

Compressive review on plant profile, phytochemistry and pharmacology of *Cordiaobliqua* willd

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ABSTRACT

Diabetic nephropathy is the leading cause of end-stage renal disease. Hyperglycemia, oxidative stress, and inflammation are some of the mechanisms involved in renal damage. Diabetes mellitus is one of the major health problems in the world, the incidence and associated mortality are increasing. Inadequate regulation of the blood sugar imposes serious consequences for health. Conventional antidiabetic drugs are effective, however, also with unavoidable side effects. On the other hand, medicinal plants may act as an alternative source of antidiabetic agents. Examples of medicinal plants with antidiabetic potential are described, with focuses on preclinical and clinical studies. The beneficial potential of each plant matrix is given by the combined and concerted action of their profile of biologically active compounds. Cordiaobliqua willd plant (Common name-Clammy Cherry) belongs to family Boraginaceae. It is a medium-sized deciduous tree and very vigorous in growth. According to traditional system, it possesses anthelmintic, purgative, diuretic, expectorant, antipyretic, hepatoprotective and analgesic action. The fruits are edible and used as pickle. The gum obtained from mucilage is used for pasting sheets of paper and as matrix forming material in tablet formulations. Phytochemical investigations show the presence of alkaloids, flavonoids, phenolics, tannins and reducing sugar. Evaluation of pharmacological activities confirmed C. obliqua plant as antimicrobial, hypotensive, respiratory stimulant, diuretic and anti-inflammatory drug. A number of traditional activities of this plant still need scientific approval which will increase its medicinal potential.

Keywords: *Cordiaobliqua*, pharmacological activities, phytoconstituents, antidiabetic; diabetic complications; nephropathy; nephroprotective.

Introduction

The Boraginaceae family consists of about 2,700 species, which are distributed in tropical, sub-tropical and warmer regions around the world. It is composed of about 130 genera and six sub families, in which *Cordioideae* is one. It contains the genus *Cordia*, which is comprised of evergreen trees and shrubs. About 300 species of genus *Cordia* have been identified worldwide. There are 13 species of this genus found in India [1]. One of them is *Cordiaobliqua* Willd. It is a medium-sized deciduous tree, found scattered throughout the mid-Himalyas up to elevations of 1,470 meters. It shows vigorous growth. There are two forms of *Cordiaobliqua* Willd., which are found in Himachal Pradesh and the major difference in between these two forms is the size of their fruits, one have smaller fruit than other. The plant having small fruits is commonly found [2]. Its fruit is sweet and possess diuretic, anthelmintic, purgative, expectorant, maturant, useful in dry cough, in the diseases of chest and urethra, in biliousness and chronic fever and pains in the joints. As per Yunani system, it is good in diseases of spleen. According to ayurveda, it is valuable in all diseases of lungs and used as a substitute for *Cordiawallichii*[3].Plants have been used for thousands of years to flavour and conserve food, to treat health disorders and to prevent diseases including epidemics Cordiaobliqua is also called as clammy cherry. It is a flowering plant species in the genus *Cordia*belonging to the family Boraginaceae. It contains about 2700 species of trees and shrubs that are found worldwide, mostly in warmer

Vol 12 Issue 03 2023

ISSN NO: 2230-5807

region. *Cordiaobliqua* is a medium-sized deciduous tree, found scattered throughout the mid-Himalyas up to elevations of 1,470 meters. It shows vigorous growth. Traditionally, Local people use *Cordiaobliqua* in different ways depending on religious belief, culture, ceremony, topography and vegetation, pickles, gums, traditional ceremonies and also havepotential medicinal values. In addition clammy cherry has well documented pharmacological activities.

