Cephalandra indica Naud. - A Review

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ABSTRACT

Cephalandra indica Naud (Syn. *Coccinia indica* Wight. & Arn, *Coccinia grandis* (L.) Voigt, *Coccinia cordifolia* (L.) Cogn), commonly known as Ivy Gourd, Little Gourd and Kovai belongs to family Cucurbitaceae. The plant had been used in Ayurvedic and Unani practice in the Indian subcontinent, as antidiabetic. *C. indica* is traditionally used as anti-inflammatory, antipyretic, analgesic, antispasmodic, antimicrobial, cathartic, antibacterial and expectorant. This review includes 138 references and emphasizes microscopic characteristics, chemical constituents, pharmacological reports, clinical trials and patents of *C. indica*. The review has been compiled using references from major databases like Chemical Abstracts, Medicinal and Aromatic Plants Abstracts, PubMed, Scirus, Science Direct and, other online and electronic databases. The plant has been reported to exhibit anti-inflammatory, antipyretic, antimicrobial, antidiabetic, antiulcer, antioxidant activities. Terpenoids, steroids, carotenoids and flavonoid have been isolated from *C. indica* aerial parts.

Keywords: Antidiabetic, *Cephalandra indica*, Cucurbitaceae, Flavonoid, Triterpenoids.

INTRODUCTION

Indian systems of traditional medicines namely Ayurvedic, Siddha and Unani index nearly about 2500 plant species for treatment of various ailments from ancient times[27]. About 70,000 plant species were used for medicinal purpose worldwide[90]. The world health organization (WHO) estimated near about 70 % of world population both in developing and developed countries use herbal drugs.

Cephalandra indica Naud, an Indian traditional plant, has long been used in the treatment of diabetes mellitus, and other ailments[7,130]. A survey of literature on *C. indica* revealed that the plant and its derived products could be developed as newer and safer drugs for the treatment of various ailments. Interests of researchers throughout the world in exploring plant drugs for the search of newer drugs, prompted us to compile an updated review article on this medicinally promising plant. The present review emphasizes microscopic characteristics, chemical constituents, pharmacological reports, clinical trials and patents of *C. indica*. The objectives of the present work are to validate that traditional uses of *C. indica* have been systematically justified with preclinical and/or clinical studies, and chemical constituents responsible for these activities have been isolated following bioactivity-guided-fractionation studies.

Cephalandra indica: *Cephalandra indica* Naud, commonly known as Bimbi, Ivy Gourd, Little Gourd and belongs to family Cucurbitaceae. It is native from Africa and Asia including India, Philippines, China, Indonesia, Malaysia, Thailand, Vietnam, Eastern Papua, New Guinea and Northern territories (PIER, 2001). In India, the plant grows in large quantities and widely distributed from upper Gangetic plains to Kerala and Lakshadweep. Traditionally, *C. indica* roots are useful in vomiting, burning sensation and uterine discharges[6]. The leaves exhibit astringent, bitter and cooling effects, and also useful in sores, skin diseases, skin eruption like small pox[146]. The fruits have astringent, antipyretic, galactogogue along with expectorant properties, and roots are used in treatment of diabetes and intermittent glycosuria[104]. The root bark is used for the treatment of asthma[111].

Pharmacognostical characters: *C. indica* is dioecious perennial herb with tap root system which is flexible, soft and break with a fibrous fracture. A transverse section of root shows circular outline made of parenchyma, which is full of starch grains. The cork is composed of six rows of cells. Phellogen is not distinct while phelloderm consists of 3-4 rows of cells. Few scattered groups of pericyclic fibers and stone cells are present. Primary xylem is tetrarch, pentarch or hexarch and visible near centre of root surrounded by secondary xylem[6]. Leaves are alternate, simple, blade broadly ovate, 5-lobed, acute and mucronate at the apex, cordate with a broad sinus at the base. Surface is glabrous or scaly with 3-8 glands near the base, lower surface with reticulate venation and margins are denticulate. Inflorescence is usually of solitary and petiole is 1-5 cm long. Transverse section of leaf shows presence of spongy parenchyma, vascular bundle, collenchyma, lower and upper epidermis with cuticle, pericyclic fibers, palisade cells, and having anisocytic type of stomata. Stems are finely grooved and tendrils are long, slender and spring like. Flowers are white in colour, corolla is campanulate and 3-4 cm long with deeply divided into 5 ovate lobes and calyx of 5 subulate. Stamens are three, present as staminodes in female flowers, ovary inferior. Style is divided to six branches. Petals are five in number, joined at

base, 6 to 9 mm long, white in colour with a shallow notch at the apex. Sepals are pale green, triangular, acute about 6 to 9 mm. Stamens are many in number and arise from a tube. Fruits are smooth, bright red, ovoid to ellipsoid berry, 2.5-6 cm long, also contains pericarp, epicarp, mesocarp, placenta and unilocular ovary. Seeds are small, reddish brown black in colour, roughly triangular, 1.5 mm in size, long with a deep depression on each side[126].

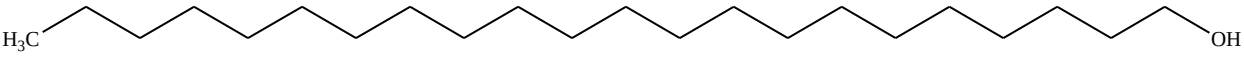
Chemical constituents: The whole plant contains various phytochemical constituents such as triterpenoids, steroids, carotenoids, aliphatic hydrocarbons and certain vitamins[33]. Reported chemical constituents of *C. indica* have been summarized in table 1.

Pharmacological reports: *C. indica* has been reported to exhibit anti-inflammatory, antipyretic, antimicrobial, antidiabetic, antiulcer and antioxidant activities. A survey of literature revealed that though few scientific reports have validated traditional claims of *C. indica* aerial parts but employed crude uncharacterized extracts. Reported pharmacological activities of *C. indica* have been summarized in table 2.

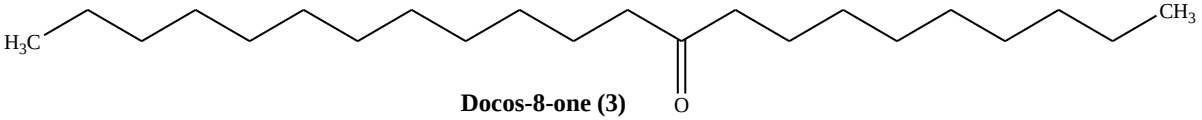
Toxicity studies: Acute and sub-acute toxicity studies showed that *C. indica* is safer herbal drug[51]. The methanol extract of *C. indica* at the doses of 5, 50, 300, 2000 mg/kg body weight was studied for toxicity, and mice were continuously observed for their mortality and behavioral response for 48 h and thereafter once in day for 14 days[81]. The methanol extract of the plant did not show any sign of toxicity in animals. Aqueous and methanolic extracts of *C. indica* proved to be safe after oral administration at dose levels upto 1000 mg/kg[8].

Clinical studies: *C. indica* is used to treat "sugar urine" (madhumeha) in Ayurveda, a traditional Indian healing system. The mechanism of action is not well understood but appears to have insulin-mimetic properties[147]. While assessing the quality of the herb for glycemic control by the American Diabetes Association Criteria for Clinical Guidelines, which rated *C. indica* with an A-rating and having supportive evidence with at least one adequate randomized clinical trial. Table 3 showed clinical studies of *C. indica.*

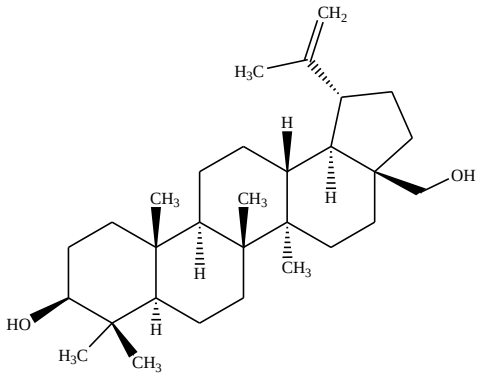
Heptacosane (1)



