



Contents lists available at ScienceDirect

Asian Pacific Journal of Tropical Biomedicine

journal homepage: www.elsevier.com/locate/apjtb



Document heading doi:10.1016/S2221-1691(13)60194-X © 2013 by the Asian Pacific Journal of Tropical Biomedicine. All rights reserved.

Plant profile, phytochemistry and pharmacology of *Cordia dichotoma* (Indian cherry): A review

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PEER REVIEW

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Comments

Authors did detailed collection regarding the topic including graphics, pharmacological uses of several parts of the plant and phytochemicals potentially evaluated for the management of range of disease.

Details on Page 1015

ABSTRACT

More than half of the world's population relies on the traditional medicine and major role of the traditional medicine including the use of plant extract and their active constituents. Among them, *Cordia dichotoma* Forst., a small to moderate size plant of family Boraginaceae, commonly called bhokar, lasura, gonda, Indian cherry and shlesmataka. Plant parts such as leaves, fruit, bark and seed have been reported for possessing antidiabetic, antiulcer, anti-inflammatory, immune-modulator and analgesic activity. Screening of fruit, leaves and seed shows the presence of pyrrolizidine alkaloids, coumarins, flavonoids, saponins, terpenes and sterols. Present review focuses on details of geographical distribution, physicochemical parameters, phytoconstituents and pharmacological properties of *Cordia dichotoma* reported so far.

KEYWORDS

Cordia dichotoma, Cytotoxic, β -sitosterol, Indian cherry, Diabetes, Pharmacology

1. Introduction

Plant derived medicines are considered to be first line of defense in maintaining health and combating diseases and even today plant source is principal source of new drug of therapeutic property[1]. Approximately 72000 plant species were estimated for having medicinal properties of which, India recognizes more than 3000 plant species having medicinal values[2]. Ayurveda is "science of life", pointed out concept of positive health means metabolically well-balanced human beings. Foremost indigenous systems listed medicinal plants such as Siddha (600), Ayurveda (700) and Amchi (600), Unani (700), allopathy which 30 plant species for ailments[1]. *Cordia dichotoma* (*C. dichotoma*) is one of the traditional medicinally important deciduous plants available all over India. The fruit has been reported to be rich in polysaccharide. Ripe fruit of *C. dichotoma* produces a jelly-like, sticky mass. Unani system of drug medicine uses

plant as antibacterial, antiviral and antitussive. Joshandah, polyherbal formulations, are extensively used by the masses in India for the treatment of common cold, catarrh, cough, respiratory distress, fevers of which *C. dichotoma* is chief ingredient[3,4]. From the ancient time, leaves and stem bark are used in the treatment of dyspepsia, fever, diarrhea, leprosy, gonorrhoea and burning sensation. Leaf of plant traditionally shows the therapeutic uses and actions such as anthelmintic, astringent, diuretic, demulcent, purgative, expectorant, tonic, ulcer and cough[5-9].

1.1. Geographical distribution

C. dichotoma (Table 1) is commonly present in tropical and subtropical regions. It grows in the sub-Himalayan tract and outer ranges, ascending up to about 1500 m elevation. It is found in divers of forests ranging from the dry deciduous forests of Rajasthan to the moist deciduous forests of

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Article history:

Received 30 Aug 2013

Received in revised form 4 Sep, 2nd revised form 10 Sep, 3rd revised form 15 Sep 2013

Accepted 27 Oct 2013

Available online 28 Dec 2013

Table 1Scientific classification, vernacular names and local names of the *C. dichotoma*[8,10,11].

Scientific classification	Vernacular name	Local names
Kingdom: Plantae	Malaysia: Sekendai, Sekendal, Petekat	Bangali: Buhal, Bahubara
Division: Magnoliophyta	English: Soap berry, Sebestan plum, Fragrant manjack	English: Sebesten, Clammy Cherry, Indian cherry
Class: Dicotyledons	India: Leshora, Gonda, Lasora	Gujarati: Vadgundo, Gunda
Subclass: Astaridae	Javanese: Kendal	Hindi: Lasura, Bhokar, Borla
Order: Lamiales	Sumatran: Nunang	Javanese: Kendal
Family: Boraginaceae	Thailand: Paw man	Lao: Man, Sino-Tibetan, Man khok
Genus: Cordia		Malay: Petekat, Sekendai
Fragrant: Manjack		Tamil: Kalvirusu, Vidi, Naruli
Species: <i>C. dichotoma</i> Forst.		Nepali: Bohori, Kalobohori
		Thai: Mandong, Manma, Phakmong
		Sanskrit: Shelu, Bahuvarka, Shleshmatak

Western Ghats in India and tidal forests in Myanmar. In Maharashtra, it grows in moist monsoon forest^[10]. It does not grow gregariously, but is found growing singly in moist shady ravines and valleys^[11]. The species is widespread in the Philippines and found in thickets and secondary forests at low and medium altitudes. It also distributed Southern China and Formosa and throughout other like Peninsular Malaysia to tropical Australia and Polynesia. The species is propagated by seeds^[12].

