

Traditional uses, phytochemistry and pharmacology of *Croton bonplandianum* - A review

Review Article

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Abstract

Croton bonplandianum L. (Euphorbiaceae) has been widely used in traditional medicine for a wide range of ailments like jaundice, acute constipation, abdominal dropsy, dysentery, external wounds, hypercholesterolemia, hypertension, and infectious disorders. This aim of the present study is to comprehend the fragmented information available on the traditional uses, phytochemistry, pharmacology of *C. bonplandianum* to explore its therapeutic potential and future research opportunities. All the available information on *C. bonplandianum* was collected via electronic search (using Google Scholar, Scopus, Pubmed, and SciFinder) and a library search. Traditional uses of *C. bonplandianum* are recorded throughout the Asia and South America, where it has been used for about various types of disease. The research on bioactive compounds had led to the isolation of diterpenes, alkaloids, flavonoids, steroid glycosides, volatile components and some other classes of secondary metabolites from *C. bonplandianum*. Extracts and bioactive constituents of *C. bonplandianum* exhibited a wide range of pharmacological activities like, hepatoprotective, anti-inflammatory, antifungal, wound healing, antimicrobial, antioxidant, and anti-tumor. *C. bonplandianum* emerged as a rich source of traditional medicine for the treatment of various disease although various *in vitro* and *in vivo* studies validated its traditional medicinal uses.

Key Words: *Croton bonplandianum*, Phytochemistry, Pharmacology, Wound healing Hepatoprotective.

Introduction

Since long ago plants are the primary source of food and medicine for human (1). Four billion people or about 80% of the world's population uses herbal medicine today as part of health care. Different cultures use herbs located in their geographical locations for curing common illnesses (2, 3). They have been successful to a certain extent and over many centuries some of the herbal cures have proved to be far more useful than allopathic drugs. It is a natural form of healing or alternative therapy where medicinal plants are used in the form of extracts, decoctions, or powder to cure ailments or diseases of human beings and in some cases of animals too (4, 5). Failure of some allopathic drugs and its side effects have prompted some patients to go back to ancient healing methods which use herbal medicines to give relief (6, 7).

Croton bonplandianum (Euphorbiaceae) is the most popular member of the Croton species and is known by over several names (Appendix A). *C. bonplandianum* is native to the Southern Bolivia, Paraguay, and Northern Argentina. Due to the

resemblance of the leaves and flower cymes to that of Tulasi (*Ocimum sanctum*), *C. bonplandianum* is often called Ban Tulsi (jungle tulsi). The plant is growing on the roadside, bank of the river, wastelands, and yards. *C. bonplandianum* is a small annual herb, growing up to 28 inches tall and 24 inches wide. Alternately arranged leaves, 3-5 cm long, are lance-shaped, with a toothed margin. The leaves of *C. bonplandianum* is leathery, smaller size, less pigmented due to lack of light and are mainly colourful under bright light. Greenish fruits have a 5 mm oblong capsule, with a warty surface. Flowers have tiny, peach colour, 12 racemes, tiny globe-shaped flower buds arranged in upright spikes and also have 5 sepals and 5 petals and numerous long stamens protruding out. The flowering season of *C. bonplandianum* is September to November (8-10). In the present study, an attempt is made to present the traditional value, phytochemistry and pharmacology of *C. bonplandianum* in order to highlight research gaps and provide an area requiring further research works on the *C. bonplandianum*.

Appendix A. Common names of *C. bonplandianum*

S. No.	Region / Language	Name
1	English	Ban tulsi
2	Hindi	Kala Bhangra
3	Assamese	Bana Tulasi
4	Bengali	Bon-tulsi
5	Kannada	AlpaBedhiSoppu
6	Irula	Soraikuruvi poo

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7	Tamil	Reilpoondu, Rail Pindu, Aathuppoondu
8	Telugu	B h o o t h a l a b h a i r i , galivanachettu, galivanamokka
9	Bodo	Titabahaphisa
10	Nepali	Mirchahiya Jhaar
11	Others	Soraipoo, Seemainai Pundu, Ban Tulsi