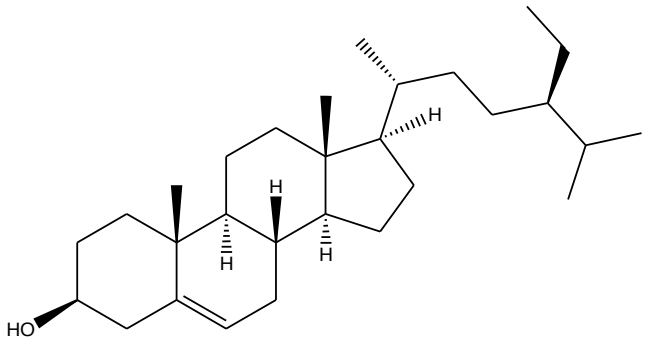
Docos-1-ol (2)



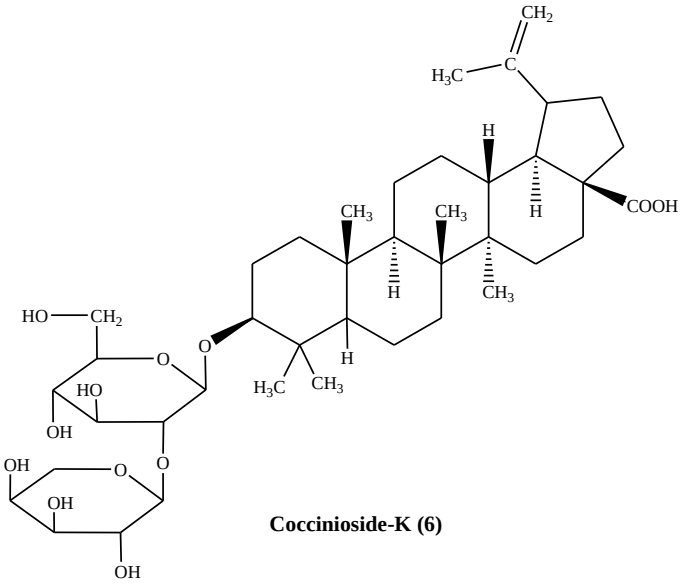
Docos-8-one (3)



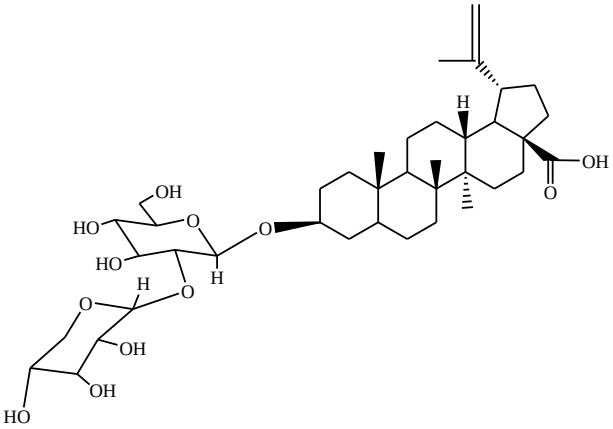
Betulin(4)



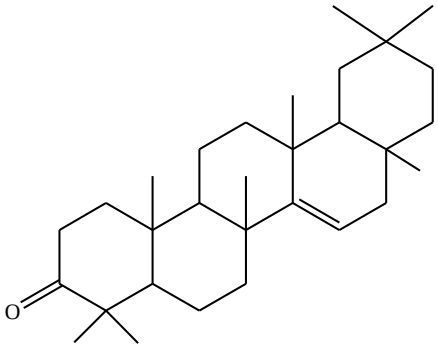
β-sitosterol(5)



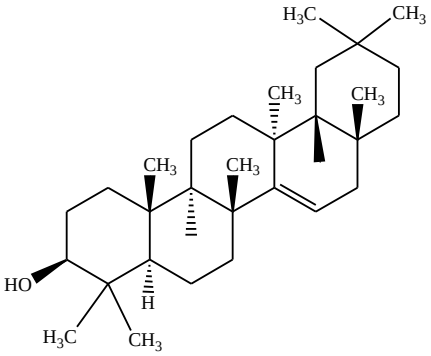
Coccinioside-K (6)



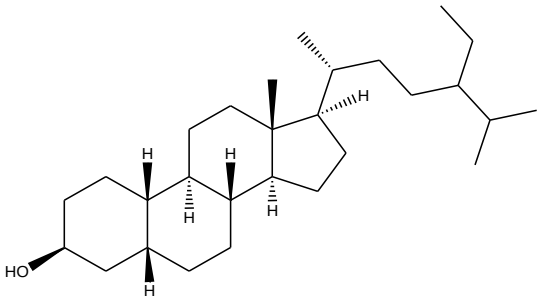
3-*O*-β-(α-L-arabinopyranosyl)-(1➔ 2)-β-D-glucopyranosyl-(1➔ 3)-β- hydroxylup-20(29)-en-28-oic acid (7)



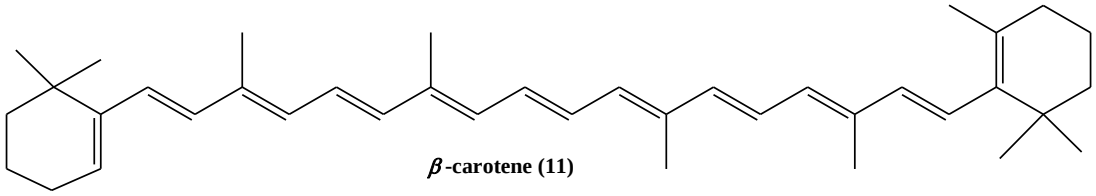
Taraxerone (8)



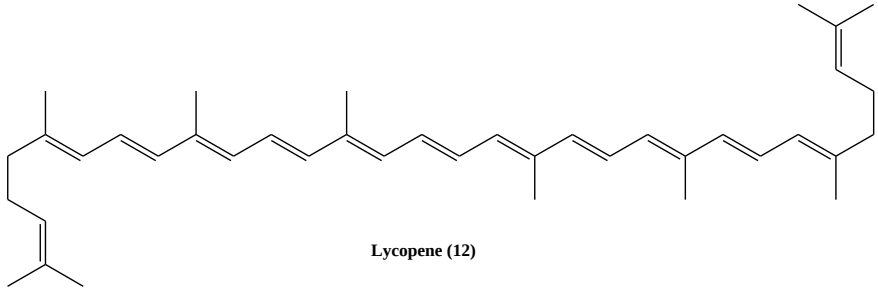
Taraxerol (9)



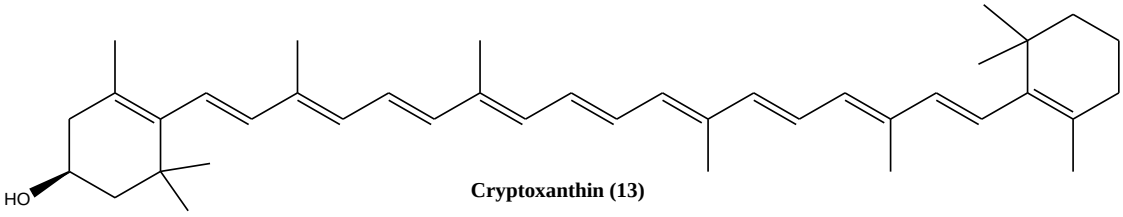
(24R)-24-ethylcholest-5-en-3β-ol (10)



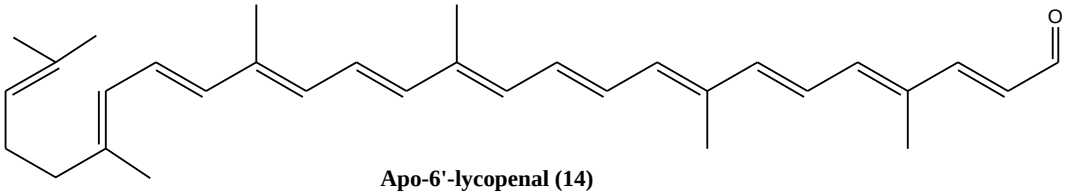
***β*-carotene (11)**



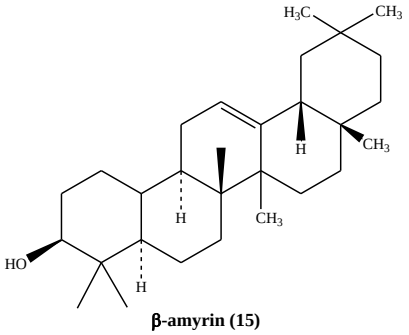
Lycopene (12)



