Chapter 2
Review of Literature

The review of literature on *Croton bonplandianus* has been concentrated particularly on its medicinal and pharmacological aspects, with special emphasis on its ethno-medicinal use and evidence based scientific reports of its pharmacognostic activities. University of North Bengal library web portal (http://10.10.2.100/opac/opac.asp) and manual internet search were performed using various keywords related to the plant such as '*Croton bonplandianus*', 'Croton *bonplandianum*', 'Croton and traditional medicine, 'Croton and therapeutic', 'Croton and anti-cancer' etc. In addition, reference and bibliographies of several published articles were searched for related keywords. Search for published research articles were separately performed in Medline, Scopus, Google Scholar and EBSCO. Different criteria of inclusion were adopted like:

Croton bonplandianum, *Croton sparsiflorus* Morong, *Croton rivinoides* Chodat, *Croton pauperulus* Müll.Arg, Oxydectes bonplandiana (Baill.) Kuntze and locally Ban tulsi or kukka tulsi were considered to be the synonyms of *Croton bonplandianus*.

2.1. Botanical description

The plant *C. bonplandianus* (synonym Croton bonplandianum, Croton sporsiflorus Morong) is commonly known as Ban-tulsi, Kala bhanghra or Paitiya (Marma). *C. bonplandianus* is a much branched, woody herb, 22-50 cm tall, branches satellite hairy to glabrous. Flowers of this plant are tiny, peach color, tiny globe shaped, flower buds arranged in up right spikes with green fruits (Dutta *et al*., 2013).

Classification of the plant is as follows:

Kingdom: Plantae
Division: Magnoliophyta
Class: Magnoliopsida
Order: Euphorbiales
Family: Euphorbiaceae
Genus: *Croton*
Species: *bonplandianus*

C. bonplandianus was collected from the garden and road side areas of the campus of University of North Bengal (NBU) and identified by the taxonomist Prof. A. P. Das, of the Department of Botany, NBU. The voucher specimen was stored at the

Figure 6: Picture of *Croton bonplandianus.*

NBU herbarium of Department of Botany with an accession number 09870.

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Croton bonplandianus Baill. (Euphorbeaceae), commonly known as 'ban tulsi' is a perennial herb grows mainly as a bush, profoundly grows around the canal, river bank, wastelands and road side area. The plant is native to the southern Bolivia, Paraguay, South Western Brazil and Northern America but also found in the Sub-Himalayan region of West Bengal, India (Dutta *et al*., 2013).

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2.2. Ethnopharmacology and traditional use of *C. bonplandianus*

The traditional medicine all over the world is now-a-days evaluated by an extensive activity of research on different plant species consumed by the local or tribal populations of different parts of the world and their therapeutic principles. Based on indigenous theory, Herbal medicines are belief and experiences that are handed down from generation to generation (World Health Organization, 2000). Practices of traditional medicine have been developed in accordance with the life style and cultural practices of the society. Hands on practical training with traditional knowledge of herbal medicines have enriched throughout the globe. Herbal medicine have evolved as a complementary and alternative medicines to treat various kind of diseases caused by different kinds of stresses, anxious, industrial hazards,