Traditional uses

The origin of this plant was found to be in South America and Asia. Due to antiseptic properties, *C. bonplandianum* is used to treat skin diseases like ringworm infection, body inflammation, and respiratory disorders. Bark and roots of *C. bonplandianum* are cholagogue and purgative (11-14). Leaves of *C. bonplandianum* is used to treat cuts and wounds on the body to stop the bleeding, cholera, and venereal sores. The seeds of this plant are used in the treatment of internal abscesses, liver disorders, acute constipation, and abdominal dropsy. Fresh juice of *C. bonplandianum* is used in headaches (12, 15). In the rural areas of Malda, West Bengal, *C. bonplandianum* is grown abundantly and is used as both a fuel and a detergent. The stems and branches of *C. bonplandianum* are used as fuel. Then the ash is collected and kept in a bottle for five or six days. The ash is put in warm water and used as a detergent for cleaning cotton garments. In the Rural area of West Bengal, India ethnic groups are using roots and leaves of *C. bonplandianum* against snake venom and high fever (16).

Phytochemistry

The methanol extracts of *C. bonplandianum* leaves showed the presence of alkaloids, flavonoids, steroids, resins, phenols, and saponins (17). A 3 α -hydroxy-urs-12,15-dien (triterpenoid of ursane skeleton) was isolated from the methanol extracts of the root of *C. bonplandianum* along with two known triterpenic acids, oleanolic acid, and ursolic acid. While β -sitosterol was isolated from methyl acetate fraction (16). The GC-MS analysis of ethanolic latex, leaves, and fruit extract of *C. bonplandianum* showed the presence of 16-Hexadecanoyl hydrazide, Myo-Inositol, 2-C-methyl, 9, 12, 15-Octadecatrienoic acid, methyl ester (z,z,z)-, 2-Hexen-1-ol, 2-ethyl (18). In addition, GC-MS analysis of essential oil isolated from the aerial parts of *C. bonplandianum* showed the rich source of sesquiterpene hydrocarbons along with the presence of β -caryophyllene, germacrene D, borneol, Z- β -damascenone, isobornyl acetate, α -humulene, germacrene A and caryophyllene oxide (19). The ethanolic latex extract of *C. bonplandianum* showed the existence of 2-C-methylmyoinositol, mequinol, 4-methylphenol, 1,2,3-benzenetriol, 3-methylquinoline, n-hexadecanoic acid, and octadecanoic acid (20). The dichloromethane extract of *C. bonplandianum* the presence of n-pentacosanyl-n-nonadeca-7'-en-9'- α -ol 1'-oate, n-tridecanyl n-octadec-9,12-dienoate, nonacosylhexadecanoate, heptacosanoic acid, 1,3,5-trihydroxy-2-hexadecanoylamino- (6e,9e) heptacosdiene, cumarin, betulin, stigmaterol, and 3,5-

dimethoxy 4-hydroxy cinnamic acid (21). The GC-MS analysis of chloroform extract of *C. bonplandianum* leaves showed the presence of Z-5-Nonadecene, Cyclotetracosane, N-Nonadecenol-1, Cycloecosane, 3-Eicosene, Z-8—Hexadecene, 6-5Heptadecenal, Phenol,2,4-bis(1,1-dimethyl) (22).