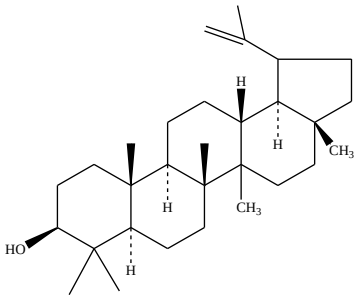
Cryptoxanthin (13)



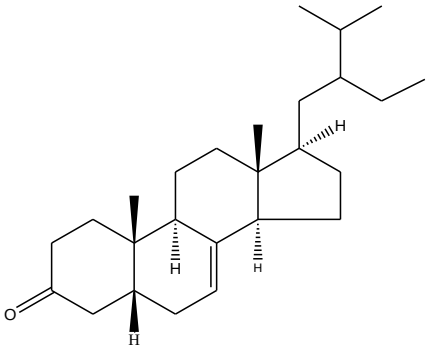
Apo-6'-lycopenal (14)



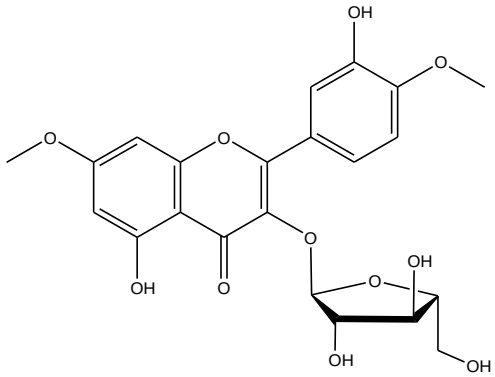
β-amyrin (15)



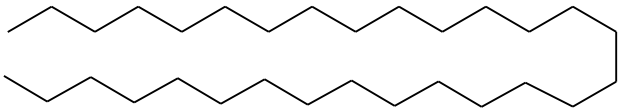
Lupeol (16)



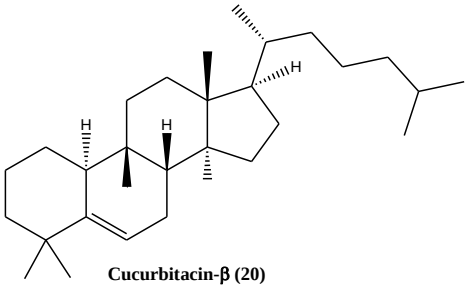
Stigmast-7-en-3-one (17)



Ombuin 3-O-arabinofuranoside (18)



Tritriacontane (19)



Cucurbitacin-β (20)

Table 1: Phytoconstituents isolated from *C. indica.*

Plant part	Compounds	References
Aerial parts	Heptacosane (**1**)	(Khaleque, 1968; Dhargalkar and Guha, 1959)
	Cephalandrol, Tritriacontane (**2**) , *β*-sitosterol (**3**), Cephalandrine A and Cephalandrine B	(Qudrat-i-Khuda,1965)
Whole plant	Docos-1-ol (**4**) and Docos-8-one (**5**), Betulin (**6**), *β*-sitosterol (**3**)	(Ajithabai, 2011)
	Stigmast-7-en-3-one (**7**)	(Sucrow, 1968)
	Arabinogalactan, Xyloglucan and Xylan (polysaccharides)	(Rahman, 1990)
Fruits	Taraxerone (**8**), Taraxerol (**9**) and (24R)-24-ethylcholest-5-en-3β-ol glycoside (**10**)	(Kundu and Ray, 1987) (Gantait, 2010)
	β-carotene (**11**), Lycopene (**12**), Cryptoxanthin (**13**), and Apo-6'-lycopenal (**14**)	(Barua and Goswami, 1979)
	β-amyrin (**15**), Lupeol (**16**) and Cucurbitacin-β **(17)**	(Bhakuni et al.1962)
	β-sitosterol (**3**) and Taraxerol (**9**)	(Basu and Ghosh, 1972)
Roots	Coccinioside-K (**18**)	(Vaishnav, 2001)
	3-*O*-β-(α-L-arabinopyranosyl)-(1 2)-β-D-glucopyranosyl-(1 3)-β- hydroxylup-20(29)-en-28-oic acid (**19**)	(Vaishnav and Gupta, 1995)
	β-amyrin (**15**), Lupeol (**16**) and β-sitosterol (**3**)	(Khastgir et al.,1958)
	Ombuin 3-*O*-arabinofuranoside (Flavonoid glycoside) (**20**)	(Vaishnav and Gupta, 1996)

Table 2: Pharmacological reports of *C. indica* aerial parts.

Activity	Extract/ fraction /isolate	Dose/route of admin-istration	Positive control (Dose)	Control	Animals/ organisms used	Experimental model	Mechanism of action	Miscellaneous information	Reference
Anti-inflammatory	Aqueous extract of leaves	25 to 300 mg/kg, i.p	Diclofenac (20 mg/kg)	Normal saline	Wistar rats	Carrageenan- induced rat paw oedema	The inhibition of histamine and serotonin release	----------	(Niazi, 2009)
	Aqueous and Ethanol extracts of leaves	250 and 500 mg/kg p.o.	Diclofenac sodium (10 mg/kg)	2 % tween 80	Wistar rats	Carrageenan- induced paw oedema and Dextran-induced paw oedema	Inhibition of lipoxygenase enzyme	Activity due to presence of tannins, flavonoids, alkaloids, glycosides, saponins and carbohydrates	(Sutar, 2010b)
	Aqueous extract of fruits (hydro-gel using chitosan as a gel base)	150 mg/kg p.o.	Diclofenac sodium (50 mg/kg); Diclofenac diethylamine (50 mg/kg)	Normal control	Wistar rats	Carrageenan- induced rat paw oedema	----------	Extract hydrogels stability might be due to the antibacterial effects of chitosan	(Salunkhe, 2005)
	Fruit juice powder	50 and 200 mg/kg p.o.	Brufen (100 mg/kg)	Normal saline	Adult male Sprague-Dawley rats	Carrageenan- induced rat paw oedema and histamine induced paw oedema	----------	----------	(Rao,2004; 2005)
	Aqueous extract of leaves and stems	50, 100 and 200 mg/kg p.o.	Indomethacin (10 mg/kg)	Disease control	Sprague-Dawley rats and Swiss mice	Formaldehyde-induced rat hind paw oedema	----------	Antiproliferative activity	(Deshpande, 2011c)
	Aqueous, pet ether and 60% methanolic extract	200 mg/kg p.o.	Diclofenac sodium (10 mg/kg)	Normal saline	Adult Wister rats	Carrageenan-induced rat paw oedema	---------	----------	(Chatterjee and Chatterjee, 2012)
	Pet ether, chloroform, ethanol and Aqueous extract of fruit powder	100, 200 and 400 mg/kg p.o.	Indomethacin (10 mg/kg)	Normal saline	Wistar rats	Carrageenan-induced rat paw oedema and cotton pellet granuloma	----------	The presence of glycosides, triterpenoids, flavonoids, tannins and phenolic compounds	(Bambal, 2010)
Anti-nociceptive	Aqueous extract of leaves	25-300 mg/kg, i.p	Morphine (2mg/kg) and Diclofenac (20 mg/kg)	Normal saline	Swiss mice	Tail flick assay	Effect due to preferentially action on central nervous system	----------	(Niazi' 2009)
	Methanolic extract of leaves	100,200 400 mg/kg p.o.	Aspirin (250 mg/kg)	1% Tween	Male Swiss Albino mice	Acetic Acid-induced writhing	Inhibition of prostaglandin synthesis	----------	(Sutradhar, 2011)

