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Antimicrobial activities of *Coleus aromaticus* Benth.

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ABSTRACT

Medicinal plants play a vital role to preserve human health. Currently plants are attracting more attention for new drugs as human diseases caused by antibiotic resistant microorganisms have gained worldwide concern. *Coleus aromaticus* Benth. (syn. *Coleus amboinicus* Lour. or *Plectranthus amboinicus* Lour. Spreng) is an aromatic plant species from the family Lamiaceae having therapeutic and nutraceutical importance. It is large succulent aromatic perennial herb found throughout India. It has wide medicinal properties including antimicrobial activities. The leaves of the plant are bitter, acrid and were being widely used traditionally for the treatment of severe bronchitis, asthma, diarrhoea, epilepsy, vaginal discharge, renal and vesical calculi, fever, etc. It is reported to act as an antilithotic, chemopreventive, antiepileptic and antioxidant. The juice of leaves has been used in wound healing and swelling disorder by the tribal people. This article is an effort to compile the information reported on its antimicrobial activities.

KEY WORDS: *Coleus aromaticus*, antibacterial, antifungal, antiprotozoal activity, solvent extracts, essential oils, nanoparticles

1. INTRODUCTION

Human beings have been dependent on plants for their health care needs since the beginning of civilization. Of the 2,50,000 higher plant species on earth, more than 80,000 are medicinal in nature[1]. Many secondary metabolites of plant are commercially important and find use in a number of pharmaceutical products. Different plant parts are used for medicinal purposes i.e., bulb, gel, leaves, roots, barks, peels etc.[2]. Development of microbial resistance to the available antibiotics and increasing popularity of traditional medicine has led researchers to investigate the antimicrobial compounds in plants[3]. Globally, plant extracts are employed for their antibacterial, antifungal, antiviral and many other therapeutic activities[4]. India has one of the richest ethnobotanical traditions in the world with more than 7000 species of plants found in different agro-ecosystems and used by various indigenous systems of medicine and industries[5].

1.1 Coleus aromaticus

Coleus aromaticus Benth. (Lamiaceae), syn. *Coleus amboinicus* Lour. or *Plectranthus amboinicus* Lour. Spreng, is commonly known as Indian / country borage[6]. In Sanskrit it is called as *Parnayavani* and in Kannada as *Karpurahalli, Dodda pathre.* The fresh or dried leaves are used for culinary purposes in most of the countries including India for flavouring, seasoning and as condiment and spice for different food preparations. The decoction of its leaves is administered in cases of chronic cough and asthma[7]. The leaves are mainly used for the treatment of stomach disorder, asthma, headache, fever, epilepsy and renal diseases. It is used to treat conditions such as indigestion, diarrhea, nervous tension, insect bites, tooth ache, ear ache, rheumatism, whooping cough, and bronchitis[8]. The plant also finds prominent importance in modern medicine[9].

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Scientific classification

Kingdom	:	Plantae
Order	:	Lamiales
Family	:	Lamiaceae
Genus	:	*Coleus*
Species	:	*C. aromaticus*
Binomial name	:	*Coleus aromaticus* Benth.
Synonyms	:	*Coleus amboinicus* Lour.
		Plectranthus amboinicus (Lour.) Spreng

C. aromaticus appears as a green, perennial, shrub having heart shaped, and leathery leaves with scalloped edges (Figure 1). The tip

is acute and the base truncate. The leaves are highly aromatic with a strong flavor of mixed herbs. The roots are fibrous; stems square, succulent without tuberous base. The inflorescence measures 10-50 cm subspicate, simple or with a pair of side bracts; dichasia subsessile, with 4-10 flowered. The bracts are ovate to suborbicular, measuring 2-3 mm. The peduncle measures 1.5-2.5 mm. The plant grows to around 50 cm tall with horizontal stems up to 180 cm long[10].

Figure 1: ***Coleus aromaticus***
(Source: http://www.stuartxchange.com/Oregano.html)

1.2 Nutritional content

Coleus aromaticus is an edible, nutritive plant, which contains proteins (0.6%), vitamins (0.003% ascorbic acid, 0.00008% thiamine), minerals (0.158% calcium, 0.016% phosphorus, 0.138% potassium, 0.0047% sodium, 0.088% magnesium), trace metals (0.262% iron, 0.0003% zinc, 0.00012% copper, 0.000022% chromium), soluble dietary fibers (0.31%), insoluble dietary fibers (1.56%), phytic acid (0.00092%), soluble oxalate (0.02%). Thus, *C. aromaticus* is a good source of nutritious compounds and can be used as a food supplement. It also contains α- carotene (0.157mg/g of dry weight) and β- carotene (0.0035mg/g of dry weight)[11].

