



REVIEW ARTICLE

MEDICINAL CHEMISTRY

COLEUS AROMATICUS BENTH – A NUTRITIVE MEDICINAL PLANT OF POTENTIAL THERAPEUTIC VALUE**RASHMI SAHAY KHARE¹, SHANTA BANERJEE² AND KANIKA KUNDU¹ ***¹Department of Chemistry, MMV, Banaras Hindu University, Varanasi, India²Plantachem GbR, Industrie- und Gewerbegebiet 21, 16278 Pinnow (UM), Germany.**KANIKA KUNDU**

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ABSTRACT

Coleus aromaticus Benth (Lamiaceae) is known as a must-have plant in medicinal herb garden. The plant is well known for its antimicrobial and pharmacological activities. It is also reported to possess antioxidant and food additive properties. Antioxidant activity is reported to be mainly due to rosmarinic acid, chlorogenic acid and caffeic acid. The essential oil of *Coleus aromaticus* has great anti-microbial activity on Gram negative as well as Gram positive bacteria, drug resistant microorganisms, phytopathogenic microorganisms and fungi. Promising fungi-toxic activity against *Aspergillus flavus*, *Aspergillus niger*, *Aspergillus ochraceus* CFR 221, *Aspergillus oryzae*, *Candida versatilis*, *Fusarium* sp. GF-1019, *Penicillium* species and *Sacharomyces cerevisiae* are reported in literature. Carvacrol and /or thymol and β -caryophyllene are the major active constituents of essential oil of the plant. The compositions of oil vary considerably depending upon the locality, season of collection and maturation of plant. *Coleus aromaticus* is useful in natural antibiotic formulation as an active gradient. The plant is also used as a food supplement and a flavoring for drinks. *Coleus aromaticus* leaves are reported to possess remarkable diuretic property. The result shows therapeutic potential of *Coleus aromaticus* which can be used as potential source of bioactive compounds.



KEYWORDS

Coleus aromaticus, Review, Pharmacology, Phytochemistry, Antimicrobial activities.

INTRODUCTION

Throughout the ages, human beings are dependent on nature for their basic needs such as food, shelter, clothing, fertilizers, transportation and medicine. Plants as medicine have been in use from thousands of years and continuing are in use. Plants are good source of a wide variety of compounds, such as phenolic compounds, terpenoids, nitrogen containing compounds, vitamins, and secondary metabolites which have antioxidant, antimicrobial, anti-inflammatory, antitumor, antimutagenic, anti-carcinogenic and diuretic activities. In the present scenario our medicines and drugs for clinical purposes contain natural products and their derivatives. According to WHO 70% to 80% of the population in many developed countries have used some form of alternative or complementary medicine which are traditionally plant products¹. So it becomes necessary that traditionally used medicinal plants should be explored on the basis of bioactivity, pharmacological activities and their active constituents responsible for bioactivities. The present review incorporates therapeutic potential, antimicrobial activity, food and nutritive value of *Coleus aromaticus* (Indian borage or Ajwain patta) as well as comparison of the active constituents of the plants from different sources and locality. The survey will give a frame work for exploration of the herb for optimum use, analysis of active constituents from different sources and scope for further research work.

Among the plants known for medicinal value, the plants of the genus *Coleus* belonging to the family Lamiaceae or Labiatae are well known for their therapeutic potentials. The plants of Lamiaceae are usually aromatic and known for kitchen herbs like *Rosemary*, *Ocimum sanctum*, and *Oregano*. Many of the plants of this family are used in traditional medicine because of their antimicrobial, antioxidant, antiseptic and other pharmacological activities. *Coleus* is a large and

