Academic Sciences Asian Journal of Pharmaceutical and Clinical Research
Vol 5, Issue 1, 2012 ISSN - 0974-2441

Review Article

RECENT UPDATES ON THE GENUS *COLEUS*: A REVIEW

HIMESH SONI[1*] & AKHLESH KUMAR SINGHAI[2]

[1]Suresh Gyan Vihar University, Jaipur-302025, India, [2]Lakshmi Narain College of Pharmacy, Bhopal, Madhya Pradesh-462021, India
Email: himeshsoni@rediffmail.com

Received: 17 October 2011, Revised and Accepted: 2 December 2011

ABSTRACT

Nature has been a source of medicinal agents for thousands of year and an impressive number of modern drug have been isolated from natural sources, many based on their use in traditional medicine. Plants from the genus *Coleus* have been used in traditional medicine by many cultures. Flavonoids, glycosides, phenolic compounds and volatile constituents have been reported as the major phytoconstituents of the *Coleus species*. This review describes the morphology, traditional and folklore uses, phytoconstituents and pharmacological reports of the prominent species of the genus *Coleus*. Various virgin areas of research on the species of this genus have been highlighted with a view to explore, isolate and identify the medicinally important phyto-constituents which could be utilized to alleviate various diseases affecting the mankind.

Keywords: *Coleus*; Ethnopharmacology; Phytoconstituents; Pharmacological-reports.

INTRODUCTION

Medicinal plants are of great significance to the health of individuals and communities [1]. India is well known as the "Emporium of Medicinal Plants". Due to their great importance, demand of medicinal plants has increased numerous folds. The genus *Coleus* was first described by De Loureiro (1970). The name *Coleus* is derived from the Greek word *Koleos*, which means sheath around the style [2]. There are about 150 plants belonging to the mint herb family. Today, there are more than 500 varieties of coleus in cultivation all over the world. *Coleus* plants are very colorful and can be grown indoor as well as outdoors. Medicinal plants have curative properties due to the presence of various complex chemical substances of different chemical nature, which are found as secondary plant metabolites in one or more parts of these plants[3]. The focus of this review is to provide information on the morphology, active constituents and pharmacological activities of the genus *Coleus*. Plants from this genus known to contain various active principals of therapeutic value and possesses biological activity against number of diseases. There are number of pharmacological effects reported on these plants.

GEOGRAPHICAL DISTRIBUTION

The Coleus group of plants grows in tropical to subtropical situations and in warm temperate climatic zone on mountains of India, Nepal, Burma, Sri Lanka, Thailand and Africa. It comes up well on the sun exposed dry hill slopes from 300m to 1800m altitude. A well drained medium fertile soil is suitable for its cultivation. It is propagated vegetatively through stem and root cuttings. Vine cuttings to a length of 10-15cm from the top portion are most ideal for planting. The land is ploughed or dug to a depth of 15-20cm and ridges are formed 30cm apart[4].

BOTANICAL IDENTIFICATION

Coleus is a member of the Lamiaceae family(mint),a perennial, branched, aromatic herb. The entire plant is aromatic. Members of the genus have square stems, branched and the nodes are often hairy. The pale blue corolla is bilabiate, the lower lobes are elongated and concave and it grows to a height of 30 cm to 60cm. The roots are thick, tuberous, fasiculated up to 20cm long, 0.5-2.5 cm thick, conical, fusiform, straight and strongly aromatic. Leaves appear when plant becomes pubescent and are narrowed into petioles. Flowers vary from a very slowly bluish to pale lavender. Racemes are perfect, the calyx is fine toothed and deflexed in the front. The plant possess four parted ovaries. The leaves and tuber have quite different odors.

MORPHOLOGY

The universal morphology of *Coleus* genus has been extensively reviewed. The genus Coleus of the family Lamiaceae (Labiatae) comprises a number of herbaceous medicinal plants which are particularly employed in home remedies for various ailments. Three species are most popular and commonly cultivated. They are *Coleus aromaticus, C. vettiveroides and C. forkoshlii.*

Fig1: ***Coleus aromaticus***

Fig2: ***Coleus vettiveroides***

Fig3: ***Coleus forskohlii***

Coleus aromaticus Benth.

syn. C. amboinicus Lour., Plectranthus amboinicus (Lour.) Spreng.

English: Country borage, Indian borage; Sanskrit: Karpuravalli, Sugandhavalakam; Hindi: Patharchur; Bengali: Paterchur; Malayali: Panikkurkka, kannikkurkka; Tamil: Karpuravalli. It is found throughout the tropics and cultivated in homestead gardens. It is a large succulent aromatic perennial herb with hispidly villous or tomentose fleshy stem. Leaves are simple, opposite, broadly ovate, crenate and fleshy. Flowers are pale purplish in dense whorls at distant intervals in a

long slender raceme. Fruits are orbicular or ovoid nutlets. The leaves are useful in cephalagia, otalgia, anorexia, dyspepsia, flatulence, colic, diarrhoea, cholera, halitosis, convulsions, epilepsy, cough, asthma, hiccough, bronchitis, strangury, hepatopathy and malarial fever [5].

