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REVIEW PAPER

Exacum tetragonum Roxb. - an endemic medicinal herb

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Abstract

Exacum tetragonum Roxb. is one of the important medicinal herbs of India and it belongs to Gentianaceae. The plant is used for treating fever, stomach disorders, gout, diabetics and eye diseases. It also function as antioxidant, anti-inflammatory, anti-helminthic and anti-hyperglycemic activities. However, drastic changes in its habitat due to various reasons can certainly cause severe threats to its continued existence and hence appropriate actions to conserve the natural habitats of this species are vital. The present paper reviews the present status of the species in terms of its taxonomy, origin, distribution, morphology, phytochemistry, pharmacological studies and conservation.

Keywords: *Exacum tetragonum*, Medicinal properties, Conservation.

Introduction

Kerala State is known for its medicinal plant wealth and the tradition of its indigenous system of therapy. *Exacum tetragonum* Roxb. is one of the important medicinal herbs of India and it belongs to Gentianaceae. In Kerala, it is distributed in the hilly tracts. Roxburgh (1832) stated that this is one of the most elegant plants, the flowers not only numerous, large and beautiful but retaining their beauty and expansion for many days, which is a rare circumstance in an Indian plant.

The systematic position of *Exacum bicolor* Roxb. is: Kingdom Plantae, order Gentianales, family Gentianaceae. The various synonyms were *Exacum hamiltonii* G.Don., *Exacum perrottetii* Grisb., *Exacum roseum* Royle, etc. (Shahina and Nampy, 2016).

The plant is known as Persian blue violet in English, *kannanthali* in Malayalam, *cheti* in Tamil, *dodda chirayutha* in Kannada, *koochuri* in Bengali, *avachiretta* in Hindi and *sher-ri-takti* in Assamese (Sreelatha *et al.,* 2007). The Malayalam name of *Exacum tetragonum,* often enjoys a place in film songs and Malayalam poems. About three to four decades ago, the plant was seen abundantly in different parts of Kerala. The earthen deity, *Thrikkakkarayappan*, worshipped during the national festival *Onam,* was adorned using flowers of *kannanthali* (Sreelatha *et al.,* 2007). The plant was regarded as a promising anti-oxidant, thrombolytic and anti-inflammatory agent (Ashwini, 2016).

Origin and distribution

The species was believed to be originated in Madagascar and was the only one species, which was common in Indomalesia (India, the Himalayas,

mainland Southeast Asia including southern China, and Malaysia) that reaches the extreme North of Australia (Yuan *et al*., 2005). *Exacum tetragonum* was distributed in India, Philippines, New Guinea and northern Australia (Klackenberg, 1985) and was the most widespread species of this genus in India, distributed from sea level to about 2000 m altitude (Shanavas and Nampy, 2016). Grassy hill slopes of Deccan Peninsula, grasslands and scrub savannas were the major habitats of *Exacum bicolor*. Major associating floras in low altitude grasslands were *Heteropogon contortus, Striga densiflora*, etc. In high altitude grasslands, *Exacum bicolor* was seen associated with *Ageratum conyzoides*, *Osbeckia* sp., *Swertia* sp., etc. In Kerala, the plant occurs in almost all districts (Sreelatha *et al.,* 2007).

Morphology

The species *Exacum tetragonum* is a 15 cm to 120 cm tall herb. Stems are tetranglular and winged which is 0.2–0.4 cm broad, branched basally and apically. Leaves are sessile-subsessile and the lamina is broadly elliptic-ovate, spathulate or linear lanceolate to broadly oblong. The leaf lamina is 3 to 5 nerved at base, acute at apex and cuneate at base. Inflorescence is a dichasial cyme, which is terminal or axillary in position. Each inflorescence is 1 to 5 flowered and pedicels of the flowers are 0.5-3 cm long. The floral calyx is green coloured, persistent and dorsally winged. Wings of the calyx are 3-5 mm wide. Corolla tube of the flower is yellowish white in colour and 0.5-1 cm long. Colour of the corolla is violet at the apex, white the rest and yellow at throat. Corolla is obovate-elliptic and cuspidate. Each flower has got four stamens whose filaments are pale green yellow coloured, short and 0.3-1.5 cm long. Anthers are orange yellow in colour, linear, curved, sagittate and 1-1.8 cm long. Dehiscence is through apical pores later widening in to slits. Ovary of the flower is green and ovate. Style is greenish white, 1-2 cm long and deflexed. Stigma is simple, rounded and faintly bilobed. Fruit is a capsule, which is brown in colour, oblong-ovate and unilocular. Many seeds are present in each capsule. Seeds are tetrahedral in shape with reddish brown testa (Shanavas and Nampy, 2016).

