International Journal of Research in Pharmacy and Life Sciences
CODEN (USA): IJRPL | ISSN: 2321–5038
Journal Home Page: www.pharmaresearchlibrary.com/ijrpls

R E V I E W A R T I C L E

Phytopharmacological Review on *Couroupita guianensis*

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Abstract
Couroupita guianensis is a type of medicinal plant commonly known as cannonball tree, belongs to family Lecythidaceae. Almost all parts of the tree is used traditionally for treating various ailments. The whole plant of *Couroupita guianensis* has several biological activities such as the Hypolipidimic, antimicrobial, antiulcer, antiinflammatory, antinociceptive, anthelmintic, antiulcer, antioxidant, antipyretic, antiarthritic, immunomodulatory, antibacterial, antistress, antidiarrheal, insecticidal, anxiolytic, ovicidal, antidepressant, antifertility, antibiofilm, neuropharmacological, wound healing, vermicopositng, allopathic and hepatoprotective activities. It is also used in traditional medicines to treat various diseases such as gastritis, scabies, bleeding piles, dysentery, scorpion poision etc., *Couroupita guianensis* is a ever green tree native to tropical northern America, southern Caribbean and India. In India, it has religious significance and it can be seen in Shiva temples and it is known as Mallikarjuna flowers in telugu. In the present study the comprehensive study about the phytochemistry, pharmacological activities and the bioactive compounds of *Couroupita guianensis* can be performed.
Keywords: *Couroupita guianensis*, antioxidant activity, hypolipidimic activity, antimicrobial activity, immunomodularoty activity.

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A R T I C L E H I S T O R Y: Received 04 March 2022, **Accepted** 06 May 2022, **Available Online** 26 June 2022

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Citation: *P. Lakshmi Prasanna et al.*, Phytopharmacological Review on *Couroupita Guianensi*. *Int. J. Res. Pharm, L. Sci.*, 2022, 10(1): 01-08.

C O N T E N T S

1. Introduction

In ancient times, medicinal plants plays an important role to mankind owing to their healing properties and also used as a traditional forms to relief several diseases. Now a days millions of adults are depending on a medicinal plants for their primary health care needs. Commitment of the safety, quality, and efficacy of medicinal plants and herbal products has now become a key issue in industrialization and in developing countries. *Couroupita guianensis* belongs to Lecythidaceae family and commonly called as cannon ball tree as well as Ayahuma tree. Why it is called

cannonball tree, because the fruit appearance like cannon ball. It is a fast growing deciduous tree. All parts of the plant namely leaves, fruits, flowers, stems, roots, and seeds, has reported to *Couroupita guianensis* Aubl has a well known medicinal and ornamental values. *Couroupita guianensis* contain chemical constituents, such as triterpenes, phenolics, couroupitine, indirubin, isatin, and oils. In India *Couroupita guianensis* is called as a sacred tree by Hindus the reason behind this is generally it is grown in Lord Shiva temples and the flowers look like hood of Naga [Snake] protecting the Shivalinga, it is also called as Naga pushpa.

The tree were overexploited during the past for timber,settlement, and agriculture and so it is under the category of threatened medicinal plant and it has been enrolled in Internationl union for conservation of Nature (IUCN) red list. It is distributed throughout India as ornamental tree and its native to central and south America (Brazil, Colombia, French, Guyana, Peru and Venezuela) it grows in the thick humid forests, often along the river belts and low altitude. The fresh fruits pulp is used in the preparation of cooling medicinal drinks. The aerial parts of *Couroupita guianensis* has antibacterial(2), antimalarial and anthelmintic (3) antimicrobial activity, hypolipidimic activity, antioxidant activity, anticancer activity, anti hypertensive activity, anti inflammatory, antiulcer activity, antioxidant activity, immunomodulatory activity etc., The bark which consists of constituents like α,β−amyrin and β−sitosterols. An alkaloid Courapitine,stigmasterol and campesterols are isolated from fruits (5) and the volatile constituents isolated from the flowers of the tree(7).

2. Plant Profile

2.1 Synonyms:

Telugu : Mallikarjuna, Naagamalli, Naagalingam
Tamil : Naagalingam
Hindi : Tope Gola, Nagalinga
English : Cannon ball tree
Odia : Nagakesara
Malayalam : Naaga danthee
Indonesia : Sala
Thai : Sala Lankaa
Marathi : Kailasapati

Fig.:1. *Couroupita guianensis* flowers, fruits and leaves

2.2 Taxonomical classification:

Kingdom : Plantae –Plants
Sub kingdom : Tracheobionta
Superdivision : Spermatophyta
Division : Magnoliophyta
Class : Magnoliopsida
Sub class : Dilleniidae
Order : Lecthidales
Family : Lecythidaceae−Brazil−nut family
Genus : Couroupita Aubl
Species : Couroupita guianensis Aubl (18).