1.3 Chemical constituents

Many chemical constituents have been isolated from *C. aromaticus* including 76 volatiles and 30 non-volatile compounds. *C. aromaticus* is reported to contain several classes of phytochemicals including monoterepenoids, diterpenoids, triterpenoids, sesquiterpenoids, phenolics, flavonoids and others. The details of these bioactive constituents have been reported[12].

Monoterpene hydrocarbons: δ-3-Carene, p-Cymene, Limonene, β-Myrcene, Ocimene, α-Phellandrene, β-Phellandrene, α-Pinene, β-Pinene, α-Terpinene, γ-Terpinene, α-Terpinolene, α-Thujene[13-25].

Oxygenated monoterpenes: Carvacrol, Camphor, Carvone, Carvone, 1,8-Cineole, Eugenol, Geraniol, Linanol, Linalool, Methyl carvacrol, Methyl eugenol, α-Terpineol, Terpinen-4-ol, Thymol, Thymol methyl ether[09,13-29].

Sesquiterpene hydrocarbons: α-Amorphene, Aromadendrene, trans-α-Bergamotene, trans-β-Bergamotene, γ-Cadinene, δ-Cadinene, α-Calacorene, cis-Calamenene, β-Caryophyllene, γ-Caryophyllene, α-Copaene, α-Cubebene, (E,Z)-α-Farnesene, Germacrene D, γ-Gurjunene, Humulene, α-Muurolene, Patchoulene, β-Selinene, β-Sesquiphellandrene[13,15-24,27,30,31].

Oxygenated sesquiterpenes: Caryophyllene oxide, β-Cedrene epoxide, β-Copaen-4-α-ol, 1-Epi-cubenol, β-Eudesmol, β-Himachalene oxide, Humulene oxide, Spathulenol[13,15-24,27,30,31].

Phenolic acids: Caffeic acid, Gallic acid, p-Coumaric acid, Rosmarinic acid, Salvianolic acid A, Shimobashiric acid[32-34].

Flavonoids: Chrysoeriol, Cirsimaritin, Eriodictyol, Luteolin, Rutin, Salvigenin, Thymoquinone, Quercetin, 5,41-Dihydroxy-6,7-dimethoxy flavones, 5,41-Dihydroxy-3,7-dimethoxy flavones, 5-O-Methyl-luteolin, 3,5,7,31,41-Pentahydroxy flavanone, 41,5,7 Trihydroxyflavone (apigenin)[32-35].

Others: 1,2-Benzenediol 4-(1,1 dimethylethyl), Chavicol, Methyl chavicol, α-Corocalene, Dihydro carveol, Durohydroquinone, 1,4 Eicosadiene, Ethyl Salicylate, (Z)-1,3-Hexadiene, (Z)-3-Hexen-1-ol, Methyl octanoate, 1-Octen-3-ol, Oleic acid, 2-Phenyl ethyl tiglate, Phytol, Squalene, Tetradecanal, 3,7,11,15–Tetramethyl-2-hexadecen-1-ol, Thymol acetate, Trans-sabinene hydrate, Undecanal [9,13,17,19,20,22,27,28,30].

1.4 Medicinal uses

In indigenous system of medicine, Ayurveda, *C. aromaticus* is used against various disorders such as severe bronchitis, asthma, diarrhoea, epilepsy, renal and vesicle calculi, fever, common cold, cough, headache, indigestion, urinary diseases, vaginal discharges, colic, dyspepsia, convulsions, stimulates the functions of liver, indicated in kidney and bladder stones, dysentery, cholera, bilious affections, poisonous bites and vitiated conditions of *Kapha* and *Vata*[9]. In folk medicine, *C. aromaticus* leaves are used to expel kidney stone and hence the herb is known as *Paashanbhedi*[36]. In India, leaves are used traditionally for diarrhea[37]. Many pharmacological properties of *C. aromaticus* have been reported[38] including urolithiasis, antiepileptic, anti- tumorogenic, antimutagenic, radioprotective effect, antiviral, antifungal and neuropharmocological

properties. A decoction of its leaves is used for treatment of cough, throat infection, nasal congestion, asthma, and also as an antispasmodic, stomachic, and for the treatment of headache, fever, epilepsy and dyspepsia. It is also used in the treatment of skin ulcerations and urinary diseases, as well as to alleviate inflammation, kidney troubles, nervous disorders and in conditions of congestive heart failure[39,40]. *C. aromaticus* is also useful in natural antibiotic formulation as an active gradient[15]. It can help in treatment of cancer as it has anti tumor and cytotoxic activities[41]. The leaves also have bronchodilator and antimycobacterium tuberculosis activity. Application of bruised leaves in burns is also reported[11]. This plant is used for reproductive issue such as child birth and infertility in both genders: male and female[42]. The leaves are consumed as breast milk stimulant[43].

