

Review Article

A REVIEW ON PHYTOCHEMISTRY AND PHARMACOLOGY OF *CALYCOPTERIS FLORIBUNDA* ROXB. LAM

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ABSTRACT

The medicinal plant *Calycopteris floribunda* Roxb. Lam. commonly known as "Ukshi" belongs to the family *Combretaceae*. *Calycopteris floribunda* is a large evergreen climbing shrub native of Bangladesh and India. It is widely distributed in the central and southern parts of India and also found in south-east Asian countries. The branches store abundant water for its own purpose as well to quench the thirst of the forest dwellers. Hence the forest habitants are referring this plant as a lifesaver. *Calycopteris floribunda* finds a place in traditional Asian medicinal systems, including Ayurveda, Folk and Unani. The anti-inflammatory flavonoid compound calycopterin is present in the leaves of the plant. In Ayurveda this plant is used to treat for leprosy, malarial fever, dysentery, ulcers, vomiting, wound healing and cytotoxic. It is hepatoprotective, antimicrobial, antiviral and used for numerous ailments. A review on the medicinal plant *Calycopteris floribunda* was done in the period from 1934 to 2020. Here, we are focusing on the isolation, phytochemical constitution and pharmacological potential of *Calycopteris floribunda* plant.

Keywords: *Calycopteris floribunda*, Phytochemical, Pharmacological activity

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INTRODUCTION

In the early century of mankind, plant-derived bioactive compounds, secondary metabolites played an important role in humans to combat diseases. The medicinal value of plants depends on some chemical compounds that produce a certain physiological action on the human body [1]. The most important secondary metabolites of plants are alkaloids, flavonoids, tannins and phenolic compounds. Many herbal medicines are prepared from Secondary metabolites of the plants. For various kinds of illness, single and polyherbal preparations have been used for the treatment. By using natural product origin, over 50 % of all modern clinical drugs are prepared [2]. *Calycopteris floribunda* Lam (*C. floribunda*) was one of the ethnomedicinal plant widely used to prepare some specific herbal medicines. The large climbing shrub *C. floribunda* Lam belongs to the Rangoon creeper family. They found extensively in Bangladesh, India, South-East Asian countries and low lying tropical forests of Western Ghats [3]. In India, they also found in Kavus of Kerala and the Eastern Ghats of coastal Andhra. The synonyms of *C. floribunda* are *Calycopteris coccineum* Lam., *Calycopteris nutans*, *Combretum extensum* Roxb. and *Getonia floribunda* Roxb. The plant parts are used medicinally for various ailments such as jaundice, ulcers, pruritus, colic, leprosy, malarial fever, dysentery, vomiting, skin diseases, anthelmintic, astringent, laxative, hepatotoxicity, neurotoxicity, cardiotoxicity, antimicrobial, antioxidant, anti-viral, anti-inflammation and so on [3-7]. This plant *C. floribunda* has extensive therapeutic potential for curing diseases with minimal toxic effects.

Taxonomy and botanical description-*Calycopteris floribunda* lam

Calycopteris floribunda Lam is a straggling shrub that is 5-10 m in height with 5-10 cm in diameter. It bears slender, hairy rust-colored streaked branches with thick fluff on the surface. The branches with vine are storing plenty of water. The keratinous leaves are 5-12 cm long, ovoid or oval, opposite, acuminate and round. The dense cluster of flowers occurs at the end of branches. The bracts of the small flowers are ovoid or oval. The flowers are devoid of petals and ten stamens are arranged two whorls of five each. The fluffy sham-winged fruit inception bears a ventricle and 3 pendulous ovules inside. The fruit is about 8 mm long and the sepals are prominent hairy and green [8, 9]. Fig. 1 represents the *C. floribunda* plant and its herbarium.



Fig. 1: *Calycopteris floribunda* plant

Table 1 represents the taxonomic hierarchy of the medicinal plant *C. floribunda*.

