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CROTON *BONPLANDIANUM* BAILL-A REVIEW ON TRADITIONAL USES, PHYTOCHEMISTRY AND PHARMACOLOGICAL STUDIES.

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ABSTRACT

Commonly Crotons are well-known foliage plants. From Euphorbiaceae or spurge family, the plant *Croton bonplandianum* Baill is a heteroicous exotic weed. It is a perdurable herb and normally 30-40 cm in height, with whorled ranches which grows in sandy clay soil, found in all situations, railway lines and roadsides, in open and follow fields in India. Due to the resemblance of the leaves and flower cymes to that of Tulsi, *Croton bonplandianum* Baill is often called *Ban Tulsi* (Jungle tulsi). The parts of plant are widely used in traditional system of medicine such as hepatoprotective, swelling of the body, cure against ring worms and skin disease, antihypertensive, antioxidant, wound healing, antifungal, antimicrobial, antidiabetic, antitumor, anticancer, acute constipation, abdominal dropsy, internal abscesses, antifertility, antispasmodic, antiseptic, antidote, analgesic, repellent property against insects, nematicide, anticoronary, anti-inflammatory, larvicidal activity, antihelmentic, this is also used for treatment of cholera, boils, bowel complaints, chicken pox, diarrhoea, dysentry, eye diseases, cold and coughs, epilepsy, gastric disorders, insanity, jaundice, liver complaints, scurvy, sprains, malaria, rheumatism, and so on. This plant is also considered as chologogue and purgative. The fresh juice of the plant is used against headache. Due to its slow rate of conventional multiplication, the plant is very high in

demand. In this review report we collected information related to taxonomy, monographs, distribution, morphology, phytochemistry, traditional uses and pharmacological studies of *Croton bonplandianum* Baill plant in details.

KEYWORDS: *Croton bonplandianum* Baill, traditional uses, phytochemistry, pharmacology.

INTRODUCTION

Taxonomy

Kingdom	:	Plantae
Subkingdom	:	Tracheobionta
Infrakingdom	:	Streptophyta
Superdivision	:	Spermatophyta
Division	:	Magnoliophyta
Class	:	Magnoliopsida
Subclass	:	Rosidae
Order	:	Malpighiales
Family	:	Euphorbiaceae
Subfamily	:	Crotonoideae
Tribe	:	Crotoneae
Genus	:	*Croton L.*
Species	:	*Croton* bonplandianus

Synonyms

Croton bonplandianus (BAILL), Croton pauperulus**,** Croton rivinoides**,** Croton sparsiflorus Morong.

Monographs

English - Bonpland’s croton

Hindi - Kala Bhangra , Ban tulsi

Odiya- Bana tulashi

Telugu - Bhoothalabhairi, galivana chettu

Tamil - Rail Poondu, Reilpoondu,Attupuntu

Marathi - Krotona, Krotona tela

Kannada - Alpa bedhi soppu, nela bedi soppu

Bengali - Bon tulshi

Nepali - Mirchaiya Jhaar

Poortuguese - Croton (Brazil)

Spanish - Tupucharo

French - Croton de Bonpland

Irula - Soraikuruvi poo

Morphology

The plant *Croton bonplandianum* Baill is a small perdurable herb, 30-40 cm in height, can be grow in any situations like sandy clay soil, railway lines, read sided areas, irrigation canal bank, open and follow fields in India. September to December months time for flowering and fruiting. The plant is a common herb, found in pan-tropic , partly subtropic areas and worldwide. It has been reported that *Croton bonplandianum* Baill. is native to the Southern Bolivia, Paraguay, Southwestern Brazil, Northern Argentina, Bangladesh, Southern India and Pakistan[7,8]. In Pakistan, this plant is found near Khyber, Attock, Wah, Rawalpindi, Sargodha, Gujarat, Sialkot, Lahore and Karachi.