2. ANTIMICROBIAL ACTIVITY

Microorganisms such as virus, bacteria, fungi and protozoa are well-known to cause various human diseases. Throughout life, every person will suffer from at least a few infections. Many infections need treatment through antimicrobial drugs to prevent them from spreading further and causing complications. The spread of drug resistant pathogens is one of the most serious threats to successful treatment of microbial diseases. Down the ages, essential oils and other extracts of plants have evoked interest as sources of natural antimicrobial agents. They have been screened for their potential uses as alternative remedies for the treatment of many infectious diseases. Antimicrobial activities of extracts, oils and nanoparticles of *C. aromaticus* have also been reported.

2.1 Antibacterial activity

Different solvent extracts, essential oils as well as nanoparticles of *C. aromaticus* have great antibacterial activity (Table 1). Carvacrol and essentials oils, present in *Plectranthus amboinicus,* modifiy the constitution and increase the fluidity of the cell membrane, typifying a dose-dependent effect. Studies have demonstrated absence of toxicity of plant extracts *in vitro* and *in vivo*[44], which makes the use of this species very safe in the treatment of multi-resistant infections[41]. The plant extracts damage cell membrane and bacterial cells[45]. Antimicrobial activity of *P. amboinicus* extracts is similar to wide spectrum antimicrobials used in human and veterinary medicine[41].

The antibacterial activity of *C. aromaticus* was tested as a cure for reproductive tract infections (RTI) among women. Discs of fresh leaves of this plant was tested against RTI causing *Proteus mirabilis, Escherichia coli, Staphylococcus aureus, Enterococcus feacalis, Klebsiella pneumoniae,* and *Neisseria gonorrhoeae*. *C. aromaticus* exhibited marked antibacterial activity against all the bacteria tested except *N. gonorrhoeae*[46]. Antibacterial activity of ethanol and hot water leaf extracts of *C. aromaticus* against human pathogenic bacteria: *Staph. aureus, Bacillus subtilis, B. cereus, E. coli*, and *Salmonella enteritidis* was studied following disc diffusion method.

Table 1. Antibacterial activity of *Coleus aromaticus*

Sl. No.	Bacteria (activity against)	References
1	*Aeromonas hydrophilia*	50
2	*Bacillus subtilis; Bacillus cereus; Bacillus sp., Bacillus megaterium*	40, 47, 52, 54, 59, 60, 62, 63, 67, 69, 72, 74, 75, 76, 79, 80, 81, 82
3	*Bacteroides vulgatus* and *Bacteroides fragilis*	66
4	*Burkholderia cepacia*	53
5	*Citrobacter freundii*	53
6	*Edverchila tarda*	50
7	*Enterobacter aerogenes*	50
8	*Enterococcus feacalis*	48, 63, 75,
9	*Escherichia coli*	11, 17, 40, 46, 51, 53, 54, 55, 56, 61, 63, 67, 72, 74, 75, 79, 80, 81, 83, 84, 85
10	*Flavobacterium*	50
11	*Haemophilus influenzae*	54
12	*Klebsiella oxytoca; Klebsiella pneumoniae; Klebsiella vulgaris; Klebsiella sp.; Klebsiella planticola*	11, 46, 48, 49, 53, 54, 55, 56, 61, 62, 63, 69, 75, 78, 79, 82, 84
13	*Lactobacillus acidophilus*	79
14	*Leptospira biflexa*	77
15	*Neisseria gonorrhoeae*	46
16	*Nocardia asteroides*	66
17	*Propionibacterium acne*	64
18	*Proteus vulgaris; Proteus mirabilis; Proteus* sp.	11, 46, 53, 55, 56, 61, 62, 65, 72, 75, 80, 81
19	*Pseudomonas aeruginosa; Pseudomonas sp.; Pseudomonas fluorescens*	11, 48, 52, 53, 54, 56, 61, 62, 63, 69, 72, 75, 76, 79, 80, 81
20	*Salmonella* sp.; *Salmonella enteritidis; Salmonella typhi; Salmonella paratyphi* A	17, 47, 49, 51, 55, 59, 60, 61, 74
21	*Serratia marcescens*	81
22	*Shigella dysenteriae; Shigella boydii; Shigella* sp.*; Shigella flexnerii; Shigella sonnei*	17, 49, 51, 52, 55, 59, 60, 75
23	*Sporothrix schenckii,*	66
24	*Staphylococcus aureus; Staphylococcus sp., Staphylococcus epidermidis; Staphylococcus citreus*	11, 40, 41, 46, 47, 48, 49, 52, 53, 54, 55, 56, 59, 60, 61, 63, 65, 67, 69, 72, 74, 75, 79, 80, 81, 83, 84, 86
25	*Streptococcus pyogens; Streptococcus aureus; Streptococcus mutans*	48, 49, 68, 69, 71, 79,
26	*Vibrio* sp.	17
27	*Xanthomonas campestris*	72
28	*Yersinia enterocolitica*	40, 67