Table 1: Systematic position of *Calycopteris floribunda* [Taxonomy ID-134915]

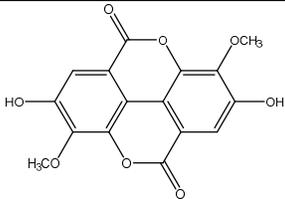
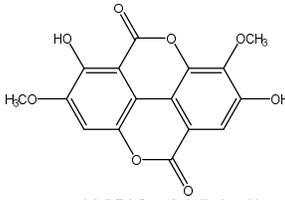
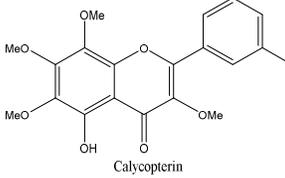
Plant name	<i>Calycopteris floribunda</i> Lam
Subkingdom	Tracheophyta
Class	Magnoliopsida
Order	Myrtales
Family	Combretaceae
Genus	<i>Calycopteris</i>
Vernacular names	Hindi: Kokoray Tamil: Pullanji valli Sanskrit: Susavi Kannada: Enjarigekubsa Bengali: Gaichha Lata Malayalam: Varavalli, Pullanji, Pullanni Telugu: Murugudutige Marathi: Ukshi English: Paper flower climber
Flowering season	January to May

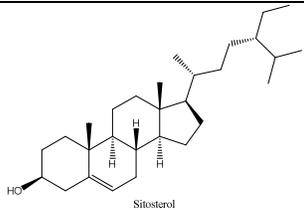
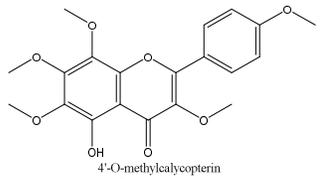
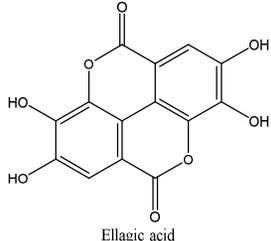
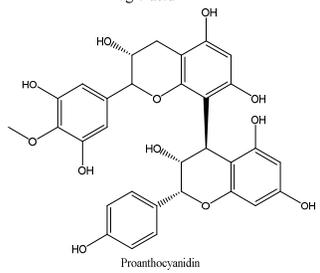
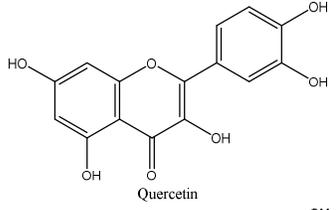
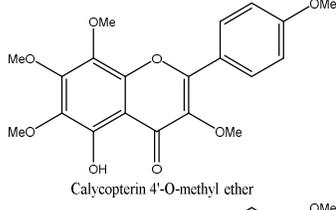
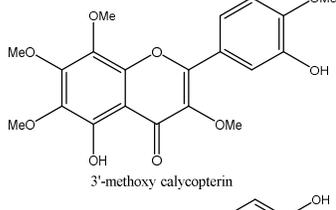
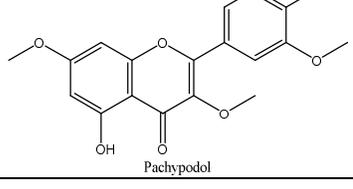
In the present study, all available phytochemical and pharmacological literature on *Calycopteris floribunda* from 1934 to 2020 is reviewed in the following sections. The collection of literature was carried by the search tool SciFinder which was accessed by Madurai Kamaraj University, Madurai.

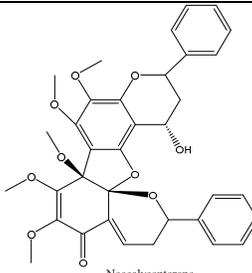
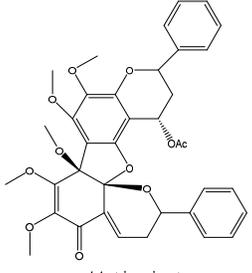
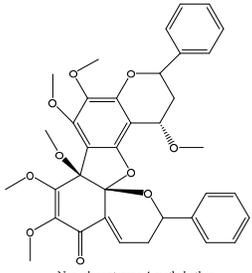
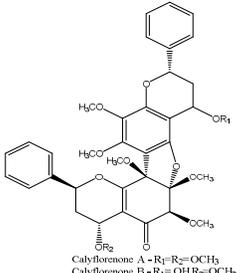
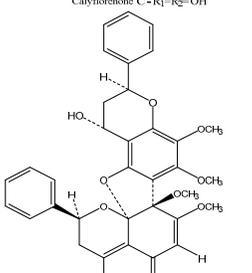
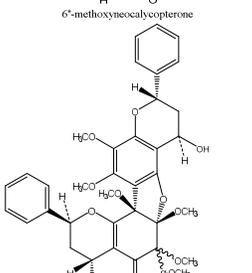
Isolation of chemical constituents

