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Ethnobotanical and Pharmacological Potential of Trichosanthes Species

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Abstract:
Plants are a vital source of drugs, serving both traditional and modern medicine, as well as pharmaceutical intermediates, synthetic drugs, nutraceuticals, and food supplements. The discovery of plants with novel medicinal properties is crucial for herbal drug development. In countries like India, China, Burma and Bangladesh, traditional medicine is widely practiced, with most medicinal plants sourced from the wild. *Trichosanthes* genus of family Cucurbitaceae, consists of about 84 species with several exhibiting important medicinal properties. Although many *Trichosanthes* species are used in traditional medicine, not all are fully investigated with respect to their active phytoconstituents. This review summarizes information available on the traditional uses, phytochemistry and pharmacology of 4 medicinally important species of genus *Trichosanthes* namely *T. kirilowii*, *T. tricuspidata*, *T. dioica* and *T. bracteata*. It further gives perspective on future research and possible investigations that need to be carried out in these and other species of genus *Trichosanthes*.

Keywords: Trichosanthes kirilowii, T. tricuspidata, T. dioica, T. bracteata. Cucurbitaceae, Pharmacological activities, Ethnobotanical, Phytoconstituents

1. Introduction

Plants are the richest bio-resource of drugs not only for traditional systems of medicine but also for modern medicines, pharmaceutical intermediates, chemical entities for synthetic drugs, Nutraceuticals as well as food supplements. Discovery of new plants with novel medicinal properties is crucial in the development of new herbal drugs. Approximately 80% of patients in India, 85% in Burma, and 90% in Bangladesh are treated by practitioners of traditional medicine [1]. Majority of medicinal plants are collected from the wild, however, farmers have recently begun to cultivate some medicinal plants to make these available for pharmaceutical companies for isolation of medicinally important phytoconstituents [2,3]. Distinct categories of secondary metabolites are produced by plants as by-products of primary metabolic processes. These include terpenoids, phenolics, flavonoids, glycosides, alkaloids, saponins, etc. [4]. Some of these compounds exhibit distinct pharmacological activity which is often proportional to the quantity of some specific metabolite present in the respective plant part. Few such medicinally important plants also belong to the genus *Trichosanthes* of family Cucurbitaceae classified by Benthem and Hooker [5].The *Trichosanthes* genus consists of about 84 species and is the largest genus under family Cucurbitaceae [6]. 34 of these are seen in China. In India, *Trichosanthes* is represented by 22 species, which are distributed

in three major regions, namely Peninsula, Northeast, and Eastern Himalaya [7]. *Trichosanthes* species are distributed in India, Sri Lanka, China, Japan, Southeast Asia, Malaysia, New Guinea, Australia, Fiji, and Vanuatu [8,9]. The genus includes dioecious, mostly perennial, tendrillar climbers with globose or egg-shaped distinctly fringed petals and with fleshy, bright, red-colored fruits. [10]. Further, *T. tricuspidata* and *T. bracteata*, although remarkably similar, are two distinct species considered medicinally important. *T. tricuspidata* does not occur in India, but is restricted to countries such as Malaysia, south China, Thailand, and Vietnam [10]. *T. kirilowii* and *T. rosthornii* grown in Henan and Shandong provinces of China for medicinal uses. They thrive best in warm to moist habitats and prefer fertilized, well drained sandy soil [11].