Kingdom	Plantae
Subkingdom	Tracheobionata
Superdivision	Spermatophyta
Division	Magnoliphyta
Class	Magnoliopsida
Subclass	Asteridae
Order	Lamiales
Family	Boraginaceae
Genus	Cordia
Species	obliqua

Table1: Scientific Classification of	Cordia <i>obliqua</i> [2]
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Clammy cherry is a medium sized deciduous tree, 10.5 meters high, the girth of trunk of a full bearing tree being 75.5 cm, branchlets glabrous, wood soft, light grey, no heartwood [3]. Phytochemical investigation shows the presence of Phenolics, Flavonoids, Pyrrolizidine Alkaloids, Tannins, Triterpenes and Phenylpropanoid derivatives [1]. The raw fruits are used as vegetable and a very good pickle. The mucilaginous substance of the fruit can be used as a gum for pasting sheets of paper and cardboard [2]. A study carried out at Tamilnadu described that fruits of Cordiaobliqua Willd. var. obliqua and var. tomentosa (known as local name Virusu and Kalvirusu respectively) family Boraginaceae, are used as edible by palliyars[4]. Common names are Clammy cherry, Sebesten plum, Lasura, Lessora, Lasora, Bhirala, Bhokar, Chhotalaslasa, Chhotalasora, Gondi, Guslasah and Rasallaetc. Cordiaobliqua leaves are simple, alternate, estipulate; petiole 25-50 mm long, slender, pubescent, grooved above, elliptic, ovate or orbicular; base acute, truncate, subcordate or rounded, apex acute or obtuse; margin entire or crenate, chartaceous, glabrous above, tomentose beneath; nerves 3-5 from the base, palmate, lateral nerves 4-7 pairs, prominent, pinnate, tomentose beneath especially on the axils of nerve; intercostaescalariform, prominent. Flowers are bisexual, complete, shortstalked, actinomorphic, white and glabrous. Fruit is drupe, when ripe yellowish brown, pink or nearly black, shinning but minutely rugose, endocarp rugose, very hard, in a sweetish viscid, almost transparent pulp. Epicarp is thick while mesocarp is mucilaginous and endocarp is hard and stony. Each stone contains two seeds, which are separated by a stony septum. The seeds are mildly sweet in taste. The flowering starts during the last week of April and continues till the end of May. The fruiting season lasts from the beginning of July to the end of August.



Figure 1:Cordiaobliqua [11]

Vol 12 Issue 03 2023 ISSN NO: 2230-5807

5245

Occurrence and distribution

It is widely distributed nearly the whole of the warmer parts of India and Ceylon. Also found in other parts of the world like Philippines, New Guinea, Hainan, Formosa, Java and Tropical Australia [3]. Cordiaobligua matures in about 50 to 60 years by when its girth at the breast height is about 1 to 1.5 m. Its bole (main trunk) is generally straight and cylindrical, attaining a height of nearly 3 to 4 m. The branches spread in all directions by virtue of which its crown can be trained into a beautiful inverted dome like an umbrella. When fully grown up, the total height of the tree comes to nearly 10 to 15 m. In less favorable climates and/or unfavorable environments, however, it has a lesser growth and may attain a somewhat crooked form. In still worse environments it can even remain a stunted shrub. Keeping in view the numerous utilities of the plant it is widely cultivated in the arid zone too. The species is indigenous to China and is widely cultivated in lower plains and tropical regions. Though this plant flourishes well in deep clayey loam and sandy soils, it does still better in areas experiencing nearly 100 to 150 cm of annual rainfall. It is a medium-sized deciduous tree, found scattered throughout the mid-Himalyas up to elevations of 1,470 meters. It shows vigorous growth. There are two forms of CordiaobliquaWilld., which are found in Himachal Pradesh and the major difference in between these two forms is the size of their fruits, one have smaller fruit than other. It is widely distributed nearly the whole of the warmer parts of India and Ceylon. Also found in other parts of the world like Philippines, New Guinea, Hainan, Formosa, Java and Tropical Australia. It is a is a medium sized deciduous tree, 10.5 meters high, the girth of trunk of a full bearing tree being 75.5 cm, branchlets glabrous, wood soft, light grey, no heartwood [6]