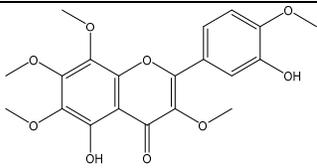
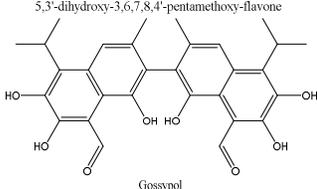
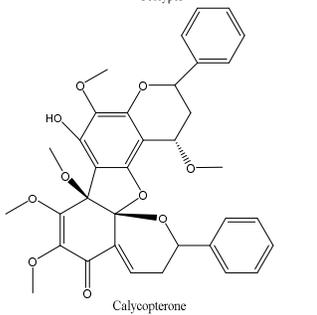
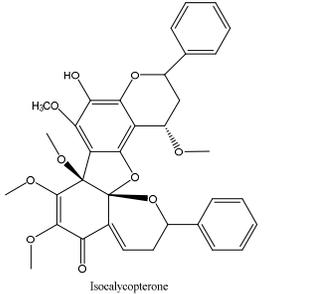
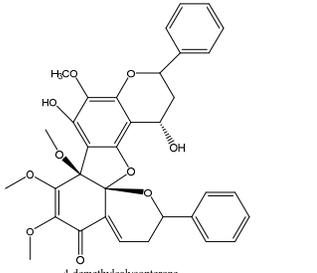
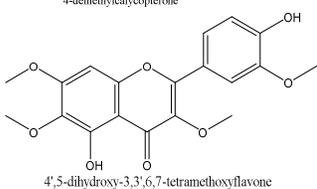
Studies in the presence of chemical constituents of *Calycopteris floribunda* were initiated as early as 1934 with the isolation and characterization. Various kinds of solvents were used for the extraction and isolation of chemical constituents. Mostly, the soxhlet extraction method has been carried out. The plant is found to largely contain the flavonoids and its derivatives. Polyphenols, long-chain aliphatic alcohols, esters and other small molecules have also been identified from *C. floribunda*. The chemical constituents isolated from *C. floribunda* are listed in alphabetical order a to x. Table 2 gives the detailed layout of the isolation of chemical constituents from the different parts of *C. floribunda* plant.

Table 2: Isolation of chemical constituents from *Calycopteris floribunda*

S. No.	Part of the plant	Solvents	Compound	Structure	References
1	Leaves	Dichloro methane methanol	a) 3,8-di-O-methyl ellagic acid	 3,8-Di-O-methyl ellagic acid	[7]
2	Leaves	Dichloro methane- methanol	b) 2,3,7-tri-O-methyl ellagic acid	 2,3,7-Tri-O-methyl ellagic acid	[7]
3	Leaves	Acetone, Benzene, Methanol	c) Calycopterin	 Calycopterin	[10-14]
4	Leaves	Petroleum ether	d) n-octacosanol	 n-octacosanol	[13]

5	Leaves	Petroleum ether	e) Sitosterol		[13]
6	Leaves	Petroleum ether	f) 4'-O-methylcalycopterin		[13]
7	Leaves	Petroleum ether	g) Ellagic acid		[13]
8	Leaves	Petroleum ether	h) Proanthocyanidin		[13]
9	Leaves	Petroleum ether, Methanol	i) Quercetin		[13-14]
10	Leaves	---	j) Calycopterin-4'-methyl ether		[15]
11	Leaves	---	k) 3'-methoxy calycopterin		[15]
12	Leaves	Dichloro methane-methanol, Ethanol	l) Pachypodol		[16, 17]