Croton *bonplandianum* is a lactiferous, green herb, growing up to 1-2 ft. long, leaves of the plant are simple, petiolate, alternately arranged, 3-5 cm long, lance shaped with toothed margin. Flowers are small,white, unisexual,, contain 5 sepals, 5 petals, and numerous long stamens protruding out. Fruits are deciduous with two valved cocci, 5 mm oblong capsule having warty surfaceseeds are small,smooth and albuminous. Bark and roots of *C.bonplandianum* are alternative and chologogue. It bears female flowers in inflorescences which are arranged in a regular pattern. The stem is cylindrical, branched, woody, light brown in color, odourless and bitter in taste. Roots are small, dark brown to black in color, cylindrical, odourless and bitter in taste. Histological observations revealed the presence of discontinuous layer of lignified sclerenchymatous cells (stone cells), paracytic stomata, stellate trichomes, xylem with scalariform thickenings and libriform fibres.

Phytochemistry

Croton bonplandianum Baill contains Primary metabolites such as carbohydrates, amino acids, proteins, resin and chlorophylls while secondary metabolites are alkaloids, saponins, steroids, flavonoids, tannins, terpenoids and phenolic compounds. Name of some important compounds which are responsible for produce particular biological activity derive from different plant parts are collected from review articles.

- Plant and leaves contain alkaloids, sparsiflorine, crotoflorine, crotsparine, crotosparinine, proporphine,isoquinoline dionone, N-methylcrotsparine and N-methylcrotsparinine
- Leaves and stem contains β-sitosterol and taraxerol, vomifoliol, uric acid and tetrahydroglazievine. Leaves also contain Rutin. (C_{18} H $_{36}$O $_{19}$). 16-Hexadecanoyl hydrazide (88.69%), 1,2-Benzenedicarboxylic acid, diisooctyl ester (5.56%), 2-Piperidinone, N-[4-bromo-n-butyl] (2.56%), Phthalic acid, bis (7-methyloctyl) ester (1.80%) and Phytol (1.39%) were found in leaf.
- The seed of *Croton bonplandianum* contains diterpines, phorbol ester, including 12-orthotrideconeoly-phorbol-13-acetat (TPA) and myristoyl phorbol acetate (MPA).
- The roots in addition to ß-sitosterol contain phenolic quinonoid alkaloid norsinoacutine and 3-methoxy-4, 6-dihydroxy morphinan-dien-7-one. An unusual finding of this species is the hyper accumulation of copper in it.
- The phytocompounds mequinol (0.74%), 4- methylphenol (6.86%) and 3-methylquinoline (0.44%) are present in the latex of *C. bonplandianum*.
- The fruits of *C. bonplandianum* showed the presence of fifteen major phytocompounds including 9,12,15-Octadecatrienoic acid, methyl ester (z,z,z)- (41.81%), Diazoprogesterone (19.03%), Decanoic acid, ethyl ester (4.86%), 1- Propene, 2- nitro-3-(1-cyclooctenyl) (4.58%) and 6,9,12- Octadecatrienoic acid, 13-Tetradece-11- yn-1-ol (3.47%).

Traditional Uses

Croton bonplandianum Baill used traditionally for curing different types of health related problems: gastro intestinal disorders (cholera, boils, bowel complaints, diarrhoea, dysentery, insanity, acute constipation, abdominal dropsy, internal abscesses), respiratory diseases (cold and cough , lungs infection, bronchitis, asthma), hepatic problem (jaundice, liver complaints), analgesic (reduce pain, sprains, headache), it is also used for the treatment of scurvy, malaria, chicken pox, eye diseases**,** skin diseases**,** rheumatism, epilepsy and many other diseases. For Chologogue and purgative this is the most important plant. From literature it has been recognized and reported that the leaves extract was used for treatment of cancer, venereal diseases, ulcer and so on.

