibacterial activity of *A. calamus* extracts [34-36] Joshi *et al*., (2012) both the rhizome essential oil and beta-asarone extracted from sweet flag exhibited antibacterial activity against four pathogenic bacteria including three gram negative bacteria such as *Pasteurella multicoda, E coli* and *Salmonella enterica* and one gram positive bacteria such as *Staphylococcus aureus* and Beta-asarone exhibited relatively stronger antimicrobial activity than alpha-asarone [37]. Kho See Li *et al*., (2017) studied the antioxidant and antibacterial activities of both hydrophilic and hydrophobic of *A. calamus* leaf and rhizome extracts and stated that the highest antibacterial activity was observed in methanol extracts and no antibacterial activities were examined for water extracts [38].

Wan-Jae Kim *et al*., (2011) evaluated antimicrobial activity of the antimicrobial activities of the essential oil, hexane extract and the main constituents of A. calamus i.e. Methyl isoeugenol against *Escherichia coli, Salmonella typhimurium, Staphylococcus aureus, Bacillus subtilis, Propionibacterium acne* and *Candida albicans.* The essential oil has shown a strong and wide range of antimicrobial activity, except against *Escherichia coli* [39].

DISCUSSION

Aforesaid various research studies illustrated that the ingredients of Tarunyapidikahara Lepa possess antimicrobial activity. Through different researches conducted in this area have explored that various bioactives **Table 2** present in the ingredients of Tarunyapidikahara Lepa contribute to their antimicrobial property **Table 1**.

Table-1: Summary of Bacteria and Fungus susceptible to the Tarunyapidikahara Lepa ingredients

Ingredients	*S racemosa*	*C. sativum*	*A. calamus*
Bacteria	***Propionibacterium acnes***, *S. epidermis staphylococcus aureus, E. coli, Enterococcus faecalis, Bacillus cereus, Klebsiella neumonia, Micrococcus pyogens,*	*Escherichia coli, Streptococcus pyogenes Acinetobacter calcoaceticus, B. subtilis Aeromonas hydrophila, Alcaligenes faecalis, Beneckea natriegens, Brevibacterium linens Brocothrix thermosphacta, Citrobacter freundii, Clostridium periringens, Enterobacter aerogenes, Erwinia carotovora, Flavobacterium suaveolens, Klebsiella pneumonia, Lactobacillus plantarum Leuconostoc cremoris, Micrococcus luteus*	***Propionibacterium acne,*** *Staphylococcus aureus, E. coli, Salmonella typhi, P. aeruginosa, Klebsiella pneumoniae, Salmonella enteric, Pasteurella multicoda, Bacillus subtilis,*

		Proteus vulgaris, Pseudomonas aeruginosa Salmonella pullorurn, Serratia marcescens Streptococcus faecalis, Pseudomonas, Erwinia, Yersinia enterocolitica B. megaterium, Xanthomonas, Clavibacter, Agrobacterium, Curtobacterium, Rhodococcus, Proteus mirabilis, Bacillus cereus	
Fungi		*Aspergillus niger, Candida albicans, Microsporum canis*	*Aspergillus niger, Candida albicans, Saccharomyces cerevisae, Cryptococcus neoformans,*

Table-2: Phytochemicals and Bioactives of ingredients of the Tarunyapidikahara Lepa [40]

Ingredients	*S. racemosa*	*C. sativum*	*A. calamus*
Phytochemicals	Glucosides, Alkaloid, Saponin, Terpenoid, Carbohydrates	Flavonoides, Tannin, Phenolic compounds, Resine, Lignin, Phytosterol, Fixed oil, Fat, Glycosides, Essential oil	Alkaloids, Palmitic acid, Linoliec acid, Acorin
Bioactivities	Anti-inflammatory, Analgesic, Antibacterial, Anti-acne	Anti-inflammatory, Analgesic, Antibacterial, Antioxidant	Anti-inflammatory, Analgesic, Antibacterial, Antioxidant

CONCLUSION

In the present era due to extensive use of antibiotics and vast majority of synthetic drugs, numerous multidrug resistant strains are developing. Therefore, to overcome drug resistance and to avoid side effects associated with the commonly available antibiotics, there is a surge of another treatment. The alternate management can be achieved by the use of traditional medicinal herbs which are potent antibacterial agents, clinically safer, cost effective and affordable. All previous research work has shown the extensive antimicrobial activity of ingredients of Tarunyapidikahara Lepa. Present review builds a foundation for further *in vitro* and *in vivo* studies to understand the mechanism of antimicrobial action of Tarunyapidikahara Lepa and its constituents which may help in developing better healthy and therapeutic products. Additionally, the bioactive constituents of all ingredients also have anti-inflammatory and antioxidant action, which make this formulation a perfect remedy to cure acne vulgaris. Moreover, ingredients of this formulation are easy available throughout the year.

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