Coleus vettiveroides

Syn. Plectranthus vettiveroides

Sanskrit: Valakam, Hriberam; Hindi: Valak; Malayali: Iruveli; Tamil: Karuver; Telegu: Karuveru. It is seen in tropical countries and cultivated in gardens. It is a small profusely branched, succulent aromatic herb with quadrangular stems and branches and deep straw coloured aromatic roots. Leaves are glandular hairy, broadly ovate with dentate margins and prominent veins on the bark. Blue flowers are borne on terminal racemes. Fruits are nutlets. The whole plant is useful in hyperpiesia, vitiated conditions of pitta, burning sensation, strangury, leprosy, skin diseases, leucoderma, fever, vomiting, diarrhoea, ulcers and as hair tonic[6].

Coleus forskohlii

Syn. C. barbatus Benth.

Hindi: Garmai, Gujarati: Maimul

The species name forskohlii was given to commemorate the Finnish botanist, Forskel. It is a perennial aromatic herb grown under tropical to temperate conditions for its carrot-like tubers which are used as condiments in the preparation of pickles. Plant height is approximately 1-2 feet and its striking leaves are teardrop shaped, shimmering green framing a bright purple centre; leaf color varies depending on the amount of shade. A cluster of stalked pale purple or blue flowers branches off a single stem. The rootstock is typically golden brown, thick, fibrous, and radially spreading. The roots are harvested in the fall, when forskolin is at its most concentrated and the color is the brightest[7].

Table 1: Comparative anatomical characters of leaves of species.

Leaf anatomical Characters	*Coleus aromaticus*	*Coleus vettiveroides*	*Coleus forskohlii*
Epidermal cell shape	rectangular to polygonal	Polygonal	Polygonal
Stomatum type	diacytic(caryophyllaceous)	Anomocytic	Anomocytic
Trichome type	Glandular trichomes	Stellate	Capitates, peltate
Mesophyll	Dorsiventeral	Dorsiventral	Dorsiventral
Midrib	Plano convex with flat adaxial side and	hypoderm and secretory cells concave-convex	Biconvex
Calcium oxalate crystals	hemispherical abaxial side[8]	rare raphides[8]	rare druses[9]

ETHNO-PHARMACOLOGY

The leaves are bitter, acrid, thermogenic, aromatic, anodyne, appetizing, digestive, carminative, stomachic, anthelmintic, constipating, deodorant, expectorant, lithontriptic, diuretic and liver tonic. They are useful in cephalgia, otalgia, anorexia, dyspepsia, flatulence, colic, diarrhoea and cholera especially in children, halitosis, convulsions, epilepsy, cough, chronic asthma,hiccough, bochitis, renal and vesical calculi, strangury, hepatopathy, malarial fever, antispasmodic and cathartic[10]. *Coleus forskohlii* has been used to treat hypertension, congestive heart failure, eczema, colic, respiratory disorders, painful urination, insomnia, and convulsions. Clinical studies of the plant and the forskolin constituent support these traditional uses, but also indicate that it may have therapeutic benefit in asthma, angina, psoriasis, and prevention of cancer metastases[11].*C.vettiveroides* used for skin diseases , rheumatism ,bronchitis and chronic allergies. It is also used as stimulant and carminative. Iruveli is most commonly used against ailments like vomiting, diarrhoea, leucoderma, fever, chronic liver diseases etc. It is used against indigestion and urinal disorders, and is a chief ingredient of many ayurvedic preparations like iruveli kashayam, devashtagandha, snana choornam etc[12].

Table:2 Traditional uses of some Coleus species

Species	Part used	Area	Uses
C. barbatus	leaves	Africa, Brazil	stomachalgia
C. floribundus	root tuber	Nigeria	as food
C. amboinicus	seed	India	acute oedematous, acute otitis
C. asirensis	whole leaf	Saudi Arabia	Antiseptic & wound-dressing
C. vettiverioides	Whole plant	India	vomiting and nausea
C. sylvestris	volatile oil	Australia	skin diseases

PHYTOCONSTITUENTS

Flavonoids, glycosides, phenolic compounds and volatile constituents have been reported as the major phytoconstituents of the *Coleus species*. Literature survey has revealed that a number of reports are available on *C.aromaticus* and *C. forskohlii* while only sporadic reports are there on other species of *C.vettiveroides*. Various phytoconstituents have been presented in a tabular form

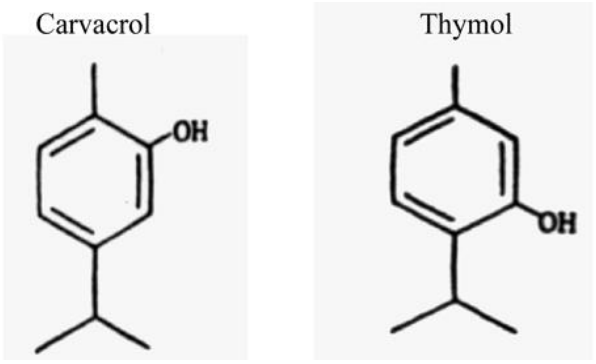
Table 3: Phytoconstituents of various *Coleus* species.