Pharmacological reports

Antibacterial activity

Alkaloid leaves extract of *C. bonplandianum* its isolated compounds (sparsiflorine and crotsparine) were performed for antibacterial activity against *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*. The alkaloid leaves extract of *C. bonplandianum* showed activity particularly against the *S. aureus* and *P. aeruginosa* while the isolated compound crotsparine and sparsiflorine were found inactive and moderate activity respectively against *S. aureus* and *P. aeruginosa* (23). Methanolic leaves and fruits extract of *C. bonplandianum* showed the highest antimicrobial activity against gram positive bacteria while acetone extract of leaves showed the highest activity against gram negative bacteria (24). At 125 mg/mL concentration, the methanolic extract of *C. bonplandianum* possessed antimicrobial activity against *P. aeruginosa* (25). *In vitro* assay, the antibacterial effect of fresh latex of *C. bonplandianum* was investigated against the isolated bacterial pathogens from pus cells causing wound infections like *P. aeruginosa*, *S. aureus*, *E. faecalis*, *E. aerogenes*, and *E. coli* by well diffusion method. The fresh latex of *C. bonplandianum* exhibited maximum inhibitory activity against *E. coli* and *E. faecalis* while aqueous and ethanolic extracts of the latex of *C. bonplandianum* possessed maximum inhibitory activity against *E. aerogenes*. The ethanolic and benzene leaves were found to be maximum inhibitory activity against *S. aureus*. The chloroform extract of fruits of *C. bonplandianum* showed the highest inhibitory activity against *E. coli* (26). Antibacterial activity of methanolic fraction of leaves of *C. bonplandianum* was tested by Minimum Inhibitory Concentration method and showed antibacterial activity against various microorganisms (27). Petroleum ether, chloroform, acetone, and methanolic leaves extracts of *C. bonplandianum* showed antimicrobial potency against *S. aureus*, *Pseudomonas sp.*, *E. coli*, *Bacillus subtilis*, and *Salmonella typhi* (17).

Antifungal activity

3 α -hydroxy-urs-12,15-dien was exhibited antifungal property against *Calletotrichemecamellie*, *Fussarium equisitiae*, *Alternaria alternate*, *Curvularia aeragrostidies*, and *Colletrichum gleosporoides* fungal pathogens (16). The methanol extracts of *C. bonplandianum* leaves exhibited the highest inhibition against the *Mucor sp.*, *Aspergillus flavus*, *Rhizopus sp.*, and *Pencillium sp* (17). The latex of *C. bonplandianum* exhibited absolute toxicity inhibiting the mycelial growth of *Microsporium gypsrum* and *Trichophyton mentagrophytes* (28). The antifungal activity of chloroform, acetone and methanolic extract of leaves

of *C. bonplandianum* were showed antifungal activity against *Aspergillus flavus*, *Candida albicans*, *Microsporiumfulvum*, and *Trichophyton mentagrophytes* (29).

Antidiabetic activity

Cumarin isolated from dichloromethane extract of *C. bonplandianum* exhibited significant α -glucosidase inhibitory activity in a concentration-dependent manner (IC₅₀=23.0 to 26.7 μ g/mL) in comparison with acarbose (positive control, IC₅₀=38.2 μ g/mL) (21). The chloroform fraction of leaves of *C. bonplandianum* showed the rich number of polyphenols, flavonoids, and tannins and also exhibited effective inhibitory activity against α amylase (IC₅₀=95.78 μ g/mL) and α glucosidase (IC₅₀=126.81 μ g/mL) (22). The α -amylase inhibitory activity of ethanolic leaves extracts of *C. bonplandianum* was evaluate against porcine pancreatic amylase. The ethanolic extract showed significant α -amylase inhibitory activity (IC₅₀=17.22) (30).

Antioxidant activity

Methanolic extracts of *C. bonplandianum* showed DPPH and hydroxyl radical scavenging activities (31). The hydro-methanolic extract of *C. bonplandianum* leaves showed potent free radical scavenging capacity (32). The chloroform fraction of *C. bonplandianum* leaves showed free radical scavenging activity, reducing power capacity, and nitric oxide scavenging assay. In addition, the chloroform fraction of *C. bonplandianum* leaves showed higher antioxidant activity as compared with n-hexane, ethyl acetate fraction (22). The ethanolic leaves extract of *C. bonplandianum* showed good free radical scavenging activity (IC₅₀=170.3 μ g/mL) while the total antioxidant was found to be 214 \pm 0.20 μ g/mL (30). Ethanolic extract of dried leaves of *C. bonplandianum* showed free radical scavenging and nitric oxide scavenging activity (33).