2.3 Botanical classification:

Couroupita guianensis is a large deciduous evergreen tree growing up to 20 meters height. Leaves are alternate, oblong−obovate they are grown up to 20 cm long, entire to slightly serrate and hairy beneath veins. Inflorescence is racemose, arising from the trunk to other branches of plant. Flowers are reddish with yellow tinge on the outside, fragrant odour, and stamens borne on an overarching androphore. Fruits are a long, reddish−brown globose, 15 to 24 cm, with a woody capsule, and each containing 200 to 300 seeds. Each fruit weight about 36 pounds (7). The plant is propagated by seeds. However, the seeds are reported to be recalcitrant with short life span. Most of the stamens are fertile, but some abortive stamens are also seen at the base of the band surrounding the ovary. Ovary is 5−7 celled and the cells are many−ovuled(4,12,14).

MORPHOLOGY:

Leaves: *Couroupita guianensis* leaves are simple, alternate, oblong or oblong−ovate up to 10 cm long with entire to slightly serrate margin and a short petiole and hairy on the veins beneath. They are arranged in whorls at the end of the shoot.

Flowers: *Couroupita guianensis* flowers are large and flashy, it appears in various colours like orange, scarlet or pink with a pleasant fragrance, almost throughout the year. They are strongly fragrance (or) sweet−smelling especially at the night and in the early morning.

Fruit: *Couroupita guianensis* fruit weighing about 36 pounds and the fruit contain seeds (200−300) they are in white colour, vinous and acidic pulp. Each tree bears around 150 fruits and takes up 1 year or nearly 18 months to mature. The pulp fills the whole shell and differs in their colour indicates the degree of maturity. The fruits of about 15−24cm diameter and encased in a hard shell.

Seed: *Couroupita guianensis* seeds are present in fruit pulp they appears like white, unpleasant smelling with edible jelly type, which are exposed when the upper half of the fruit goes off like a cover.

Chemical constituents:

Couroupita guianensis having rich with medicinal values, almost all parts of the tree contain API. Flowers yield an alipathic hydrocarbons, stigmasterol, alkaloids, phenolics and flavonoids. It also contains active principles like isatin and indirubin which are vital to its antimicrobial activity.

Couroupita guianensis fruits yielded 6,12−dihydro−6, 12−dixoindolo(2,1−b) quinazoline (tryptanthrin), as well as indigo (CR et al., 2013) indirubin (8a) and isatin. From the fruit of *C.guianensis* nursing compounds are isolated stigmasterol , campesterol (Rastogi, 1995) and one more compounds also isolated they are linolenic acis, nerolic acid, tryptanthrin ect., *Couroupita guianensis* leaves

contain triterpenoid esters of fatty acids as β−amirin palmitate and it also contain dyes as indigo and indirubin. The whole tree has rich in providing anthocyanin, flavanoids, volatile constituents like eugenol and farsenol.

3. Pharmacological Activities

Hypolipidimic activity

Methanolic extract of Couroupita guianensis Abul flowers was orally given in High cholesterol fed diet rats. Treatment with methanolic extract of Couroupita guianensis Aubl Flowers significantly declined in total serum cholesterol, triglycerides, low density lipoproteins, very low density lipoproteins and enhanced the high density lipoproteins in obese rats and it was comparabled with that of standard atorvastatin.

Antioxidant activity

Extracts obtained from different parts of CG have exhibiting a significant antioxidant effect was demonstrated in several studies. Leaf, stem and flower extracts exhibits variable scavenging activities with respect to DPPH, hydrogen peroxide, nitric oxide and hydroxyl radicals. Importantly, ethylacetate leaf extract has shown the highest scavenging activity against DPPH, hydrogen peroxide and hydroxyl radicals with IC50 values of 17.25, 55.1 ± 0.04 and 240 ± 0.81 µg/mL, respectively. Similarly, ethylacetate stem extract inhibited nitric oxide radical with an IC50 value of 50.4 ± 0.31 µg/mL. In another study carried out by Kekuda, marked scavenging activity against 2,2′-azino-bis-3-ethylbenzthiazoline-6-sulfonic acid was provided by the methanol extract of the leaf (IC50 value 7.63 µg/mL) (11). Likewise, the methanol extract of flowers and ethanol extract of the leaves have also been found to exhibit antioxidant activities (13).