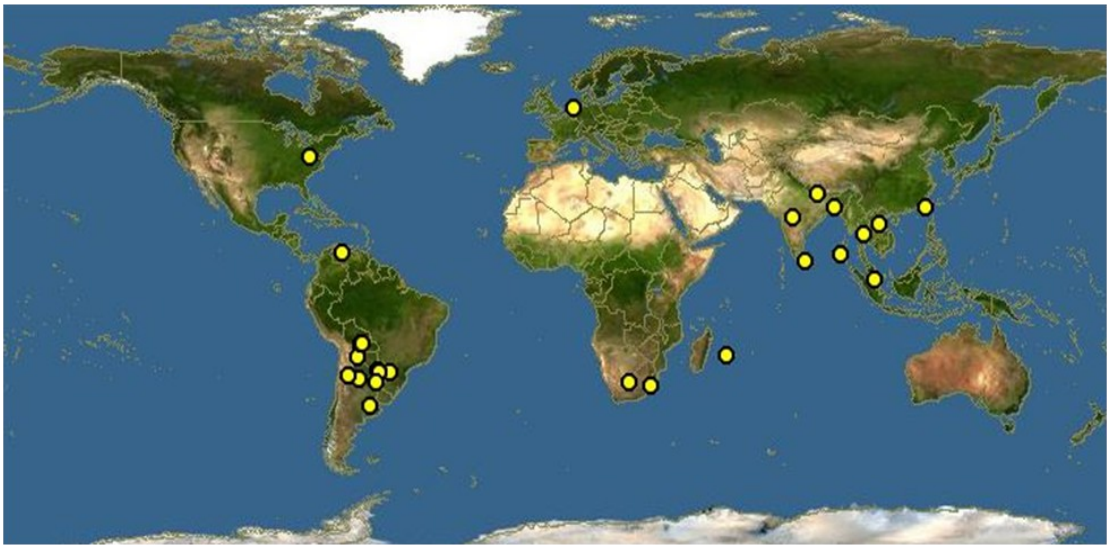

Figure 7: Worldwide distribution of *Croton bonplandianus.* (Discover Life)

pathogenic bacteria etc. In spite of modern synthetic drugs and antibiotics, herbal drugs still have their place in modern medicinal field and day to day therapy. There are many properties like effectiveness, ease in access, low cost and comparative freedom from serious side effects, makes herbal medicine not only popular but also an acceptable mode of treating diseases even in modern times.

The knowledge for long life, Ayurveda is originated in India in the Vedic period (AYUSH, 2013). Susrata Sanhita and Charaka Sanhita, the core of the Ayurvedic medicinal system mentioned therapeutic uses of different medicinal plants.

C. bonplandianus has many medicinal usages including the repellent property against the insect (Jeeshna *et al*., 2010). It has also anti-bacterial (Vadlapudi, 2010), anti-fungal (Asthana *et al*., 1989), anti-oxidant (Divya *et al*., 2011), analgesic (Saggoo *et al*., 2010), nematicide (Maria *et al*., 2008), anti-coronary (Bhakat and Sen, 2008; Chaudhuri, 2007; Nishanta *et al*., 2002), hepatoprotective (Das *et al*., 2008) and wound healing activities (Chandel *et al*., 1996; Reddy, 1995). In the remote areas of West Bengal, local people use its root as a medicine against snake venom and the leaf extract used as a medicine for high fever (Ghosh *et al*., 2013). *C. bonplandianus* have been used to cure liver diseases against ring worm and skin diseases. Leaves of this plant have got high medicinal value and are used for controlling blood pressure, cuts and wounds. The seeds of *C. bonplandianus* are used for the treatment of jaundice, acute constipation, abdominal dropsy and internal abscesses. The fresh juice of this plant is used by tribal populations to cure head acne (Divya *et al*., 2011). The plant is also used by some migratory workers for the treatment of skin disorders. Less commonly, the juice of this plant is used

against helminthiasis and toothache (Singh, 2011).

2.3. Bio-molecules of *C. bonplandianus*

There are several bio-molecules or bio-active compounds present in *C. bonplandianus*, responsible for preventing many diseases. Phyto-chemically the plant has been reported to contain rutin, crotsporinine, crotosparine and its methyl derivatives aphorbol play a key role in wound healing activity (Divya *et al*., 2011). *C. bonplandianus* is a good source of steroids, unsaturated steroids, phenolics, alkaloids, flavon, flavonols, carotinoids, leuco-anthocyanine and flavonoids (Kothale, 2011). The plant also contains two groups of compounds, terpinoids and glycosides. *C. bonplandianus* is rich in bio -polymars such as cellulose, hemi-cellulose and lignin. Oil and ethanol can be obtained from this plant (Sharma, 1990). 3 -α hydroxyl-urs 12, 15-dien of ursane skeleton, oleanolic acid, ursolic acid and β-sitosterol are the isolated compounds from the root of *C. bonplandianus* (Ghosh, 2013), and 3-methoxy 4, 6-hydroxymorphinandien-7-one, norsinoacutin are the alkaloids isolated from the extract of *C. bonplandianus*.