Both extracts showed potent antibacterial activity, of which the ethanol extract demonstrated the strongest antibacterial activity with the MIC value of 25-39 µg/ml where as water extract showed MIC around 46 62 µg/ml[47]. Crude water, crude alcohol, soxhlet water and soxhlet alcoholic extracts of *C. aromaticus* leaves were screened for antibacterial activity against five human pathogens isolated from sputum. Crude water extract produced higher zone of inhibition against *Pseudomonas aeruginosa* (20mm) followed by *K. pneumoniae* (18mm), *Streptococcus pyogens* (17 mm), *Staph. aureus* and *E. coli* (15 mm each). In crude alcohol extract *Staph. aureus* and *E. coli* showed 13 mm as high zone of inhibition. In soxhlet water and soxhlet alcohol *Ps. aeruginosa* showed 18 mm as highest zone of inhibition. Among all the extracts, crude water extract showed best antibacterial activity[48]. The methanolic extract of *C. aromaticus* was efficient against human pathogenic *S. typhi, Strep. aureus, Staph. aureus, Klebsiella vulgaris, Shigella dysenteriae and Shigella boydii,* obtained from MTCC, Chandigarh. *C. aromaticus* extract had MIC of 12.5 mg/ml[49]. The ethanolic extracts of *C. aromaticus* in the concentrations of 75 and 100 µg /ml were effective against different pathogens namely *Aeromonas hydrophilia, E. coli, Edverchila tarda, Enterobacter aerogenes* and *Flavobacterium*[50]. The methanol and ethanol extracts *of C. aromaticus* were screened against enteric pathogens such as *Shigella* sp., *Salmonella typhi and E. coli.* Both the leaf extracts exhibited antibacterial activity against the tested enteric pathogens[51].

The hydro alcoholic extract was screened against the Gram positive (*B. subtilis, Staph. aureus*) and Gram negative bacteria (*S. boydii, Ps. aeruginosa*) and the extract showed a zone of inhibition of 23.5mm and 20mm against Gram positive and Gram negative bacteria respectively[52]. Acetone, ethanol and water extracts of *C. aromaticus* was screened against pathogens associated with respiratory conditions *i.e. E. coli, K. pneumoniae, Ps. aeruginosa, Citrobacter freundii, Staph. aureus,* Methicillin Resistant *Staph. aureus, Proteus mirabilis* and *Burkholderia cepacia.* The leaf extracts demonstrated significant activity in the disc diffusion assay and the zones of inhibition ranged from 5mm to 14mm, while the MIC values ranged from 0.312mg/ml to 20.0mg/ml[53]**.** The ethanol extract of *C. aromaticus* also had high impact on the waste water pathogenic bacteria with inhibition zone of 21mm, 19mm, 16mm, 13mm,12mm against *E. coli, Bacillus* sp., *Pseudomonas* sp., *Staphylococcus* sp., *Klebsiella* sp., respectively[54]. Methonolic leaf extract of *C. aromaticus* showed moderate to high activity against all the tested bacterial pathogens viz., *E. coli, Haemophilus influenzae, K. pneumoniae, Proteus mirabilis, S. typhi, Shigella flexnerii* and *Staph. aureus*[55]. The ethanolic extract of *C. aromaticus* leaves and roots were screened against wound pathogenic bacteria using disc diffusion method. Ethanolic extracts demonstrated good antibacterial activity against *E. coli, Proteus mirabilis* and *Staph. aureus* and moderate activity against *Ps. aeruginosa* and *K. pneumoniae*. The efficiency of ethanolic extract against wound pathogens was dose and time dependent since greater activity was noted with the higher dose and prolonged time of exposure[56]. Ethanolic extract of *C. aromaticus* leaves showed good activity against *Klebsiella*, *Staphylococcus* and *Pseudomonas*[57].

Coleus amboinicus crude methanolic (CACM) leaves extract inhibited MRSA growth completely. The MIC value of CACM leaves extract against MRSA was 200µg/ml[58]. Hexane, chloroform and alcohol extracts from the leaf of *C. amboinicus* exhibited antibacterial activity against *B. cereus, B. subtilis, Staph. aureus, Shigella flexneri and Salmonella paratyphi* A[59]. Alcoholic extracts from the leaves of *C. amboinicus* exhibited antibacterial activity against *B. cereus, B. subtilis, Staph. aureus, Shigella flexneri* and *Salmonella paratyphi* A[60]. Ethanolic extract of *C. amboinicus* leaves was evaluated against six bacterial strains (*Staph. aureus*, *S. typhi*, *Ps. aeruginosa*, *E. coli, K. pneumoniae* and *Proteus* sp.). The highest antibacterial activity was observed against *S. typhi* and lowest antibacterial activity against *Staph. aureus*[61]. Acetone extract of *C. amboinicus* inhibited *Pseudomonas* sp., *Proteus* sp., and *Bacillus* sp., Benzene extract inhibited *Klebsiella* sp., and Petroleum ether extract inhibited *Proteus* sp.[62].

