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Prashith Kekuda TR
Department of Microbiology, SRNMN College of Applied Sciences, N.E.S Campus, Balraj Urs Road, Shivamogga, Karnataka, India

Smruthi BS
Department of Microbiology, SRNMN College of Applied Sciences, N.E.S Campus, Balraj Urs Road, Shivamogga, Karnataka, India

Saima Banu
Department of Microbiology, SRNMN College of Applied Sciences, N.E.S Campus, Balraj Urs Road, Shivamogga, Karnataka, India

Swathi BG
Department of Microbiology, SRNMN College of Applied Sciences, N.E.S Campus, Balraj, Urs Road, Shivamogga, Karnataka, India

Correspondence
Prashith Kekuda TR
Department of Microbiology, SRNMN College of Applied Sciences, N.E.S Campus, Balraj Urs Road, Shivamogga, Karnataka, India

A comprehensive review on the ethnobotanical uses and pharmacological activities of *Cochlospermum religiosum* (L.) Alston (Bixaceae)

Prashith Kekuda TR, Smruthi BS, Saima Banu and Swathi BG

Abstract
Plants represent an indispensable need of human life every day. *Cochlospermum religiosum* (L.) Alston is one among the most important medicinal plants belonging to the family Bixaceae. In this review, we present a comprehensive data available on the ethnomedicinal uses and pharmacological activities of *C. religiosum*. Fruits of *C. religiosum* are edible. Leaves and shoots are often used as vegetable in some parts of India. Various parts, such as stem bark, root and leaves, of the plant including the gum are traditionally used in several conditions such as cough, bone fracture, ulcer, jaundice, itching, asthma, diarrhea, dysentery, tuberculosis, syphilis, sore throat, gonorrhea, piles, and dandruff. *C. religiosum* is used as sedative, to enhance face glow and memory. The plant is also widely employed in ethnoveterinary uses. The plant is shown to exhibit antibacterial, antifungal, insecticidal and antioxidant activity. A gum, designated as katira gum (also known as kondagogu gum), obtained from the stem bark of the plant is shown to exhibit various bioactivities including wound healing activity. The gum is also proven to exhibit promising bioremediation property with respect to removal of heavy metals. It is very important to conserve this plant species as the plant is medicinally important and is one of the threatened plant species because of its overexploitation.

Keywords: *Cochlospermum religiosum*, Ethnomedicine, Pharmacological activities

Introduction
Plants serve mankind in various ways and are considered as an important element in the daily life. Plants are an inevitable source of food, fodder, construction tools, medicines, spices and flavoring agents and textile. The history of utilization of plants is as old as human civilization. Traditional practitioners rely on various medicinal plants for treating several ailments of humans and animals including dreadful diseases such as cancer. People living in remote places utilize medicinal plants preferentially as they do not have access for modern medicine. A vast majority (>75%) of population, living especially in developing and under-developing countries, depends on traditional medicine for meeting the primary healthcare. Whole plant or various parts such as roots, leaves, and flowers of plants have found medicinal importance in various indigenous systems of medicine. Medicinal virtues of plants are attributed to the presence of secondary metabolites such as alkaloids, polyphenolic compounds and terpenes. The secondary metabolites from plants have been extensively used in modern medicine. Many plant metabolites such as morphine, vincristine, vinblastine, codeine, camptothecin, taxol, quinine and digoxin have been used in many conditions. Plant secondary metabolites have been shown to exert various bioactivities such as antioxidant, anti-inflammatory, antimicrobial and anticancer activity [1-7].

Cochlospermum religiosum (L.) Alston (synonym *C. gossypium* DC) is one of the medicinally important tree species belonging to the family Bixaceae. The plant is popularly known by the names Golden silk cotton tree/butter cup tree in English, Girisalmalika in Sanskrit, Gabdi in Hindi and Arasina buruga in Kannada. The plant *C. religiosum* is used as medicine for various purposes. The plant is used as sedative, stimulant, and is used in gonorrhea, jaundice, cough, trachoma, syphilis etc. The young leaves are used for cooling, and for washing hairs. The gum obtained from the plant is useful in treating pharyngitis, dysentery, diarrhea, asthma, eye problems and stomachache. The plant has got wide ethnoveterinary use. The gum obtained from the plant is often marketed and is useful in several complications or conditions [8-16]. In India, the plant is grown near temples due to its bright flowers that are to be used for offerings to god and also for aesthetics [17].

An updated information of ethnobotanical uses and pharmacological activities of *C. religiosum* is presented in this review. An intensive literature survey is carried out by an insight into search engines such as Google Scholar, PubMed and ScienceDirect and by referring journals.