Flowering occurs during August to November (Ashwini, 2016). Flowering period lasts for 30-45 days and a single flower remains for 8-10 days. The most attractive part of the flower is its white petals with dark purple coloured tips. After 5-6 days of opening of the flower, the tip colour slowly spread downwards and finally the entire petal becomes purple coloured (Sreelatha *et al.,* 2007). Gardening in Tropics by Woodrow (1910), described *Exacum bicolor* as the most difficult plant to cultivate.

Diseases

Commonly observed disease of *Exacum bicolor* was damping-off of seedlings. Wilting of the plant was commonly observed in soils with poor drainage. Another problem was the attack of nematodes (Sreelatha *et al.,* 2007).

Phytochemistry

Exacum bicolor is a phytochemicaly unexplored traditional, medicinal herb (Meethaley and Paulsamy, 2011; Ashwini *et al.,* 2015). The extraction of *E. tetragonum* furnished the secoiridoids, gentiopicroside and methyl grandifloroside. Luteolin and chlorogenic acid, two flavonoid compounds were detected in *E. bicolor* by HPLC. Compounds belonging to alkaloid, polyphenolic and glycoside groups were detected by GCMS analysis of whole plant extract of *E. bicolor* (Vinayaka *et al*., 2016). The study of Ashwini and Majumdar (2014) using different solvent extracts of leaf of *E. bicolor* showed the presence of various phytochemicals such as phenols, saponins, flavonoids and alkaloids. The major phytocomponents reported in *Exacum bicolor* were methyl 2-(3-oxocyclohexyenyl) imidazole (5.8%), erythrocentaurin (1.0%), neophytadiene (4.0%), hexadecanoic acid (5.4%), 6-octadeccenoic acid (12.0%), (+-)-inophylum D (2.7%), 4,6,8(14)-cholestatriene (6.0%) and methyl 3,4diphenylpyrrolo[2,1,5-cd] indolizine-1-carboxylate (5.5%) (Ashwini *et al.,* 2015).

Ethnopharmacology

Traditional medicine forms the basis of primary healthcare system among various communities across the world (Vinayaka *et al.,* 2016). Whole plant of *Exacum tetragonum* was taken for treatment of fever and stomach trouble by the Chamaka community in Arunachal Pradash (Sarmah *et al*., 2008) and the people of Namdapha National Park use *Exacum tetragonum* as febrifuge (Dey and De, 2012). Naga people have been using *Exacum tetragonum* against malaria fever since long (Rao, 1983). *E. bicolor* was used for curing human ailments like diabetes, malaria, skin disorders, fungal diseases and inflammation (Marles and Farnsworth, 1995; Reddi *et al*., 2005; Pullaiah, 2006; Khare, 2007). In Khao Kho District, Phetchabun Province, Thailand *Exacum tetragonum* was considered as a valuable medicinal herb (Chuakul, 2000). Juice of *Exacum tetragonum* was used thrice a day as substitute for

Swertia chirayita (Shankar *et al*., 2012). The roots of *Exacum bicolor* contain a colouring matter and it was used in alcoholic drinks in Germany and Switzerland (Torfida, 1944). Decoction of leaves and bark of *Exacum tetragonum* was used by Angaminagas for curing malarial fever (Rao, 1983). The plant yields a dye (Srivastava, 1989). This species has been extensively used for curing diabetes (Marles and Farnsworth, 1995; Sreelatha *et al*., 2007), skin disorders (Reddi *et al*., 2005) and for inflammation, to purify blood and in the treatment of malaria (Rao, 1983). It is used as stomachic (Shiddhamallayya *et al*., 2010) and in asthma (Lingaraju *et al*., 2013). The plant exhibits anthelmintic, antioxidant, anti-inflammatory and thrombolytic activities also (Ashwini and Majumdar, 2014; 2015 and Ashwini *et al*., 2015). Decoction of whole plant for washing eyes is prescribed by traditional medical practitioners. However, the medicinal properties of *E. bicolor* are yet to be fully exploited scientifically (Sreelatha *et al*., 2007; Brilliant *et al*., 2010).