13	Leaves	Ethanol	m) Neo calycopterone	 <p>Neo calycopterone</p>	[18]
14	Leaves	Ethanol	n) 4-Acetyl neo calycopterone	 <p>4-Acetylneo calycopterone</p>	[18]
15	Leaves	Ethanol	o) Neocalycopterone 4-methyl ether	 <p>Neocalycopterone 4-methyl ether</p>	[18]
16	Leaves	Ethanol, Ethyl acetate	p) Calyflorenone A-C	 <p>Calyflorenone A - R₁=R₂=OCH₃ Calyflorenone B - R₁=OH R₂=OCH₃ Calyflorenone C - R₁=R₂=OH</p>	[18, 19]
17	Leaves	Ethyl acetate	q) 6"-demethoxy neocalycopterone	 <p>6''-methoxyneocalycopterone</p>	[19]
18	Leaves	Ethyl acetate	r) 6"-epi-calyflorenone	 <p>6''-Epi-calyflorenone</p>	[19]

19	Leaves	Dichloro methane	s) 5,3'-dihydroxy-3,6,7,8,4'-pentamethoxy-flavone		[20]
20	Flowers	Methanol	t) Gossypol		[14]
21	Flowers	50% Methanol/Chloroform	u) Calycopterone		[21]
22	Flowers	50% Methanol/Chloroform	v) Isocalycopterone		[21]
23	Flowers	50% Methanol/Chloroform	w) 4-demethyl calycopterone		[21]
24	Flowers	50% Methanol/Chloroform	x) 4',5-dihydroxy-3,3',6,7-tetra methoxy flavone		[21]

Qualitative phytochemical screening

The phytochemical screening of *C. floribunda* leaves revealed the presence of flavonoids in methanol and ethanol extracts, steroids in petroleum ether and chloroform extracts and alkaloids in methanol, ethanol and chloroform extracts [6]. The preliminary phytochemical screening of methanolic and aqueous extracts of *C. floribunda* plant revealed the presence of tannins, terpenoids, alkaloids, saponins, steroids and flavonoids [22, 23]. The phytochemical analysis of chloroform stem extract of *C. floribunda* showed the presence of sterols, flavonoids and alkaloids and the methanol extract showed the presence of glycosides, saponins, tannins and carbohydrates [24].

The methanolic extract of flowers *C. floribunda* revealed the presence of phytochemicals such as saponins, tannins, triterpenoids and flavonoids [25]. The ethyl acetate leaf extracts of *C. floribunda* contain alkaloids, terpenoids, steroids, cardio glycosides, flavonoids, saponins, tannins, resins and phenols. Additionally, the chloroform, methanol, petroleum ether and aqueous extracts of *C. floribunda* showed the strong presence of

terpenoids and moderate presence of alkaloids, steroids and flavonoids [26]. The phytochemical analysis of methanolic and aqueous root extracts of *C. floribunda* shows the positive results for carbohydrates, glycosides, proteins, alkaloids, steroids, terpenoids, flavonoids and phenolics. The phytochemical saponins present only in the aqueous extract [27].

Quantification of phytoconstituents

The total flavonoid content of petroleum ether, methanol and ethyl acetate extracts of *C. floribunda* was evaluated using spectrophotometric methods. Petroleum ether extract contains 0.038 ± 0.076 mg/g, methanol extract contains 1.489 ± 0.043 mg/g and ethyl acetate extract contains 3.545 ± 0.023 mg/g of flavonoids [8]. The total phenolic content of methanolic and aqueous root extracts of *C. floribunda* was determined by Folin-Ciocalteu calorimetric method. The methanol extract and aqueous extract contains 343.77 ± 2.02 and 87.87 ± 6.06 gallic acid equivalent/mg of phenolic content [27]. The total phenolic content and flavonoid contents of various extracts of *C. floribunda* were estimated by the Folin-Ciocalteu reagent and Aluminium-chloride colorimetric estimation method. The estimated results of the total phenolic content of petroleum ether, chloroform and methanol extracts were 25.68, 55.85 and 280.31 $\mu\text{g GAE/mg}$ and the flavonoid content were 14.50, 16.50, 48.50 $\mu\text{g GAE/mg}$ respectively [28].