Morphology

The bark of *Cordiaobliqua*is grayish brown in color with longitudinal and vertical fissures. The tree can be easily identified from a distance by observing the fissures which are so prominent in the bark of the main bole of a tree approaching maturity. The leaves of *Cordiaobliqua*are broad, ovate, alternate and stalked with the spread being 7 to 15 cm x 5 to 10 cm. In matter of external appearance these are glabrous above and pubescent below. The young leaves tend to be hairy. The fresh foliage is quite useful as fodder for cattle more so during grass famines. These are also used for wrapping biddies and cheroots. *Cordiaobliqua*tree flowers during March-April. The inflorescence, mostly terminal, is, white in color. Individual florets are nearly 5 mm in diameter. At places these are somewhat hairy and white. Being a deciduous plant, the species bears male and female flowers on the same tree. The calyx part of an independent flower is about 8 mm long and glabrous, but not pubescent. It splits irregularly at the opening of its bud into flower. The filaments are hairy. The fruit of *Cordiaobliqua*start appearing during July–August. It is a kind of a <u>drupe</u> (stone fruit), light pale to brown or even pink in color. The appearance tends to darken when ripening sets in. Being full of viscid glue like mucilage, the pulp is somewhat translucent. When fully ripe the pulp becomes quite sweet in taste and is fully enjoyed by children. The pulp in a half ripe fruit can even be used as an alternative to paper glue in office work.

Macroscopic

Leaves are alternate, entire to slightly dentate and glabrous, but may be more or less rough when full grown, variable in shape, from elliptic-lanceolate to broad ovate, often with a rounded or cordate base, basal nerves 3, rarely 5, blade 3-6, petioles 2.5-5 cm long. Flowers are bisexual, complete, short-stalked, actinomorphic, white and glabrous. A fully open flower is 6 mm in average diameter. The inflorescence is terminal or an axillary cyme, which almost resembling to a biparous cyme. It has 14 flowers per cluster. The calyx is cup-shaped. Sepals are about 4mm in length, slightly dentate from top, light green in color and gamoseplous. The corolla has four creamish white color petals which are 6mm in length and polypetlous. The androecium contains two stamens, each having a very small filament and epipetalous. The gynoecium is bifurcated, 4 mm in length and having a globose shaped ovary at the base [2]. Fruit is drupe, 1.3-2.5 cm long, when ripe yellowish brown, pink or nearly black, shinning but minutely rugose, endocarp rugose, very hard, in a sweetish viscid, almost transparent pulp [3]. Epicarp is thick while mesocarp is mucilaginous and endocarp is hard and stony [2]. Stone is found in fruit and it is of 8.5×7 mm in size, 298 microlitres in volume, 375 mg in weight and each stone contains two seeds, which are separated by a stony septum. The seeds are mildly sweet in taste.

A Journal for New Zealand Herpetology

flowering starts during the last week of April and continues till the end of May. The fruiting season lasts from the beginning of July to the end of August [2].

Microscopy

Leaf - The transverse section of leaf shows that mesophyll is differentiated into palisade and spongy parenchyma cells. Epidermis is of single layer, covered externally with prominent cuticle in upper and lower surface. Palisade tissue is consists of one layer of columnar cells, which occupies a little less than half of the width of mesophyll and the spongy mesophyll is covered with cells of irregular size. The midrib is almost circular in out line. Following the epidermis, there is a zone of cortex composed of 1 or 2 layers of collenchyma surrounding the central portion. The vascular bundle is ovoid in shape and circularly arranged, centrally forming pith. Sclerenchyma sheath is found lignified with thick walled cells that cover the vascular bundles and xylem consists of small tracheids and vessels with large lumen [5,6]. Stem - The transverse section of stem shows single layer epidermis with barrel shaped cells. Cortex is made up of 2-4 layers of collenchyma hypodermis and 8-9 layers of parenchymatous cells. Distinct endodermis and pericycle (2-3 layers) was also observed. The secondary phloem is made up of sieve elements and parenchyma. The xylem is consists of tracheids, vessels of large lumen and parenchyma. In between the xylem cells 1-3 layered medullary rays are also found with many starch grains. The pith is consists of scattered several conspicuous sclerenchyma aggregates. In the pith parenchyma, Starch grains are abounded [5]. Root - The outermost part is the cork consists of 10-12 layers of brown cells with thick walled. The phellogen consists of some layers of thin walled colourless cells. The phelloderm having thick walled rectangular cells consists of rhomboidial calcium oxalate crystals and starch grains. This part is followed by a zone consisting of cortical cells having polygonal shape and many starch grains. There were a number of large stone cells scattered in this region. The vascular part consists of prominent medullary rays which are biseriate. Xylem consists of large tracheids and vessels [5].