Pharmacological Activity

V. Vennila et.al. (*Article no.IJBcRR.2015.022)* carried out research on phytochemical constituents from leaves of *Croton bonplandianum* Baill. By chromatographic technique and

mass spectroscopic analysis the phytoconstituents are isolated and identified. The GC-MS results showed that the presence of twenty one major compounds in different parts of *C. bonplandianum.* Among these Six phytocompounds such as quercetin-3-O-rutinoside (rutin) 16-Hexadecanoyl hydrazide (88.69%), 1,2-Benzenedicarboxylic acid, diisooctyl ester (5.56%), 2-Piperidinone, N-[4-bromo-n-butyl] (2.56%), Phthalic acid, bis (7-methyloctyl) ester (1.80%) and Phytol (1.39%) were found in leaf. The latex of *C. bonplandianum* showed the presence only one phytocompound Myo-Inositol, 2-C-methyl (30.8%). The fruits of *C. bonplandianum* showed the presence of fifteen major phytocompounds including 9,12,15-Octadecatrienoic acid, methyl ester (z,z,z)- (41.81%), Diazoprogesterone (19.03%), Decanoic acid, ethyl ester (4.86%), 1 Propene, 2- nitro-3-(1-cyclooctenyl) (4.58%) and 6,9,12-Octadecatrienoic acid, 13-Tetradece-11- yn-1-ol (3.47%).

Wound healing activity

S. Divya et.al. 2011 studied wound healing effect of Ethanolic and aqueous leaves extract of *Croton bonplandianum* by preparing 10% Ointment and applied topically on wound in experimental rats. The plant showed a definite, positive effect on wound healing, with significant increase in wound contraction. The efficacy of this plant in wound healing may be due to its chemical constituent rutin. Rutin, also called rutoside, quercetin-3-O-rutinoside and sophorin,isthe glycoside combiningthe flavonol quercetin and the disaccharide rutinose (α-L rhamnopyranosyl-(1→6)-β-D-glucopyranose) [1, 2, 3]. *G. Selvaraj et.al,* 2016, MMPs (Matrix metalloproteinase) are proteolytic and matrix degrading enzymes play multiactions in the pathology of the nervous system. Matrix metalloproteinase level was increased in diabetic patients who simultaneously causes inflammation, atherogenic effect and increased the tumour necrosis α-factor[4]. In diabetic foot ulcer, the inflammatory response accelerated the synthesis of matrix metalloproteinase to degrade the ECM fibrous structural proteins, which decreased the blood supply, delayed wound healing, atherosclerosis, and gangrene of the foot finally leading to amputations[5]. Rutin as an effective matrix metalloproteinase inhibitor and most important phyto constituent for wound healing. *Mittal et al.* 2013, Wound healing is an anabolic process that requires both energy and nutritive substrates. It is reported that serum albumin level of 3.5 gm/dl or more is necessary for proper healing [20]. Protein is essential for collagen synthesis on wound site. A state of malnutrition may provide an inadequate amount of protein and this can result in the decreased rate of collagen synthesis wound tensile strength or an increased chance for infection [6, 7].

Antiseptic

Croton bonplandianum Baill (Entire plant) in Argentina although it has gotten its way into Kenya where it is found as a common weed and used as antiseptic for treatment of wound healing and other skin diseases[8].

Antioxidant activity

It has been found that many plants or plant-derived compounds possess high levels of antioxidant properties. *Muhammad Naeem Qaisar et.al* 2013, Antioxidant activity of the Dichloromethane and methanol extracts *Croton bonplandianum* were measured in this assay as ability to scavenge stable DPPH radicals according to[9]. The activities of antioxidants have been attributed to various mechanisms including prevention of chain initiation, decomposition of perox- ides, radical scavenging and reducing capacity[10]. Manal A. Ibrahim *et al.,* DPPH stable free radical method is an easy, rapid and sensitive way survey to the anti oxidant activity of specific compound or plant extracts[11]. Propyl galate was used as standard compound. The highest radical scavenging activity was showed bye thanolic extract (89%) whereas chloroform and ethylacetate extracts were showed a weak presence with a value of 16% and 29% respectively. Ethanolic extract had high antioxidant efficacy. *Aggarwal Sushma et.al* Free-radical-scavenging enzymes are cytoprotective enzymes that have an essential role in the reduction, deactivation and removal ofROS as well as in regulating the wound healing process. Hence, if the plant or its extract having antioxidant potentials could be a good therapeutic agent for accelerating the wound healing process and could be expected to promote epithelisation by controlling oxidative stress.[12],[13]. Riti Thapar Kapoor, 2015, The leaf extract of *Croton bonplandianum* was mixed in the aqueous solution of the silver nitrate; it started to change in colour from green to light brown. According to Parashar et al[14]. the change in colour was due to the excitation of surface plasmon vibrations, which indicated the formation of silver nanoparticles. This change in colour from green to light brown may be due to the reduction of silver nitrate into silver nanoparticles**.** According to Ganesan et al.[15] secondary metabolites such as alkaloids, terpenoids, phenolic compounds and flavonoids are responsible for the formation and stabilization of the silver nanoparticles. The phytochemicals present in the leaf extract of *Croton bonplandianum* may act as the surface active stabilizing molecules for the synthesis of silver nanoparticles. Reduction of Ag+ ions into silver nanoparticles by using the aqueous leaf extracts of *Croton bonplandianum*, shows that this plant play a significant role to increase antioxidant potency. G.Keerthana *et.al.2013* Oxidative stress plays a pivotal role in the development of diabetes