Pharmacological potential of *Calycopteris floribunda*

The pharmacological potential of *C. floribunda* plant is widely established. The extracts from the plant are investigated for antimicrobial, antioxidant, anti-inflammatory, anticancer, antiproliferative activity, hypoglycemic activity, hepatoprotective activity and anthelmintic activity. The toxicity studies for this plant have also been determined.

Antibacterial activity

Leaves of *C. floribunda* dichloromethane-methanol extract of and its aqueous 90% methanol soluble fractions were studied for antibacterial activity by agar-well-diffusion method against two Gram-positive bacteria *Streptococcus pyogenes*, *Staphylococcus aureus* and two Gram-negative bacteria *Escherichia coli*, *Pseudomonas aerogenes* and *Salmonella typhi*. The leaf extracts showed significant antibacterial activity against *Bacillus subtilis*, *Streptococcus pyogenes*, *Staphylococcus aureus* and *Salmonella typhi*. The highest zone of inhibition 23 mm was found in 90 % aqueous methanol extract against *Staphylococcus aureus* and *Salmonella typhi* [7].

The antibacterial efficacy of methanol and aqueous extracts of *C. floribunda* plant was done by an agar-well-diffusion method. The plant extracts were treated against two Gram-positive bacteria *S. aureus*, *Clostridium perfringens* and four Gram-negative bacteria viz. *E. coli*, *Klebsiella pneumoniae*, *S. typhimurium*, *Pseudomonas aeruginosa* was treated against the plant extracts. Both the extracts were more active against Gram-positive bacteria than Gram-negative bacteria and the methanol extract exhibited higher antibacterial activity than the aqueous extract [23]. The antibacterial activity of the various solvent (petroleum ether, chloroform, ethyl acetate, methanol and aqueous) leaf extracts of *C. floribunda* like extracts have been evaluated against the pathogenic microorganism such as *B. subtilis*, *P. aeruginosa*, *Actinomyces sp.* and *Serratia sp.* Comparing with the other solvents, methanolic extract shows an 8 mm maximum inhibition zone against *Bacillus strain* [26].

The solvent extracts of *C. floribunda* flowers were studied for antibacterial activity against *S. aureus*, *B. cereus*, *P. aeruginosa* and *E. coli*. The methanol and chloroform extract show higher inhibition of about 2.2 to 2.4 mm [28]. The disk diffusion method was employed to evaluate the antibacterial efficacy of the volatile oil of leaves and barks of *C. floribunda*. Four pathogenic test organisms *S. aureus*, *B. subtilis*, *E. coli* and *P. aeruginosa* test organisms were used. The leaf oil shows a strong bacterial inhibitory effect against *S. aureus*, *B. subtilis*, *E. coli*, and moderate effect were observed in *P. aeruginosa*. The bark oil shows a high bacterial inhibition for *S. aureus*, *B. subtilis*, *P. aeruginosa*, while it shows moderate inhibitory activity for *E. coli* [29].

Antifungal activity

The disk diffusion method was employed to evaluate the antimicrobial efficacy of the volatile oil of leaves and barks of *C. floribunda*. The antifungal efficacy of methanol and aqueous extracts of *C. floribunda* was studied by agar well diffusion method against human dermatophytes, namely *Microsporium gypseum*, *Chrysosporium keratinophilum*, *Chrysosporium indicum* and *Trichophyton rubrum*. The aqueous extract exhibited higher inhibition zone 14 mm for *C. keratinophilum* and 12 mm for *M. gypseum* while the methanol extract exhibited effective inhibition 14 mm for *T. rubrum* and 12 mm for *C. indicum*. These extracts can treat human skin infections caused by these pathogenic fungi [22].