wide spread genus containing 300 species and is found in different parts of tropical Africa, Asia and Australia². *Coleus* species are found as herbs, subshrubs or shrubs. They are often succulent with opposite leaves. Inflorescence is terminal or in the upper leaf axils and flowers are in compact cymose clusters. *Coleus aromaticus* Benth syn. *Coleus ambionicus* (Lour) Spreng or *Plectranthus ambonicus* Lour, one of the plant of genus *Coleus* which is native to India and Mediterranean. The plant is also known by different folk names such as Country-borage, Indian-borage (English), Ajwain patta, Karpuravalli (Tamil), Pattharachuur (Bengal)³, Bangun-bangun leaves, Indian-mint, French-thyme, Mexican-mint, Soup-mint, Spanish-thyme, Oreille, Hung chanh, Maxian thyme⁴, which confirms its large diffusion in tropical areas. In Ayurvedic medicine, the plant is known as Parna- Yavaani.

COLEUS AROMATICUS AT A FIRST GLANCE:

At first appearance, *Coleus aromaticus* looks as a green, perennial, shrub having heart shaped, and leathery leaves with scalloped edges (figure1). The plant grows to around 50 cm tall with horizontal stems up to 180 cm long. The leaves are highly aromatic with a strong flavor of mixed herbs and make an excellent addition in stuffing for meat and poultry. Finely chopped, they can also be used to flavor meat dishes, especially beef and lamb^{5, 6}. *Coleus aromaticus*, a plant of medical and food interest is told as "must- have" plant in medicinal herb garden⁷. It is known to possess antimicrobial^{8, 9, 10}, antiepileptic, leishmanial, and antioxidant activities^{11, 12}. The leaves are also used for treatment of cough, throat infection and nasal congestion. The last decade has witnessed considerable research on *Coleus aromaticus* in different parts of world as evident from the increase in publication during last decade



including the review articles by different authors^{2, 13}. There are major differences in chemical composition between samples of different

locations of this species that may result from genetic, environmental and developmental differences.



Figure 1
Coleus aromaticus

NUTRITION 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%)¹⁴. Thus, *Coleus aromaticus* is a good source of nutritious compounds and can be used as a food supplement. This plant has chlorophyll a 0.44 ± 0.13 and chlorophyll b 0.29 ± 0.10 ¹⁵. It also contains total xanthophylls (0.356mg/g of dry weight of plant); neoxanthin, violaxanthin, leutin, zeaxanthinics, α - carotene (0.157mg/g of dry weight) and β - carotene (0.0035mg/g of dry weight)¹⁶.

ETHNO BOTANICAL USES:

In India the leaves of green type of country borage are often eaten as fried stuff or seasoning meat dishes and food products to remove disagreeable smell^{5, 6}. Batakese people in Indonesia use the plant as a breast

milk stimulant (a lactagogue) for hundreds of years¹⁷. The plant is used more commonly as medicinal herb due to its strong antioxidant property and therapeutic value. *Coleus aromaticus* is also useful in natural antibiotic formulation as an active gradient¹⁸. Juice obtained from leaves of *Coleus aromaticus* is effective to cure constipation and other digestive problems¹⁹ including indigestion, stomach ache, and congestive heart failure. It can help in treatment of cancer as it has anti tumor and cytotoxic activities^{11, 20}. *Coleus aromaticus* leaf extract is also given in bronchitis, asthma, cold, chronic cough and epilepsy^{3, 21, 22}. In India, leaves are used traditionally for diarrhea²³. The plant is used in South India primarily as a medicinal plant where it is called as "Karpuravalli". In the Philippines, *Coleus aromaticus* is commonly considered as a medicinal plant, useful for relieving headache, colic, flatulence, rheumatism, otalgia (ear aches)^{2, 22}. In eastern Cuba it is used as herbal mixture in traditional medicine for treatment of catarrhal infections²¹. The leaves of *Coleus aromaticus* have bronchodilator and antimycobacterium tuberculosis activity^{24, 25}. Application of bruised leaves in burns is also reported. The leaf extract



shows regulatory influence on calcium oxalate stone formation in experimental rats. In folk medicine, *C. aromaticus* leaves are used to expel kidney stone and hence the herb is known as Paashanbhedi³. In Rodrigues, *Coleus aromaticus* is used for curing of cholera and in treatment of fever or infections^{26, 27, 28}. Leaves of *Coleus aromaticus* are helpful for checking of alleviate inflammations²⁶. This plant is used for reproductive issue such as child birth and infertility in both genders: male and female²⁹. Plant part, other than leaves are also known to be of therapeutic value. *C. aromaticus* roots are used for menorrhagia³⁰, for the treatment of diphtheria and tetanus³¹, and for curing infant fever²⁷.