				80 in water					
	Fruit juice powder	50 and 200 mg/kg p.o.	Brufen (100 mg/kg)	Normal saline	Swiss mice	Acetic Acid-induced writhing and hot plate induce pain	----------	----------	(Rao, 2004;2005)
	Methanolic extract of leaves	50, 100 and 200 mg/kg p.o.	Aspirin (200 mg/kg)	0.5 % CMC	Wistar rats	Acetic acid induced writhing, Tail immersion method and Eddy's hot plate method	---------	Effect mediated through peripheral but not central mechanism(s)	(Aggarwal, 2011)
Antipyretic	Aqueous extract of leaves	100, 200 and 300 mg/kg p.o.	Paracetamol (150 mg/kg)	Normal saline	Wistar rats	Brewer's Yeast-induced hyperpyrexia	Antioxidant property of plant cause decrease in body temperature	Pyrexia is associated with increased oxidative stress	(Niazi, 2009)
	Methanolic extract of leaves	50, 100 and 200 mg/kg p.o.	Aspirin (100 mg/kg)	0.5 % CMC	Wistar rats	Yeast induced pyrexia	----------	----------	(Aggarwal , 2011)
Antiulcer	Methanol and aqueous extracts of leaves	0.5,1 and 2 g/kg p.o.	Famotidine (20 mg/kg); Aspirin (200 mg/kg)	1 % CMC	Wistar Albino rats	Asprin induced gastric ulcer model	Decreased levels of lipid peroxidation and superoxide dimustase	Increased mucus secretion and having antioxidant property	(Majumde, 2008)
	Ethanolic and Aqueous extracts of leaves	200 and 400 mg/kg p.o.	Omeprazole (2 mg/kg)	Solvent control	Wistar Albino rats	Pylorus ligation induced ulcer model	Decrease the Na^+ ions and increased in K^+ ions levels in dose dependent manner.	Anti-secretory effects	(Preeth, 2010)
	Ethanolic and Aqueous extracts of leaves	200 and 400 mg/kg p.o.	Omeprazole (2 mg/kg)	Solvent control	Wistar Albino rats	Pylorus ligation induced ulcer model	----------	----------	(Santhara, 2013)
Anti-microbial	Water extract of leaves and ethanol extract of stems	200 µg/100µl	Ampicillin and Amoxicillin	----------	Gram +ve bacteria (4); Gram – ve bacteria (6)	Well diffusion technique	----------	----------	(Farrukh, 2008)

	Ethanol, pet ether, chloroform and aqueous extracts of leaves	25, 50 and 75 mg/well	Antibiotics	DMSO	*E. aerogenes, P. aeruginosa, S. epidermidis, B. subtilis and S. typhimurium*	Well diffusion method and broth dilution method	----------		(Hussain, 2010)
	Methanolic extract of leaves	200 µg/ml	Ciprofloxacin (200 µg/ml); Griseofulvin (2000 µg/ml)	----------	(5)Gram +ve bacteria; (20)Gram – ve bacteria); (4) Fungal strain	Disc diffusion assay and agar diffusion method	----------	----------	(Dewanjee, 2007b)
	Petroleum ether and methanol extracts of fruits	100 µl of 100 mg/ml	Streptomycin (10 mg/ml)	----------	Gram +ve bacteria (2); Gram – ve bacteria (4)	Bacterial susceptibility testing; agar diffusion method	----------	----------	(Shaheen, 2009)
	Protease inhibitor (PI) 14.3 kDa isolated from leaves	200 µl	Levofloxacin	----------	Gram +ve bacteria (2); Gram – ve bacteria (3); fungal strain (4)	Antimicrobial assay (*In vitro* growth inhibition)	Protease inhibitor form a channel on cell membrane and cell die due to the out flow of cellular content	Disulfide bridge is essential for protease inhibition and antifungal activity	(Satheesh and Murugan, 2011)
	Aqueous, acetone and ethanol extracts of leaves	200 to 1000 µg/ml	----------	----------	Biofilm and ESBL producing UPEC	Agar well diffusion method	----------	Activity related to the presence of tannin, alkaloids and triterpenoids	(Poovendr, 2011a)
	Aqueous, acetone and ethanol extracts of leaves	200 to 1000 µg/ml	----------	----------	ULPH 1, ULPH 2, ULPH 3 and ULPH 4	Agar well diffusion method	----------	Activity related to the presence of tannin, alkaloids and triterpenoids	(Poovendr, 2011b)

	Aqueous, acetone, hexane, methanolic and ethanol extracts of leaves	31.52 to1000 µg/ml	----------	DMSO	*S. pyogenes*, *S. aureus*, *K. pneuminiae* , *B. cereus* and *E. coli*	Agar well diffusion method	----------	----------	(Sivaraj, 2011)
	Aqueous, acetone, pet ether, methanolic and distilled extracts of leaves	20 µg/ml	Cephalexin (20 µg/ml)	DMSO	*E. coli* , *S. auerus*, *B. subtilis*, *P. aeruginosa*, *C. albicans* and *A. nigrus*	Agar well diffusion method	----------	----------	(Rodge and Biradar, 2010)
	Chloroform n-hexane and ethyl acetate extracts of leaves	500 µg/disc	Kanamycin (30 µg/disc)	Blank disc (impreg-nated with solvent)	Gram +ve and -ve bacteria	Antibacterial assay (disc diffusion method)	----------	----------	(Bulbul, 2011)
	Ethanolic and aqueous extracts of leaves	700-1500 µg/ml	Chloram-phenicol (15-20µg/ml)	--------	Gram +ve, gram -ve bacteria and fungal strain	Zone inhibition method	----------	----------	(Bhattacha rya, 2010)
	Chloroform, ethyl acetate, methanol and aqueous extracts of fruits	25 and 50 mg/mL	---------	-------	*Pheritima posthuma*	Anthelmintic Assay	---------	---------	(Shivhare , 2011)
	Methanolic extract of leaves	5 and 10 mg/mL i.p	Albenzazole (10 mg/ml)	DMSO in normal saline	*P. posthuma*, *T. solium* and *A. lumbricoid es*	Anthelmintic Assay	---------	---------	(Dewanjee, 2007a)
	Mucilage of fruit	Film, length (1 cm) and thickness of 1mm	----------	----------	*Staphylo-coccus aureus and Asperfigllu s foetidus*	Agar diffusion method	----------	----------	(Raghava, 2013)

Anti obesity	Alcoholic and aqueous extract of *C. indica* fruits	100 and 200 mg/kg, p.o.	Sibutramine (5 mg/kg, p.o)	Normal control	---------	Cafeteria Diet (CD) Induced Obesity Model	----------	----------	(Ahmed and Manoj, 2012)
Antioxidant	Methanolic extract of leave	3163.28 mg/kg	Ascorbic acid	----------	----------	DPPH method	----------	Antistress due to strong free radical scavenging activity	(Chandira, 2010)
	Chloroform n-hexane Ethyl acetate extract of leaves	20,40,60, 80 and100 µg/mL	Ascorbic acid	Normal control	----------	DPPH method	----------	----------	(Bulbul, 2011)
	Ethanolic extract of leaves	50,100 and 200 mg/kg, p.o.	Glibenclamide (600 µg/kg)	Diabetic control	Male Albino rats	STZ induced Diabetes	Protective action on lipid per-oxidation and against oxidative damage	Hypoglycaemic action	(Venkateswara and Pari, 2003a)
	Chloroform, ethyl acetate and pet ether extracts of leaves	50-800 µg/ml	Ascorbic acid, BHT, Quercetin, α-tocopherol, Curcumin	--------	--------	*In vitro* assay	--------	Phenolic compounds exhibits antioxidant effects	(Umamaheshwari and Chatterjee, 2008a)
	Aqueous extract of leaves	30 -6452 µg/ml	Ascorbic acid	---------	---------	*In vitro* assay	---------	Total phenol and flavonoid content	(Biswas et al., 2010)
	Methanolic extract of fruits	50 -250 µg/ml	Butylated hydroxy-anisole (50 -250 µg/ml)	---------	---------	DPPH assay, Reducing power ability and H_2O_2 scavenging assay	---------	Activity due to presence of flavonoids and anthraquinone glycosides	(Deshpand, 2011b)
	Pet ether, chloroform and ethyl acetate extracts of stems	50 -250 µg/ml	Butylated hydroxy-anisole (50 -250 µg/ml)	----------	---------	DPPH assay, Reducing power ability and H_2O_2 scavenging assay	---------	---------	(Deshpand, 2011a)
Antistress	Pet ether chloroform and ethyl acetate extracts of leaves	200 mg/kg p.o.	Vitamin E (100 mg/kg)	Normal saline	Wistar rats	Ethanol-induced cerebral oxidative stress	Increase in the activities of serum transaminases, alkaline phosphatase, uric acid and lipid levels.	No sign of toxicity and mortality were observed	(Umamaheshwari and Chatterjee, 2009)