Evaluation of the antifungal activity of the volatile oil of leaves and barks of *C. floribunda* was carried out by four pathogenic fungi test organisms. The volatile leave oil exhibits a strong inhibitory effect against pathogenic organisms *Candida albicans* and *Trichophyton rubrum*, moderate result observed in *Aspergillus niger* and no effect against *Penicillium citrinum*. The bark oil shows a strong inhibitory effect against the growth of *Candida albicans* and *Penicillium citrinum* and the effect is absent against *Trichophyton rubrum* and *Aspergillus niger* [29].

By using a poisoned food technique, the aqueous flower extract of *C. floribunda* treated against two fungi organisms *Fusarium oxysporum* and *Pythium aphanidermatum*. The flower extract exhibited higher antifungal potency of 2.2 cm and 2.1 cm for *Fusarium oxysporum* and *Pythium aphanidermatum*, respectively [30].

Antioxidant activity

2,2-diphenyl-1-picrylhydrazyl (DPPH) free radical scavenging antioxidant activity of the dichloromethane-methanol extract, aqueous 90% methanol and 1-butanol soluble fractions of the leaves of *C. floribunda* were studied. Aqueous 90% methanol and 1-butanol soluble fractions show a highly active percentage of scavenging activity about 89 and 92 [7].

The two *in vitro* antioxidant models were used to evaluate the free radical scavenging potential of various extracts from the whole plant of *C. floribunda*. The total antioxidant activity (phosphomolybdic acid method) and ferric reducing antioxidant potential (FRAP) assay methods were adopted for this study. By comparing with the standard ascorbate, the ethyl acetate extract was found to be extremely effective with half-maximal inhibitory concentration (IC_{50}) values 360 $\mu\text{g/ml}$ while for standard 410 $\mu\text{g/ml}$. For both antioxidant assays, the ethyl acetate extract was found more efficient than that of petroleum ether and methanolic extract [8].

Leaves of *C. floribunda* extracts were obtained from supercritical fluid extraction and classical organic solvent extraction. The flavonoid compound pachypodol was isolated from these extracts. The extracts and the pachypodol were screened for antioxidant activity by superoxide anion radical scavenging method. The compound pachypodol exhibited high antioxidant activity while the extracts results probable activity [17]. The chloroform and methanol stem extracts of *C. floribunda* were subjected to *in vitro* antioxidant methods like superoxide radical, hydroxyl radical, lipid peroxidation and DPPH radical methods. The scavenging IC_{50} values of chloroform extract and methanol extract for superoxide radicals were found to be 193.50 μg , 273.89 μg ; hydroxyl radical were 290.69 μg , 343.37 μg ; lipid peroxidation inhibiting activity was 324.33 μg , 376.87 μg and DPPH radical were 90.71 μg , 117.68 μg respectively. The chloroform extract exhibit better scavenging activity than methanol extract [24].

The antioxidant activity of methanolic and aqueous roots of this plant was determined by reducing power assay and total antioxidant capacity. The methanolic extract exhibit higher antioxidant activity while aqueous extract exhibit lower activity [27]. DPPH free radical scavenging and ferric reducing assay were employed to determine the antioxidant activity of flower extracts of *C. floribunda*. The methanol flower extract results in higher scavenging potential, followed by chloroform and petroleum ether extracts [28].

Anti-inflammatory activity

The anti-inflammatory activity was determined for methanolic extract and chloroform fractions of the stem of *C. floribunda* by carrageenan-induced rat hind paw oedema method. The percentage inhibition for 100 and 200 mg/kg dosage of methanolic extract were 54.02 ± 2.05 , 70.21 ± 0.44 and for chloroform extract were 45.97 ± 0.32 , 59.77 ± 0.42 respectively. Compared with the standard diclofenac sodium both the stem extracts show maximum anti-inflammatory efficacy [31].