1.2. Morphology of *C. dichotoma*

Cordia dichotoma is small to medium-size deciduous tree with a short crooked trunk, short bole and spreading crown (Figure 1). Leaves are simple, entire and slightly dentate, elliptical-lanceolate to broad ovate with a round and cordate base. The stem bark is grayish brown smooth or longitudinally wrinkled^[10]. Flowers are short stalked, bisexual and white to pinkish in colour and appear in loose corymbose cymes. Fruits are edible with sticky flesh mass. It

is a yellow or pinkish-yellow shining globose or ovoid drupe seated in a saucer-like enlarged calyx. It turns black on ripening and the pulp gets viscid^[11].

1.3. Nutritional information

The whole plant of *C. dichotoma* is edible and is used as food. Immature fruits are pickled and are also used as vegetable^[10]. Mixture of flower and curd applied two times in a day used to protect body against heavy sun heat waves^[13]. The rural people of coastal areas of Orissa eat the ripe fruits raw^[14]. The seed kernels of *C. dichotoma* contain high quantity of fatty oils and proteins which has potential as cattle feed^[15]. The polysaccharide gum (97%) obtained from the plant used for various pharmaceutical purposes. Chromium present in the fruit has therapeutic value in diabetes. A fruit also contains some anti-nutritional factors such as phytic acid (355 mg), phytate phosphorus (100 mg) and oxalic acid (250 mg) per 100 g (Table 2)^[16]. New natural cellulose fabrics were identified from the branches of the *C. dichotoma*^[17].

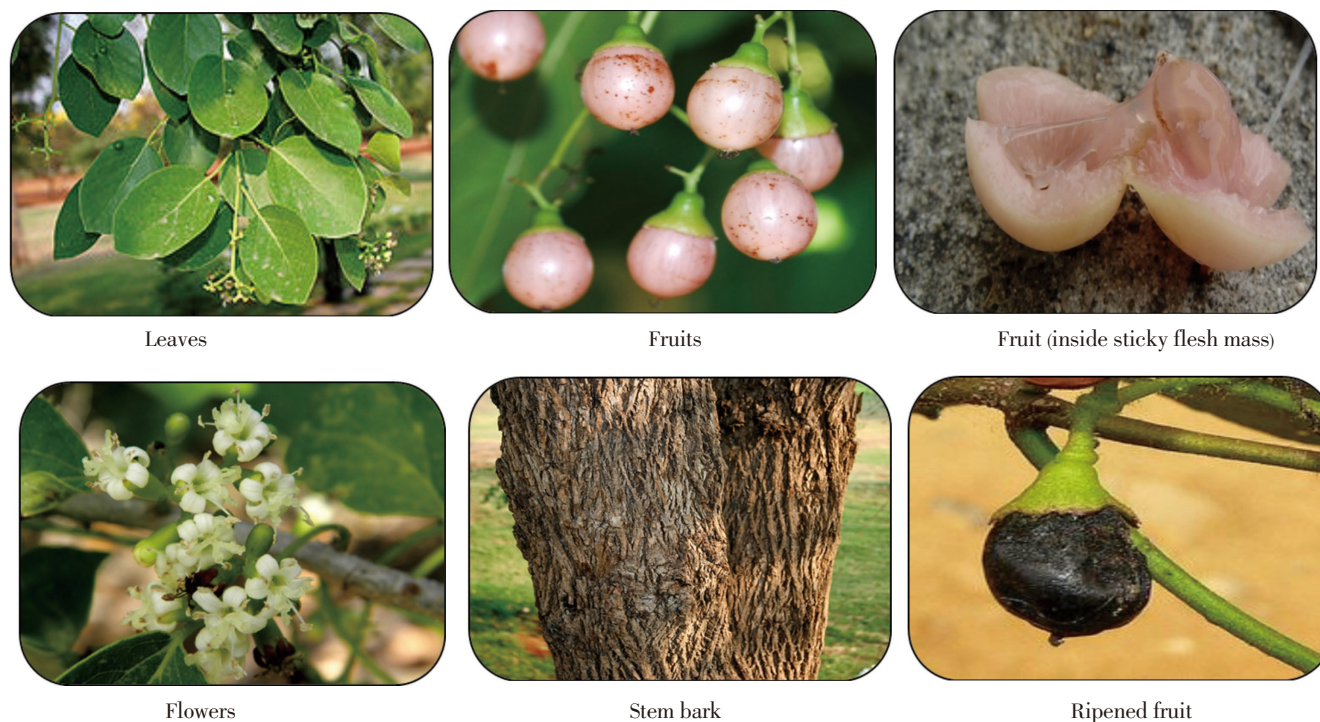


Figure 1. Parts of *C. dichotoma* plant.