The hydro alcoholic extract of *Plectranthus amboinicus* had a great activity on methicillin resistant *Staph. aureus* (MRSA) strains with minimum inhibitory concentration ranging from 9.3 to 18.7 mg/ml[41]. The aqueous, acetone and methanol extracts of *P. amboinicus* leaves were tested against *B. subtilis, Staph. aureus, Staph. epidermidis, Enterococcus feacalis, E. coli*, *Ps. aeruginosa* and *K. pneumoniae.* Highest antibacterial activity was observed with methanol extract followed by acetone and aqueous extracts[63]. Aqueous extract of *P. amboinicus* exhibited good antibacterial activity against *Propionibacterium acne*[64]. The acetone extract of the leaves of *P. amboinicus* showed good antibacterial activity with least MIC values (400 – 1000 ppm) against the tested foodborne pathogens namely *Staph. aureus*, *B. cereus*, *E. coli* and *Yersinia enterocolitica*[40]. The methanolic leaf extract of *P. amboinicus* inhibited gram positive bacteria *Staph. citreus* and gram negative bacteria *Proteus mirabilis*[65]. Antimicrobial activity of petroleum ether, ethanol and aqueous extracts of *P. amboinicus* was studied against four respiratory pathogens such as *Sporothrix schenckii, Nocardia asteroides, Bacteroides vulgatus* and *B. fragilis*. Petroleum ether and aqueous extracts exhibited significant antibacterial activity against all the pathogens tested except *B. fragilis,* while methanolic

extract exhibited moderate antibacterial activity against all the four strains[66]. The acetone extract of *P. amboinicus* showed higher antibacterial activity than ethyl acetate extract, and both the extracts showed highest activity against *B. cereus* (375 and 625 µg/ml, respectively) and lowest activity against *Y. enterocolitica* (1000 and 1125 µg/ml, respectively). Antibacterial activity was in the order of *B. cereus* < *E.coli* < *Staph. aureus* < *Y. enterocolitica*[67]. Aqueous and ethanolic leaf extracts of *P. amboinicus* were tested against *Streptococcus mutans* causing dental caries through disc diffusion test and minimum inhibitory concentration (MIC) test. *S. mutans* was found to be sensitive to ethanolic and aqueous extracts of *P. amboinicus* at MIC 50 µg/ml[68]. Aqueous, acetone, and ethanol extracts of *P. amboinicus* showed significant activity against *Staph. aureus, Strep. pyogenes, B. subtilis, K. pneumoniae* and *Ps. aeruginosa*[69]. The ability of acetone and ethyl acetate extracts of the *P. amboinicus* leaves to prevent spoilage of artificially inoculated model food systems (cabbage and papaya) and natural microflora of chicken meat was evaluated. These extracts were able to reduce the bacterial counts in all food systems. A probable mode of action was by the changes they cause in bacterial cell wall and leakage of nucleic acid from bacterial cells[70]. Methanol extract of *P. amboinicus* leaves could be used as an anti-biofilm agent against *Streptococcus pyogens* biofilms[71].

Essential oils: Deena *et al.*[72] reported antibacterial activity of the essential oils of *C. aromaticus* against seven bacteria *viz., Bacillus megaterium, B. subtilis, E. coli, Staph. aureus, Proteus vulgaris, Ps. aeruginosa* and *Xanthomonas campestris*. Essential oils of *C. aromaticus* showed remarkable activity against urinary tract infection (UTI) causing bacteria: *Staph. aureus, Klebsiella oxytoca, K. pneumoniae, Proteus vulgaris, P. mirabilis*, *E. coli, Ps. aeruginosa*[11]. The minimum inhibitory concentration (MIC) of *C. aromaticus* leaf essential oil against tested bacteria ranged 40–80 µl/l and the minimum bactericidal concentration (MBC) 80–150 µl/l[73]. The antibacterial activity of essential oil extracted from leaf of *C. aromaticus* was tested against both Gram-positive and Gram-negative organisms. The essential oil showed maximum activity against *S. typhi, Staph. aureus, B. subtilis*, while no activity was observed against *E. coli* [74]. The antibacterial activities of *C. aromaticus* essential oil were conducted against multi drug resistant (MDR) urinary tract infection causing Gram positive (*B. subtilis, Staph. aureus, Enterococcus faecalis*) and Gram negative pathogens (*E. coli, Shigella sonnei, Ps. aeruginosa, K. pneumoniae, Proteus vulgaris*) by agar diffusion. Maximum zone of inhibition was found against Gram positive pathogens than Gram negative at the higher concentration of 80µl/ml[75]. The essential oil of aerial parts of *C. amboinicus* exhibited antibacterial activity against *B. subtilis* and *Pseudomonas fluorescens*[76]. The essential oil of *C. amboinicus* showed antibacterial activity against important enteric pathogens (*Salmonella* sp., *Shigella* sp., diarrheagenic *E. coli* and *Vibrio* sp.), with MIC values of 10 µg/ml[17].