	50 % ethanolic extract of whole plant	100, 300 and 600 mg/kg p.o.	Ginseng (100 mg/kg)	Normal saline	Swiss Albino mice and Sprague-Dawley rats	Swimming performance time test, Antifatigue test, Hypoxia time and Cold-restraint stress induced ulcers	---	Phytochemical screening and having free radical scavenging activity	(Chandira, 2010)
Antidiabetic	Ethanolic extract of aerial parts	100 and 200 mg/kg p.o.	Glibenclamide (0.5 mg/kg)	0.5% CMC solution	Adult male Sprague-Dawley rats	STZ induced diabetes	Reduction of serum enzymatic activities cloud contribute to	Increase in content of glycogen could contribute to the decrease endogenous glucose	(Balarama, 2010)
	Methanolic extract of leaves	50,100, 200 and 400 mg/kg p.o.	Glibenclamide (10 mg/kg)	1% Tween 80 in water	Swiss Albino mice (male)	Oral glucose tolerance tests	---		(Sutradhar, 2011)
	Aqueous extract of leaves	500 mg/kg p.o.	----------	Citrate buffer	Male adult cross-bred Albino rats	STZ induced diabetes	Protect the pancreas or regenerate the damaged pancreatic cells	Preventing the development of tactile allodynia (diabetic neuropathy)	(Kazi, 2009)
	Aqueous extract of leaves + *Abroma augusta* extract of leaves	500 mg/kg p.o.	Diabetic untreated	Normal saline	Wistar Albino rats	STZ induced diabetes	Increase in blood insulin along with utilization of glucose by liver and extra hepatic tissues	Anti-hyperlipidemic effects, corrects retinopathy, neuropathy and musculopathy	(Eshrat, 2003)
	Alcoholic extract of fruits	200 mg/kg p.o.	Glibenclamide (2.5mg/kg)	Normal saline	Wistar Albino rats	Alloxan induced diabetes	---	Decrease in amylase activity	(Gunjan, 2010)
	Crude powder of fruits	50,100, 200, 375 and 500 mg/kg, p.o.	----------	1 % gum acacia	Adult male Sprague-Dawley rats	STZ induced diabetes and evaluation on normoglycaemic rats	---	---	(Mishra, 2009)
	Pet ether, chloroform and ethyl acetate extracts of leaves	150 mg/kg, i.p	Metformin (150 mg/kg)	Normal control	Long-Evans female rats	Glucose induced hyper-glycemic	---	Presence of β-carotene & first time intraperitoneal administration of the plant extract	(Islam, 2009)

	Leaves decoction	1 ml p.o.	Glibenclamide (10 mg/kg)	Normal control	Wistar Albino rats	Alloxan induced diabetes	Potentiating the pancreatic secretions or increasing the glucose uptake	Stimulate glycogenesis or inhibit glycogenolysis	(Doss and Dhanabalan, 2008)
	Aqueous extract of leaves	500 mg/kg p.o.	Diabetic control	Citrate buffer	Male adult cross-bred Albino rats	STZ induced diabetes	Protection of pancreas or regeneration of damaged pancreatic cells	Neuropathic pain cured by anti-hyperglycemic effects or anti-oxidant compounds	(Rafiq et al., 2009)
	Ethanolic extract of leaves	250 mg/kg p.o.	Metformin (100 mg/kg)	1 % gum acacia	Adult male Sprague-Dawley rats	STZ induced Diabetes	---------		(Akanksha et al., 2010)
	Ethanolic extract of leaves	150 and 300 mg/kg i.p	Glibenclamide (0.05 mg/kg); Metformin (100 mg/kg)	DMSO	Wistar Albino rats	Alloxan induced diabetes	Enhances secretion of insulin	Hypolipidemic effects	(Akhtar et al., 2007)
	Freeze dried (aqueous) extract of leaves	25 mg/kg p.o.	Tolbutamide (200 mg/kg)	---------	Wistar Albino rats	Alloxan induced diabetes	---------	---------	(Sullivan and Janis, 2000)
	Freeze dried (aqueous) extract of roots	200 and 400 mg/kg p.o.	Tolbutamide (200 and 400 mg/kg)	---------	Wistar Albino rats	Alloxan induced diabetes	---------	---------	(Niedzielski 2002)
	Hydro-alcoholic extract of leaves	200 mg/kg p.o.	Phenformin (30 mg/kg)	----------	Wistar Albino rats	STZ induced diabetes	Depression of key gluconeogenic process or the increase in the levels of glucose transporters and stimulation of uptake in peripheral tissues	Antilipidperoxidative and Antioxidative Effects; Corrects the protein disorder	(Mallick et al., 2007 a)
	Aqueous extract of fruits + aqueous extract of fruits of *Morinda citrofolia*	300 mg/kg p.o.	Tolbutamide (200 mg/kg)	Normal saline	Wistar Albino rats	Alloxan induced diabetes and OGTT	Increase in the levels of glucose transporters	Preserve the cells of islet of Langerhans	(Prakash et al., 2010)

	Hexane extract of aerial parts	200 mg/kg p.o.	Phenformin 30 mg/kg	Normal saline	Wistar Albino rats	STZ induced diabetes	---	---	(Shakya, 2008)
	Aqueous extract of roots	2cc = 11G of crude powder for 16 days	Diabetic control	Normal saline	Rabbit	Alloxan induced diabetes	---	---	(De and Mukerji, 1953)
	Ethanolic extract of whole plants	250 mg/kg p.o.	---	2% gum acacia	Male Albino rats	Fasted model; Glucose loaded model; STZ induced diabetes	---	---	(Chandrasekar, 1989)
	Ethanolic extract of leaves	200 mg/kg p.o.	Glibenclamide (600 µg/kg)	Diabetic control	Male Albino rats	STZ induced diabetes	Increase pancreatic secretion of insulin from existing β-cells or its release from bound form	Increased glycolysis, decreased gluconeogenesis, increased hydrogen shuttle reactions and normo-glycemia	(Venkateswaran and Pari, 2002)
	Coccinia leaves milk suspension (CMS)	500 mg/mL p.o.	---	---	Mongrel male dogs	Alloxan induced diabetes	---	---	(Singh, 1985)
	Pet ether, ethyl acetate and chloroform extracts of leaves	150 mg/kg i.p	Metformin (150 mg/kg)	Diabetic control	Long-Evans female rat	STZ induced diabetes	Enhanced secretion of insulin	Hypolipidemic effects	(Islam, 2011)
	Aqueous extract of fruits + *Morinda citrifolia*	300 mg/mL p.o.	Diabetic control	Normal saline	Male Albino rats	Alloxan induced diabetes	Depression of key gluconeogenic enzymes or the increase in the levels of glucose transporters	Inhibition of cholesterol synthesis and having antihyperlipidemic effects	(Kumar and Verma, 2011)
	Ethanolic extract of leaves	50 to 200 mg/kg p.o.	Glibenclamide (600 µg/kg)	Diabetic control	Male Albino rats	STZ induced diabetes	Enhancing effects on cellular antioxidant defense	Increase in the pancreatic secretion of insulin from the existing β-cells	(Venkateswaran and Pari, 2003b)

	Aqueous extract of leaves of *C. indica* and *Trigonella foenum-graecum*	250, 350 and 750 mg/kg p.o.	Glimepiride (800µg/kg)	Normal control	Long-Evans male rat	STZ induced diabetes	---------	The body weight gain were increased significantly	(Das, 2008)
	Ethanolic extract of leaves of *C. indica* and Glibenclamide	100, 150 and 200 mg/kg & 0.125 mg/kg p.o.	Diabetic control	Normal control	Sprague-Dawley Albino rats	Alloxan induced diabetes	---------	Hypolipidemic and antioxidant effects	(Jose and Usha, 2011)
	Ethanolic extract of leaves	200 mg/kg p.o.	---------	Distilled water	Long-Evans male rat of black and white strains	Enzyme assay (Glucose-6-phosphatase and Arginase)	Repression of the key gluconeogenic enzyme glucose-6-phosphatase and inhibition of arginase	Hypoglycemic effect in normal fed animals could be also due to inhibition of intestinal glucose absorption	(Hossain, 1992)
	Hydro-alcoholic extract of leaves	200 mg/kg p.o.	---------	Distilled water	Wistar Albino rats	STZ induced diabetes	Suppression gluconeogenic enzyme and lowering of intra-cellular cyclic AMP	The red-cell and hepatic glucose-6-phosphate dehydrogenase activities were found to be elevated	(Shibib, 1993)
	Ethanolic extract of leaves	200 mg/kg p.o.	Glibenclamide (0.25 mg/kg)	3 % tween 80	Sprague-Dawley rats	Alloxan induced diabetes	Stimulate hepatic glucose uptake, and also inhibit gluconeogenesis and glycolgenolysis in liver	Terpenes having insulin like activit	(Jose and Usha, 2010)
	Ethanol, chloroform and aqueous extracts of fruits	250 mg/kg p.o.	Glibenclamide (1 mg/kg)	Normal saline	Wistar Albino rats	Alloxan induced diabetes	Activation of the existing pancreatic cells in diabetic rats	Leaves are more active than fruits	(Ramakrishnan, 2011)
	Aqueous, pet ether and chloroform extracts of leaves	250 mg/kg p.o.	---------	1 % glucose	Guinea-pigs	(OGTT)	---------		(Mukherje, 1972)