Chemical composition

The fruit contains moisture 75 g, pectin 4.5 g, total sugars 3.55 g, reducing sugars 3.41 g, non-reducing sugars 0.08 g, protein 2.06 g, ash 2.132 g, phosphorus 0.091 g, potassium 1.066 g, magnesium 0.067 g, calcium 0.062 g and iron 0.005 g (all data is per 100 g of the edible portion). The total soluble solids of the fruit pulp constitute 10.2% [2]. The leaf, stem and root powders with various extracts showed the presence of phenols, alkaloids, tannins and reducing sugar [5]. In a phytochemistry study of *Cordiaobliqua* leaf aqueous extract, a number of chemical tests were performed to find out various chemical constituents and this study confirmed that only steroids are present in leaf aqueous extract and other constituents like saponins, flavonoids, terpenoids, cardiac glycosides and tannins were absent [9]. Chemical examination of *Cordiaobliqua* seeds, resulted in isolation and characterization of various constituents like alpha-amyrin, betulin, octacosanol, lupeol-3-rhamnoside, beta-sitosterol, beta-sitosterol-3-glucoside, hentricontanol, hentricontane, taxifolin-3,5-dirhamnoside and hesperitin-7-rhamnoside [10].

Other isolated chemical compounds from various parts of *Cordiaobliqua* plant are Hesperetin-7-rhamnoside from roots, [11] Lupa-20,29-ene-3-o- β -D-maltoside from roots[12], Lupa-20 (29)-ene-3-O-alpha-L-rhamnopyranoside from roots, [13] natural gums and mucilage from fruits. [14] Constituents like Allantoin- β -sitosterol and some flavonoids were also isolated from stem bark of *Cordia oblique*[15].

Medicinal properties

The fruit is sweet and have effects like slightly cooling, anthelmintic, purgative, diuretic, expectorant, and useful in diseases of the chest, urethra, dry cough, biliousness and chronic fever. It lessens thirst and the scalding of urine, removes pains in the joints, bad humours, burning of the throat and also good in diseases of the spleen (As per Yunani system). The juice of the bark is given in gripes, along with coconut oil. The

bark and unripe fruit are used as a mild tonic. The kernels are a good remedy in treatment of ringworm. The leaves are useful as an external application to treat ulcers and headache. The Santals use a powder of the bark for external application in prurigo. The Javanese use the bark in treatment of fevers [3]. Local people use Cordiaobliqua in different ways depending on religious belief, culture, ceremony, topography and vegetation. Cordiaobliqua is used for vegetables, pickles, gums, medicines for traditional ceremonies. The fruit is sweet and have effects like slightly cooling, anthelmintic, purgative, diuretic, expectorant, and useful in diseases of



Vol 12 Issue 03 2023 ISSN NO: 2230-5807

the chest, urethra, dry cough and also used as a cough suppressant, astringent, analgesic, anti-inflammatory[7], antimalarial, febrifuge, hepatoprotective, antimicrobial, respiratory stimulant, appetite suppressants and to treat urinary tract infections and leprosy. biliousness and chronic fever. It lessens thirst and the scalding of urine, removes pains in the joints, bad humours, burning of the throat and also good in diseases of the spleen (As per Yunani system). According to ayurveda, it is valuable in all diseases of lungs. The juice of the bark is given in gripes, along with coconut oil. The bark and unripe fruit are used as a mild tonic. The kernels are a good remedy in treatment of ringworm. The leaves are useful as an external application to treat ulcers and headache. The Santals use a powder of the bark for external application in prurigo. The Javanese use the bark in treatment of fevers. A good pickle is prepared from its raw fruits and these are also used as vegetable [8]. The fruit mucilage is used as a gum for pasting cardboard and paper sheets.

Utilization

A good pickle is prepared from its raw fruits and these are also used as vegetable. The fruit mucilage is used as a gum for pasting cardboard and paper sheets $[\underline{2}]$.

Biological activities

Traditionally a number of activities are reported from various parts of this plant. A few of them are scientifically proven. Some of the reported studies are following:

Anti-inflammatory activity

Cordia genus is well known in herbal medicine for its anti-inflammatory activity. It is taken internally and as well as applied topically for various types of inflammatory conditions.