Aqueous extract and volatile oil of *P. amboinicus* were effective in the concentration of 500 mcg /100µl and 50 mcg/ 100 µl respectively against *Leptospira biflexa*[77]. Essential oil obtained from leaves of *P. amboinicus* was tested against a standard strain of *K. pneumoniae* and 5 multiresistant clinical isolates of the bacteria. The minimal inhibitory concentration (MIC) and minimal bactericidal concentration (MBC) were 0.09 ± 0.01%. A complete inhibition of the bacterial growth was observed after 2 h of incubation with twice the MIC of the essential oil. Alteration in membrane permeability, prevention of urease activity, and alteration of the bacterial morphology was observed[78]. Essential oils of *P. amboinicus* leaves and stem were screened against Gram positive bacteria [*Streptococcus mutans* (clinical isolates), *Lactobacillus acidophilus* (clinical isolates), *B. subtilis* (ATCC 6051), *Staph. aureus* (ATCC 6538) and methicillin resistant *Staph. aureus* (MRSA) (ATCC 12692)], Gram negative bacteria [*K. pneumoniae* (ATCC 4352), *Ps. aeruginosa* (ATCC 9027) and *E. coli* (ATCC 8739)]. The essential oils exhibited powerful antibacterial activity against all the tested Gram positive bacteria in comparison to ceftriaxon. Concerning Gram negative bacteria, the oil of the leaves showed antibacterial activity against *E. coli*, while the oil of the stems showed activity against *K. pneumoniae*[79]. *In vitro* antimicrobial activity of *P. amboinicus* oils was conducted against *E. coli*, *Proteus vulgaris*, *B. cereus*, *Ps. aeruginosa*, *Staph. aureus*, and *Staph. aureus* (multiresistant) using microdilution method. The results of bioassay showed that all strains were sensitive to the oils, except *Ps. aeruginosa*. A synergistic effect of all essential oils combined with the aminoglycosides was demonstrated. This showed that *P. amboinicus* present antibiotic modifying activity[80]. *P. amboinicus* essential oil was tested against seven bacteria i.e. *Staph. epidermidis*, *Staph. aureus*, *Serratia marcescens*, *Ps. aeruginosa*, *Proteus vulgaris*, methicillin-resistant *Staph. aureus* (MRSA), *E. coli* and *B. subtilis*. All the bacteria were susceptible to *P. amboinicus* essential oil except *Ps. aeruginosa*[25]. *P. amboinicus* essential oil was found to exhibit bacterial resistance-modifying activity[81].

Nanoparticles: The bactericidal activity of the silver nanoparticles of *C. aromaticus* extract was carried out by disc diffusion method. The nanoparticles exhibited high toxicity against *B. subtilis* and *Klebsiella planticola*[82]. The antibacterial efficacy of the biogenic Au/Ag nanoparticles of *C. aromaticus* was tested against *E. coli* and *Staph. aureus*. The bactericidal effect of the alloy

nanoparticles was prominent against *E. coli* with an inhibition zone of 28 mm for a concentration of 150 µl[83]. The aqueous extract of *P. amboinicus* was used for the synthesis of silver nanoparticles, which showed good antibacterial effect on *K. pneumoniae, Staph. aureus* and *E. coli*[84]. The synthesized silver nanoparticles (Ag-NPs) using *P. amboinicus* leaf extract exhibited better antimicrobial property towards *E. coli*[85]. Zinc oxide nanoparticles prepared using *P. amboinicus* leaf extract controlled the growth of methicillin resistant *Staph. aureus* biofilm (MRSA ATCC 33591) at the concentration of 8–10 g/ml[86].

