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 inhabitants are referring this plant as a life-saver. 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

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 of 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, furry 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 ovaries 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.

Table 1 represents the taxonomic hierarchy of the medicinal plant C. floribunda.
Table 1: Systematic position of *Calycopteris floribunda* [Taxonomy ID-134915]

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

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***

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Part of the plant</th>
<th>Solvents</th>
<th>Compound</th>
<th>Structure</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Leaves</td>
<td>Dichloro methane methanol</td>
<td>a) 3,8-di-O-methyl ellagic acid</td>
<td><img src="structure1.png" alt="Structure" /></td>
<td>[7]</td>
</tr>
<tr>
<td>2</td>
<td>Leaves</td>
<td>Dichloro methane methanol</td>
<td>b) 2,3,7-tri-O-methyl ellagic acid</td>
<td><img src="structure2.png" alt="Structure" /></td>
<td>[7]</td>
</tr>
<tr>
<td>3</td>
<td>Leaves</td>
<td>Acetone, Benzene, Methanol</td>
<td>c) Calycopterin</td>
<td><img src="structure3.png" alt="Structure" /></td>
<td>[10-14]</td>
</tr>
<tr>
<td>4</td>
<td>Leaves</td>
<td>Petroleum ether</td>
<td>d) n-octacosanol</td>
<td><img src="structure4.png" alt="Structure" /></td>
<td>[13]</td>
</tr>
<tr>
<td>No.</td>
<td>Sample</td>
<td>Solvent</td>
<td>Compound Description</td>
<td>Ref.</td>
<td></td>
</tr>
<tr>
<td>-----</td>
<td>--------</td>
<td>----------</td>
<td>----------------------</td>
<td>------</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Leaves</td>
<td>Petroleum ether</td>
<td>e) Sitosterol</td>
<td>[13]</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Leaves</td>
<td>Petroleum ether</td>
<td>f) 4'-O-methylcalycopterin</td>
<td>[13]</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Leaves</td>
<td>Petroleum ether</td>
<td>g) Ellagic acid</td>
<td>[13]</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Leaves</td>
<td>Petroleum ether</td>
<td>h) Proanthocyanidin</td>
<td>[13]</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Leaves</td>
<td>Petroleum ether, Methanol</td>
<td>i) Quercetin</td>
<td>[13-14]</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Leaves</td>
<td>---</td>
<td>j) Calycopterin-4'-methyl ether</td>
<td>[15]</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>Leaves</td>
<td>---</td>
<td>k) 3'-methoxy calycopterin</td>
<td>[15]</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>Leaves</td>
<td>Dichloro methane-methanol, Ethanol</td>
<td>l) Pachypodol</td>
<td>[16, 17]</td>
<td></td>
</tr>
</tbody>
</table>
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13 Leaves  Ethanol  m) Neo calycopterone  [18]

14 Leaves  Ethanol  n) 4-Acetyl neo calycopterone  [18]

15 Leaves  Ethanol  o) Neocalycopterone 4-methyl ether  [18]

16 Leaves  Ethanol, Ethyl acetate  p) Calyflorenone A-C  [18, 19]

17 Leaves  Ethylacetate  q) 6'-demethoxy neocalycopterone  [19]

18 Leaves  Ethyl acetate  r) 6'-epi-calyflorenone  [19]
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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 0.098±0.076 mg/g, methanol extract contains 1.491±0.43 mg/g and ethyl acetate extract contains 3.5±0.23 mg/g of flavonoids [8]. The total phenolic content of methanolic and aqueous root extracts of *C. floribunda* was determined by Folin-Ciocalteu colorimetric method. The methanol extract and aqueous extract contains 343.77±0.02 and 87.87±0.06 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 µg GAE/mg and the flavonoid content were 14.5±0.076, 16.5±0.087 and 48.50 µg GAE/mg respectively [28].

**Pharmacological potential of Calycoperis 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 *Staphylococcus pyogen*, *Staphylococcus aureus* and two Gram-negative bacteria *Escherichia coli*, *Pseudomonas aerogenes* and *Salmonella typhi*. The leaf extract showed significant antibacterial activity against *Bacillus subtilis*, *Streptococcus pyogen*, *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 pneumonia*, *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*, *Actinomycetes sp* and *Seratia sp*.

The estimated results of the antibacterial activity 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 antifungal 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 *Microsporum 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].

The 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 leaf 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 aphidermanatum*. The flower extract exhibited higher antifungal potency of 2.2 cm and 2.1 cm for *Fusarium oxysporum* and *Pythium aphidermanatum*, 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 (phosphomolybic acid method) and ferric reducing antioxidant potential (FRAP) assay methods were adopted for this study. By comparing the standard ascorbate, the ethyl acetate extract was found to be extremely effective with half-maximal inhibitory concentration (IC₅₀) values 360 µg/ml while for standard 410 µg/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 IC₅₀ 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±0.05, 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 Cell-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 calycoperine, isocalycoperine, 4-demethylcalycoperine 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 calycoperine, isocalycoperine, 4-demethylcalycoperine exhibit a wide range of cytotoxic activity with a median effective dose (ED50) values ranging from 101 to 104 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 calycoperine 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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AUTHORS CONTRIBUTIONS

All the authors have contributed equally.

CONFLICT OF INTERESTS

The authors declare no Conflict of Interest.

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