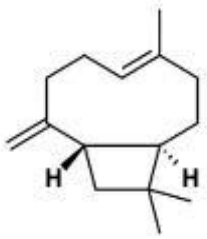
Species	Phytoconstituents
C.aromaticus	Butylaniside, -caryophyllene, carvacrol, 1-8-cineole, p-cymene, ethylsalicylate, eugenol, limonene, myrcene, and -pinenes, -selenene, -terpinene, terpinen-4-ol, thymol, verbenone (essential oil), apigenin, chrysoeriol, 5,4-dihydroxy-6,7-dimethoxy-flavone (cirsimaritin), eriodictyol, 6-methoxy-genkawanin, luteolin, quercetin, salvigenin, taxifolin, oxaloacetic acid, crategolic, euscaphic, 2-3-dihydro-olean-12-en-28-oic, pomolic, oleanolic, tormentic, 2α,3 α,19 α,23 α -tetrahydroxyurs-12-en-28-oic, ursolic acids, β-sitosterol--D-glucoside isolated from leaves[13].
C. forskohlii	Forskolin (7 β -acetoxy-8, 13-epoxy- 1α , 6 β, 9 α -trihydroxy-labd-14-ene-11-one), a diterpene compound is the active principle[14].Minorditerpenoids,deacetylforskolin,9-deoxyforskolin, 1, 9-deoxyforskolin, 1, 9-dideoxy-7-deacetylforskolin, and four other diterpenoids, have been reported to be present in the roots of C. forskohlii [15].
C.vettiveroides	phenolic abietanoids (diterpenoids).Flavonoids seem to be rare in Coleus. Only two flavonoids were identified, 4',7-dimethoxy-5,6-dihydroxyflavone and chrysosplenetin[16].

PHYTOCHEMISTRY

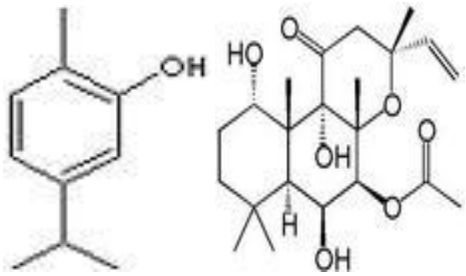
Brieskorn CH and Reidel W (1977) isolated eight triterpenic acids from the leaves of the South - American lamiaceae *Coleus amboinicus* Loureiro. 2,3-Dihydroxylean-12-en-28-oic acid, 2,3,19-trihydroxyurs-12-en-28-oic acid and 2,3,19,23-tetrahydroxyurs-12-en-28-oic acid were found first time in lamiaceae[17]. Baslas RK and Kumar P (1981) reported that the oil obtained by steam distillation (0.04-0.05%), has been found to contain terpinolene (3.75%),α -pinene (3.20%), β-pinene (2.50%), β -caryophyllene (4.20%), methyl eugenol (2.10%), thymol (41.3%), 1,8-cineole (5.45%), eugenol (4.40%), carvacrol (13.25%) and β -phellandrene (1.90%)[18]. Bos R and Hendriks FH (1983) studied the composition of essential oil in the leaves of *Coleus aromaticus* Benthum and their importance

as a component of species antiapthosae[19]. Thymol (79.6%) was shown to be the principal component of the oil[20]. Pino J *et al*., (1989) investigated the essential oil of *Coleus amboinicus* Lour. by means of LSC, GLC and GC-MS and 20 components were identified, including 13 terpene hydrocarbons and 7 oxygenated compounds. The oils contained about 64% carvacrol[21].Ammon and Kemper, 1982 and De Souza and Shah, 1988 were studied the tuberous root extracts of *C. forskohlii* contain minor diterpenoids *viz.,* deactylforskolin, 9 - deoxyforskolin, 1, 9-deoxyforskolin, 1, 9 - dideoxy - 7 - deacetylforskolin in addition to forskolin (7 β- acetoxy - 8, 13-epoxy- 1α, 6 β, 9 α - trihydroxylabd-14-en-11-one)[22]. Forskolin was discovered in the year 1974 and was initially referred to as coleonol. After the identification of other coleonols and diterpenoids the name was later changed to forskolin[23]. Shah et al. (1980) reported that forskolin occurred exclusively in *C. forskohlii* and could not be detected in six other *Coleus* species *viz*., *C*. *amboinicus*, *C. blumei*, *C*. *canisus*, *C*. *malabaricus*, *C*. *parviflorus* and *C*. *spicatus* and six taxonomically related *Plectranthus* species *viz*., *P*. *coesta*, *P*. *incanus*, *P*. *melissoides*, *P*. *mollis*, *P*. *rugosus* and *P*. *stocksii*. Studies carried out using one hundred samples belonging to species of *Coleus*, *Orthosiphon* and *Plectranthus* of the sub family Ocimoideae at Japan also revealed the absence of forskolin in all the samples. Recently, two more new labdane diterpene glycosides, forskoditerpenoside A, B were also isolated from the ethanol extract of the whole plant[24].