2.2 Antifungal activity

Fungi are destroyers of food materials, crops and grains during storage, retarding their nutritive values for human consumption. More than 25% of the world cereals are contaminated with known mycotoxins and more than 300 fungal metabolites are reported to be toxic to man and animals. Different solvent extracts, essential oils and nanoparticles of *C. aromaticus* have great antifungal activity (Table 2). The n-hexane and dichloromethane extracts of the *C. aromaticus* leaves exhibited activity against *Botrytis cinerea, Aspergillus niger* and *Candida albicans*[30]. Perumal *et al.*,[87] tested ethanolic extract of *C. aromaticus* (leaves) for antifungal activity against *Aspergillus flavus, A. terreus* and *Mucor* sp. The extract in different concentrations exhibited good fungicidal activity. Methanolic extract of *C. aromaticus* showed activity against *Candida krusei*[88]. Fresh leaves of *C. aromaticus* effectively reduced not only the incidence of the majority of seed-borne fungal pathogens of okra, but also improved the seed germination percentage and seedling vigor as well as yield[89]. The hydro alcoholic extract of *C. aromaticus* was screened against *A. niger* and the extract showed a zone of inhibition of 20.4mm[52]. Acetone, ethanol and water extracts of *C. aromaticus* were screened against pathogen associated with respiratory conditions *i.e. Candida abicans*. The leaf extracts demonstrated significant activity in the disc diffusion assay[53]. The antifungal activity of aqueous and ethanolic extracts of fresh, oven dried and shade dried leaves of *C. amboinicus* was performed by cup plate method against *Mucor* sp., *Aspergillus* sp., *A. niger, Penicillium* sp. and *Fusarium* sp. The extracts exhibited good antifungal activity against all fungi except *Fusarium* sp.[60]. Acetone and benzene extracts of *C. amboinicus* inhibited the fungal pathogen *Aspergillus tamari*[62]. The antifungal activity of methanolic extract of *P. amboinicus* was assessed against *Candida albicans, C. tropicalis, Aspergillus fumigatus, A. flavus* and *A. niger*. The extract showed significant antifungal activity at 150 µg/ml with a P value of (P<0.05- 0.01) when compared with the positive control fluconozole[90]. The methanolic leaf extract of *P. amboinicus* demonstrated antifungal activity against *Penicillium* sp., and several pathogenic yeasts like *Trichophyton rubrum, T. mentagrophytes, Candida albicans, C. parapsilosis* and *Cryptococcus* sp.[65]. Aqueous and ethanolic extracts of the leaves of *P. amboinicus* were screened against *C. albicans, C. tropicalis, C. parapsilosis, C. krusie* and *C. glabrata*. The ethanol extract was found to be having higher inhibition with low MIC against the fungal species selected for the study[91]. Aqueous and ethanol leaf extracts of *P. amboinicus* induced systemic resistance in rice plants against *Rhizoctonia solani* infection causing sheath blight disease[92].

Table 2 : Antifungal activity of *Coleus aromaticus*

Sl. No.	Fungi (activity against)	References
1.	*Alternaria brassicicola*	72
2.	*Aspergillus ochraceus; Aspergillus oryzae; Aspergillus niger; Aspergillus* sp.*; Aspergillus flavus, Aspergillus tamari; Aspergillus parasiticus; Aspergillus terreus; Aspergillus fumigatus*	16, 30, 52, 60, 62, 72, 74, 79, 84, 87, 90,
3.	*Botrytis cinerea*	30,
4.	*Candida albicans; Candida parapsilosis; Candida krusei; Candida tropicalis; Candida glabrata; Candida guilliermondii, Candida stellatoidea; Candida gattii; Candida neoformans*	25, 30, 53, 60, 65, 72, 74, 79, 84, 88, 90, 91, 94, 95, 96
5.	*Cladosporium cucumerinum*	76
6.	*Colletotrichum musae*	72
7.	*Cryptococcus* sp.	65
8.	*Fusarium* sp.; *Fusarium solani*	60, 72
9.	*Malassezia furfur*	93
10.	*Mucor sp.*	60, 87,
11.	*Penicillium* sp.	16, 60, 85
12.	*Rhizoctonia oryzae-sativae; Rhizoctonia oryzae; Rhizoctonia solani*	72, 92
13.	*Saccharomyces cerevisiae*	16, 96
14.	*Trichophyton rubrum, Trichophyton mentagrophytes*	65

Essential oils: The essential oil of *C. aromaticus* inhibited the growth of *Botrytis cinerea, A. niger* and *C. albicans* (MIC values between 0.125 and 0.25 mg/ml)[30]. Essential oils of *C. aromaticus* exhibited antimicrobial activity against eight fungi *viz., A. niger, A. parasiticus, Rhizoctonia oryzae-sativae, R. oryzae, Colletotrichum musae, Fusarium solani, Alternaria brassicicola* and *C. albicans*[72]. The essential oil of *C. aromaticus* exhibited effective antifungal activity with minimum inhibitory concentration of (MIC) 25-50 µl/l[15]. The antifungal activity of essential oil extracted from leaf of *C. aromaticus* was studied against two fungal species *C. albicans* and *A. niger*

and the essential oil exhibited maximum zone of inhibition against *C. albicans*. The essential oil exhibited concentration dependent activity[74]. The essential oil of aerial parts of *C. amboinicus* exhibited antifungal acitivity against *Cladosporium cucumerinum*[76]. Pure essential oil of *C. amboinicus* showed antidandruff activity against *Malassezia furfur* with an inhibitory zone of 31mm[93]. The antifungal activity of essential oil extracted from leaf of *C. amboinicus* was studied against two fungal species *C. albicans* and *A. niger* and the essential oil exhibited maximum zone of inhibition against *C. albicans*[60]. *P. amboinicus* oils were effective against yeasts *C. albicans, C. tropicalis, C. guilliermondii*, *C. krusei* and *C. stellatoidea*[94].