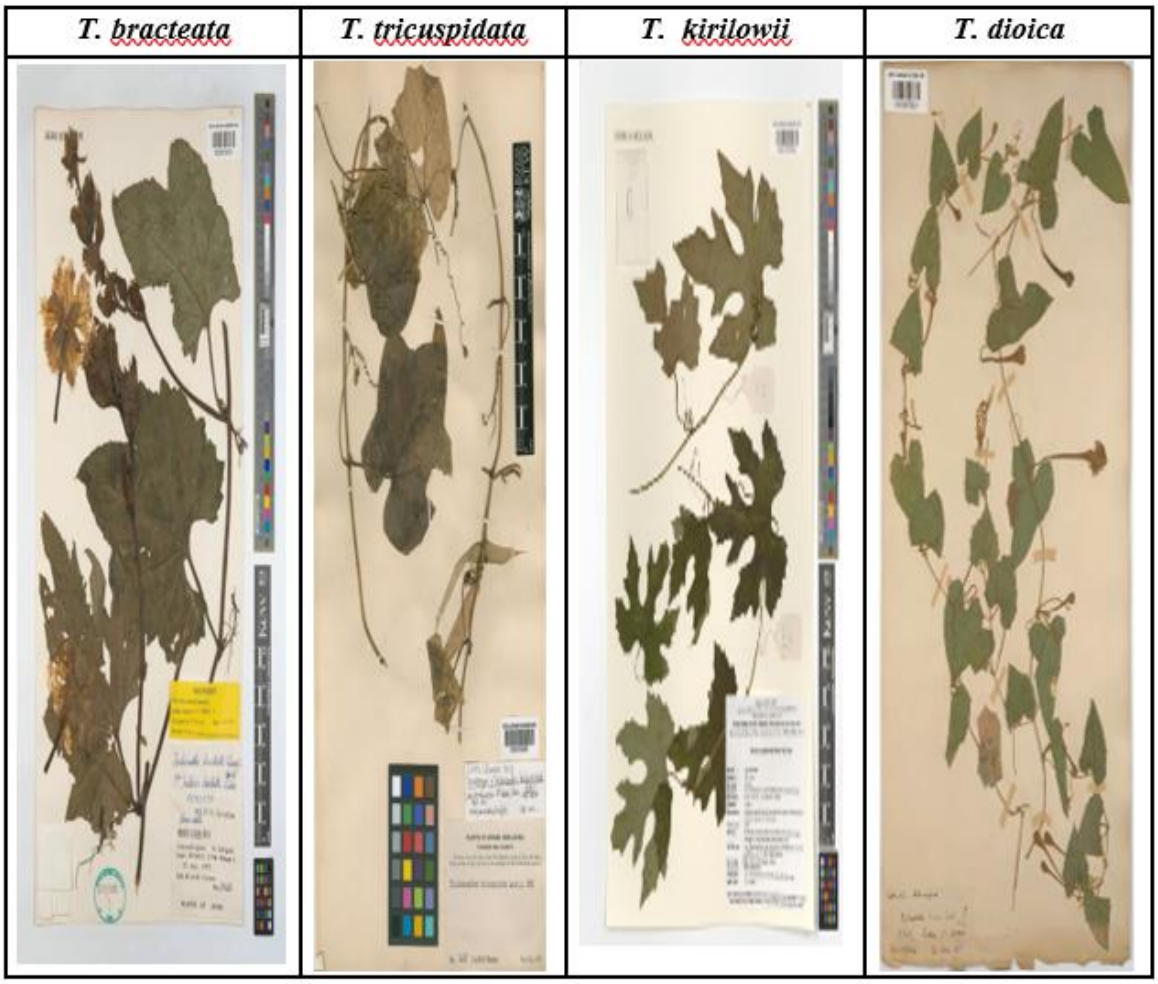

Figure 1: Herbaria of Trichosanthes species (Source: POWO site:- https://powo.science.kew.org)

T. bracteata is restricted to India. The ethnobotanical uses, phytoconstituents and pharmacological properties of four medicinally important species of *Trichosanthes* genus are discussed in this review.

2. *Trichosanthes kirilowii* Maxim

T. kirilowii, also known as Chinese cucumber, is an herbaceous climber belonging to the Cucurbitaceae family growing up to 10 meters in height. This plant is cultivated for its excellent for medical uses in Henan and Shandong provinces of China. It is a dioecious plant mainly distributed in East Asia and northern Australia and is native to North and East China, Japan, and Indo China. These plants have

unisexual flowers with white corolla and fringed apex and bloom from May to August. The multibranched climbing stem is covered with soft white hairs and possess axillary tendrils. Leaves are rounded to cordate, hairy and lobate. Fruits are spherical and turn yellowish brown on maturity and can be harvested from August to October. The fruit encloses flat, ovate seeds with ribbed margins. Seeds turn yellowish brown on maturity [11].