complications. Free radicals are formed disproportionately during diabetes due to glucose oxidation and the subsequent oxidative degradation of glycated proteins[16]. In addition, the diabetic patients have enhanced cellular oxidative stress and reduced antioxidant potential leads to defective antioxidant status. Evaluation of antioxidant capacity which showed good DPPH scavenging activity due to the presence of some phytoconstituents like E-15 Heptadecanol, 1-Nonadecene, 5-Eicosene, Asparagine, 2-Tetradecene[17].

Cytotoxicity activity

Muhammad Naeem Qaisar et.al. 2013, The brine shrimp lethality test (BST) was used to predict the presence, in the extracts, of cytotoxic activity. The Dichloromethane and methanol extracts were tested for brine shrimp lethality. The mean percentage mortality was observed. Etoposide was used as a standard test drug. In the brine shrimp lethality test methanolic extracts was toxic with a LD50 value of Dichloromethane extract was not toxic. Bioactive compounds are often toxic to shrimp larvae. Hence, *in vivo* lethality to shrimp larvae can be used as a rapid and simple preliminary monitor for bioactive com- pounds during the isolation of natural products. The eggs of the brine shrimp *Artemia salina* (Leach) are readily available as fish food in pet shops. When placed in artifi- cial sea water, the eggs hatch within 48 hours, providing large numbers of larvae. These tiny shrimp larvae have been extensively used as a tool to monitor the cytotoxic- ity of samples under study.[18].

Antitumor activity

Islam *et.al*. 2010. Methanol twigs extract of *C. bonplandianum* Baill plays an important role in antitumor activity.It was shown that tumor formation was observed when *Agrobacterium* strains alive on living potato disc. The potato discs were often damaged due to the contamination and other physiological factors when there was no tumor formation. Thus successful attachment of *Agrobacteirum* on living potato disc is needed for antitumor test of plant extracts. Tumor formation ability of *Agrobacterium* was distinctly inhibited on potato disc in presence of methanol extract. Tumor inhibition was increased with the increasing of concentrations of plant extract. The bioactive compound of this plant may play an important role in developing antitumor drugs for human beings, as there is a similarity between human and plant tumor formation mechanism. This is a rapid, inexpensive, in-house, general bioassay which has been developed for screening, fractionation and monitoring of physiologi- cally active natural products[19-23].

***In-vitro* alpha amylase and alpha glucosidase inhibitory activity**

In-Vitro Alpha Amylase inhibitory activity

Sumathy et al. 2013 Ethanolic extract of the leaves of *Croton bonplandianum* Baill showed potent alpha amylase inhibitory activity indicating the presence of potential inhibitors such as Tannins, phenols, flavonoids etc. These alpha amylase inhibitors are also called as starch blockers since it prevents or slows the absorption of starch in to the body mainly by blocking the hydrolysis of 1, 4-glycosidic linkages of starch and other oligosaccharides into maltose, maltriose and other simple sugars[24].