The variations in antioxidant activities might be due to the method of extraction and the solvent used. In a study amongst all the extracts studied, cold percolation aqueous extract of leaf showed high phenol content (91.87±0.113 mg/g) and thus maximum DPPH free radical scavenging activity and ferric reducing antioxidant power with a percentage inhibition of 85.43 ± 0.155 and 11.85 ± 0.155 respectively at a concentration of 100 µg/mL (8). Meanwhile, on assessing the effect of maturation on the in vitro antioxidant activities, it has been evident that young stages of leaf and fruit exhibited higher total phenols, flavonoids, ortho-dihydric phenols and anthocyanin and also maximum scavenging activity (20).

Anti-inflammatory activity

Inflammation is a body's physiological response against intrinsic and/or extrinsic factors. In-vitro and in-vivo studies are implicated that role of CG in counteracting inflammation. In an in-vitro study, the methanolic flower extract stabilizes the human red cell membrane at a dose of 500 µg/mL compared with the ethanolic flower extract by taking the diclofenac as standard drug. The flower extracts inhibited hypotonicity induced RBC membrane lysis. Since the RBC membrane is similar to the lysosomal membrane, the inhibition is taken as a measure of anti-inflammatory activity (22). Different extracts from leaves were explored in an in vivo study for inflammatory pain (formalin-induced licking) and acute inflammation (carrageenan-induced peritonitis). The study showed that hexane, ethanol and ethyl acetate extracts inhibited leukocyte migration at higher doses (30 and 100 mg/kg). The extracts were found to reduce cytokines such as tumor necrosis factor-α, and inhibit interleukin-1b and nitric oxide production.

The flower extract was also reported to reduce the paw licking during first and second phases (22). Similar anti-inflammatory study was carried out with flowers and bark of CG in the carrageenan-induced hind paw edema model and the observed mean paw volume was compared with the standard drug, indomethacin. Benzene, ethanol and aqueous extracts obtained from the flower and aqueous extracts obtained from bark showed a marked reduction in inflammation after 3 hours of administration.

Anthelmintic activity

Helminthic infection is one of the major problems for livestock all over the world. Development of antihelminthic resistance made the researchers overlook for plant-based product. In vitro studies revealed that CG leaves and flowers possess antihelminthic property (23).

The extracts of leaves and flowers were tested against Pheretima posthuma by worm motility assay. By observing the time of paralysis and time of death, it was reported that chloroform, ethanol and acetone extracts obtained from CG flowers and methanol extract obtained from CG leaves showed better antihelminthic effect at the concentration of 100 mg/mL.

Antihyperglycemic and antidiabetic activities

Different parts of CG were tested to evaluate its antidiabetic activity. The alloxan induced mice with the aqueous and methanolic extracts obtained from flowers at a dose of 100 mg/kg body weight. The extracts showed significant ($P < 0.05$) reduction in blood glucose level compared with the standard, metformin (24). One of the therapeutic approaches for diabetes is to control postprandial hyperglycemia which can be accomplished by inhibiting gastrointestinal carbohydrate hydrolyzing enzymes such as α-amylase and α-glucosidase. A study was carried out to find the effect of methanolic extract of leaves on the subject carbohydrate hydrolyzing enzymes and found that the extract control the enzymes dose-dependently highlighting inhibition of α-amylase and α-glucosidase with sucrose as substrate and α-glucosidase with maltose as substrate at an IC50 value of 2.86 mg/mL, 2.38 mg/mL and 2.49 mg/mL, respectively.

Leaves are rich in polyphenolic compounds including hydroxycinnamic acids, rosmarinic acid, caffeic acid and kaempferol-3-neohesperidoside, triterpenoid and β-amyrin palmitate. These compounds were reported to have inhibitory activity against carbohydrate hydrolyzing enzymes (24). Further, reactive oxygen species are considered to be the underlying cause for β cell dysfunction, insulin resistance, impaired glucose tolerance and type 2 diabetes. Gold nanoparticles obtained from CG leaves have increased lipid peroxidation, and antioxidant enzymes such as superoxide dismutase, glutathione

reductase and catalase enzyme activities in diabetic rats and thus alleviating hyperglycemia condition by regulating oxidative stress.