ANTIOXIDANT ACTIVITY:

Antioxidants are widely used as ingredients in dietary supplements in the hope of maintaining health and preventing diseases. Antioxidants also prevent food spoilage via food additive. But use of synthetic antioxidants is not safe due to their health risks and toxicity³². The search for antioxidants from natural sources has received much attention to identify compounds that act as suitable antioxidants and replace the synthetic ones. In addition, these naturally-occurring antioxidants can be formulated to give nutraceuticals that can help to prevent oxidative damage from occurring in the body³³. Palani et al. have shown antioxidant activities of the ethanol extract of *Coleus aromaticus*³⁴. Phenolic and polyphenol constituents namely carvacrol, flavonoids, rosmarinic acid, caffeic acid and chlorogenic acid are reported to be responsible for antioxidant activity of *Coleus aromaticus*^{33, 35}. The hydroalcoholic and methanolic extracts of this plant show free radical scavenging activity^{36, 37}. Hydroalcoholic extract at 10, 20, 40, 60, 80, 100 and 120 µg/ml resulted in a dose-dependent increase in radical scavenging ability against various free radicals. The order of scavenging property towards free radicals were 1, 1-diphenyl-2-picrylhydrazyl (DDPH), 2,2-azinobis (3-ethylbenzothiazoline-6-sulfonic acid) (ABTS), super oxide anions, hydroxyl radicals, nitric oxide radical respectively³⁶. Being the major

polyphenol in *C. aromaticus*, rosmarinic acid was more likely to be responsible for most of the observed antioxidant activity of the plant. The potency of these compounds could provide a chemical basis for some of the health benefits claimed for *C. aromaticus* in folk medicine e.g. anticancer, bronchodilator activity³⁵. Triazole treatments can be used as enhancer for antioxidant potentials in the plant³⁸. Methanolic extract of *Coleus aromaticus* seed shows antioxidant activity with reducing power in percentage 300.7 ± 3.1 ³⁹.

PHARMACOLOGICAL ACTIVITY:

Pharmacological activities of *Coleus aromaticus* have been studied by different groups of workers which can account for reported ethno botanical use of the plant. Brindha P. et al. have reported the pharmacognostic, exomorphology, histomorphology and physico-chemical properties of the leaf and stem of *Coleus aromaticus*⁴⁰. Indian borage has anti tumor promoting and cytotoxic activities^{11, 20, 41}. Hydroalcoholic and water extract of this plant shows anti-inflammatory¹¹, induced body immunity⁴². Gurgel et al. have shown that hydroalcoholic extract on dosing to mice at rate of 100, 150, 250 and 350 mg/kg suppressed the growth of sarcoma-180 and Ehrlich ascite carcinoma tumors¹¹. Ethanol extract of *Coleus aromaticus* is reported to have anticlastogenic potency against anticancer drugs⁴³, diuretic properties^{34, 44}, nephroprotective activities³⁴. Aqueous extract of *Coleus aromaticus* increases phagocytosis capacity of neutrophil cells⁴⁴ and mast cell stabilization⁴², diuretic properties property in rat peritoneal mast cells⁴⁵. Perez et al. reported neuropharmacological profile of *Coleus aromaticus*⁴⁶. A work on Insect antifeedant activity was reported by Valera et al. He reported that *Sitophilus oryzae* on treatment with 1.25% w/w with *Coleus* oil did not show any negative response in insect⁴⁷. Singh et al. have reported insecticidal activity of oils at a dose of 2.5×10^{-2} mg/cm³⁴⁸. Polysachharides extracted from dried plant parts of *Coleus aromaticus* shows anticoagulant activity⁴⁹. *Coleus*