C. religiosum is one among the most important tree species that yield gum. The bark of *C. religiosum* yields an exudate i.e. gum, termed as katira or kondagogu, which is exploited as one of the most important non-timber forest products. The gum is obtained by blazing or stripping the tree bark. The gum is sweet, pale, semi-transparent, nontoxic, less expensive, swells in water, safe for consumption (as food additive) and is shown to contain several important elements having profound health benefits. The gum is used in ice cream, cigar and paste industries. Besides, the gum finds potential use as sedative, stomachic, coolant and in conditions such as asthma, cough, diarrhea, dysentery, eye problems, gonorrhea, syphilis and throat infections. The biopolymer is a heteropolysaccharide and is composed of sugars such as glucose, galactose, arabinose, mannose, rhamnose, glucuronic acid and galacturonic acid. The gum katira is shown to contain D-galactose, D-galacturonic acid and L-rhamnose in a molar ratio 2:1:3. Katira is grouped under substituted rhamnogalacturonans. Katira gum is shown to contain elements namely calcium, magnesium and potassium in higher quantity, however, the content of aluminium, nickel and cobalt is less. The gum is reported as a biosorbent for the removal of toxic metals such as lead and cadmium [16, 18-24].

Systematic position [23]

Kingdom:	Plantae
Class:	Magnoliopsida
Order:	Violales
Family:	Bixaceae
Genus:	*Cochlospermum*
Species:	*religiosum*

Plant description

C. religiosum is a small deciduous tree (Figure 1). Stem is smooth and ash colored. Bark contains gum. The leaves are 7-20cm across, orbicular in outline, palmately 3-5lobed, cordate at base, tomentose beneath, 5-7 nerved at base. Petiole is up to 25cm long. Flowers appear after leaf fall. Flowers are large, cup shaped, up to 8cm or more across, in terminal recemes or loosely branched panicles. Sepals are 5 in number, deciduous and imbricate. Petals are 5 in number, bright golden yellow in color and contorted in bud. Stamens are free and numerous. Ovary is one celled or incompletely 3-5celled. Fruit is a capsule, large, 9-13cm long, obovoid. Seeds are brown in color, reniform and covered with wooly hairs [25].

Fig 1: *Cochlospermum religiosum* (L.) Alston

Ethnobotanical uses of *C. Religiosum*

Literature survey revealed the utilization of various parts of *C. religiosum* (including the gum) for treating several diseases or disorders besides the edible use. A brief description of the utilization of various parts viz. fruits, roots, gum, bark and leaves of the plant in various regions is described. *C. religiosum* is an active ingredient in the polyherbal formulation of Unani medicine Majoon-e-Azaraqi. The drug is prescribed for hemiplegia, nerve strengthening, facial paralysis, trembling, tremor, rheumatism, neurasthenia and epilepsy [26]. The decoction prepared from leaves and stem bark has ethno-veterinary use in order to treat infertility in Andhra Pradesh, India [27]. In Nallamalais, Andhra Pradesh, the plant is used in the treatment of tuberculosis [28]. Basha *et al.* [29] reported the utilization of *C. religiosum* for the treatment of gonorrhea and dysentery in Nagarjuna Sagar Srisailam wildlife sanctuary, Andhra Pradesh, India. The tribal communities of Chitrakoot, Madhya Pradesh use the root powder mixed with water to reduce wrinkles on the face [30]. Adhikary [2] showed the ethnoveterinary application of stem fibers of *C. religiosum* for the management of ticks in cattle and sheep. The study of Singh *et al.* [31] highlighted the utilization of the plant in Balangir and Deogarh districts, Odisha, India to increase sexual desire. The leaves have ethnoveterinary significance for treating the reproductive disorders in cattle and buffalos in the district Sargodha, Pakistan [32].

In Nagpur district, India, the plant is used in the treatment of gonorrhea, cough and cold [33]. The local medicine men of Kappat hill area of Gadag district, Karnataka, India, administer the fine powder of flowers mixed with honey to children in empty stomach in order to enhance memory and to improve memory [8]. The tribal communities in Palakkad district, Kerala, India use the fruits of *C. religiosum* traditionally [34]. Various parts such as leaf, stem and bark of *C. religiosum* are used as ethnoveterinary medicine in Maharashtra state, India [35]. In Godavari district, Andhra Pradesh, India, the plant is used as hair tonic and in the treatment of ulcers [36]. In Chimur Tahsil of Chandrapur district, Maharashtra, India, the roots of *C. religiosum* are used to treat jaundice in children and the leaves as well as flowers are used as stimulant [37]. The stem bark of the plant is used as sedative by ethnic people of Gundlabrahmeswaram wildlife sanctuary, Andhra Pradesh, India [38]. The flowers of *C. religiosum* are used as wild food plants by tribal communities in Orissa, India [39]. Leaves of the plant are used as a remedy for piles in Andhra Pradesh, India [40]. Leaves are used to treat jaundice in Madhya Pradesh, India [41]. In Chitter, India, the leaves are used as hairtonic and gum is used in ulcers [42]. The gum obtained from the bark of the plant is used as a remedy for cough and gonorrhea in Andhra Pradesh, India [43]. More information on the ethnomedicinal uses of *C. religiosum* in various states of India is presented in Table 1.