Caryophyllene



Cavacrol **Forskolin**

PHYTOPHARMACOLOGY

Irrespective of the presence of a large variety of phytoconstituents in the genus *Coleus*, only a few reports regarding the pharmacological investigations on the plants of this genus are available. Study was undertaken to check the efficiency of *C. aromaticus* extract in modifying cyclophosphamide and mitomycin-C induced clastogenicity in mouse bone marrow cells[25]. It was calculated that Coleus extract micronucleus and lower dose of the extract are more effective than higher dose. Study was done to check antioxidant and free radical scavenging activity of an aqueous extract of *C. aromaticus.*An activity directed fractionation purification process was used to identify the DPPH free-radical scavenging components of *C. aromaticus* Beath. Fresh leaves of *C. aromaticus* were extracted with water & then separated into hexane, ethyl acetate and water fractions. Three components showing strong DPPH radical scavenging activity were shown to be rosmarinic acid, Chlorogenic acid, Caffic acid Rosmarinic acid was major constituent for free radical scavenging potential[26]. Study was done to examine essential oil composition of *Coleus ambonicus* lour. The volatile constituents of the whole herb of *Coleus amboninus* Lour (Labiatae) were analyzed by GC-MS following isolaiton by hydrodistillation. Ten compounds were identified among which carvacrol (50.7 percent), Gamma - caryophyllene (13.1 percent) and patchoulane (8.7 percent) were dominant[27]. Study was done to check antifungal activities of traditional medicinal plant extract. In preliminary survey ethanolic extract of nine medicinal plant parts such as *C. aromaticus* (leaves), *Euphorbia tricalli. C longa, Aloe vera (aerial part) Zingeber officinale* were tested for antifungal activity against *Aspergillus flaves*[28].Study was done to examine mast cell stabilization property of *Coleus aromaticus* leaf extract in rat peritoneal mast cells. *Coleus aromaticus* stabilizes mast cells in the rat mesenteric tissue. As most cells play a major role in Type I hypersensitivity - mediated diseases like allergic asthma and rhinitis, studies are under way to evaluate the efficacy of *Coleus aromaticus* due to its mast stabilization property in these animal allergic models[29]. Vera R *et al*., (1992) investigated essential oils of *Plectranthus amboinicus* by GLS & MS. Juice of its leaves is used for curing wounds and an infusion is said to possess anti-influenza properties[30]. Baskar R *et al*., (1992) administered *Coleus aromaticus* leaf juice (at the rate of 1ml/rat/day) for 10-30 days in experimental urolithiatic rats. Reduction in the deposition of Ca and oxalate in the kidney tissues has been reported[31]. Buzenego MT and Perez- saad H (1999) reported antiepileptic effect of *Plectranthus amboinicus* (Lour) Spreng[32]. Annapurani S *et al*., (1999) exhibited significant antitumor and antimutagenic activities of *Coleus aromaticus*, *Ocimum sanctum* and *Aegle marmelos* and estimated polyphenol content in each[33]. Santosa CM (2002) reported that *Coleus amboinicus* leaves exhibited increasing milk secretion of lactating animals and seemed to be superior to other treatment groups on milk secretion and also containing iron and potassium composition[34]. Morallo RB *et al*., (1992) evaluated the biological activity of 18 medicinal plants along with *Coleus amboinicus*. It was found that *Coleus amboinicus* did not exhibited pronounced insecticidal activity[35].Kathiresan RM (2000) reviewed the allelopathic potential of native plants for use as an alternative bio-control tactic. Dried powder of the leaves of Omavalli *Coleus amboinicus* L. at 40gl-1 as a water suspension killed water hyacinth with 24 h reducing the fresh weight by 80.72% and dry weight by 75.63% within one week[36]. Gupta S *et al*., (2004) analysed nutrient and antinutrient contents of 13 locally available underutilized green leafy vegetables along with *Coleus aromaticus* Benth[37]. Patel R *et al*., (2010) evaluated the diuretic properties of ethanolic and aqueous extracts of leaves of *Plectranthus amboinicus* in male albino rats[38]. Palani S *et al*., (2010) investigated the nephroprotective , diuretic and antioxidant activities of the ethanolic extract of *Plectranthus amboinicus* at two dose 250 and 500 mg/kg bw on APAP-induced toxicity in rats[39].In a small study of seven patients with dilated cardiomyopathy,intravenous forskolin administered at 3 µg/kg/minute significantly reduced diastolic blood pressure (17%) without increasing myocardial oxygen consumption;left ventricular function also improved. In a similar study (patient sample size not available), 4 µg/kg/minute of intravenous forskolin given to dilated cardiomyopathy patients, resulted in decreased vascular resistance and a 19-percent improvement in left ventricle contractility. Heart rate increased an average of 16 percent in study patients. Subjects also exhibited a 20-percent reduction in arterial pressure accompanied by symptomatic flush. Forskolin's ability to inhibit platelet aggregation is of additional benefit in cardiovascular disease[40, 41]. Forskolin also demonstrates a direct effect on cerebrovascular vasodilatation via cAMP activation. In rabbits,