Hepatoprotective activity

The hepatoprotective activity of hydro-methanolic extract of *C. bonplandianum* leaves extract showed the highest hepatoprotective activity by ameliorating haloalkane induced liver injury in the murine model. Silymarin was used as a standard drug. The increased level of biochemical activity was significantly restored by hydro-methanolic extract of *C. bonplandianum* treatment. A molecular docking study revealed that the compound α -amyrin present in the leaves extract of *C. bonplandianum* has better capability to ameliorate hepatocellular damages than the positive control Silymarin (32).

Wound healing activity

Ethanolic and aqueous extract of dried leaves of *C. bonplandianum* is prepared with 10% ointment and topically applied to experimental wounds in rats. Both extracts showed a positive effect on wound healing, with a significant increase in wound contraction (33). Ethyl acetate, chloroform, benzene extracts of leaves of *C.*

bonplandianum possessed haemolytic activity towards human erythrocytes (34). Herbal preparations from fruits, leaves, and latex of *C. bonplandianum* were evaluated for wound healing activity in Wistar albino rats. The increased levels of collagen content and wound contraction rate were observed in fruits, leaves, and latex of *C. bonplandianum* treated rats. Increased levels of superoxide dismutase and catalase and reduced level of lipid peroxidation were found in both serum and granulation tissue of wounded rats treated with fruits, leaves, and latex of *C. bonplandianum*. The wounded rats treated with the latex of *C. bonplandianum* showed more antioxidant activity, significant wound contraction rate, and a higher level of collagen content as compared to fruits, and leaves of *C. bonplandianum* treated rats (35).

Antitumor activity

Antitumor activity of twigs methanolic extract of *C. bonplandianum* was evaluated using potato disc and radish seed paradigms. The methanolic extract of *C. bonplandianum* (10, 100, and 1,000 ppm) inhibited the tumor formation ability of agrobacterium on potato disc. By reduction in the root length and percentage of seed germination throughout radish seed bioassays confirmed the antitumor activity of *C. bonplandianum* (36).

Anti-inflammatory activity

The ethanolic extract of *C. bonplandianum* leaves was evaluated in Human Red Blood Cell Membrane. Ethanolic extract (200mg/mL) prevented hypotonicity-induced Human Red Blood Cell Membrane lysis to an extent of 83.2% (37). The anti-inflammatory properties of hydro-alcoholic leaves extract of *C. bonplandianum* was evaluated carrageenan induced paw edema model in rats. Hydro-alcoholic leaves extract of *C. bonplandianum* produced significant inhibition of carrageenan-induced rat paw edema after a period of 4 h (38).

Toxicology

The cytotoxic and biochemical investigation of water leaves extract of *C. bonplandianum* (3.25, 4.65, and 6.97 mg/kg, b.w.) was evaluated in male rats. To test ameliorative effects, the extract was mixed with cyclophosphamide (0.2 mg/gm, b.w.) and then injected in animals. The water leaves extract of *C. bonplandianum* showed insignificant amelioration however, differences in serum LDH isoenzymes, ALP, SGOT, SGPT activities, and bilirubin were found notable (39). Methanolic extract of *C. bonplandianum* showed in vitro cytotoxic activity (LD₅₀ = 115.76 μ g/mL) (31).

Conclusion

Overall, this study presents the connections among traditional practices, bioactive constituents, pharmacological activity, and toxicity. The ethnomedicinal survey showed *C. bonplandianum* to be a sacred and essential medicinal herb used for the

ailments of jaundice, acute constipation, abdominal dropsy, dysentery, external wounds, hypercholesterolemia, hypertension, and infectious disorders in Asian countries. Experimental *in vitro* and *in vivo* studies carried out on the fruits, latex, root, aerial parts, leaves, and bioactive components of *C. bonplandianum* offer pragmatic support for its several traditional medicinal uses. Current pharmacological studies have been focused on assessing the antidiabetic, antimicrobial, antifungal, antitumor, wound healing, anti-inflammatory, antioxidant and hepatoprotective activities. Latex and leaves of *C. bonplandianum* depicted interesting biological efficacies, which can be further explored to utilize them as a treatment in future clinical application. Besides, more in-depth researches are required to elucidate the pharmacodynamic, pharmacokinetics, and specific pathways of *C. bonplandianum* to lead their clinical uses and develop efficient medicines.

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