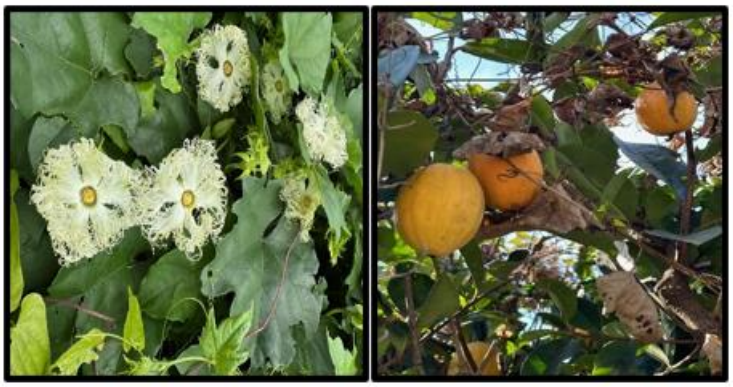

Figure 2: *Trichosanthes kirilowii* Flower and Fruits (Source: Official POWO site: - https://powo.science.kew.org)

2.1 Ethnobotanical uses of *Trichosanthes kirilowii*

Amongst the various *Trichosanthes* species, *T. kirilowii*, is widely used in Chinese traditional medicine (TCM). It is considered as one of the 50 fundamental herbs used in TCM. The tubers of this plant were used as folk medicine in the ancient East to reduce mid-term abortion. The fruit, fruit peel, seed, and root of *T.kirilowii* have often been used medicinally and is popularly known to be "drug homologous food" to treat cough constipation, inflammation [6].The fruit rind was used to cure certain heart and lung diseases , The seeds of this plant have long been used in Korean medicine to loosen bowels and relieve chronic constipation. The plant was therefore tested to study and detect phytoconstituents responsible for a wide range of pharmacological actions that the plant exhibited.

2.2 Phytoconstituents and pharmacological reports of *T. kirilowii*

T. kirilowii has also been reported to show the presence of a different unique class of protease inhibitor from the roots of *Trichosanthes kirilowii*, which showed inhibitory activity against the integrase enzyme [12]. A serine protease TKP isolated from *T. kirilowii* inhibits human colorectal adenocarcinoma cell proliferation through inducing apoptosis [13]. Further, an alpha-amylase inhibitor (*TkAAI*) was reported in the seeds of *T. kirilowii*. This inhibitor was reported to be active against porcine pancreatic amylase. It is suggested that *TkAAI* might play a physiological role during the seed development. The presence of this inhibitor also provides reasoning for the possibility of *T. kirilowii* derived medicine to treat diabetes related diseases. The presence of ten flavones, three tetracyclic triterpenoids, and one pentacyclic triterpenoid were reported in the extracts of *T. kirilowii* [14]. *T. kirilowii* var. japonica showed the presence of 7-, 3′- and 4′-glucosides of luteolin, the 7-glucoside and 6,8-di-C-glucoside of apigenin. Some novel kinds of phytoconstituents were found in this plant. These included the ribosome inactivating proteins (RIPs) which occur in fungi, bacteria and plants and are believed to play a role in plant defense. RIPs are so-named because their rRNA N-glycosidase activity can depurinate the large ribosomal subunit rRNA at a selective universally conserved site on r RNA [15]. RIPs thus exhibit a translational inhibitory activity by inactivating the rRNA irreversibly and preventing the binding of elongation factor II [16].This leads to stopping the process of protein synthesis. RIPs thus display some unique bioactive properties, including

antiviral, antifungal and anti-tumor activity [17, 18] and have attracted a great deal of attention because of their potential use in medical research and development. Some RIPs with different bioactivities are found in various parts of the same plant, like leaves, seeds, roots, and tubers. A type I RIP was purified from the tubers of *T. kirilowii* and was labelled as trichosanthin (TCS). It was successfully used to treat acquired immune deficiency syndrome and chorioadenoma[19]. TCS has also been reported to inhibit cell growth of a diversity of cancers, including cervical cancer, choriocarcinoma, and leukemia/lymphoma.
Due to the presence of important pharmacological activities of trichosanthin, other plant parts of *T. kirilowii* were further investigated. RIPs with a molecular mass of 10 kDa have high levels of bioactivity and exhibit lower allergic reactions and lower toxicity toward normal cells [20, 21]. Such a novel RIP with a molecular mass of 10,964.617 Da showing high bioactivity and low immune toxicity, was purified from the seeds of *T. kirilowii*, and was named as Trichosanthrip [22]. Anti-cancer effects of ethanolic seed extract of *T. kirilowii* was reported in 2019.This ethanolic extract was shown to effectively suppress both colorectal cancer cell lines namely HT-29 and CT-26 and the observed cytotoxic effect was greater than that of positive control 5-fluorouracil (5-Fu) in HT-29 cells. This anti cell proliferative effect was believed to be due to down regulation of some proliferation related signaling pathways which resulted in inducing mitochondrial-mediated apoptosis in cancer cells. These findings supported the use of TKSE as complementary and alternative medicine in the treatment of colorectal cancer [23].