aromaticus offers to have biologically control activity for water hyacinth. It is reported that 40g/l as a highest dosage and 20g/l as a medium dosages cause complete killing of water hyacinth within 24 hours where as 10g/l offers complete killing of water hyacinth in 9 days⁵⁰. *C. aromaticus*, causes reduction in egg laying capacity, retard in adult emergence and weight loss in the pulse beetle *Callosobruchus maculatus* F⁵¹. Periyannayagam et al. have studied effect of aqueous extract of this plant on *Plasmodium berghei yoelii*⁵². Aqueous extract of fresh leaves of *C. aromaticus* and tissue culture-raised plants posses a dose-dependent positive inotropic effect on isolated frog heart⁵³.

ANTIMICROBIAL ACTIVITY:

Different solvent extracts as well as essential oils of *Coleus aromaticus* have great anti-microbial activity on Gram negative as well as Gram positive bacteria, drugs resistant microorganisms and phytopathogenic microorganism. Fungi are destroyers of food materials, crops and grains during storage, retarding their nutritive values for human consumption⁵⁴. 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. Rao et al. have reported antimicrobial activity of *Coleus aromaticus* oil against pathogenic and non-pathogenic fungi and bacteria⁵⁵. It is reported that essential oil of *Coleus aromaticus* is effective against fungal and bacterial strain with minimum inhibitory concentration (MIC) 25-50 µl /L and 20-100 µl /L respectively¹⁸. The medicinal properties and antibacterial action of *Coleus aromaticus* is reported to have activity against *Pneumococcus* and *Staphylococcus* 209 P⁵⁶. The essential oil of *Coleus aromaticus* (10 µl) has promising fungi-toxic activity against *Aspergillus flavus*, *Aspergillus niger*⁵⁷, *Aspergillus ochraceus* CFR 221, *Aspergillus oryzae* beside *Fusarium* sp. GF-1019, *Penicillium* species and *Sacharomyces cerevisiae*. It is also seen that ochratoxin production from *Aspergillus ochraceus* was completely inhibited by the essential oil of

*Coleus aromaticus*⁸. Oils are also effective against yeast *Candida albicans*⁵⁸, *Candida tropicalis*, *Candida guilliermondii*, *Candida krusei* and *Candida stellatoidea*⁵⁹. Anti microbial flavonoid, viz. salvigenin and cirsimaritin isolated from *Coleus aromaticus* are also reported to have low antimicrobial activities against *Pseudomonas aeruginosa*, *Bacillus subtilis*, *E. coli*, *Staphylococcus aureus*, *Candida albicans*, *Tricophyton*, *mentagrophytes* and *Aspergillus niger*⁹.

Fresh leaves of *Coleus aromaticus* Benth are effective not only at reducing the incidence of the majority of seed borne fungal pathogens, but also improving the seed germination percentage as well as the seedling vigor and ultimately the yield of okra⁶⁰. *Coleus aromaticus* is also effective against microorganism of reproductive tract infection. Discs of fresh leaves of this plant was tested against RTI causing *Candida albicans*, *Candida krusei*, *Proteus mirabilis*, *E. coli*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsilla pneumoniae*, *Neiseri*¹⁰. This plant is also effective against *Streptococcus mutans*⁶¹. The hydroalcoholic extract of *Coleus aromaticus* has a great activity on methicillin resistant *Staphylococcus aureus* (MRSA) strains with minimum inhibitory concentration ranging from 18.7 to 9.3 mg/ml⁶². Perumal et al. have shown ethanolic extract of nine medicinal plants parts along with *Coleus aromaticus* for antifungal activity against *Aspergillus flavus*, *A. terreus* and *Mucor* species⁶³. Methanolic extract of *Coleus aromaticus* shows activity against *Candida krusei*, *Leishmania chagasi* and *Leishmania amazonensis*⁶⁴. Ether extract of dried leaves of *C. aromaticus* do not show effect on the Inaba and Ogawa strains of *Vibrio comma*⁶⁵.