Table 2Nutritional value of leaves, seed kernels and fruits of *C. dichotoma*.

Plant part	Nutritional value
Leaves	12%–15% crude protein
	16%–27% crude fibers
	42%–53% nitrogen free extract
	2%–3% ether extract
	13%– 17% total ash
	2%–4% total calcium
Seed kernels	0.3% phosphorus
	32 g water: per 100 g
	46% fatty oils
Fruits	31% proteins
	70% pulp which contains per 100 g
	6 g water
	35 g proteins
	37 g fats
	18 g carbohydrate
	Ca (55 mg), P (275 mg), Zn (2 mg), Fe (6 mg), Mn (2 mg) Cr (0.2 mg), Cu (1.6 mg/100 gm)

2. Biological investigation

Numerous *Cordia* species were mentioned in traditional literatures of Ayurveda and Materia Medicas for the treatment of various disease and disorder conditions. Moreover, the plant species has been reported for various pharmacological activities and are listed in Table 3^[18–22].

3. Phytochemicals

Several chemicals have been identified from seeds of *C. dichotoma*. The seed contains α -amyryns, betulin, octacosanol, lupeol-3rhamnoside, β -sitosterol, β -sitosterol-3glucoside, hentricontanol, hentricontane, taxifolin-3-5-dirhamnoside, hesperitin-7-rhamnoside and fatty acids such as palmitic acid, stearic acid, arachidic acid, behenic acid, oleic acid and linoleic acid. Four flavonoid glycosides (robinin, rutin, rutoside, datiscoside and hesperidin), a flavonoid aglycone (dihydrorobinetin) and 2 phenolic

Table 3Biological investigations of plants from *Cordia* species.

<i>Cordia</i> species	Part used	Reported activity
<i>Cordia alliodora</i> (Ruiz & Pav.) Oken.	Root bark	Antifungal, Larvicidal
<i>Cordia corymbosa</i> Willd. Ex Roem. & Schult.	Fruits	Antimicrobial, Cytotoxic, Tumour inhibition
<i>Cordia curassavica</i> (Jacq.) Roem. & Schult.	Roots	Antifungal, Larvicidal, Antibacterial
<i>Cordia cylindrostachya</i> Roem. & schult	Fruits	Antibacterial, Anti-inflammatory
	Fruits	Anthelmintic
<i>Cordia dichotoma</i> G. Forst.	Fruits	Wound healing
	Leaves	Antifertility, Juvenomimetic Biliary obstruction, Nutritional food
<i>Cordia fragrantissima</i> Kurz.	Wood	Leishmanicidal
<i>Cordia francisci</i> Ten.	Leaves	Analgesic, Anti-inflammatory, Antiarthritic
	Leaves	Rheumatism, Painful menstruation, Gastric ulcer
<i>Cordia globosa</i> (Jacq.) Kunth.	Root	Cytotoxic
	Leaves	Vasodilator, Spasmolytic
<i>Cordia goetzei</i> Gürke.	Stem bark	Antifungal
<i>Cordia latifolia</i> Roxb.	Ripen fruits	Anti-ulcer, Antihistaminic
<i>Cordia linnaei</i> Stearn.	Roots	Antifungal, Larvicidal
<i>Cordia martinicensis</i> (Jacq.) Roem. & Schult.	Leaves	Cytotoxic, Hepatotoxic, Anti-inflammatory, Analgesic
<i>Cordia monosperma</i> (Jacq.) Roem. & Schult.	Aerial parts	Antimicrobial
<i>Cordia multispicata</i> Cham.	Leaves	Antiandrogenic
	Leaves	Anti-inflammatory, Analgesic, Anti-arthritis
<i>Cordia myxa</i> L.	Fruits	Cytotoxic, Chest and urinary infections, Anthelminthic, Diuretic, Astringent, Demulcent, Expectorant
	Fruits, Leaves	Astringent, Anthelmintic, Diuretic, Demulcent, Antimicrobial, Alcoholic liver cirrhosis
	Bark	Antifertility, Antihistaminic, Antitumour
<i>Cordia oblique</i> wild.	Seeds	Anti-inflammatory
<i>Cordia perrottettii</i> DC.	Fruits	Antioxidant
<i>Cordia plauhiensis</i> Fresen.		Larvicidal
<i>Cordia rufescens</i>		Abortive, Anti-inflammatory, Dysmenorrheal treatment
<i>Cordia salicifolia</i> Cham.	Whole plant	Antiviral, Excitatory & negative ionotropic effect
<i>Cordia serratifolia</i> Kunth.	Leaves	Analgesic, Anti-inflammatory, Antiarthritic
<i>Cordia sinensis</i>	Bark	Stomach disorders, Chest pains
<i>Cordia spinescens</i> L.	Leaves	Antiviral, Anti-HIV
<i>Cordia subcordata</i>	Nut/seed	Famine treatment
<i>Cordia ulmifolia</i> Juss. Ex Dum. Cours.	Leaves	Cytotoxic, Hepatotoxic, Anti-inflammatory, Analgesic
	Leaves	Anti-inflammatory, Analgesic, Fetus toxicity
<i>Cordia verbenacea</i> DC.	Aerial parts	Antimicrobial
	Leaves	Antiserum action, Potentiation