A study was carried out on various isolated constituents from *Cordiaobliqua* seeds to find out antiinflammatory effect and it showed potent anti-inflammatory action of these seed constituents [9].

Hypotensive and respiratory stimulation activity

A comparative study was carried out to find hypotensive and respiratory stimulant effects of both ripe and unripe fruit mucilage of *Cordiaobliqua* and *Cordiamyxa*. The experimental animals were used guinea pigs and rabbits. The *Cordiaobliqua* fruit mucilage both ripe and unripe, decreased rabbit blood pressure and also showed stimulation of respiratory rate. But hypotensive effect of *Cordiamyxa* fruit mucilage was 12.37 times more potent than the effect of *Cordiaobliqua* fruit mucilage. Although the respiratory stimulant effect of *Cordiaobliqua* fruit mucilage is 7 times more than its own hypotensive effect and *Cordiamyxa* fruit mucilage showed no effect on respiratory stimulation [16].

The comparative pharmacological activity of Cordia fruit mucilage at daerent stages of maturity was investigated to determine the stage at which active substances were present in high proportions. The fruit mucilage of ripe and unripe Cordiamyxa (RCm and URCm) decreased rabbit arterial blood pressure in a dose dependent manner without affecting the respiratory rate. Mucilage From both ripe and unripe Cordiaobliqua (RCo and URCo) decreased rabbit blood pressure and stimulated the respiratory rate. RCm is 12.37-fold more potent as a hypotensive agent than RCo. However the respiratory stimulant effect of RCo is 7-fold more than its own hypotensive effect. Investigation of the mode of action revealed that the hypotensive effect was more likely due to activation of parasympathetic ganglia and dilatation of peripheral blood vessels, whereas the respiratory stimulant effect on rabbit and nicotine ganglionic stimulant effect on the isolated guineapig ileum. This is the first report on the comparative pharmacological activity of Cordia mucilage at different stages of fruit maturity. This information may allow the use of the ripe fruit mucilage of Cordiaobliqua as a respiratory stimulant and that of Cordiamyxa as a hypotensive agent [10].

This study suggests that methanolic fraction from seeds and leaves of Cordiaobliqua possesses significant antimicrobial activity at very low concentration (20ug/disc) on oral pathogenic strains of Gram-positive bacteria such as Streptococcus mitis can cause infective endocarditis[11], Streptococcus mutans is a significant contributor to tooth decay and Streptococcus sanguinis is found in dental plaque, Gram-negative bacteria such as Porphyromonasgingivalis is found in oral cavity, where it is implicated in periodontal disease[12]. Tannerella forsythia is a member of the red complex of periodontal pathogens[13]and

5247

Vol 12 Issue 03 2023 ISSN NO: 2230-5807

Actinobacillusactinomycetemcomitans causes periodontitis and fungal strain like Candida albicans is an opportunistic human fungal pathogen that causes candidiasis[14]. The activity of methanol extract was compared with standard antibiotics Gentamycin, Chloramphenicol, Ciprofloxacin, Erythromycin and Fluconazole. The methanolic extract form leaves and seeds of plant Cordiaobliqua as a potential antimicrobial agent in prevention of oral infections and diseases [15].

The study explored the antimicrobial activity of methanol, ethanol and distilled water extracts of six Indian medicinal plant species growing in different kind of habitats. These plant species showed different range of antimicrobial activity against test microorganism (Streptococcus mutans, Staphylococcus aureus, Candida albicans, Lactobacillus acidophilus and Streptococcus gordonii). Out of these six plant species Dahlia could serve as broad spectrum antibiotic whereas plants such as Bombaxceiba and Cordiaobliqua could serve as narrow spectrum antibiotics[16]. Diuretic activity A study was carried out on 266 identified plants from 222 plant families for various biological activities. In this study, Cordiaobliqua var. wallichii plant of family Boraginaceae, was also studied. The fruits were used to study various activities like antiprotozoal, antiviral, CNS effects, antifertility, effects on respiration, diuretic activity and other. They reported diuretic activity with LD50 > 1000 mg/kg body weight of mice [17].