PHYTOCHEMISTRY:

Leaves of *Coleus aromaticus* contain flavones salvigenin, 6-methoxygenkwanin, quercetin, chrysoeriol, luteolin and apigenin, the flavanone eriodyctol and the flavanol taxifolin⁶⁶, triterpenic acids; oleanolic acid, 2,3-dihydroxyoleanolic acid, crategolic acid, ursolic acid, pomolic acid, euscaphic acid, tormentic acid and 2,3,19,23-tetrahydroxyursolic acid⁶⁷.



Bioactivity of *Coleus aromaticus* is reported to be mainly due to the steam volatile essential oil fraction of the plant and it has been widely studied in different parts of the world. The main constituents present in the oils largely depend upon of locality, environment (Table 2) and season. Essential oil of *Coleus aromaticus*, grown in India, is rich in carvacrol, thymol, eugenol, chavicol, ethyl salicylate⁶⁸. The data also shows that percentage of carvacrol, β -caryophyllene and other oxygenated compounds are more in the month of September as compared to May^{58, 69}. On the other hand, volatile constituent of Mauritius's *Coleus aromaticus* contains camphor (39%) along with carvacrol (41.3%)²⁸. Other constituents reported are (Z)-1, 3-hexadiene (0.1%), (Z)-3-hexenol (0.6%), (E,Z) farnesene (0.2%), (E,E) farnesene (0.2%), (E,E) farnesene (0.2%) and muurolene(0.2%)⁷⁰. GC/MS of *Coleus aromaticus* in Pakistan shows the thymol as a major constituent instead of carvacrol along with p-cymene, terpinen-4-ol, caryophyllene, verbenone, tert-Bu anisole, oxygenated sesquiterpene⁷¹, but according to Malik et al. carvacrol is a major component (40.42%) of *C. aromaticus* volatiles in Pakistan; with other compounds limonene, eugenol, thymol, ethyl

salicylate, terpinene, selinene, p-cymene, pinene, caryophyllene and myrcene⁷². The presence of patchoulane: 8.7% along with carvacrol: 50.7% and caryophyllene: 13.1% was reported by Mangathayaru et al.⁷³. Weehuizen has isolated carvacrol from oils of *Coleus aromaticus* and identified by its urethan and NO derivatives⁷⁴.

Due to good antioxidant and pharmacological activities, this plant and its different types of extracts were analyzed for active constituents. Methanolic extract of seed of this plant contains total phenol 55.1 ± 1.0 (mg/g)³⁹. Methanolic extract of leaves of *Coleus aromaticus* contains chlorogenic acid, caffeic acid, coumaric acid poly phenolic compounds with strong antioxidant property³³. Alcohol (75%) extraction yields cirsimaritin, sitosterol-D-glucosides and oxalacetic acid⁷⁵. Chloroform fraction of this plant shows the presence of three flavones; Salvigenin, Cristimartin and Chrysoeriol⁹. Knab et al. have reported presence of eucalyptol in *Coleus aromaticus* leaves when extracted through steam distillation and solid phase micro extraction (SPME) methods⁷⁶. Rout et al. have reported different types of compounds present in different solvent fractions of *Coleus aromaticus* given in table 1⁷⁷.