	Toluene, chloroform, ethyl acetate, n-butanol fraction from alcoholic extracts of aerial parts	150 mg/kg p.o.	Phenformin (30 mg/kg)	0.3 % CMC	Wistar Albino rats	Alloxan induced diabetes	β-cell restorative properties of active principle	Triterpenes found to be responsible for the antidiabetic and correction of metabolic disorder	(Dhanabal et al., 2004)
	Alcohol extract of leaves	250 mg/kg p.o.	Glibenclamide (5 mg/kg)	Normal saline	Male Wistar Albino rats	STZ induced diabetes	---------	No acute toxicity reported	(Singh, 2009)
	Aqueous and alcoholic extract of leaves	1.25 g./kg p.o.	Tolbutamide (0.25 g/kg.)	----------	Rabbit	Fasted model, fed model and glucose loaded model	---------	---------	(Brahmachari and Augusti, 1963)
	Ethanolic extract of whole plant	250 mg/kg p.o.	---------	2 % gum acacia	Male Wistar Albino rats	Fasted model, Fed model and Glucose loaded model	Stimulate insulin release.	Possesses insulin secretogogue activity.	(Bajpai, 2007)
	Mother tincture of aerial parts	30c p.o.	---------	Normal saline	Male Wistar Albino rats	High fat and high fructose induced type -2 diabetes	Increased the serum insulin and expression of proteins	---------	(Sampath, 2013)
	Methanol extract of leaves	150, and 300 mg/kg p.o.	Glibenclamide (5 mg/kg)	Normal saline	Male Wistar Albino rats	STZ induced diabetes	---------	---------	(Ghosh and Roy, 2013)
	Methanolic extract of leaves	200 mg/kg p.o.	Diabetic control	Normal saline	Female Wistar Albino rats	STZ-nicotinamide induced diabetes	Stimulation of insulin secretion by the closure of K^+-ATP channels, membrane depolarization and stimulation of Ca^{2+} influx	Activate the glucose uptake into cells and enhanced reduction in gluconeogenesis	(Palanisamy, 2011)
	Ethanolic extract of leaves	150 mg/kg p.o.	Glibenclamide (600 µg/kg)	Diabetic control	Swiss Albino rats	STZ induced diabetes	---------	Hypoglycemic effect	(Venkateswaran, 2003)

	Aqueous-methanolic (60:40) extract of leaves	80 mg(1:1)/ 0.5mL olive oil per 100 mg b.w	Diabetic control	Citrate buffer + olive oil	Wistar strain Albino rats	STZ induced diabetes	Sensitize the β-cell and elevate serum insulin, rectify glycated hemoglobin		(Mallick, 2009)
	Ethanolic extract of leaves	200 mg/kg p.o.	Glibenclamide (600 µg/kg)	Diabetic control	Male Albino rats	STZ induced diabetes	Improved glycaemic control and increased plasma insulin	Hypoglycemic and hypolipidaemic effects	(Pari and Venkateswaran, 2003)
	Ethanolic extract of aerial parts	100 and 200 mg/kg p.o.	Glibenclamide (0.5 mg/kg)	0.5% CMC solution	Adult male Sprague-Dawley rats	STZ induced diabetes	Level of HDL-cholesterol increased due to increased activity of lecithin-cholesterol acyl transferase. which may contribute to the regulation of blood protein	Effect could be through the control of hyperglycemia	(Balaraman, 2010)
	Ethanolic extract of leaves	200 mg/kg p.o.	Glibenclamide (0.25 mg/kg)	3 % tween 80	Sprague-Dawley rats	Alloxan induced diabetes	Terpenes produced suppression of lipolysis and mobilization of free fatty acid from the fat deposit	Reduced glutathione scavenges free radicals and renders protection against lipid peroxidation caused by free radical; no toxicity is reported	(Jose and Usha, 2010)
	Aqueous-methanolic (40:60) extract of leaves	80 mg/kg p.o.	Diabetic control	Citrate buffer	Male Wistar Albino rats	STZ induced diabetes	Pancreatic β-cell regeneration or stimulation of insulin secretion	---------	(Mallick, 2007 b)
	Fruits and leaves extract	Fed 10 and 5 % w/w	Diabetic control	--------	Male Wistar Albino rats	STZ induced diabetes	---------	---------	(Gurukar, 2013)
	Methanol extract of leaves of *C. indica* and *Salvadora oleoides*	150 mg/kg p.o	Glipizide (5 mg/kg)	1% CMC solution	Male Wistar Albino rats	Alloxan induced diabetes	---------	---------	(Saklani,, 2102)

Anti-dyslipidemic effects	Chloroform, ethanol, butanol and aqueous extracts of leaves & Polyprenol	250 and 500 mg/kg (p.o.) & 5to 50 mg/kg (p.o.)	Fenofibrate (108 mg/kg)	(HFD)	Golden Syrian hamster	Dyslipidemic hamster model	Effect mediated through (PPARα), by catabolizing triglyceride (TG)	Polyprenols used as active marker for standardization and improving HDLC/ ratio for the maintenance of lipid-glucose homeostasis	(Singh, 2007)
Antitussive	Methanolic extract of fruits	2.5 and 5 % w/v p.o.	Codeine solution (0.03 g/mL)	Normal saline	Male Guinea pig	Citric acid aerosol-induced antitussive evaluation	Effect may be *via* central nervous system	---	(Pattanayak and Sunita, 2009)
		100,200 and 400 mg/kg (p.o.)	Codeine phosphate (10,20,40 mg/kg)	Normal saline	Swiss Albino mice	Sulfur dioxide-induce antitussive evaluation	---	---	(Pattanayak and Sunita, 2009)
Antifungal	Ethanolic and aqueous extracts of leaves	700-4750 µg/ml	Fluconazole (15-20 µg/ml)	---	Fungal strains	Zone inhibition method	---	Non-polar fraction have higher level of antifungal properties	(Bhattacharya, 2010)
Anticancer	Ethanolic extract of leaves	200 and 400 mg/kg i.p	Vinblastine (1mg/kg)	Normal saline with EAC cells	Swiss Albino mice	*In vivo* and *in vitro* anticancer assay	Causes lysis of EAC cells by direct cytotoxic mechanism	Restore haematological parameter	(Bhattacharya, 2011)
	Aqueous extract of leaves	1-4 ml	----	No drop of conidial suspensions	*Neurospora crassa* Ema (5297)	Culture method	---	Inhibition of growth and mutagenesis	(Bhuiyan, 2009)
	Chloroform, n-hexane and ethyl acetate extracts of leaves	5,10,20,40 and 80 µg/mL	Vincristine sulphate	DMSO	*Artemia salina* (brine shrimp)	Brine shrimp lethality bioassay	---	Extracts might have antitumor or pesticidal activities	(Bulbul, 2011)
Anti-anaphylactic effects	Ethanolic extract of fruits	100, 125 and 150 mg/kg p.o.	Sodium chromoglycate (50mg/kg)	1 % Tween 80	Swiss Albino rats	Passive cutaneous anaphylaxic test	Antihistaminic and anti inflammatory mechanism	Effect due to presence of flavonoids and saponins	(Taur and Patil, 2011)
Anti-histaminic	Ethanolic extract of fruits	100, 125 and 150 mg/kg p.o.	Chlorpheni-ramine maleate (10 mg/kg)	1 % Tween 80	Swiss Albino mice	Clonidine-induced catalepsy	Mast cell stabilization	Antihistaminic activity in dose dependent manner in asthma	Taur and Patil, 2011)