derivatives (chlorogenic acid and caffeic acid) were isolated from seeds. The significant anti-inflammatory activity of seeds is because of α -amyrins and taxifolin-3-5-dirhamnoside (71.4%, 67.8% respectively). The seeds also contain fatty acids and flavonoids (Table 4)[10,23].

The bark is medicinal and contains several chemicals including allantoin, β -sitosterol and 3',5-dihydroxy-4'-methoxy flavanone-7-O- α -L-rhamnopyranoside[10,14]. Fruits and leaves showed presence of pyrrolizidine alkaloids, coumarins, flavonoids, saponins, terpenes and sterols[10]. Fruit has been identified for arabinoglucan, D-glucose (67.6%) and L-arabinose (13.2%)[3,20]. Leaves also contain quercetin and quercitrin (Table 4)[20].

4. Pharmacological properties

4.1. Normoglycemic and diabetes

The effect of the aqueous extract of *C. dichotoma* on alloxan induced and normoglycemic Wistar rats has been investigated. Three doses of the extract (250 mg/kg; 500 mg/kg and 1000 mg/kg) were considered for study by oral route. The 500 mg/kg extract of *C. dichotoma* did not show any significant change in the blood glucose levels in normoglycemic rats. Same effect was also observed at 250 mg/kg dose in alloxan induced diabetic wister rats, when compared to untreated control. The significant ($P < 0.5$) decrease in blood glucose levels after 4, 8 and 24 h was observed at 500 and 1000 mg/kg dose of extract. In normoglycemic rats, the dose of 1000 mg/kg of the extract significantly ($P < 0.05$) reduces the blood glucose levels at 8 and 24 h. Overall study shows that the doses of extract has shown both significant ($P < 0.05$) hypoglycemic and antihyperglycemic effects in wister rats[14,24].

4.2. Wound healing activity

The wound healing activity of fruits of *C. dichotoma* was screened using three different models, viz. excision wound, incision wound and dead space wound in Wistar rats. The fruits of *C. dichotoma* were extracted using ethanol by soxhlation and further Petroleum ether, solvent ether, ethyl acetate, butanol and butanone fractions were prepared from the alcoholic extract. The ethanol extract, ethyl acetate and butanol fraction showed positive taste for flavonoids. The doses of fractions determined by acute toxicity study using Up and Down method and was found to be 300 mg/kg. The results were analysed by student *t*-test at a significance level of $P < 0.001$. The earlier epithelization of wound and significant increase in tensile strength as compared to control was found in rats treated with fractions of ethanol extract. Results reveals that fruit extracts of *C. dichotoma* has potent wound healing property[25,26].

4.3. Antimicrobial and antifungal activity

Antibacterial and antifungal potentials of *C. dichotoma* bark investigated. Antibacterial activity of ethanol and the butanolic extracts of the bark were carried out against two Gram negative bacteria *Escherichia coli* and *Pseudomonas aeruginosa* and two Gram positive bacteria *Streptococcus pyogenes* and *Staphylococcus aureus*. The antifungal activity of the extract was carried out against that *Aspergillus niger*, *Aspergillus clavatus* and *Candida albicans*, the pathogenic fungi. Zone of inhibition of extracts was compared with that of different standards like ampicilline, ciprofloxacin, norfloxacin and chloramphenicol for antibacterial activity and nystatin and griseofulvin for antifungal activity. The extract showed remarkable inhibition of zone for bacterial and fungal growth and the result obtained were comparable with that of standards drugs against the tested organisms[6,23].