In-Vitro Alpha Glucosidase inhibitory activity

Muhammad Naeem Qaisar *et. al.* 2014, elevated postprandial hyperglycemia (PPHG) is one of the risk factors[25]. PPHG elevated by the action of α- glucosidase and α-amylase. Inhibition of these enzymes plays a major role in managing PPHG in diabetic patients. Inhibition of α-glucosidase enzyme activity leads to a reduction in disaccharide hydrolysis which has beneficial effects on glycemic index control in diabetic patients[26, 27]. Several α-glucosidase inhibitors have been isolated from medicinal plants for the development of new drugs with increased potency and lower adverse effects than existing drugs[28]. Methanol extracts of *Croton bonplandianum* showed the maximum alpha glucosidase inhibitory activity. The plants may essentially contain herbal bioactive compounds flavonoids or phenolic compounds which may inhibiting enzyme activity.

Antimicrobial activity

M.V. Jeeshna *et. al. 2011,* Antimicrobial activities of various crude extracts of *C. bonplandianum* Baill may also be explained due to the presence of many kinds of secondary metabolites or compounds like glycosides, saponins, tannins, flavanoids, terpenoids, alkaloids (Okeke et al. 2001; Shamala Gowri and Vasantha 2009)[29]. These antimicrobial activities against bacteria and fungi confirm the presence of broad spectrum antibiotic compounds in the leaves of this species (Srinivasan et al. 2001). The inhibitory activity of the methanol extract of the leaf part of *C.bonplandianum* Baill was also considerably higher against the fungi (*Rhizopus sp.)* tested in comparison with other extracts and also methanol extract activity was higher against bacteria tested (*Salmonella typhi*)[30]. M. Mishra et.al. *Croton bonplandianum* Baill leaves were extracted in different solvents of increasing polarity and their antimicrobial response were examined against skin disease (dermatophytosis, aspergillosis & candidiasis) causing fungi including *Trichophyton mentagrophytes* (MTCC 7250), *Microsporum fulvum* (MTCC 7675), *Aspergillus flavus* (MTCC 8636) and *Candida*

albicans (MTCC 227). Chloroform extract showed boosting effect against Dermatophytes. Antibacterial activity revealed that the acetone extract showed strong activity against MRSA (MTCC 96). The leaf was screened for phytochemistry and was found to contain flavonoids, terpenoids, alkaloids and glycosides etc.[31-33]. Mohammad Nafees Iqbal et.al. The antibacterial activity of leaf extracts of *C. bonplandianum* was tested against *Escherichia coli, Klebsiella pneumoniae* and *Staphylococcus aureus* using disc diffusion method and zone of inhibition was detected in mm. The chloramphenicol (30mg/ml) was used as positive control for the analysis. All the positive results indicate moderate antibacterial activity against microbes tested. Aqueous leaf extracts showed moderate inhibition (05-08mm) against all tested microbes. The methanolic leaf extract was found to inhibit the growth of *E. coli* and *S. aureus* but not *K.pneumoniae.* The antibacterial activity of medicinal plants is due to the presence of secondary metabolites.

The leaf extracts were also screened for their antifungal activity in comparison with standard antibiotic Clotrimazole (20mg/ml) in vitro by well diffusion method[34, 35]. Lawn culture was prepared using the test organism on Yeast Potato Dextrose Agar (YPDA). The inoculated plates were kept aside for few minutes using well cutter, four wells were made in those plates at required distance. A fixed volume (0.1ml) of the selected extracts of *Croton bonplandianum* was then introduced into the wells in the increasing concentration. The plates with fungi were incubated at room temperature for 7 days. The activity of the extract was determined by measuring the diameters of zone of inhibition.