There is a close association between obesity and type 2 diabetes. Type 2 diabetes is characterized by insulin insensitivity. Obesity along with insulin resistance and hyperlipidemia are related to macrovascular diabetic complications. CG has been explored for its anti-obesity potential and a positive result was obtained. The methanolic extract (100, 200 mg/kg body weight) of the plant reduced total serum cholesterol, low-density lipoproteins, triglycerides, very low-density lipoproteins and increased the high-density lipoproteins in obese rats when compared with the standard, Atorvastatin. Further, the extract has demonstrated significant inhibition of atherosclerotic plaque formation.

Antinociceptive

CEE (crude ethanol extract) and fractions significantly inhibited the number of mutilation induced by acetic acid. All fractions showed antinociceptive activity in the tail flick model, being the hexane and ethyl acetate the most potent and long acting fractions. In the hot plate method the highest effects was observed at the dose of 100mg/kg from allfractions. Administration of Naloxone inhibited the antinociceptive effect of fractions. The most prominent effect was identified in the antinociceptive activity initiated by CEE and butanol fraction.

Hepatoprotective activity

The hepatoprotective activity of ethanolic leaf extract of Couroupita guianensis against CCL persuaded liver damage in four rats. Actions of liver marker enzymes such as, serum glutamate oxaloacetate transaminase, serum glutamic pyruvic transaminase, asparate aminotransferase, alkaline phosphatase, total bilirubin, and total protein which are visible under considerable hepatoprotective effect in evaluation with the drug of silymarin.

Wound healing activity

Ethanol extract of the whole plant was evaluated for its potential to heal the wound in rats by carrying out two methods: excision and incision models. Parameters such as wound contraction, epithelisation, tensile strength and hydroxyproline content were determined and it was reported that there was decrease in the surface area of the wound and increase in the tensile strength and hydroxyproline concentration. Furthermore, complete epithelisation was observed within 15 days (2). In another study, hydroethanolic leaf extract containing flavonoids such as 2′,4′-dihydroxy- 6′-methoxy-3′,5′-dimethylchalcone and 7-hydroxy-5- methoxy-6,8-dimethyl flavanone and the phenolic acid 4-hydroxybenzoic acid was reported to stimulate human skin fibroblast proliferation was promote UV absorption. Fibroblast plays an incredible role in wound healing by enhancing wound contraction (2).

Anti-ulcer activity

Methanol extract of flowers in Wistar rats revealed that at doses of 400 mg/kg b.w, the ulcer protection level and ulcer index score were found to be 86.82% and 4.93 ± 0.22%, respectively. Furthermore, the extract reduced gastric juice, free acidity (61.83 ± 4.71), total acidity (88.50 ± 5.09) and pepsin (15.36 µg/mL) when compared with ulcer induced control group. It was suggested that the protective action of the CG flowers might be due to the richness in phytochemicals such as tannins and flavonoids. Another study performed using the ethanolic extract of CG leaves in experimental rats indicated that at doses of 150 and 300 mg/kg body weight there was a significant decrease in ulcer index, gastric volume and free acidity compared to control. The extract has recorded significant inhibition of the gastric lesions induced by pylorus ligation induced ulcer and ethanol-induced gastric ulcer. It has been claimed that the anti-ulcer property is attributed to the anti-secretory activity of the extract (16).

Immunomodulatory activity

Both in-vitro and in-vivo studies have claimed CG to modulate (suppress or stimulate) the components of the immune system. Methanol extract of CG leaves was tested for hypersensitivity reactions using sheep red blood cell as the antigen in both the studies. It has been found to increase phagocytosis. It enhances the phagocytic functions of neutrophils and also stimulates the cell-mediated and humoral mediated immune responses (19).

Antipyretic activity

Antipyretic activity of flower and a bark of Couroupita guianensis in chloroform, ethanol, water, ether, petroleum ether extracts was done by victimization yeast induces febrility methodology. The antipyretic action of all the extracts was chloroform, ethanol, water extracts have vital onset of action on fall of temperature (within 30minutes) almost like that of paracetamol (30 minutes).

Ovicidal activity

The hexane, chloroform and ester extracts of Couroupita guianensis plant on the eggs of Helicoverpa armigera. All the extracts showed ovicidal activity, and among them alkane extract exhibited additional ovicidal activity.

Antiarthritic activity

Antiarthritic activity of Couroupita guianesis leaves in methanolic extract by using of Protein denaturation methodology. The activity of the extract was increased depends upon the concentration.