4.4. Analgesic, antibacterial and cytotoxic activity

Crude ethanolic extract of *C. dichotoma* was evaluated for the analgesic, antibacterial and cytotoxic activity. The extract produced significant writhing inhibition in acetic acid induced writhing in mice at the oral dose of 500 mg/kg body weight respectively ($P < 0.001$) which was compared to the standard drug diclofenac sodium at the dose of 25 mg/kg of body weight. When tested for antibacterial effects by disc diffusion method, it showed dominant zone of inhibition of against both gram negative and gram positive bacteria such as *Streptococcus aureus*, *Streptococcus pyogenes*, *Vibrio cholerae*, *Streptococcus epidermis*, Hafnia and *Escherichia coli* which is comparable with kanamycin (30 μ g/mL). Moreover, when tested for toxicity using brine shrimp lethality bioassay, the extract showed potent activity against the brine shrimp *artemia salina* (LC₅₀: 20 μ g/mL and LC₉₀: 180 μ g/mL). The overall result represents significant analgesic, antibacterial and cytotoxic activities of the extract[27].

4.5. Degenerative disorder

Free radical induced stress is common line etiology of various degenerative disorders. Singh *et al.* correlated free radical scavenging potential of methanolic extract of seeds and leaves of *C. dichotoma* for the management of degenerative disorders such as ageing and age associated oxidative stress related disorders. Activity was evaluated by *in-vitro* models viz. DPPH and hydrogen peroxide model. These models showed positive antioxidant activity in a concentration dependent manner and highest concentration exhibits highest (100 μ g/mL) antioxidant activity. This activity was more pronounced in methanolic extract of leaves as compared to seeds[28].

Table 4Structures of some phytochemicals from *C. dichotoma* [3,10,14,20,23].