Table 1: Ethnobotanical uses of *C. religiosum* in different states of India

State	Part used	Uses	Reference
Tamil Nadu	Fruit	Fruit is edible	Ramachandran *et al*. [44]
Andhra Pradesh	Stem bark	Jaundice	Maheswari *et al*. [45]
Kerala	Leaves and leafy shoots	Edible	Yesodharan and Sujana [46]
Telangana	Bark, gum	Bark is used in bone fracture; gum is used in ulcer.	Saidulu *et al*. [47]
Andhra Pradesh	Stem bark	Jaundice (ethnoveterinary use)	Reddy *et al*. [48]
Maharashtra	Stem	Bone fracture	Bhadange [49]
Karnataka	Flowers	Face glow	Shivakumar and Parashurama [50]
Andhra Pradesh	Gum	Aphrodisiac	Basha and Priyadarshini [51]
Andhra Pradesh	Resin	External application for treating itching	Subbaiah and Savithramma [52]
Maharashtra	Root	Jaundice	Satpure [53]
Tamil Nadu	Leaf	Cough	Arulappan *et al*. [54]
Andhra Pradesh	Stem bark	Bone fracture	Bapuji and Ratnam [55]
Odisha	Leaves and shoots	Used as vegetable.	Mohanty *et al*. [56]
Andhra Pradesh	Fruit	Fruit juice is used in dysentery and gonorrhea	Savithramma *et al*. [57]
Telangana	Leaf	Piles	Mohan *et al*. [58]
Madhya Pradesh	Gum	Cough, menorrhagia, asthama, syphilis, sore throat, tuberculosis, diarrhea, dysentery, gonorrhea, leucorrhea, spermatorrhoea, and general debility	Mishra *et al*. [59]
Uttar Pradesh	Root, stem bark	Root in albuminuria, stem bark in sores and fistula	Singh *et al*. [60]
Andhra Pradesh	Stem bark	Jaundice	Saheb *et al*. [61]
Tamil Nadu	Petals, gum	Petals are used for general health; gum from stem is used for external application in case of bone fracture	Suresh *et al*. [62]
Andhra Pradesh	Stem bark	Bone fracture	Rao *et al*. [63]
Telangana	Bark	Diarrhea, dysentery	Murthy and Madhav [64]
Madhya Pradesh	Root	Powder of roots is used as tonic.	Jain *et al*. [65]
Karnataka	Leaf	Bronchial asthma	Shiddamallayya *et al*. [66]
Andhra Pradesh	Leaf	Leaf paste is used in dandruff.	Madhu and Naik [67]
Tamil Nadu	Seeds	Juice made from the seeds is taken as sedative.	Balagengatharathilagam *et al*. [68]
Maharashtra	Leaf	Infusion prepared from leaves is taken in asthma.	Khyade *et al*. [69]
Andhra Pradesh	Gum	Aphrodisiac	Neelima *et al*. [70]
Andhra Pradesh	Stem bark	Bone fracture	Suneetha *et al*. [71]
Andhra Pradesh	Leaf	Leaf decoction is used for hair wash	Suneetha *et al*. [72]

Phytochemicals detected in *C. Religiosum*

The plant *C. religiosum* is shown to contain a range of phytochemicals. A glycoside compound named as 5,7,3',4'-tetrahydroxy-3-methoxy-flavone-7-O-β-D-glucopyranosyl-(1-4)-O-β-D-galactopyranoside was isolated from the seeds of *C. religiosum* [73]. Phytochemicals viz. phenols, tannins, flavonoids and alkaloids have been detected in the leaves and stem bark of *C. religiosum*. The content of phenols and tannins were higher in stem bark while flavonoids and alkaloids were found in higher quantity in leaves [74]. A bioactive flavonoid designated as Isorhamnetin-3-glucoside (Figure 2) was isolated from the leaves of *C. religiosum*[75]. More information on phytochemicals detected in *C. religiosum* is presented in Table 2.