Table 1
Types of compounds present in *Coleus aromaticus*⁷⁷

Test	Petroleum ether	Chloroform	Methanol	Water
Flavonoid	-	-	+	+
Fixed oils	-	-	-	-
Proteins	-	-	+	+
Amino acids	-	-	+	+
Saponin	+	+	-	-
Tannins	-	-	+	+
Phenolic compounds	-	-	+	+
Terpenoids	-	+	+	+
Steroids	+	+	-	-
Carbohydrates	-	-	+	+
Glycosides	-	-	+	+
Alkaloid	-	-	+	+
Gum & resin	-	-	-	-



Table 2
Volatile constituents of Coleus aromaticus leaves

Place	Chemical constituent of volatiles (percentage)	References
Mysore, India	Carvacrol (70), β -caryophyllene (6.2), p-cymene (5.6), gamma-terpinene (5.3)	Murthy et al. 2008 ⁸
Cambodia	Carvacrol (44.01), terpinene(14.75), Cyperene(11.46), p-Cymene(10.47)	Koba et al. 2007 ¹⁸
Rancherias	Carvacrol(55.3) p-cymene(18.8), γ -terpinene(7.2)	Valera et al. 2003 ⁴⁷
Merida	Carvacrol (64.7), p-cymene (9.8)	Valera et al. 2003 ⁴⁷
Andhra Pradesh, India	Thymol (94.3), Carvacrol (1.2)	Singh et al. 2002 ⁴⁸
India	Carvacrol (53-67), p-cymene (6.5-12.6), terpinene (5.9-15.5),	Mallavarapu et al. 1999 ⁶⁹
Pakistan	Thymol (79.6)	Haque et al. 1998 ⁷¹
Egypt	Thymol (88)	Hafez et al. 1994 ⁵⁸
Martinique	Carvacrol (72)	Prudent et al. 1995 ⁷⁰
Mauritius	Carvacrol (41.3), camphor (39)	Gurib-Fakim et al. 1995 ²⁸
Pakistan	Carvacrol (40.40), thymol(8.12), eugenol (7.35), chavicol (4.250)	Malik et al. 1985 ⁷²
Surabaja, Java	Carvacrol (60.1), β -caryophyllene (20.6), p-cymene (5.3)	Bos et al. 1983 ⁷⁸
India	Thymol (41.30), carvacrol (13.25), 1,8-cineole(5.45), eugenol (4.40), β -caryophyllene (4.20)	Baslas et al. 1981 ⁷⁹
India	Carvacrol (43.1), thymol (7.2), eugenol (6.4), chavicol (5.3), Et-salicylate (3.2)	Dutta et al. 1959 ⁶⁸