Insecticidal activity

The aqueous extract of Couroupita guianensis plant was reflected for insecticidal activity against eggs, nymphs and adults of Bemisia tabaci, on tomato plant grown in the greenhouse condition. The aqueous extracts of C. guianensis leaves show high insecticidal effects on nymphs and adult flies although low effect on the eggs of B. tabaci as paralleled to control.

Neuropharmacological activity

In a study exploring the neuropharmacological activity, Gupta et al analyzed the effect of methanolic extract of flower with respect to spontaneous motor activity, rota-rod performance and phenobarbital induced hypnosis in mice. The extract exhibited a significantly reduce the spontaneous motor activity and the onset of phenobarbitone induced sleep, dose-dependently (100, 250 and 500 mg/kg). However, the extract had no effect in motor coordination as evident from the rota-rod performance. In addition, anti-depressant activity of CG has been confirmed in its roots and leaves. Methanol extract obtained from leaves were

given orally to mice at a dosage of 125, 250, and 500 mg/kg body weight and the tail suspension test (TST), forced swim test (FST) and reserpine antagonism were carried out in the tested mice.

The extract has been shown to reduce immobility time in TST and FST, and in reserpine antagonism, it significantly reduced the duration of catalepsy and ptosis. Furthermore, compounds isolated from petroleum ether extract of the leaf was found to implicate the same result with respect to TST and despair swim test but at lower concentration (1, 2.5, 5 mg/kg) suggesting its antidepressant activity.

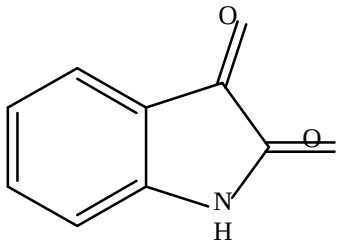
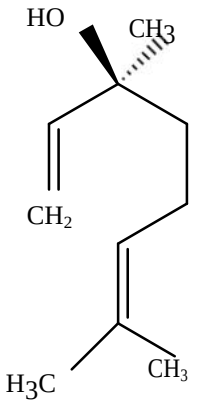
The use of anxiolytic drugs helps to induce relaxation and hypnosis. C. guianensis extracts were explored for its effect in controlling anxiety. Methanolic and aqueous flower extracts were found to have anxiolytic activity at a dose of 500 mg/kg as observed from the results of the elevated plus maze, light and dark, and open field test (21).

Antimicrobial, antimycobacterial, antibiofilm Properties: Antimicrobial, antimycobacterial and antibiofilm properties in chloroform extract of fruit of Couroupita guianensis. Chloroform extract of Couroupita guianensis fruit showed sensible antimicrobial and antibiofilm forming activities however it showed less antimycobacterial activity. Chloroform extract showed effective antibiofilm activity against gram-negative microorganism referred to as genus Pseudomonas aeruginosa ranging from two mg/mL biofilm repressive concentration (BIC), with 52 inhibition of biofilm formation.

The metanolic extract Couroupita guianensis flowers showed antimicrobial property. The results of the antimicrobial activity showed effective repressing activity against Plesiomonas Shigelloides, Cocci aureus, Vibrio mimicus, and Proteus vulgaris. Moderate antimicrobial activity was recorded against E.coli, Klebsiella pneumonia and Salmonella typhi.

The current review article represents that Couroupita guianensis having the chemical constituents and pharmacological and therapeutic effects. Couroupita guianensis was widely used to treat the diseases like obesity, hypertension, ulcers, bacterial infections, tumors, diabetes, depressant, anxiety, ovicidal, hepatotoxicity, inflammation, fertility, pyretic, have been reported for c.guianensis. The extensive literature survey revealed that Couroupita guianensis is important medicinal plant with diverse pharmacological spectrum. The plant shows the presence of many chemical constituents such as notably isatin, indirubin and tryptanthrin. Which is responsible for varied pharmacological and medicinal properties.

Table: 2 Phytoconstituents with IUPAC names and structures

Name	IUPAC Name	Structure
Isatin	Indoline-2,3-dione	
Linalool	3,7-dimethylocta-1,6-dien-3-ol	