2.4. Bioactivity of *C. bonplandianus*

2.4.1. Antimicrobial and genotoxic activity

A wide range of diseases are caused by bacteria such as cholera, tetanus, diphtheria, tuberculosis, typhoid fever, etc. Numerous antibiotics derived from plant extract have displayed potent antimicrobial activity against a vast spectrum of pathogenic bacteria. *C. bonplandianus* has genotoxic and anti-microbial activities. The aqueous extract of leaf produced 24.17% aberration in the root tip cells allium at the stage of anaphase and telophase. On the other hand methanolic and acetone extract produced 22.08% and 21.55% aberration. Methanolic extract of leaf and fruit of *C. bonplandianus* are more effective against microorganisms like *Bacillus subtilis, Escherichia coli, Klebsiella pneumonia, Pseudomonous aeruginosa* and *Staphylococcus aureus* (Singh *et al.,* 2010). Sarkar *et al.,* (2004) proved that the leaf extract made in chloroform and benzene were most effective against *Bacillus subtilis*, B. *megaterium*, *Escherichia coli*, Proteus *vulgaris*, *Pseudomonas aeruginosa* and *Staphylococcus aureus*.

2.4.2. Anti-fungal activity

A vast array of diseases such as athlete's foot, pneumocystis pneumonia, candidiasis, chronic pulmonary aspergillosis, etc. occurs due to the fungal infections. Under complementary and alternative medicinal approaches various plants are tested for their antifungal efficiency. *C. bonplandianus* has antifungal activity against two ringworm fungi like *Microsporum gypseum* and *Trichophyton mentagrophytes* (Ashma 1989). Jeeshna *et al*., (2011) proposed that

the methanolic extract of leaf of *C. bonplandianus* was very active against the fungus *Rhizopus* sp. and *Fusorium lycopersici*. *C. bonplandianus* aqueous extract inhibis the growth of Aspergillus niger approximately MIC 100 mg/ml according to Singh *et al*. (2011). Divya *et al.,* (2011) suggested that the latex of *C. bonplandianus* (1.5 v/v in 50 % acetone) showed anti-fungal activity against Microsporum gypseum and Trichophyton mentagrophytes.

2.4.3. Anti-tumor activity

Anti-tumor activity of *C. bonplandianus* was established by potato disc and radish disc bioassay, which showed that the root length and percent of seed germination was decreased (Islam *et al*., 2010).

2.4.4. Cytotoxic and pro-apoptotic activity

Acetone extract of *C. bonplandianus* was used for the study of cytotoxic and pro-apoptotic study using MTT assay, acridine orange/ ethidium bromide (AO/EB) staining and cell cycle analyses (Bhabana *et al.,* 2016). They proposed that the number of cells in G2/M phase increases with concurrent accumulation of cells in sub G0/G1 phase and this indicates the induction of apoptosis at G_2M phase. They also suggested that A_{549} cells were more sensitive to acetone extract of *C. bonplandianus* with an IC_{50} of 15.68 ± 0.006 µg/ml compared to the standard drug cisplastin (2.20 ± 0.008 µg/ml).

2.4.5. Antioxidant activity

'Oxidative stress' is the effect of free radicals, reactive oxygen species (ROS) and reactive nitrogen species (RNS), causing potential biological damage. It is nothing but the imbalance between oxidants and antioxidants in favor of the oxidants which are formed as a normal product of aerobic metabolism. Reactive oxygen species (ROS) are the causative agents behind a wide range of disorders. Several plant based products possess tremendous ROS scavenging capacity. Antioxidant activity of *C. bonplandianus* was evaluated by (Sridhar *et al*., 2013). They proposed that the plant extract has DPPH scavenging activity with IC_{50} value 416.82 µg/ml when compared to standard BHT.