3. Trichosanthes tricuspidata

T. tricuspidata also known as red ball snake gourd, is also a rare wild liana, remarkably similar to *T. bracteata* in morphological appearance, flowering and fruiting time but does not occur in India. It is restricted to countries such as Malaysia, South China, Thailand, and Vietnam. Flowers and fruits are also like *T. bracteata* with some minor differences as follows. Male sepals are with serrate margin or with side lobes. Female sepals are entire along margins. Male bracts are with finely densely deeply serrate-laciniate margins. Leaf margins are entire or wavy with small dentations. Fruits ovoid, acute, beaked at apex, without any longitudinal streaks and this character distinguished *T. tricuspidata* from *T. bracteata*. Seed coats not marginate [10].

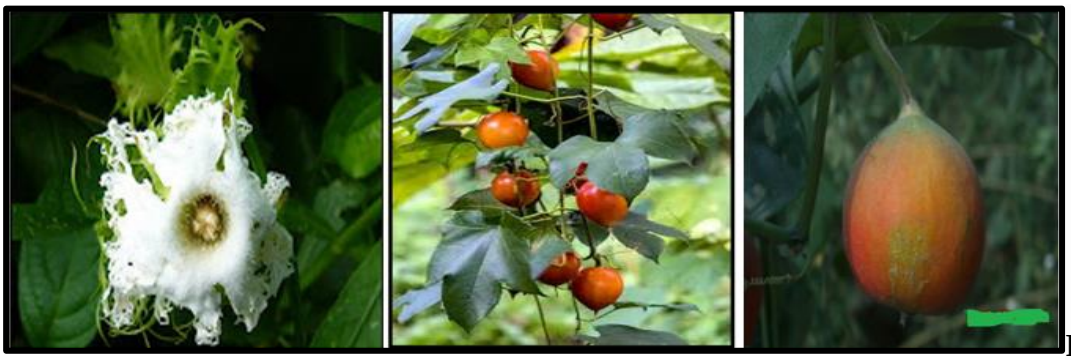

Figure 3: *Trichosanthes tricuspidata* Flower and Fruits (Source: eFlora of India and Official POWO site:- https://powo.science.kew.org)

3.1 Ethnobotanical uses of *Trichosanthes tricuspidata*:

T. tricuspidata has been used in traditional Indian medicine for a long period of time to treat a variety of stress-related issues, as well as ophthalmic illnesses, epilepsy, asthma, inflammations, rheumatism, and leprosy [12, 2].The whole plant is used as an anti-fever remedy, a laxative, an anthelmintic as well as in

migraine treatments. The juice of the plant is applied externally for skin eruptions. In Bastar District, Chhattisgarh, India, the fruit of *T. tricuspidata* is reportedly used for curing snakebite poisoning. The Vaidya's, or practitioners of ayurveda, also use the fruits in treating stomatitis Application of seed paste is reported to be used for hoof and mouth disease in cattle [22, 24]. The roots of the plant are used to treat lung diseases in cattle and for the treatment of diabetic carbuncles and headaches. In Nepal, the roots are used to cure bleeding in chickens. The oil extracted from the roots is used as a painkiller [25]

3.2 Phytoconstituents and pharmacological reports of *T. tricuspidata*

Seeds of *T.trisucpidata* contain punicic acid and it is a painkiller [25]. Leaves of *T. tricuspidata* are reported to have anticonvulsant and antioxidative effects on pilocarpine induced mice [26]. Tetrahydroxy pentacyclic triterpene "Trichotetrol" was isolated from the root extract of *T. tricuspidata* [22]. Fruits of *T. tricuspidata* show the presence of cucurbitane glycosides [27].Roots of *T.tricuspidata* have also been investigated and reported for various pharmacological actions like antipyretic activity, anti-hyperglycemic activity, which significantly lowered the blood sugar level in alloxan induced diabetic rats [12]. Pharmacological studies also proved that the roots of *T. tricuspidata* showed antimitotic and anticancer activity [28].A protease was reported from the sarcocarp (fruits) of *T. tricuspidata* [29]. Thus, there are numerous therapeutically important bioactive compounds reported to be present in this *Trichosanthes* species. There is a possibility of similar compounds to be detected in *other species of Trichosanthes* and these need to be investigated.