Fertility effect	Aqueous extract of leaves	500 and 1000 mg/kg p.o.	Bromocriptine (30 mg/kg); Clomiphene citrate (100 µg/kg); Danazol (100 mg/kg)	Normal saline (1ml/kg)	Female Wistar rats	Hyperprolactinemia induced infertility; Endometriosis induced infertility; TII	Inhibit cell proliferation in endometrial tissue	Plant may be effective only in inducing fertility on patients suffering from hyperprolactinemia	(Jha, 2010)
Hepato-protective	Aqueous extract of leaves	250 mg/kg p.o.	---------	Ethanol (7.9 g/kg)	Wistar male rat	Ethanol induced hepatotoxicity	Protection from oxidative damage by reducing the rate of lipid peroxidation	Repair the hepatic injury and/or restore the cellular permeability and increasing the antioxidant defense mechanism in rats	(Sivaraj, 2010)
	Ethanolic extract of fruits	50 and 100 mg/kg p.o.	Liv-Fit, Dabur formulation (100mg/kg)	1 % Tween 20	Wistar rats	CCl_4 induced hepatotoxicity	Controlling damage effects on hepatocyte membrane	Inhibition of cytochrome P_{450}; Increased total proteins levels	(Sumanth and Vazir, 2006)
	Ethanolic extract of roots	200 and 400 mg/kg p.o.	Silymarin (25 mg/kg)	0.5 % CMC	Wistar rats	Paracetamol induced hepatic oxidative stress	Increase the activities of catalase and prevent the accumulation of excessive free radical and protects liver	Extracts having antioxidant effects	(Moideen, 2011)
	Methanolic extract of fruits	100, 200 and 400 mg/kg p.o.	Silymarin (100 mg/kg)	0.5 % tween 80 and olive oil (1:1)	Wistar Albino rats	CCl_4 induced hepatotoxicity	Able to condition hepatocytes, accelerate regeneration of parenchyma cells	Extracts are protecting against membrane fragility and decrease of leakage of the marker enzymes into the circulation	(Swamy, 2007)
	Methanol, chloroform and aqueous extracts of fruits	200 and 400 mg/kg	Silymarin (100 mg/kg)	Liquid paraffin	Male Albino rats	CCl_4 induced hepatotoxicity	----------	----------	(Rao, 2005)
	Diethyl ether extract of leaves	400 mg/kg p.o.	Silymarin (125 mg/kg)	Propylene glycol	Wistar Albino rats	CCl_4 induced hepatotoxicity	----------	Leaves found to be non toxic upto 2000 mg/kg	(Kumar et al., 2010)
	Alcoholic extract of fruits	250 mg/kg p.o.	Silymarin (100 mg/kg)	1% w/v of tragacanth gum	Male wistar Albino rats	CCl_4 induced hepatotoxicity	Protection from oxidative damage by free radical generation	Antioxidant property exerted by flavanoids in the fruits.	(Vadivu et al., 2008)

	Aqueous extract of leaves	250 mg/kg p.o.	Olive oil (1 ml/kg)	Distilled water	Wistar Albino rats	CCl_4 induced hepatotoxicity	Inhibit lipid peroxidation	Flavonoid, a vasculo protector prevent hemorrhage	(Kumar, 2009)
	Aqueous and ethanolic extracts of leaves	200 mg/kg p.o.	Silymarin (20 mg/kg)	Liquid paraffin	Wistar rats	CCl_4 induced hepatotoxicity	----------	Flavonoid and Cucurbitacin glycosides are responsible for hepatoprotective property	(Sunilson, 2009)
	Ethanolic extract of fruits	100 mg/kg p.o.	Disease control	Liquid paraffin	Sprague-Dawley rats	CCl_4 induced hepatotoxicity	----------	----------	(Rao et al., 2003)
	Alcoholic extract of leaves	100 and 200 mg/kg p.o.	----------	Normal saline	Male Wistar rats	Alcohol-CCl_4 induced hepatotoxicity and Paracetamol induced hepatotoxicity	----------	Antioxidant properties of flavonoids contribute to hepatoprotective effects	(Maheswari et al., 2011)
	Hydro-alcoholic extract of leaves and fruits	----------	----------	----------	Wistar Albino rats and Swiss mice	CCl_4 induced hepatotoxicity	----------	Free radical scavenging property	(Vazir and Asdaq, 2005)
	Hydro-methanolic extracts of leaves	200, 400 and 600 mg/kg	----------	Normal saline	Swiss albino male mice and Wistar rats	CP-induced oxidative stress, genotoxicity, and hepatotoxicity.	Significantly decreased in the serum ALP, ALT, and AST levels, thus indicating the protective activity against the liver damage	No toxic effects	(Nitharwal, 2013)
	Aqueous extract of fruits	200 and 400 mg/kg	Paracetamol (2 mg/kg)	2% w/v gum acacia	Albino rats	Paracetamol induced hepatotoxicity	----------	----------	(Sanapala and Kumar, 2013)
Hypo-uricaemic	Hydro-alcoholic extract of leave	200 mg/kg p.o.	Allopurinol (10 mg/kg)	Normal control	Swiss Albino mice	Potassium oxonate induced hyper-uricaemia	----------	Xanthine oxidase inhibition due to phytoconstituents and posses anti-inflammatory and antioxidant activities	(Umamaheswari, 2007)
	Hydro-alcoholic extract of leaves	200 mg/kg p.o.	Allopurinol (10 mg/kg)	0.5 % CMC	Swiss Albino mice	Potassium oxonate induced hyper-uricaemia	Lowering of Xanthine oxidase/ xanthine dehydrogenase activities	The antioxidant activity of the fractions may also contribute to its hypo-uricemic and xanthine oxidase inhibitory activities	(Umamaheswari and Chatterjee, 2008b)

Larvicidal efficacy	Methanolic extract of leaves	1.0 ml	---------	Petroleum ether and polysorbate	*A. aegypti* L. and *C. quinquefasciatus* Say.	Larvicidal bioassay	---------	Cyclotide (small disulphide-rich peptide) showed toxic and growth retardant activity	(Rahuman and Venkatesan, 2008)
	Essential oils from leaves	50,100, 150 and 200 mg/L	----------	DMSO	*A. stephensi* Liston (Diptera)	Egg hatching inhibition assay	Essential oils increase the tendency of tracheal flooding and chemical toxicity in mosquito larvae	Embryogenesis processes and egg hatching are inhibited	(Rajkumar ,2011)
Mast cell stabilizing	Ethanolic extract of fruits	100, 125 and 150 mg/kg	Sodium chromoglycate (50mg/kg)	1 % Tween 80	Swiss Albino mice	Antigen induced degranulation	---------	---------	(Taur and Patil, 2011)
Testicular disorder	*C. indica* extract of leaves + MPHF extract of leaves	2 mg/0.2 ml olive oil/100 g	---------	Olive oil	Wistar rats	STZ induced diabetes	---------	Corrects testicular germ cell apoptosis	(Mallick, 2010)
	MTEC	60mg/d	Diabetic control	Citrate buffer	Wistar rats	STZ induced diabetes	---------	No toxic effects	(Mallick , 2007c)
Wound healing	Ethanolic and aqueous extract gel of fruits	---------	Framycetin sulfate cream (1% w/w)	Blank gel	Wistar rats	Excision wound model and incision wound model	---------	Improve vascularity and inhibit lipid peroxidation	(Bambal, 2011)

Table.3.List of patented formulation containing *C. indica*.