Table 2: Phytoconstituents in *C. religiosum*

Part	Phytochemical detected	Reference
Leaf	Sterols, triterpenes, saponins, alkaloids, tannins, flavonoids, phenols, glycosides	Ponnamma *et al*. [76]
Leaf	Steroid, coumarins, anthocyanins	Savithramma *et al*. [77]
Leaf	Sterols, glycosides, saponins, flavonoids, tannins and phenols	Bai *et al*. [78]
Stem bark	Saponins, tannins, phenolic compounds, alkaloids, phytosterols	Kawde *et al*. [79]

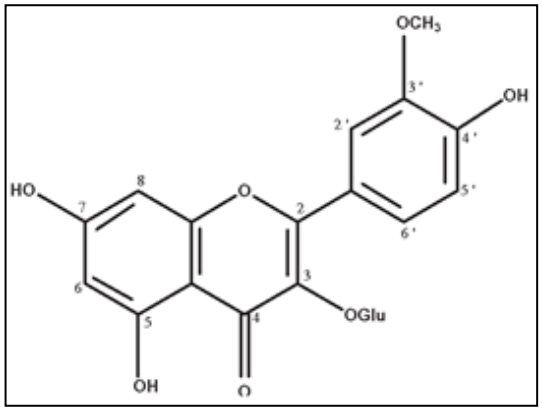

Fig 2: Isorhamnetin-3-glucoside [75]

Pharmacological activity of *c. Religiosum*

Antibacterial activity

Methanolic extract of leaves of *C. religiosum* was effective against *Staphylococcus aureus* while other bacteria were not affected [80]. Ethanolic extract obtained from the leaves of *C. religiosum* displayed concentration dependent inhibition of *Staphylococcus aureus* and *Escherichia coli*. *S. aureus* was more susceptible than *E. coli* [81]. The acetone and ethanolic extract obtained from the stem of *C. religiosum* were effective against gram positive and gram-negative bacteria. Chloroform extract was not effective [28]. Bai *et al*. [78] showed antibacterial activity of methanol extract of *C. religiosum* leaves against human and plant pathogenic gram positive and gram-negative bacteria. The study carried out by Ponnamma

et al. [76] revealed concentration dependent antibacterial activity of solvent extracts of *C. religiosum* leaves. Among extracts, marked antibacterial activity was shown by ethyl acetate extract. Marked inhibitory activity was observed against *E. coli*. At concentration 25 and 50µg, chloroform extract did not cause inhibition of any of the test bacteria. The study of Pumpaluk *et al*. [82] revealed the inefficacy of methanolic extract of seeds/fruits against cariogenic bacteria viz. *Streptococcus mutans*, *Lactobacillus casei* and *Actinomyces viscosus*. Kawde *et al*. [79] evaluated antibacterial potential of various solvent extracts of stem bark of *C. religiosum*. Solvent extracts displayed concentration dependent inhibition of test bacteria with marked activity against gram positive bacteria. Recently, the study carried out by us showed the efficacy of methanolic extract of flower of *C. religiosum* to inhibit gram positive and gram negative bacteria [83].

Antifungal activity

Methanolic and aqueous extracts of leaves of *C. religiosum* were screened for three phytopathogenic fungi of *Gossypium herbaceum* against *Alternaria alternata*, *Chaetomium globosum* and *Fusarium oxysporum*. The extracts caused concentration dependent inhibitory activity against fungi. Overall, methanol extracts were more inhibitory than aqueous extracts [84]. The study of Goud *et al*. [28] did not reveal antifungal activity of stem bark extracts against *Aspergillus niger*. Recently, we reported antifungal efficacy of methanolic extract of flower to inhibit mycelial growth of two molds namely *Curvularia* sp. and *Rhizopus* sp. [83]

Antioxidant activity

A bioactive flavonoid compound Isorhamnetin-3-glucoside isolated from the leaves of *C. religiosum* was shown to exhibit concentration dependent scavenging of superoxide radicals [84]. The kondagogu gum was shown to exhibit weaker inhibitory activity against DPPH radicals with a scavenging activity of 11.6% at 1% w/v concentration [85]. The study of Bai *et al*. [78] failed to reveal antioxidant activity of methanolic extract of leaves of *C. religiosum* as evaluated by ferric reducing assay. Kawde *et al*. [79] revealed scavenging of DPPH radicals by methanolic extract of stem bark with an IC_{50} value of 50µg/ml. Ponnamma *et al*. [76] screened antiradical activity of various solvent extracts of *C. religiosum* leaves by DPPH assay. The extracts were shown to inhibit DPPH radicals in a dose dependent manner. In a recent study, Swathi *et al*. [83] reported the antioxidant activity of flower extract of *C. religiosum* as evaluated by DPPH and ABTS radical scavenging assays and ferric reducing assay. The extract was effective in scavenging DPPH radicals dose dependently with EC_{50} values 2.72 and 1.50µg/ml, respectively.