4. Trichosanthes dioica

T. dioica, commonly known as pointed gourd or Parval is an herbaceous vine with stem having distinct thick tendrils. This plant is believed to be originated in the Indian subcontinent or the Indo Malayan region and cultivated largely in India, Bangladesh, Myanmar, Sri Lanka, Pakistan, and Nepal. Solitary whitish green sessile flowers with an oblong-cylindrical calyx tube are found on a racemose inflorescence borne in the leaf axils. Leaves are dark green, cordate, oblong, acute, sinuate-dentate but not lobed. Pericarp and mesocarp form the edible part of globose and oblong dark green fruits with characteristic striations having white to pale green stripes. Fruits are found from February to September. The tuberous tap roots of this plant are usually used for propagation along with stem cuttings as the seeds show poor germination. *T. dioica* is one of the most consumed species of genus *Trichosanthes* specially in Asian Tropical countries like Bangladesh and India where fruits are eaten as a vegetable [30].

Figure 4: *Trichosanthes dioica* Flower and Fruits (Source: Official POWO site: - https://powo.science.kew.org)

4.1 Ethnobotanical uses of *Trichosanthes dioica*

T. dioica usually cultivated as a vegetable have excellent medicinal properties. No report of toxicity of the fruits in humans has been documented.Various parts of the plant are used by tribal folks as well as ayurvedic doctors to treat a wide range of human ailments. Bangladesh tribals in Jhenaidah use of leaves of this plant to treat hyperacidity with constipation [31]. Some other tribals in Bangladesh use the fruit in the treatment of teeth, fungal infection in nail and the skin of the fruit against Badmouth smell [32]. The juice of roasted fruits is applied on chicken pox scar [33]. In India the tribals in Orissa largely use the leaf to treat enlargement of liver and spleen, boils, skin diseases, Alopecia and as a laxative [30]. Leaf is also reported to be used against fever, hemorrhage, anal fistula, leprosy, and certain mouth diseases and to treat inflammation and wounds [34, 35, 36, 37]. They are reported to use the fruit as tonic, febrifuge, boils, skin disease, laxative, enlargement of liver and spleen [35,38]. Some tribals use the leaf decoction mixed with Piper nigrum fruit powder to treat diarrhea. The stalk of the plant is also used as an expectorant [35]. The root is also used by Indian tribals as a febrifuge, cathartic, tonic, jaundice, anasarca, ascites[38,39 ,40]. Leaves and fruits are also reported to treat alcoholism and Jaundice (liver ailments). Additionally, fruits are known to be used for improving appetite and digestion [35].