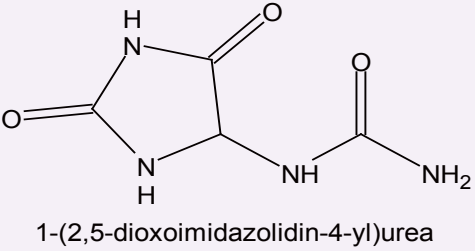
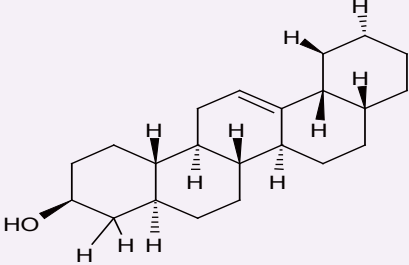
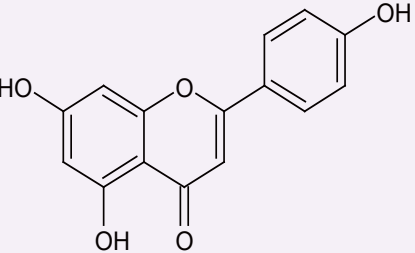
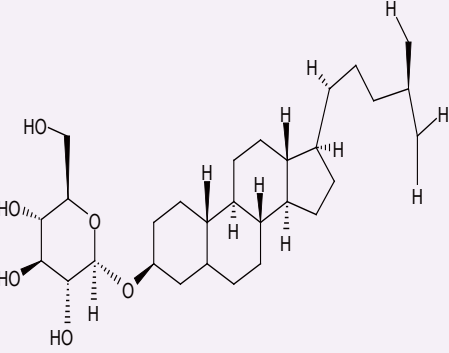
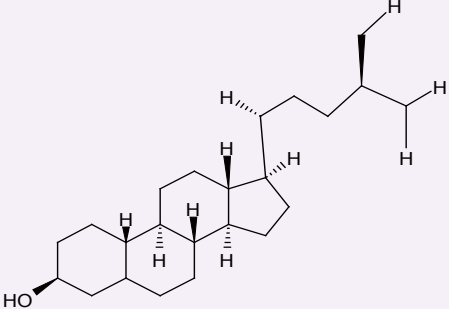
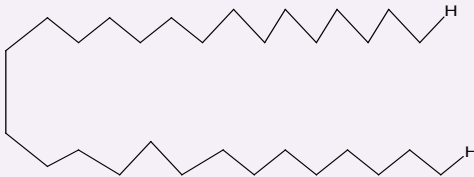
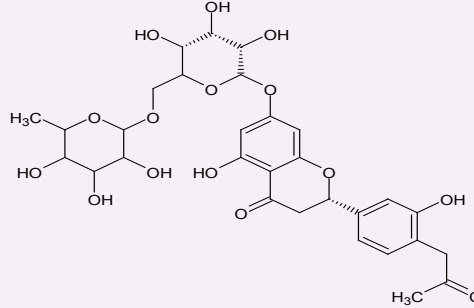
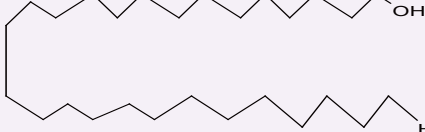
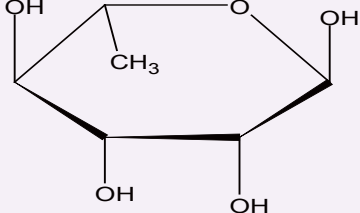
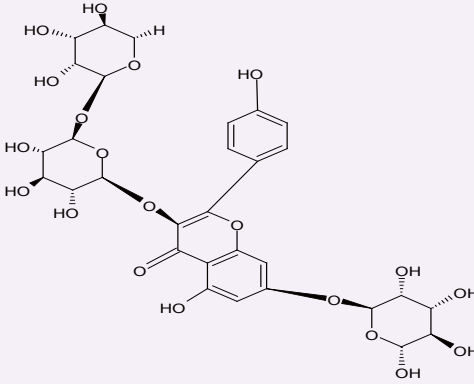
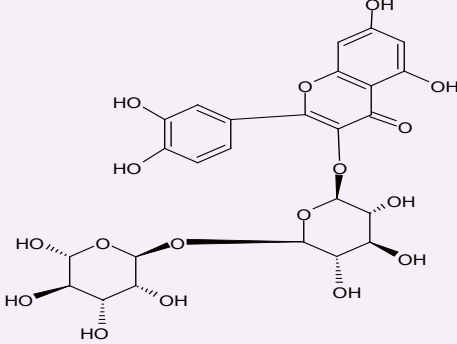
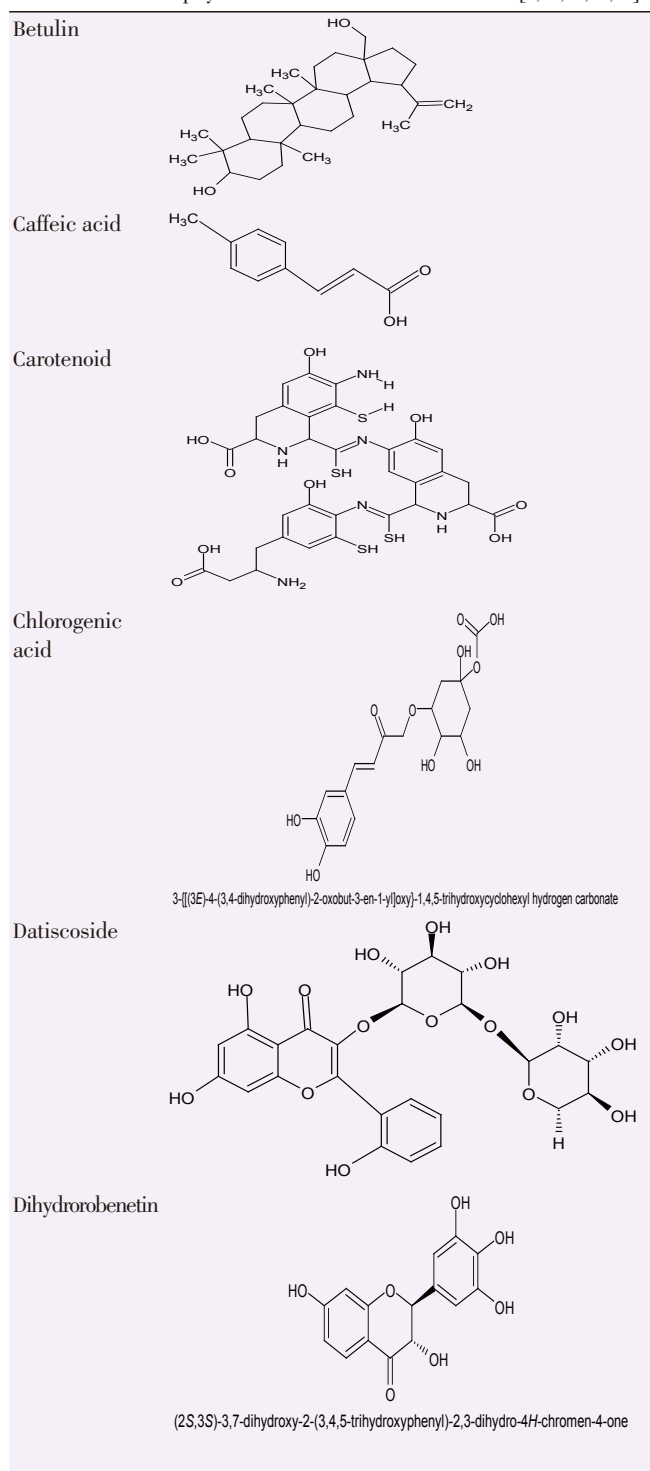
Name of phytochemical	Structure
Allantoic acid	 1-(2,5-dioxoimidazolidin-4-yl)urea
α -amyrin	
Apigenin	
β -sitosterol glycoside	
β -sitosterol	
Hentricontanol	
Hesperidine	
Octasanol	
Lupeol	
Robonine	
Rutin	