Insecticidal activity

The flower extract of *C. religiosum* was shown to possess insecticidal activity (in terms of larvicidal activity) in a recent study by Swathi *et al*. [83] The methanolic extract of flower was effective in causing 100% mortality of I, II and III instar larvae of *Aedes* sp. and *Anopheles* sp. at 1mg/ml concentration.

Bioactivities of gum obtained from *C. religiosum*

The gum kondagogu or katira is one of the economically valuable non-timber forest products obtained from the stem bark of the plant is shown to exhibit some biological activities. A brief description of bioactivities of the gum katira is presented below.

Wound healing activity

Girotra and Singh [86] evaluated wound healing activity of katira gum (an exudate) in terms of period of epithelialization and percent wound contraction in Wistar rats. Gels formulated with katira gum alone and combination of katira gum and silver sulphadiazine were tested for wound healing potential. The animals treated with the combination of gum and silver sulphadiazine showed marked wound contraction and the period for epithelialization taken was also significantly lesser.

Effect on α-glucosidase activity

The study carried out by Hongsing *et al*. [85] revealed no inhibitory effect of the kondagogu gum against the activity of the enzyme α-glucosidase.

Effect on tyrosinase activity

Kondagogu gum was screened for its effect on tyrosinase. The gum, at 1% w/v concentration, had a slight inhibitory activity against tyrosinase. At lower concentrations, the gum was shown to exhibit activation of tyrosinase enzyme [85].

Effect on lipase activity

At concentration 0.25%, the kondagogu gum was shown to exert lipase inhibitory activity with an inhibition of 16.2% [85].

Effect on glucose diffusion

Hongsing *et al*. [85] studied the effect of kondagogu gum on the glucose diffusion by using dialysis tubing method, which is an *in vitro* method mimicking the conditions in the lumen of jejunum. At 2% polysaccharide gel concentration, Kondagogu gum revealed 60.8±0.2% of glucose releasing indicating the ability of the gum to retard glucose absorption across the intestinal lumen.

Effect on cholesterol solubility

Hongsing *et al*. [85] determined the effect of kondagogu gum on cholesterol inhibition through its solubility. Kondagogu gum showed a slightly inhibitory effect (16±0.04%).

Immunological evaluation of gum kondagogu

Puskuri *et al*. [87] carried out immunological evaluation of three grades of gum kondagogu (KG-I, KG-II and KG-III) in terms of its ability to elicit delayed type of hypersensitivity. Interestingly, the KG-III grade elicited immunological response in the animals and was related to the presence of impurities. However, grades viz. KG-I and KG-2 were not able to cause delayed type of hypersensitivity.

Bioremediation of toxic metals by *C. religiosum* gum

Sashidhar *et al*. [88] evaluated the efficacy of gum kondagogu to remove uranium (VI) from aqueous, simulated nuclear effluents and studied the adsorption characteristic of the gum towards uranium (VI). The result obtained was promising and maximum adsorption was found at 0.1% concentration of gum and pH 4.0 with the contact time of 60 minutes. Vinod and Sashidhar [22] determined the bioremediation potential of gum kondagogu in terms of its adsorptive removal of toxic metal ions. The gum was able to competitively biosorb toxic metal ions namely cadmium, copper, iron, lead, mercury, nickel and zinc. The study of Vinod *et al*. [89] also revealed the efficacy of gum kondagogu in the bioremediation of nickel and chromium. Vinod *et al*. [90] reported competitive adsorption of heavy metals by gum kondagogu. It was

inferred that the amorphous nature of the gum facilitate metal biosorption.

Conclusions

An elaborated literature survey indicated the potential utilization of *C. religiosum* as a medicinal plant in India and other parts of the world. Various parts of the plants viz. root, leaves, stem bark, flowers and fruits have edible, aesthetic as well as medicinal applications. The plant is reported to display antibacterial, antioxidant, antifungal, insecticidal, wound healing and other pharmacological properties. The gum obtained from the plant is shown to display bioremediation of toxic metals. *C. religiosum* is being listed as threatened species due to overexploitation for the gum and medicinal uses. It is very much necessary that the plant has to be conserved and grown in larger scale due to its therapeutic benefits.

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Conflicts of Interest

None declared

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