The essential oil of *P. amboinicus* (10 µl) exhibited promising fungitoxic activity against *Aspergillus flavus, A. niger*, *A. ochraceus* CFR 221, *A. oryzae* besides *Fusarium* sp. GF-1019, *Penicillium* sp., and *Saccharomyces cerevisiae*. The ochratoxin production from *Aspergillus ochraceus* was also completely inhibited by the essential oil of *P. amboinicus*[16]. Essential oil of *P. amboinicus* showed significant antifungal activity against *C. albicans, C. tropicalis* and *C. parapsilosis* at minimum fungicidal concentration of 50 µg/ml[95]. Essential oils of *P. amboinicus* leaves and stem were screened against filamentous fungi [*A. flavus* (ATCC 15517) and *A. niger* (ATCC 16404)] and yeast [*C. albicans* (ATCC 10231) and *C. parapsilosis* (ATCC 22019)]. The oils showed high antifungal activity against all the tested fungi and yeast compared to clotrimazole as standard[79]. *P. amboinicus* essential oil was tested against *C. albicans* and *C. tropicalis*. Both the fungi were susceptible to *P. amboinicus* essential oil[25]. The effects of essential oils of *P. amboinicus* leaves on fungal growth were evaluated by disk diffusion assay. The results showed that seven fungi (yeasts) (*Candida albicans*; *C. gattii* serotype B; *C. gattii* serotype C; *C. neoformans* serotype D; and *S. cerevisiae*) were sensitive[96].

Nanoparticles: The aqueous extract of *P. amboinicus* was used for the synthesis of silver nanoparticles, which showed good antifungal effect on *Aspergillus* sp. and *C. albicans*[84]. The synthesized silver nanoparticles (Ag-NPs) using *P. amboinicus* leaf extract exhibited better antifungal property towards *Penicillium* spp.[85].

2.3 Antiprotozoal activity

Periyanayagam *et. al.*[97] studied the antimalarial activity of the aqueous extract of *C. amboinicus* leaves against *Plasmodium berghei yoelii*. They found that the extract in a dose of 250 mg/kg was able to reduce parasitaemia up to 68% after 96 hours and up to 76% in a dose of 500 mg/kg after the same duration. Methanolic extract of *C. aromaticus* showed significant activity against *Leishmania chagasi* and *Leishmania amazonensis*[88]. Essential oil of *P. amboinicus* at 2.5% was able to reduce the viability of *Leishmania braziliensis* promastigotes in the first 48 h, similar to the reference drug ($p < 0.01$)[98]. Antimalarial activity of *P. amboinicus* at different extract doses of 50, 200, 400 and 1000 mg/kg were tested *in vivo* against *Plasmodium berghei* infections in mice. The extract significantly reduced the parasitemia by the 50 ($P = 0.000$), 200 ($P = 0.000$) and 400 mg/kg doses ($P = 0.000$) in the *in vivo* prophylactic assay. The percentage chemo-suppression was calculated as 83.33% for 50 mg/kg dose, 75.62% for 200 mg/kg dose and 90.74% for 400 mg/kg dose. Thus, *P. amboinicus* extract was found to be a promising agent against *P. berghei* infection[99].

2.4 Antiviral activity

Chloroform extract of *C. amboinicus* showed active antiviral activity against Herpes Simplex Virus (HSV-2) strain 186 in plaque reduction assay using Vero cell line. The 50% Effective Dose (ED50) of the extract was 3.25 µg/ml[100]. Extracts of *P. amboinicus* were reported to have antiviral activity against Herpes Simplex Virus-1 (HSV1)[101] and anti-HIV inhibition activity[102]. Ethanolic extract of *P. amboinicus* was reported to have selective antiviral activity against HSV1 and Vesicular Stomatitis (VSV) viruses[103]. 800 ppm hexane leaf extract of *P. amboinicus* was found to be effective against *Bombyx mori* Nuclear Polyhedrosis Virus (BmNPV) infecting three different silkworm breeds[104].

3. CONCLUSION

Coleus aromaticus is a rich source of compounds with various biological activities. It is easily available in India and leaves of the plant possess a wide range of biological properties and thus can be source of low-cost medication. Till now not much work has been done on the antiviral and antiprotozoal activity of this plant and thus there is a scope for scientific studies to fully exploit the medicinal properties of this plant to support traditional claims as well as, exploring some novel and promising drugs.

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