Anticancer activity

The Cancer Coli-2 (CaCo-2) colon cancer cell line was used to determine the toxicity of the isolated flavonoid compound pachypodol by Brine shrimp lethality assay and Promega's CellTiter 96 non-radioactive cell proliferation assay. The compound possesses a median lethal dose (LD₅₀) value for general toxicity is 435.8 µM and IC₅₀ values for cytotoxicity are 185.6 µM. Thus the compound possesses moderate levels of cytotoxicity towards the CaCo-2 colon cancer cell lines [16].

The compounds isolated from the flowers of *C. floribunda* calycopterone, isocalycopterone, 4-demethylcalycopterone and 4',5-dihydroxy-3,3',6,7-tetramethoxyflavone were screened for *in vitro* cytotoxicity in several Frederick-NCI human tumor cancer cell lines. The compounds calycopterone, isocalycopterone, 4-demethylcalycopterone exhibit a wide range of cytotoxic activity with a median effective dose (ED₅₀) values ranging from 10⁻¹ to 10⁰ µg/ml. The 4', 5-dihydroxy-3, 3', 6, 7-tetramethoxyflavone was inactive in most of the cell lines. The results were compared with the known clinical antitumor drug doxorubicin [21].

The inhibitory effect of flower extracts (petroleum ether, chloroform and methanol) of *C. floribunda* was tested against carcinogenic bacteria with 4 isolates of *Streptococcus mutans* by agar well diffusion method. The chloroform flower extracts exhibited higher anticarcinogenic potential than methanol and petroleum ether [25].

Antiproliferative activity

One of the amino flavone isolated from the dichloromethane leaf extract of *C. floribunda* shows a strong antiproliferative activity [20].

Anthelmintic activity

The compound calycopterin isolated from the acetone extract of *C. floribunda* leaves has an anthelmintic activity [10].

Hypoglycemic activity

Leaves of hydro-alcoholic (70:30) extract of *C. floribunda* was carried out to study the hypoglycemic effects in normal and streptozotocin-induced diabetic rat models. The leaves of *C. floribunda* significantly having hypoglycemic activity due to the reduction of high fasting glucose levels in streptozotocin-induced diabetic rats [32].

Hepatoprotective activity

Carbon tetrachloride (CCl₄) induced liver damage in Wistar albino rats was taken to evaluate the hepatoprotective activity of chloroform and methanol stem extract of *C. floribunda*. The observations of chloroform and methanolic extract of stem extracts were effective in protecting the liver injury induced by CCl₄ in animals and they are also resulting in some biological changes like centrilobular necrosis and vacuolization in CCl₄ induced rats [33].

Other pharmacological uses

Both children and adults who are affected by dysentery can internally take the juice from the leaves of *C. floribunda* to cure the stomach aches [35]. The root of *C. floribunda* was crushed and extracted. Orally, it serves as an antidote for snakebite [36].

Toxicity studies

The toxicological studies for the methanolic leaf extract of *C. floribunda* were carried out on calf, rabbit and rat [6].

Elemental analysis

Elemental analysis of flowers of *C. floribunda* was determined by analytical techniques, mainly based on atomic spectrometry. The flower was found to have a higher amount of Sodium, Iron, Manganese, a moderate amount of Calcium, Chromium and Magnesium and a lower amount of Potassium, zinc, Copper, Nickel and Lithium [24]. Energy Dispersive X-ray Fluorescence (EDXRF) technique was used to determine the trace elements in the leaves of *C. floribunda*. They contain higher concentrations of Iron, Manganese, Nickel and a minimum concentration of Zinc [35].

CONCLUSION

This review highlights the herbal medicinal potential of *Calycopteris floribunda* Lam and the isolation of a large number of chemical constituents. It revealed that the *Calycopteris floribunda* plant possessed a large number of flavone and phenolic molecules. The presence of phenolic and flavonoid content provides high antioxidant potential to the plant. The non-toxic elements present in the plant endorse their medicinal use in folklore and Ayurvedic systems of medicine. Overall results are proving that this plant *Calycopteris floribunda* Lam has extensive therapeutic potential for curing diseases with minimal toxic effects.

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Nil

AUTHORS CONTRIBUTIONS

All the authors have contributed equally.

CONFLICT OF INTERESTS

The authors declare no Conflict of Interest.

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