Title	Composition of Formulation or plants used	Activity	Reference
Production of natural food colorant from *C. indica*	*C. indica*	----------	(Dubasi, 2003)
Novel therapeutic extracts and molecules for degenerative conditions	*Aegle marmelos, Azadirachta indica, Catharanthus roseus, Curcuma longa, Emblica officinalis, Eugenia jambolana, Glycyrrhiza glabara, Gymnema sylvestre, Lagerstroemia speciosa, Morinda citrifolia, Ocimum sanctum, Pterocarpus marsupium, Stevia rebaudiana, Swertia chirata, Tinospora cordifolia, Trigonella foenum gracum, Withania somnifera, Cinnamomum zeylanicum, Garcinia combogia, Camellia sinensis, Vanilla fragrans or C. indica.*	Used in degenerative conditions like cardiovascular diseases, diabetes mellitus, hypertension, all types of cancers, arthritis pain, alzheimer's disease, multiple sclerosis or autoimmune diseases, asthma or allergies, osteoporosis or bone health, parkinson's disease, stress, disorders or diseases of the eye.	(Patel, 2005)
Herbal health protective and promotive nutraceutical formulation for diabetics and process for preparing the same	Comprises of herbs (*Gymnema sylvestre, Momordica charantia, Syzgium cumini, Pterocarpus marsupium, Trigonella foenum-graecum,* and *Cinnamomum tamala*); Optionally herbs (*Withania somnifera, C. indica, Pueraria tuberosa, Asparagus racemosus, Boerhaavia diffusa* and *Aegle marmelos*); Legumes (*Glycine max, Cicer arietinum, Phaseolus mungo, Phaseolus radiatus, Cyamompsis tetragonoloba, Mucuna pruriens*); Cereals (*Hordeum vulgare*); Pseudocereals (*Amaranthus hypochondriacus* and *Fagopyrum*	Antidiabetic and used as food supplement to ameliorate the general health of diabetics with optimum nutrients, helps control blood sugar level, reduction in fatigue, weakness, drowsiness, numbing effect, frequent urination, unusual thirst and hunger, weight loss, swellings on leg ankles, and burning sensation on feet. It also provides increase in sleep comfort.	(Pushpangadan and Prakash, 2003)
External active oxygen scavenging agent and antimicrobial agent containing plant extracts	*Artocarpus lakoocha* Roxb, *Streblus asper* Lour, *Blumea balsamifera* DC, *Pluchea indica* (L.) *Coccinia indica* Wight & Arnott, *C. grandis* Voigt, *Gloriosa superba* L, *Heliotropium indica, Hibiscus sabdariffa* L, *Mammea siamensis, Michelia champaca* L, *Murraya paniculata* Jack, *Mitragyna speciosa* (Korth.) Havil, *Morinda citrifolia* L, *Randia siamensis* Craib, *Solanum trilosatum* L, *Diospyros mollis* Griff, *Elephantopus scber* L, *Mesua ferrea* L., *Micromelum minutum* Seem, *Orthosiphon stamineus* and *Solanum violaceum* Ortega.	The preparation has antimicrobial effect, can inhibit tyrosinase activity, melanin generation and lipid peroxidation. It can be used for relieving pigmentation, whitening skin, treating dermatitis and preventing skin aging.	(Kondo, 2000)
Method and composition using Adipocleave for management of weight and blood sugar, and screening method	Adipocleave: *C. grandis* extract with cucurbitacins B and D as active ingredients, cephalandrol, cephalandrine A and B, and cucurbitacins.	Effective to maintain normal blood sugar and levels of nonenzymic protein glycosylation	(Subbiah, 2008)
The herbal formulation used for preventing and treating diabetes and diabetic microvascular complications	Salacia chinensis and atleast one other active constituents selected from *C. indica* and Hippophae rhamnoides and optionally additives in trace amounts.	Prevention of endothelial dysfunction in diabetes mellitus and diabetic micro-vascular complications	(Dubey, 2006)

Table.4.List of clinical trials conducted on *C. indica* for antidiabetic activity

Design	Sample	Intervention	Control	Outcome	Adverse effects/events	Reference
Double- blind; 2 parallel groups	32 type 2 (Diabetic patients); uncontrolled or untreated	1800 mg/d (freeze-dried powder from fresh leaves in tablets); for 6 weeks	Placebo tablet	Decrease Fasting blood glucose, Postprandial glucose	No side effects; no effect on liver/kidney function	(Khan, 1979)
Non-randomized; open-label	60 (both types of diabetes); untreated	50mgm/kg (dried pellets from fresh leaves); for 6 weeks	No treatment	Decrease Fasting blood glucose, Postprandial glucose and enzymes levels	Not reported	(Kamble, 1998)
Three-arm controlled groups	70 type 2 (Diabetic patients) uncontrolled	6g/d (dried pellets from fresh leaves); for 12 weeks	No treatment and Chlopro-pamide	Change was similar to that of conventional drug	Not reported	(Kamble, 1996)
Non-randomized; open-label prospective	70 type 2 (Diabetic patients)uncontrolled	6g/d (dried pellets from fresh leaves); for 6 weeks	No treatment	---------	No side effects	(Kuppurajan, 1986)
Double- blind phase I randomized	122 healthy volunteers controlled	20 g (with meal)	*Erythrina indica* 20 g	Decrease Postprandial glucose and Improved glucose tolerance	Nausea, headache and drowsiness	(Munasinghe, 2011)
Random Double- blind	16 type 2 (Diabetic patients) uncontrolled or untreated	Homogenized and freeze-dried powder from fresh leaves in tablets; for 6 weeks	Placebo tablet	Improved glucose tolerance	No side effects	(Khan, 1980)
Double blind; randomized	60 type 2(Diabetic patients); controlled	1g of aqueous alcoholic extract (Freeze-dried powder from fresh leaves and fruits in tablets); for 90 days	Maltodextrin capsule (500 mg)	Decrease Fasting blood glucose, Postprandial glucose and action independent of energy/ food intake or weight loss	Very minor side effects	(Kurpad and Raj, 2008)
Double blind; randomized	60 type 2(Diabetic patients); controlled	Two 500 mg capsule daily; for 90 days	Maltodextrin capsule (500 mg)	Decrease Fasting blood glucose, Postprandial glucose	Perspiration, excessive hunger and dizziness	(Kuriyan, 2008)

Abbreviations:

BHT - Butylated hydroxy toluene
OGTT - Oral glucose tolerance test
STZ - Streptozotocin
UPEC - Uropathogenic *E.coli*
ESBL - Extended spectrum of beta lactamase
DMSO - Dimethyl sulfoxide
STZ - Streptozotocin

HDLC - High density lipoproteins cholesterol
HFD - High-fat diet
EAC - Ehrlich ascites carcinoma
ULHP - Ulcer producing *Helicobacter pylori*
- Aqueous-methanol extract of *Musa paradisiaca, Tamarindus indica, Eugenia jambolana* and *Coccinia indica*
MPHF`- *Musa paradisiaca* hexane fraction
PPARα - Peroxisome proliferator-activated receptor-α
TII - Testosterone induced infertility.

CONCLUSION

Cephalandra indica is widely prescribed for the treatment of diabetes in Ayurvedic system of Medicine. Even fruits of the plant are consumed as vegetable in many parts of North India. The whole plant is also used traditionally in the treatment of various ailments. Till date, twenty six constituents have been isolated from various parts of the plant. Triterpenoids, steroids, carotenoids and flavonoid constitute major classes of phytoconstituents. Amongst various phytoconstituents, only triterpenoids have been suggested to possess most of pharmacological activities of *C. indica*. The plant has been evaluated exhaustively for various pharmacological activities and reported to possess anti-inflammatory, antinociceptive, antipyretic, antiulcer, antimicrobial, antiobesity, antioxidant, antistress, antidiabetic, antidyslipidemic, antitussive, antifungal, anticancer, antianaphylactic, antihistamininc, hepatoprotective, hypouricaemic, Larvicidal, mast cell stabilizing, wound healing and fertility inducing activities. A through scrutiny of literature revealed a startling fact that crude uncharacterized extracts of *C. indica* have been employed in these pharmacological activities.

No systematic work has been carried out to isolate bioactive constituents responsible for afore-mentioned bioactivities. These observations suggest that detailed investigations are needed on *C. indica* with a view to isolate bioactive constituents, and to standardize the plant on the basis of isolated bioactive markers. Six formulations containing *C. indica* as one of the ingredients have been patented. Out of these, four patents have been employed in the treatment of diabetic complications. Eight clinical trials (368 diabetic patients and 122 healthy volunteers) have been conducted to observe antidiabetic potential of *C. indica*. The plant showed beneficial effects in diabetic patients in all clinical trials. Further, *C. indica* has been found to be safe in all toxicity studies.

Finally, it is concluded that *C. indica* emerged as a good source of bioactive constituents which could be developed as efficacious and safer drugs.

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