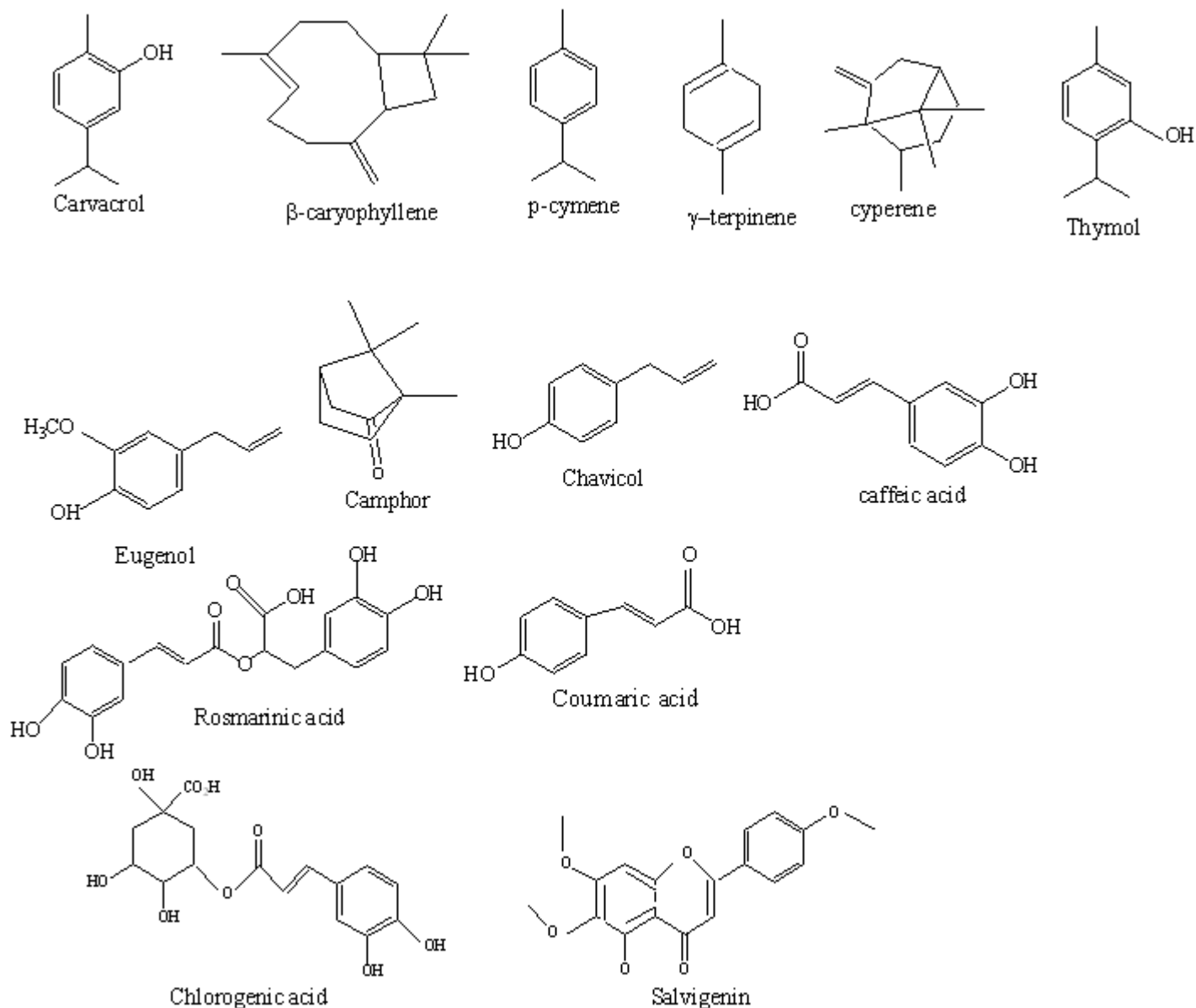


Figure 2
Structure of compounds present in *Coleus aromaticus*

RECENT WORKS:

Besides the pharmacological and medicinal activity, this plant is also important due to its nutritional, ecological and microbiological significance.

Tissue cultured studies for biosynthetic capacity of this plant reveals that tissue cultured plant has more thymol content (0.012% of fresh weight) in essential oil as compared to the parent plant (thymol composition: 0.009% of

fresh weight). It also shows that root cultured plants are enriched in thymol content as compared to leaves and auxiliary buds cultured plants⁸⁰. Other research shows the symbiotic association of *Coleus* plant and fungi. These fungi are dependent on plant for sugar uptake and help the plant by increasing uptake of minerals from soil via fungal hyphae. But these fungi also affect the root, shoot, leaves, and nodes growth of plant and biochemical



constituents. Symbiotiation of *Coleus* with AM + *Azospirillum* is reported to increase growth and biochemical activity⁸¹.

Many fungal communities such as *Absidia glauca* Hagem, *Acremonium chrysogenum*, *Aspergillus niger*, *Cephalosporim acremonium Thaxter*, *Colletotrichum dematium* (Fr.) Grove, *Glocladium roseum* Bainier, *Pestalotiopsis* sp., have been isolated from surface sterilized leaves of *Coleus aromaticus* in dry and wet seasons⁸². Karyomorphological and RAPD

studies have been also done in *Coleus aromaticus*⁸³.

FUTURE DIRECTION OF RESEARCH:

The scientific research on *Coleus aromaticus* shows its potential therapeutic values. The detailed information in this review will provide a pathway for future study. As this plant is a rich source of biologically active compounds, activity guided isolation of new compounds needs to be evaluated.

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