Anthelmintic Activity

Ethanol and Petrolium Ether extracts from the leaves of *Croton bonplandianum* Baill were investigated for anthelmintic activity against *Pheretima prosthuma* (Indian earth worms). Various concentrations (100 & 200 µg/ml) of each extract were tested by bioassay, which involved determination of time of paralysis and time of death of the worms. Albendazole was used as standard reference and distilled water as control. The Anthelmintic assay was carried as per the method fallowed by Ajaiyeoba et al with minor modifications[36]. The assay was performed on adult Indian earth worms, Pheretima prosthuma due to its anatomical and physiological resemblance with the intestinal round worm parasite of human beings[37]. Because of easy availability, earthworms have been used widely for the initial evaluation of anthelmintic compounds in vitro[38, 39, 40]. Hapse S.A. et.al. The earthworms were treated with the leaves of *Croton bonplandianum* baill extracted in Petroleum ether,

ethanol were found to be more effective as compared to standard drug albendazole at the same concentration. The petroleum ether & ethanol extract were more effective as compared to standard drug but extract in aqueous found little less effective than standard drug. Hence the study proves the traditional claim of *Croton bonplandianum* Baill as Anthelmintic drug[41].

Anticoagulant activity

K.Raja et.al Blood samples were collected from healthy volunteers, using a disposable polypropylene syringe, and then anti-coagulated using 3.8% tri-sodium citrate in a polypropylene container (9 parts of blood to 1 part of tri-sodium citrate solution). It was immediately centrifuged at 4000 × g for 15 min, and plasma was separated and pooled. The freshly prepared plasma was stored at 4^{o}C until its use. In a test tube 0.1 ml test plasma and EDTA were added and shaken briefly to mix the reagent and plasma. The tube was placed at 37^{o}C for 20 min for incubation. After the incubation, 0.1ml pre-warmed calcium chloride solution was forcibly added into the mixture of plasma and reagent. To this, one ml of aqueous extracts, ethanol extracts and was added separately in different concentrations and kept at 37^{o}C. A stopwatch was started to record the coagulation time in seconds. The tube was shaken to mix the contents and it was stopped as soon as the clot formation began. The activity is expressed in term of clotting time ratio in relation to control. The steps were repeated three times for each sample, and average of the test value was noted[42]. Normal saline was used in place of the extracts for the negative control, and 50 mg/ml of commercial heparin for the positive control[43]. Effect of aqueous and ethanol extracts of whole plant and leaves on Prothrombin time (PT).

Anti *Inflammatory activity*

Bimala et.al The inhibition of hypotonicity induced HRBC membrane lysis i.e, stabilisation of HRBC membrane was taken as a measure of the anti inflammatory activity. Lysosomal enzymes released during inflammation produce a variety of disorders which leads to tisuue injury by damaging the macro molecules & lipid peroxidation of membranes which are assumed to be responsible for certain pathological conditions as heart strokes, septic shocks and rheumotoid arthreitis etc. The extracellular activity of these enzymes is said to be related to acute and chronic inflammation. Stabilization of lysosomal membrane is important in limiting the inflammatory response by inhibiting the release of lysososmal constituents of activated neutrophil such as bacteriocidal enzymes and proteases which cause further tissue

inflamation and damage upon extracellular release upon stabilizing the lysosomal membrane. Stabilization of the HRBCs membrane by hypotonicity induced membrane lysis was studied to establish the mechanism of anti inflammatory action of *Croton bonplandainum*. Due to the presence of active principles such as flavonoids, glycosides & terpenoids and related polyphenols may responsible for this activity. Hence, *Croton bonplandainum* can be used as a potent anti inflammatory agent[44-47].

Larvicidal activity

M. V. Jeeshna et.al. Methanolic leaf extract of plant material was effective against larvae of mosquito. Furthermore, the effect of larval mortality was depended on the concentration of leaf extract. The larvicidal property of the leaf extract of the study species, *C. bonplandianum* may be due to thepresence of phorbol derivatives, the secondary metabolites of diterpenoids category (Chandel et al., 2005). Maria et al.(2006) reported that the essential oils present in four species of a genus, Croton are responsible for their larvicidal activity against the mosquito, A. aegypti. Nazer et al. (2009) reported that the stem extracts of *C. bonplandianum* was active and significantly lethal against the mosquito, Culex quinquefasciatus and he explained that the alkaloids present in the species has toxic effect on mosquito larvae. All these reports emphasized that the members of the genus, Croton are generally having lethal effects against various mosquitoes. Hence the large biomass of the weed, *C. bonplandianum* available in the wastelands of southern India can be used as a bioresource to commercially produce mosquito (A.aegypti) repellent[48-50].

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