intravenous infusion of 10 µg/kg/min forskolin increased blood flow to the brain from 39 ± 5 to 56 ± 9 mL/min. This change was accompanied by a small decrease in mean arterial pressure, although cerebral oxygen consumption remained stable. These results indicate that forskolin may be useful in cases of cerebral vascular insufficiency and post-stroke[42]. Asthma and other allergic conditions are characterized by decreased cAMP levels in bronchial smooth muscle, as well as high levels of PAF. In response to allergenic stimuli, mast cells degranulate, histamine is released, and bronchial smooth muscle contracts. Forskolin activation of cAMP inhibits human basophil and mast cell degranulation, resulting in subsequent bronchodilation[43]. Research has demonstrated aerosolized dry forskolin powder results in significant relaxation of bronchial muscles and relief of asthma symptoms. In one randomized, double-blind, placebo-controlled trial, 16 asthma patients were given a single inhaled (aerosolized) 10-mg dose of dry forskolin powder, an asthma medication (0.4 mg fenoterol), or placebo. Both fenoterol and forskolin administration resulted in significant, equivalent bronchodilation, but patients taking fenoterol experienced marked finger tremor response and a decrease in plasma potassium levels. These side effects were not observed in patients receiving forskolin[44].Ammon et al reported an improvement in symptoms of psoriasis in four patients supplemented with forskolin. The ability of forskolin to regulate cAMP levels in skin cells has been shown to have therapeutic benefit for sufferers of psoriasis[45]. Caprioli *et al* demonstrated a significant decrease in IOP in rabbits, monkeys, and humans administered a topical forskolin suspension (1% forskolin). This effect was present at one hour post application and remained significant for at least five hours. In one clinical trial of 20 young, healthy Japanese volunteers, two 50 µL topical instillations of one-percent forskolin were applied to one eye while the other eye served as control, receiving only the topical vehicle. At one-hour post instillation, the IOP fell 2.4 ± 1.3 mmHg and aqueous flow rate was reduced by 13 percent in the treatment eye compared to the control. Both results were statistically significant[46]. *In vitro* and animal studies demonstrate lipolysis in fat cells is stimulated by forskolin[47] via activation of adenylate cyclase and increased levels of cAMP. Khatun *et al*., studied antioxidant status of different parts of *Coleus forskohlii* including roots, stem, leaves and tubers. For the enzymatic antioxidant properties, the activities of superoxide dismutase, peroxidase, polyphenol oxidase and catalase were significantly higher ($P < 0.05$) in tubers than in the leaves, roots and stem. Among the non-enzymatic antioxidants, except for the chlorophyll and lycopene content, the reducing power and chelating abilities on Fe^{2+}, 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical-scavenging activity, total phenol, flavonoids and β-carotene were significantly higher ($P < 0.05$) in tubers than in the leaves, roots and stem, respectively. The tubers possessed significantly rich sources of both enzymatic and non-enzymatic antioxidants besides their medicinal properties[48].Recently, it has been found that forskolin, a potent PP2A activator, induced marked apoptosis, reduced proliferation, impaired colony formation, inhibited tumorigenesis, and restored differentiation of BCR/ABL-transformed cells regardless of their degree of sensitivity to imatinib[49].