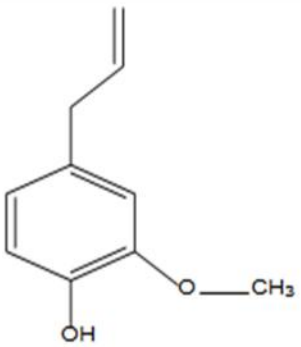
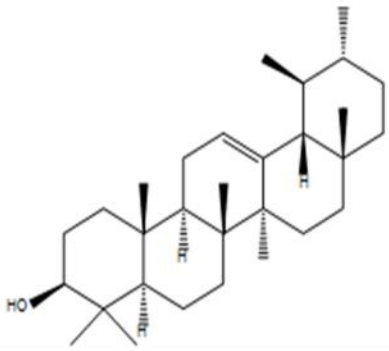
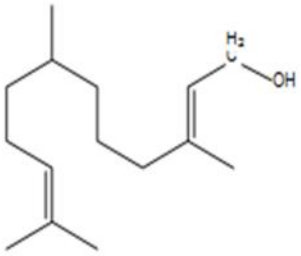
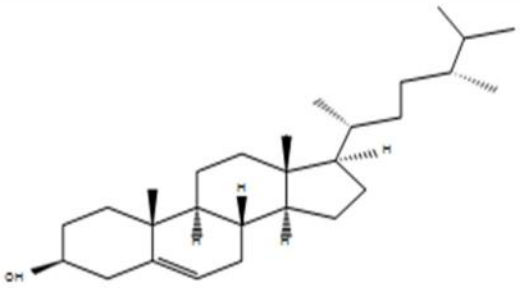
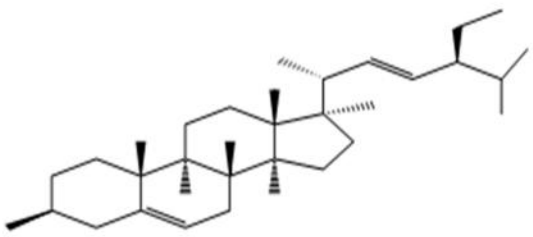
Eugenol	4-allyl-2-methoxyphenol	
α-amyrin	(3S,4aR,6aR,6bS,8aR,11R,12S,12aR,14aR,14bR)1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,14,14a,14b-icosahydro-4,4,6a,6b,8a,11,12,14b-octamethylpicen-3-ol	
Famesol	3,7,11-trimethyldodeca-2,10-dien-1-ol	
Campsterol	(3S,8S,9S,10R,13R,14S,17R)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-10,13-dimethyl-17-((2R,5R)-5,6-dimethylheptan-2-yl)-1H-cyclopenta[a]phenanthren-3-ol	
Stigmasterol	(3S,8R,9R,10S,13R,14R,17R)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-17-((E,2R,5S)-5-isopropylhept-3-en-2-yl)-3,8,9,10,13,14,17-heptamethyl-1H-cyclopenta[a]phenanthrene	

Table: 1. Chemical constituents of *Couroupita guianensis*

Part of the plant	Chemical constituents	Reference
Fruit	Couroupitine A (tryptanthrin), Couroupitine B (indirubin), malic acid, isocitric acid, stigmasterol, campesterol, hopane, rutin, quercetin, kaempherol, farmaricetin, luteolin and ursolic acid.	(20−25)
Flower	Eugenol, linalool, (E,E)−farnesol, nerol, geraniol, (Z,E)−farnesol, vanillin, limonene and geranial, (E,E)−farnesyl actate, trans ocimene, nootkatone, geraniol, 2−isopropenyl−5−mrthyl−4−hexenylacetate),cedr−8−en−13−ol, (E,Z)−farnesyl acetate, methyl (11E)−hexadecenoate, isatin, cycloart−24−en3−ol−3−exomethyleneheptadeconate, stigmasterol, p−coumaric acid, o−coumaricacid, quercetin, octyl 4−(nonanoyloxy) benzoate, myristoleic acid, linoleic acid, (8E, 10E, 12E)−icosa−8,10,12−triene)	23,36−39)
Leaf	Triterpenic ester β−amirin palmitate, hydroxycinnamic acids, caffeicacid,rosmarinicacid,kaempferol−3−O−neohesperidoside,20, 40−dihydroxy−60−mrthoxy−30,50−dimethylchalcone, 7−hydroxy−5−methoxy−6,8−dimethylflavanone, 4−hydroxybenzoic acid	(5,10)
Seed	Indigo, indirubin, stigmasterol, campesterol, linoleic acid, nerol, tryptanthrin	(4)
Stem and Bark	Phytosterol, β−amyrin, betulin−3β−caffeate and lupeol−3β−caffeate, couropitone (stigmasta−4,23(E)−dien−3−one 1), β−amyrin, β−amyrone, β−amyrin acetate, stigmasterol, ergosta−4,6,8 (14), 22−tetraen−3−one, β−sitosterol and its glycoside.	1−4)

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