4.2 Phytoconstituents and pharmacological reports of *T. dioica*

Reports on Antihyperglycemic activity of fruits of T. *dioica* were first reported in normal albino rabbits by Sharma and Pant [41]. Aqueous fruit extracts of *T. dioica* when tested in Streptozotocin (STZ)-induced diabetic rats also showed Antihyperglycemic activity Rai, et al.[42]. Leaf and seed extracts of *T. dioica* also showed dose-dependent antihyperglycemic potential. Thus, leaves, fruits as well as seed extracts of *T. dioica* showed significant antihyperglycemic property [43]. Sharma and Pant reported the antihyperlipidemic potential of T. *dioica* fruits as well as seed extracts. These researchers reported a hypocholesterolemic and hypotriglyceridemic effect on normal albino rabbits. The Phospholipids and HDL cholesterol were also seen to increase in these rabbits [44]. Thus, there was an overall improvement in the lipid profile of animals studied when treated with fruit [38]. and seed extract [44] of T. *dioica* [41, 44]. Further, an overall improvement in lipid profiles was observed in human trials[36] proving evidence of the potential use of T. *dioica* seeds in treating dyslipidemia in both diabetic as well as the non-diabetic groups. Antitumor efficacy of *T. dioica* root has been well reported by several workers. Alcoholic extract of *T. dioica* roots was reported to show antitumor and oxidative stress reducing activity in Ehrlich ascites carcinoma (EAC) cells in mice. The study reported a decrease in tumor weight, tumor volume, an increase in the life span of test animals, and improvement in other hematological parameters in the T. *dioica* treated groups [45]. The triterpenoid fraction of *T. dioica* root showed antiproliferative efficacy[37]. Several reports indicate antitumor efficacy of T. *dioica* root. Trichosanthin, a ribosome-inactivating protein (RIP), first isolated from *T. kirilowii* was also reported in root extracts of *T. dioica* [46]. Trichosanthin is a 27-kDa protein having a single chain of 247 amino acids and this protein is known for its abortifacient, immunosuppressant and antitumor activity Trichosanthin was proved to play a role in inducing apoptosis in tumor cells[47]. Methanolic and ethyl acetate extracts of *T. dioica* fruits have been reported to show an anti-inflammatory effect in carrageenan-induced paw edema in rats. Oral administration of aqueous fruit and root extracts of *T. dioica* have shown a significant ameliorative effect on arsenic-induced toxicity in rats [48]. The fruit extract alleviated arsenic-induced brain toxicity [49] and myocardial toxicity [50] while the root extract alleviated myocardial toxicity [51]. Excellent wound healing potential of ointment made using methanolic extracts of fruits of *T. dioica* was reported in study involving excision and incision rat models. There was an improvement in parameters such as wound contraction, epithelialization period,

tensile strength, hydroxyproline content indicating progression of healing process [52]. High phenolic content of 259mg/gm was reported in the leaves of T. *dioica* [53]. Leaves as well as fruit extracts have shown antioxidant activity in DPPH radical scavenging, nitric oxide scavenging, and reducing power assay in a dose-dependent manner [40]. Dose-dependent inhibition of root growth and reduction of the mitotic index was observed in *Allium cepa* root meristems indicating the cytotoxic and genotoxic potential of *T. dioica* root methanolic, dichloromethane as well as aqueous extracts [54, 55]. Several important classes of phytochemicals are reported in *T. dioica*. Roots are reported to have 14 sterols and 13 triterpenes. Of these the most abundant are the sterols and tetra- and pentacyclic triterpenes. The most significant triterpenes responsible for the wide pharmacological potential of roots are Lupeol, Taraxerol, Euphol, α-amyrin with antifungal and anti-inflammatory activity, β-amyrin with anti-inflammatory [56,57] and anti-lipoxygenase activity [68]. Seeds of *T. dioica* are also reported to contain 6 different types of tri terpenes. The most important of these is betulin known for its antiseptic, wound healing, cholesterol lowering, anti-inflammatory and hepatoprotective properties [59]. Seeds also contain fatty acids such as elaeostearic, linoleic, oleic and other saturated acids [60]. Cucurbitacin B, an oxygenated tetracyclic triterpenoid, with promising anticancer potential has been found in the fruit [61] in addition to presence of a higher concentration of calcium, magnesium, iron [62] [27].

5. Trichosanthes bracteata

T. bracteata is a rare wild perennial liana, mostly distributed in India and to some extent in its neighboring countries such as Bangladesh, Myanmar, Nepal, and Sri Lanka. *T. bracteata* grows in the semi-evergreen or mixed deciduous forests mostly on forest fringes and along roadsides or in abandoned places from sea level to 2000 meters or above. The plant is a large woody climber with grooved stems having trailing branches. Flowering & fruiting time is from May-June and fruit harvesting time is from August- October. Flowers 4-5 cm ,white with frilly margin. They occur singly or in 5-10 flowered racemes, in leaf axils. Male sepals with entire margin or occasionally with 2 or 3 side lobes. Female sepals have margins with side lobes. Male bracts are with sparsely laciniate margins. Leaves are 6-12 cm across, broadly heart-shaped, but palmately 3-5 lobed. Leaf margins are prominently dentate and never entire. Unlobed and lobed leaves are present on the same plant. Fruits are sub globose, ellipsoid, rounded at apex with 10 longitudinal orange streaks on the surface. Seeds black with marginate seedcoat [10].