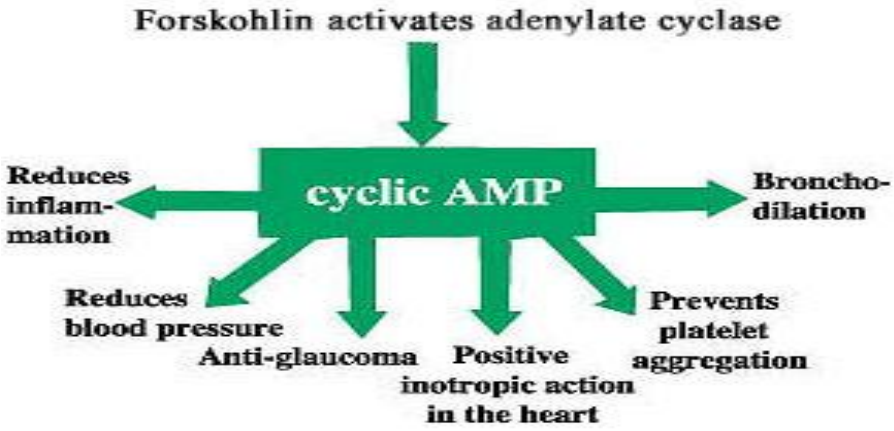


Fig 4: Mechanism of Action of Forskolin

TOXICITY STUDIES

Parra AL *et al*., (2001) determined the median lethal concentrations (LD50 value) of 20 plant extracts along with *Plectranthus amboinicus* using *Artemia salina* (tested at three concentrations: 10, 100 and 1000 mg/ml for each extract). Good correlation was found between in vivo and in vitro test (r = 0.85, *P*<0.05). Jose MA *et al*., (2005) have done the LD50 using OECD guideline for testing of chemicals revised draft guideline 423. The one tenth of the LD50 500mg/kg was chosen as a dose for further study[50]. Sclareol isolated from *C. forskohlii* reported to be non–cytotoxic to resting human peripheral blood mononuclear leukocytes and have LD50 > 5mg/kg in rats[51]. The study on forskolin also showed that it was extremely safe with an oral LD50 of 3100 mg/kg[52].The study on *C.vettiveroides* showed that it was extremely safe with an oral LD50 of >5000 µg/mL[53].

CONCLUSION

The therapeutic efficacy of the genus *Coleus* extensively used in Indian System of Medicine has been established through modern testing and evaluation (pre-clinical and clinical trials) in different disease conditions. These studies place this indigenous drug a novel candidate for bioprospection and drug development for the treatment of wound, burn, microbial infection, helmintic and liver disorder etc. The medicinal applications of these plants, countless possibilities for investigation still remain in relatively newer areas of its function. The present review of genus Coleus revealed that medicinal property of *Coleus amboinicus* is attributed to carvacrol, flavones, aromatic acids and tannins present in the plant. The essential oil from the plant contains carvacrol, ethyl salicylate, thymol, eugenol and chavicol. Leaves also contain cirsimaritin, b-sitosterol-b-D-glucoside and oxalacetic acid. Leaves are bitter, acrid, thermogenic, aromatic, anodyne, appetising, digestive, carminative, stomachic, anthelmintic, constipating, deodorant, expectorant, diuretic and liver tonic. *Coleus vettiveroides* is bitter, cooling, diuretic, trichogenous and antipyretic. *Coleus forskohlii* roots are rich in diterpenoids like forskolin, coleonols, coleons, barbatusin, cyclobutatusin, coleosol, coleol, coleonone, deoxycoleonol, 7-deacetylforskolin and 6-acetyl-7-deacetylforskolin. Its root is spasmolytic, CNS active, hypothermic and diuretic. Forskolin is bronchodialative and hypotensive. Forskolin is also useful in preventing the clotting of blood platelets, in reducing intraocular pressure in glaucoma and as an aid to nerve regeneration following trauma. Hence, phytochemicals and minerals of these plants will enable to exploit its therapeutic use. Therefore further studies may

be carried out to prove the potential of these plants. This genus Coleus are easy available in our country and leaves of the plant possess a wide range of biological properties. In future study, the isolated principles of extracts of different species of Coleus needs to be evaluated in scientific manner. It could be concluded that genus Coleus are rich source of compounds, interesting chemical structures and various biological active products.

ACKNOWLEDGEMENTS

Author acknowledge to the Dr.A.K. Singhai, Principal L.N.C.P. Bhopal (M.P.) support to carry-out research work on Coleus species.