Antimicrobial activity

The Cordiaobliqua seeds and leaves extracts were evaluated for antimicrobial activity using zone inhibition assay against some oral pathogenic strains of Gram-positive bacteria (Streptococcus mitis, S. mutans and S. gingivalis, Bacillus (Pseudomonas sanguis), Gram-negative bacteria forsythus and Aggregatibacteractinomycetemcomitans) and fungal strain (Candida albicans). The activity of methanol extract was compared with standard antibiotics Gentamycin, Chloramphenicol, Ciprofloxacin, Erythromycin and Fluconazole. The activity of methanol extract was found comparable with standards and it's use was suggested as potent antimicrobial agent [17].

Diuretic activity

A study was carried out on 266 identified plants from 222 plant families for various biological activities. In this study, Cordiaobliqua var. wallichii plant of family Boraginaceae, was also studied. It was collected from Calcutta, West Bengal in the month of April. The fruits were used to study various activities like antiprotozoal, antiviral, CNS effects, antifertility, effects on respiration, diuretic activity and other. They reported diuretic activity with $LD_{50} > 1000 mg/kg$ body weight of mice [18].

Wound healing activity

A study was carried out to evaluate wound healing potential of the aqueous and methanolic extract of the seeds and leaves of Cordiaobliuqa. Three models (incision, excision and dead space wound) were used to evaluate healing activity of the extracts. Wounds are created to the rats (albino rats), in excision model both the extracts were applied till epithelialization process completed. On other hand in incision and dead space wound model extracts were applied daily (topically) till 10th day after wound formation. While standard group was treated with povidone iodine ointment topically. Observation was carried out for percentage of wound contraction, breaking strength, epithelialization period, hydroxyproline content and granulation weight.

Other activity

As sustained release matrix forming material

A study was carried out to evaluate the efficacy of gum obtained from Cordiaobliqua Willd. Plant as a novel sustained release matrix forming material in tablet formulations using Diclofenac. The drug Diclofenac was selected because of its short half life which needs multiple dosing regimens of immediate release formulations and so requires sustained release formulation for patient compliance. The Cordia gum was obtained from fresh and raw fruits mucilage, which was expressed from fruits by tincture press. Matrix tablets were prepared by wet granulation technique using non aqueous solvents. The effect of gum in various concentrations (1, 2, 5) and 10% w/w with respect to total tablet weight) on in-vitro drug release profile was examined and it was compared with commercial sustained release Diclofenac formulation (Voveran SR-100). The results showed that the formulation containing 2% w/w gum, gave a similar dissolution profile as to the marketed product and

Vol 12 Issue 03 2023 ISSN NO: 2230-5807

it obeys first order kinetics. So this study concludes the efficacy of *Cordiaobliqua* gum as sustained release matrix forming material [19].

Conclusion

Cordiaobliqua Willdis a well known and commonly found tree. Traditionally it has a number of medicinal activities and its fruits are utilized in form of pickle and vegetable all over India. Although its distribution is very common, yet very less research has been done on this plant parts as compared to other Cordia species. Many of its traditional uses are still scientifically unproved. Beside this, very less data is available showing the morphology and histology of this plant. So it is required to explore the knowledge about its identification, investigation of its phytochemicals and biological evaluation of various traditionally mentioned activities. Plants are the "backbone" of traditional medicine and play a key role in world health. Medicinal herbs or plants have been known to be an important potential source of therapeutics or curative aids. The use of medicinal plants has attained a commanding role in health system all over the world. This involves the use of medicinal plants not only for the treatment of diseases but also as potential material for maintaining good health and conditions. Some people value these plants due to the ancient belief which says plants are created to supply man with food, medical treatment, and other effects. There are nearly 2000 ethnic groups in the world, and almost every group has its own traditional medical knowledge and experiences. On basis of our study, Traditionally Cordiaobliqua have been used for various purposes such as religious belief, culture, ceremony, topography, vegetation, vegetables, pickles, gums and medicines and also it has well documented pharmacological activities. This review is an effort to compile all available information and research data on this plant.

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Vol 12 Issue 03 2023 ISSN NO: 2230-5807

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