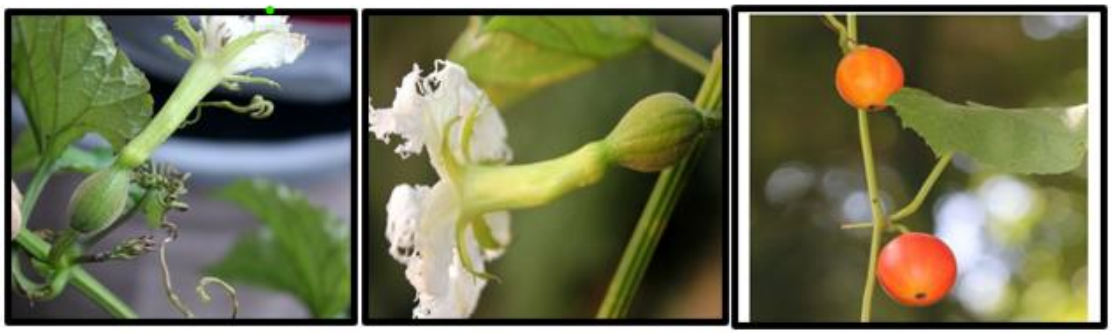

Figure 5: *Trichosanthes bracteata* Flower and Fruits (Source: eFlora of India)

5.1 Ethnobotanical uses of *Trichosanthes bracteata*

There are few reports on the ethnobotanical uses of *T. bracteata.* Some surveys in the tribal zone, however, pointed out that the fruit of *T. bracteata* is used by tribals of Maharashtra for its medicinal as well as

pesticidal property. The fruit is reported to have a bitter taste like that reported in *T. tricuspidata*. The bitter taste of sarcocarp may point to the fact that the plant may contain similar medicinally important types of secondary metabolites such as terpenoids, alkaloids, etc which could be responsible for its medicinal and pesticidal properties.

5.2 Phytoconstituents and pharmacological reports of *T. bracteata*

Sarcocarp of *Trichosanthes bracteata* shows the presence of a serine protease [63]. Seed oil of *T. bracteata* and *T. nervifolia* showed the presence of Punicic acid (41.8% and 51.9 %) which is an especially important bioactive compound also found to be present in pomegranate seed oil. Therapeutic potential of punicic acid has gained wide attention which includes antidiabetic, antiobesity, antiproliferative, and anticarcinogenic activity against various forms of cancer [25]. *T. bracteata* yet needs to be evaluated for these pharmacological properties. Flavonoids are an important class of phytoconstituents which increase the medicinal value of the plant. Although there are many *Trichosanthes* species reporting the presence of a wide range of flavonoids as well as other classes of phytochemicals, there is only one report in *T.bracteata* stating the presence of only two flavonoids namely luteolin 3′-glucoside and kaempferol 3-rutinoside [64]. *T. cucumeroides* showed the presence of Kaempferol. 3,7-di-rhamnoside and 3-glucoside-7-rhamnoside. Kaempferol 3-galactoside and 3-sophoroside were identified from *T. anguina*. Quercetin-3-rutinoside was detected from *T. multiloba* and *T. rostrata. T. bracteata* needs to be investigated further for the presence of similar flavonoids. Additionally, there are no reported studies on other important phytochemicals like alkaloids and terpenoids in *T.bracteata.*

Conclusion:

Majority of the *Trichosanthes* species studied so far have proved to have excellent medicinal and ethnobotanical properties. A wide range of exclusive and rare phytochemicals are already detected in some of the above species as mentioned in this article. However, more plants belonging to the *Trichosanthes* genus, like *T. bracteata* which is also used for its medicinal properties by tribals may have phytoconstituents similar to T. *kirilowii*, *T. tricuspidata* and *T. dioica* . There are only a few reports on phytoconstituents present in *T. bracteata.* Thus, *T. bracteata* needs to be investigated to assess its full therapeutic potential by screening for the presence of rare bioactive phytoconstituents like Lupeol, Taraxerol, Euphol, *α*-amyrin, Punicic acid, Curcubitacin B, Luteolin, betulin, trichosanthin etc. which are of great pharmacological value and specially found in other species of genus *Trichosanthes.*

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