REFERENCE

1. Hill AF. Economic Botany. A Text book of useful plants and plant products.(2 nd Edn., McGarw- Hill Book Company Inc, NewYork)1952.
2. De Loureiro J. Flora Cochinchinensis(Published by Academiac Ulyssipone, Lisbon)1970 2: 272.
3. Aswal BS, Goel GK. Screening of Indian plants for Biological Activities. Indian. Exp. Biol 1996; 34(5): 444-467.
4. Nadkararni AK, Nadkarni KM. Indian Materia Medica (Published by Popular Prakashan Pvt. Ltd., Bombay) 1976.
5. Warrier PK, Nambiar VP and Ramankutty C. Indian Medicinal Plants(Orient Longman Ltd., Madras)1995.
6. Sharma PV, Dravyaguna Vigyan, Chowkambha Sanskrit Sansthan, 1997.
7. Dubey MP, Srimal RC, Nityanand S, Dhawan BN. Pharmacological studies on Coleonol, a hypotensive diterpene from *Coleus forskohlii.* J Ethnopharmacol 1981;3:1-13.
8. Soni *et.,al*. Synergistic effect of polyherbal suspension *of Punica granatum* and *Coleus aromaticus* in evaluation of wound healing activity. Journal of Herbal Medicine and Toxicology 2011; 5 (1) 111-115.
9. Metcalfe CR, Chalk L. Anatomy of the dicotyledons. (2nd ed. Published by Oxford Clarendon Press)1988.
10. Warier PK, Nambier VP. Indian Medicinal Plants: A compendium of 500 species.(Published by Orient Longman Limited, Chennai) 1996.
11. Dubey MP, Srimal RC, Nityanand S, Dhawan BN. Pharmacological studies on coleonol, a
12. hypotensive diterpene from *Coleus forskohlii.* J Ethnopharmacol 1981; 3:1-9.
13. T. Pullaiah. Encyclopaedia of world medicinal plants (Edn reprint Regency Publication New Delhi) 2006.
14. Chatterjee A, Pakrashi SC. The Treatise of Indian Medicinal Plants. (Council of Industrial and Scientific Research, New Delhi)2001.
15. Shah V, Bhat SV, Bajwa BS, Domacur H, De Souza NJ. The occurrence of forskolin in Labiatae. Planta Med 1980; 39: 183-185.
16. Gabetta B, Zini G, Daniele B (1989). Minor diterpenoids of Coleus forskohlii. Phytochem 1989; 28: 859-862.
17. Liu G, Ruedi P. Phytochemistry(Published by Chapell and Hall New York) 1996.
18. Brieskorn CH, Riedel W. Triterpenic acids from *Coleus amboinicus* Loureiro. Arch Pharm 1977; 310(11): 910-16.
19. Baslas RK, Kumar P. Chemical examination of essential oil of *Coleus aromaticus* Benth. Journal of Indian Chem. Soc 1981; 58(1): 103-04.
20. Bos R, Hendriks FH. The compositions of essential oil in the leaves of *Coleus aromaticus* Bentham and their importance as a component of species antiapthosae. Pharm Weekly Sci 1983; 26: 129-30.
21. Haque IU. Analysis of volatile constituents of *Coleus aromaticus*. Journal of the Chem. Society of Pakistan 1988; 10(3): 369-71.
22. Pino J, Rosado A and Borges P. Volatile components in the essential oil of wild oregano (*Coleus amboinicus* Lour). Food / Nahrung 1989; 34(9): 819-23.
23. Ammon HP, Kemper FH . Ayurveda: 3000 years of Indian traditional medicine. Med Welt 1982; 33:148-153.
24. Saksena AK, Green MJ, Shue HJ. Identity of coleonol with forskolin: structure revision of a base-catalysed rearrangement product. Tetrahedron Lett 1985; 26: 551-554.
25. Shan Y, Wang X, Zhou X, Kong L, Niwa M (2007). Two minor diterpene glycosides and an eudesman sesquiterpene from *Coleus forskohlii*. Chem. Pharm. Bull 2007; 55:376-81.
26. Shyama PS, P Naik, KK Vijayalaxmi. Efficiency of Coleus aromaticus extract in modifying cyclophosphamide and mitomycin-C induced clastogenicity in mouse bone marrow cells. *J Exp Biol*, 2002, 40:1020-1025.
27. Kumaran A and Karunakaran RJ, Activity guided isolation and identification of free radical - scavenging components from an aqueous extract of *Coleus aromaticus. Food Chemistry*,2007,100:356–361
28. Mangathayaru K, Pratap DVV, Thirumurgan D, Patel PS, David DJ, Karthikeyan J. Essential oil composition of *Coleus amboinicus* Lour. Indian J. of Pharmaceutical Sci 2005; 67(1): 122-123.
29. Murthy PS, Ramalakshmi K, Srinivas P, Fungitoxic activity of Indian borage (Plectranthus amboinicus) volatiles. Food Chemistry 2009; 114: 1014–1018.
30. Kumar A, Elango K, Markanday S,Undhad CV, Kotadiya AV, Savaliya BM.,Vyas D N and Datta D, Mast cell stabilization property of *Colus aromaticus* leaf extract in rat peritoneal mast cells. *Indian J Pharmacol*,2007,39(2):119-120
31. Vera R, Mondon JM and Pieri buttesti JC. Some Medicinal Plants of reunion, 7th Asian Symposium on Medicinal Plants, Spices and other Natural Products, (ASOMPS VII), Manila. 1992.
32. Baskar R, Varalaksmi P, Amsaveni. Changes in tissue enzymes produced by *Coleus aromaticus* experimental Urolithiasis. Indian Drugs 1992; 29(6): 254-58.
33. Buznego MT, Perez Saad H. Antiepileptic effect of *Plectranthus amboinicus* (Lour.) Spreng. Rev. Neurol 1999; 29: 229-32.
34. Annapurani S, Priya R. Antimutagenic, antitumourogenic and antigenotoxic effects of polyphenol extracts of selected medicinal plants. Indian Journal of Nutrition and Dietetics 1999; 36(10): 431-35.
35. Santosa CM. The effect of 'bangun-bangun' leaves (*Coleus amboinicus* L.) consumption of the potency of milk secretion and its composition of lactating mothers. Indonesian Journal of Pharmacy 2002; 13(3): 133-39.
36. Morallo RB, Maini HA, Dayrit F and Quintana E. Biocidal action of some medicinal plants to insects, 8th Asian Symposium on Medicinal Plants, Spices and other Natural Products, (ASOMPS VII). Manila. 1996.
37. Kathiresan RM. Allelopathic potential of native plants against water hyacinth. Crop Protection 2000; 19: 705-08.
38. Gupta S, Jyothi Lakshmi A, Manjunath MN and Prakash Jamuna. Analysis of nutrient and antinutrient content of underutilized green leafy vegetables. LWT 2005; 38: 339-45.
39. Patel R, Mahobia N, Gendle R, Kaushik B and Singh S. Diuretic activity of leaves of *Plectranthus amboincus* in male albino rats. Pharmacog Res 2010; 2: 86-88.
40. Palani S, Raja S, Naresh R, Kumar BS. Evaluation of nephroprotective, diuretic and antioxidant activities of *Plectranthus amboinicus* on acetaminophen-induced nephrotoxic rats. Toxicol Mech Methods. 2010; 20(4): 213-21.
41. Agarwal KC, Parks RE Jr. Synergistic inhibition of platelet aggregation by forskolin plus PGE1 or 2- fluoroadenosine: effects of 2',5'-dideoxyadenosine and 5'-methylthioadenosine. *Biochem Pharmacol* 1982; 31:3713-3716.
42. Siegl AM, Daly JW, Smith JB. Inhibition of aggregation and stimulation of cyclic AMP Generation in intact human platelets by the diterpene forskolin. *Mol Pharmacol* 1982;21:680-687.
43. Wysham DG, Brotherton AF, Heistad DD. Effects of forskolin on cerebral blood flow: implications for a role of adenylate cyclase. *Stroke* 1986;17:1299- 1303.
44. Lichey I, Friedrich T, Priesnitz M, et al. Effect of forskolin on methacholine-induced
45. bronchoconstriction in extrinsic asthmatics. *Lancet* 1984:2:167.