Table 4, continuedStructures of some phytochemicals from *C. dichotoma* [3,10,14,20,23].

4.6. Antidiabetic activity

The fruit pulp of the *C. dichotoma* was screened for antidiabetic activity on the healthy male Wistar albino rats. The acute toxicity was determined in albino rats (170–200 g) by adopting fixed dose method of Committee for the Purpose of Control and Supervision of Experiments on Animals (OECD guidelines No. 420). Animals were administered with

increasing dose of methanolic extract (5, 50, 300, 2000 and 5000 mg/kg body weight) to determine changes in parameters for assessing toxicity. No mortality was observed upto dose as high as 2 g/kg body weight. So 200 mg/kg body weight dose was considered for further experiment. Alloxan induced diabetic studies were randomly assigned into four groups each having six rats. Significant reduction in blood glucose level and the rate of body weight loss was observed in glucose loaded rats and alloxan induced diabetic rats when treated with methanol extract of fruits pulp, which reveals antidiabetic potential of fruits pulp of *C. dichotoma* and this can be useful for the management of diabetes mellitus^[29].

4.7. Anthelmintic activity

The aqueous and ethanolic extracts of fruit of *C. dichotoma* showed significant anthelmintic activity. Study was carried out using *Eudrilus euginae* earth worms. It showed paralysis and death of worms at concentration 10–100 mg/mL in dose dependant manner. Aqueous extract of the *C. dichotoma* fruit showed potent anthelmintic activity than the ethanolic extract. Piperazine citrates (10 mg/mL) and distilled water were used as standard drug and control respectively. The result showed fruits of *C. dichotoma* possessed potential anthelmintic activity^[30].

4.8. Ulcerative colitis

The dried bark of *C. dichotoma* was powdered and methanolic extract was obtained using Soxhlet extraction. The obtained hydroalcoholic extract was fractionated into *n*-hexane, ethyl acetate and methanol fractions. Apigenin is isolated by column chromatography from methanol fraction of crude methanol extract of *C. dichotoma* bark and structure of apigenin is established by various spectroscopic studies. Ulcerative colitis was induced and confirmed by observing classical lesions of ulcer *i.e.* the destruction of epithelia, hemorrhage, infiltration of neutrophils and macrophage. Groups treated with fractions and standard (prednisolone 5 mg/kg, *i.p.*) showed significant healing. Groups treated with ethyl acetate fraction and ethyl acetate/methanol (1:1) fraction showed mild scores of pathological changes but infiltration of neutrophils and presence of edema was observed where as the groups treated with methanol and apigenin (5 mg/kg, *p.o.*) showed significant healing and reduction in inflammatory enzymes. Study concluded that apigenin from *C. dichotoma* bark may be effectively used for the management of ulcerative colitis^[31].

4.9. Gastroprotective and antiulcer effect

The gastroprotective effect of some extracts of the ripe fresh fruit of *C. dichotoma* were investigated in aspirin induced gastric ulcer model and pylorus ligation model in rats. The methanolic and water extract was obtained from fresh fruit by maceration. A safe oral dose was calculated using OECD 423 guidelines and it falls in GSH 5 category. Effective reduction in ulcer index is observed in water extract treated Wistar rats as compared to methanolic extract

and results were compared with standard ranitidine (50 mg/kg). The water extract showed significant antiulcer effect in aspirin induced gastric ulcer model ($P \leq 0.001$) as well as in pylorus ligation model^[32].