2.4.6. Larvicidal activity

The level of larvicidal activity of methanolic extract of *C. bonplandianus* at different concentration has been investigated. It is observed that IC_{50} value obtained at 124 ppm is effective against the mosquito Aedes aegypti (Jeeshana, 2010). They proposed that the leaf extract of *C. bonplandianus* at 124 ppm is better for mosquito control.

2.4.7. Anti-inflammatory activity

Inflammation is a biological response against invading bacterial and viral pathogens, autoimmune reactions, and persistent foreign bodies which results in tissue damage. Inflammatory responses are

primarily mediated by various cytokines, inflammatory proteins and nitric oxide.

2.4.8. Wound healing activity

Divya *et al.,* (2011) proposed that *C. bonplandianus* contain Rutin ($C_{18}H_{36}O_{19}$) together with crotsparine and its methyl derivatives aphorbol play a key role in wound healing activity. The studies carried out Divya *et al.,* showed that both aqueous and alcoholic extract of *C. bonplandianus* have wound healing activities. In case of aqueous extract, the percent of wound concentration was observed 29.2 % in 14 days, 63.1% in 21 days and 89.2 % in 28 days respectively. On the other hand in case of alcoholic extract, the percent of wound concentration was observed 36.6 % in 14 days, 66.2 % in 21 days and 91.6 % in 28 days. Finally Divya *et al.,* suggested that on the basis of their study alcoholic extract of *C. bonplandianus* is more effective in wound healing than the aqueous extract.

2.4.9. Phytochemical Analysis

Dutta *et al*., (2013) performed the phytochemical analysis of various parts of *C. bonplandianus* and identified the presence of a wide range of phytochemicals such as phenolics, glycosides, alkaloids, tannin, flavonoid, etc., in the plant. Quantification of these phytochemicals revealed the presence of 67.86 ± 1.54 g/100 g alkaloid, 82.53 ± 2.41 mg/g phenolics, 1.01 ± 0.06 mg/100 g ascorbic acid in the root; 12.56 ± 0.67 g/100 g saponin, 8.05 ± 0.19 mg/g flavonoid, 0.42 ± 0.04 mg/g riboflavin, and 0.48 ± 0.05 mg/g thiamine in the leaves.

2.5. Future Prospects

Plant derived medicines could provide a unique opportunity to bio-prospect diverse chemical species. They could function synergistically on multiple target, resulting in a holistic therapeutic approach to improve the therapeutic efficiency of the drugs. In the global scenario, the shift of the pharmaceutical research towards herbal remedies from modern medicine is very much apparent. In case of plant like *C. bonplandianus*, mechanism based screening of bioactivities focusing on their ethnopharmacological use is of utmost importance. Various issues, which are only applicable to herbal medicine, must be considered for proper evaluation of these products (Kunle *et al*., 2012). Different issues such as:

Herbal drugs are phytococtails which may contain multiple bioactive species.

- The active constituents are mostly unknown.
- Herbal constituents may be chemically and naturally variable as chemo-variants and
- Chemo-cultivars may be present.
- Appropriate analytical method may not be present.
- Authentication of source and quality of raw material.

- Assurance of quality, efficiency, safety and reproducibility.

Unlike conventional drugs, the botanical drugs are not target specific and therefore, could be used to treat disease associated symptoms of infection and inflammation. Present immunomodulatory strategies have revealed that monovalent approach of isolated drug therapy is unlikely to provide a holistic treatment (Patwardhan and Gautam, 2005). It is very much expected to opt for a strategy which would consider the complex interplay between different biological pathways. Thus, the requirement of designer drugs based on synergistic approach of traditional medicine would be helpful.