46. Bauer K, Dietersdorfer F, Sertl K, et al. Pharmacodynamic effects of inhaled dry powder formulations of fenoterol and colforsin in asthma. *Clin Pharmacol Ther* 1993; 53:76-83.
47. Ammon HP, Muller AB. Forskolin: from an Ayurvedic remedy to a modern agent. *Planta Med* 1985;6:473-477.
48. Seto C, Eguchi S, Araie M, et al. Acute effects of topical forskolin on aqueous humor dynamics in man. *Jpn J Ophthalmol* 1986; 30:238-244.
49. Okuda H, Morimoto C, Tsujita T. Relationship between cyclic AMP production and lipolysis induced by forskolin in rat fat cells. *J Lipid Res* 1992;33:225-231.
50. Selima Khatun, Narayan Chandra Chatterjee and Ugur Cakilcioglu. Antioxidant activity of the medicinal plant *Coleus forskohlii* Briq. African Journal of Biotechnology 2011; 10(13):2530-2535.
51. Neviani P, Santhanam R, Trotta R, Notari M, Blaser BW, Liu S.The tumor suppressor PP2A is functionally inactivated in blast crisis CML through the inhibitory activity of the BCR/ABL regulated SET protein. Cancer Cell 2005; 8:355-68.
52. Parra AL, Yhebra RS, Sardinas IG and Buela LI. Comparative study of the assay of *Artemia salina* L. and the estimate of the medium lethal dose (LD50 value) in mice, to determine oral acute toxicity of plant extracts. Phytomedicine 2001; 8(5): 395-400.
53. Dimas K *et.,al*.The effect of sclareol on growth and cell cycle progression of human leukemic cell lines. Leuk Res 1999; 23:217–34.
54. Leamon KB, Padgett W, Daly JW. Forskolin: Unique diterpene activator of adenylate cyclase in membrane and intact cells. J Natl Acad Sci 1981; 78:3363.
55. Alluri V *et.,al*. Assessment of Bioactivity of Indian Medicinal Plants Using Brine Shrimp (Artemia salina) Lethality Assay. International Journal of Applied Science and Engineering 2005; 3(2): 133.