4.10. Anti-inflammatory activity

Transdermal films were prepared using natural polymer (fruit gum) of *C. dichotoma* with different percentage of plasticizer (glycerin 0.10, 0.20 and 0.25% w/v), preservatives (methyl paraben 0.1% w/v) and drug neomycin (0.2% w/v). The films were casted on glass plates under dried controlled condition. These films were evaluated by various parameters like thickness, tensile strength, water uptake, folding endurance, and skin irritation test. The films were screened for the anti-inflammatory activity using carrageenan-induced rat paw edema model. The data was analyzed using student *t*-test and level of significance was set at $P < 0.001$. The results were compared with standard drug, diclofenac sodium. The percentage of inhibition of edema was considered as a mark of anti-inflammatory potential and it was found to be highest in 0.20% (w/v) glycerin treated animals which indicate significant anti-inflammatory activity of cordial dichotoma^[33].

4.11. Behavioral changes and hypoperfusion effect

Effect of *C. dichotoma* long-term cerebral hypoperfusion in rats was investigated. Transient cerebral ischemia was induced under ketamine anesthesia by blocking bilateral common carotid arteries for chronic hypoperfusion studies, after separating them from nerves, the carotid arteries were doubly ligated with 3-0 silk and cut in between. Animals were returned to home cage after suturing the skin for behavioral and histopathological studies were done for chronic hypoperfusion studies. One way ANOVA followed by *post hoc* Tukey test was used. The Long-term cerebral hypoperfusion in rats caused a propensity towards anxiety and listlessness (open field paradigm and elevated plus maze test) accompanied by deficits in learning and memory (Morris' water maze testing) and tendency towards depression (Porsolts swim test). Additionally, histopathological observations in forebrain revealed changes like gliosis, astrocytosis, cellular edema and inflammatory changes. The *C. dichotoma* treatment (250 mg/kg *p.o.* for 28 d) alleviated these behavioral, cognitive and histopathological changes. The study suggests that *C. dichotoma* may be useful in cerebrovascular insufficiency conditions^[34].

4.12. Antiimplantation activity

Antiimplantation activity of methanolic extract of *C. dichotoma* bark was evaluated by observing implantation site at various doses. The coarse powder material was defatted using petroleum ether (60–80) and extracted with methanol. The vaginal smear of the Wistar rats (200–250 g) was studied microscopically for estrus cycle and only female rats with normal estrus cycle were selected for study. The acute study was done according to OECD guidelines and 50 mg/kg body weight and 100 mg/kg body weight dose selected for antiimplantation activity. The rats in proestrous and

estrous stages were caged with fertile male in the ratio 2:1. The vaginal smears were examined and the appearance of the sperms clusters in the smears was recorded as Day 1 of pregnancy. The implant number and size was examined on Days 10 and 21 by laprotomy. There was no change in ovulation; hence the antiimplantation activity observed which can be attributed largely to its inhibition of number of implants. However, an investigation of the antiimplantation activity showed no increase in body weight or uterine content of blood glucose, cholesterol and triglyceride levels when compared with control group^[35].

Conflict of interest statement

We declare that we have no conflict of interest.

Comments

Background

The back bone of Indian traditional system of medication is herbal source. Ayurveda, the oldest traditional medicinal system that is based on plant medicines and treatments. *C. dichotoma* (Indian cherry) has been widely used for the preparation of traditional medicines for various ailments in diverse regions of India. Also several parts of the plant and phytochemicals potentially evaluated for the management of range of disease. As the world is facing problem of rapid resistance of synthetics like antibiotic, it is important to focus on plant as a source of therapeutic agents.

Research frontiers

The present review of *C. dichotoma* is well documented for its systematic study of various plant parts, nutritional information, biological investigation, phytochemicals and pharmacological properties. The plant information is precisely arranged and explained.

Related reports

The article is well documented with traditional medicinal system and folklore medicinal properties which is beneficial to screen their biological efficacy and isolation of biologically active phytochemicals.

Innovations and breakthroughs

The detail plant information and its uses against various ailments might be further useful for references and related research work based on traditional Indian system of medication.

Applications

The present review could help to lead the discovery of various new plant based drugs and treatment.

Peer review

Authors did detailed collection regarding the topic including graphics, pharmacological uses of several parts of the plant and phytochemicals potentially evaluated for the management of range of disease. The article is well

documented with traditional medicinal system and folklore medicinal properties which is beneficial to screen their biological efficacy and isolation of biologically active phytochemicals. The review is glowing with detailed information with ample study results.

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