Antioxidant activity

The search for alternative sources of natural antioxidant compounds from *in vitro* produced plants has gained importance nowadays since the populations of wild plants are diminishing due to anthropogenic activities (Franco *et al*., 2008). *Exacum bicolor* possess antioxidant and anthelmintic activities (Ashwini and Majumdar, 2014; 2015). *E. bicolor* extract exhibited potent antioxidant activity with lower IC_{50} in comparison to earlier findings, thus the extract might act as an effective radical scavenger (Ashwini, 2016). *E. bicolor* extracts may be exploited as a source of beneficial compounds for oxidative stress related diseases in humans (Ashwini *et al.,* 2015). Antioxidant activity and its correlation with total phenolic content in this species have been estimated for the first time by Ashwini and Majumdar (2015) and they have observed significant correlation between them (Ashwini *et al.,* 2015).

Antihyperglycemic activity

The treatment of diabetes with commercially available drugs such as acarbose may cause various side effects such as kidney, retinal and neurological disorders and hence it is desirable to use traditional and alternative medicines to cure hyperglycemia (Arulrayan *et al*., 2007). *Exacum bicolor* was considered as a substitute of *Swertia chirata* which is a potent endangered antidiabetic plant. Therefore, mass production of *E. bicolor* is needed since the plant has been over exploited because of its medicinal importance (Sreelatha *et al*., 2007; Brilliant *et al*., 2010; Behera and Raina, 2012).

Thrombolytic activity

Synthetic thrombolytic drugs are expensive and might also cause side effects such as respiratory depression, allergic reactions, urticaria, itching, nausea, headache and musculoskeletal pain (Banerjee *et al*., 2004). Therefore, there is a need for search of alternate herbal remedy as a substitute, which causes no side effects (Ashwini, 2016). In the case of *E. bicolor*, the methanol leaf extract (ML) was assessed by clot disruption method which revealed 45.1±0.8% of clot lysis at 100 µg/ml (Ashwini *et al.,* 2015) while streptokinase (positive control) and water (negative control) demonstrated 56.2±0.6% and 8.3±0.5% lysis of clot respectively. *E. bicolor* ML extract exhibited thrombolytic activity with lower concentration (100µg/ml) when compared to the above studies (Ashwini, 2016).

Anti-inflammatory activity

Methanol extract of *E. bicolor* exhibited inhibition of protein denaturation (78%) which revealed its antiinflammatory activity (Ashwini, 2016). *In vitro* antiinflammatory activity of *E. bicolor* extracts at different concentrations showed significant stabilization towards HRBC membranes (Ashwini *et al*., 2015).

Anthelmintic activity

E. bicolor exhibited improved degree of anthelmintic activities, which could be considered as herbal source for anthelmintics (Ashwini, 2016).

Bioactive compounds

Plants are important sources of free radical scavenging molecules. Free radical scavenging activity of *E. bicolor* methanolic extract was determined by Braca *et al*. (2003). Active compounds such as luteolin and chlorogenic acid were detected in *E. bicolor* from *in vitro* regenerated plantlets and wild plants (Jeeshna and Paulsamy, 2011a). In *Exacum bicolor* extract, GC-MS analysis revealed the presence of six phytochemical compounds of medicinal importance belonging to phenolic group [7"-3"- (2, 4 dichlorophenyl) – 3", 4"- dihydrodpirol (1,3-dioxolane); Cyclocorynan-16-carboxylic acid; 17-(acetyloxy)-19,20-diehydro-10-methoxy-methyl ester; 4- (4Chlorophenyl)-5morpholin-4-yl-thiophen -2-carboxylic acid ethyl

ester], one compound of glycoside group [a"-D-galactopyranoside, methyl 2,3-bis-0-(trimethylsilyl)-, cyclic phenylboronate] and one compound of steroid group [9,19cycloergostan-3-ol-7-one,4,14-dimethyl (Jeeshna and Paulsamy, 2011b). *E. bicolor* leaf extract contains various phytocompounds with functional molecules such as phenols, alcohols, amines, carboxylic acids and its derivatives. In *E. bicolor* wild (ML) and micropropagated extracts (MM) revealed similar bioactive compounds such as undecane, 1-Methyl 2(3-oxocyclohexyenyl) imidazole, erythrocenturin, neophytediene, hexadeconic acid, 6- Octadeconic acid and inophylum by GC-MS analysis (Ashwini, 2016).

Threats

Mishra (2018) has listed out the variety of plant species existing in the Ash-Dyke area of Dharnas village, National Thermal Power Corporation (NTPC), Korba recorded the presence of *E. tetragonum* within the study area. The area was one of the heavily industrialized sites in India. Godbole *et al.* (2016) assessed the biodiversity of the proposed mining lease area of Degave village in Maharashtra and found out that iron ore mining would lead to heavy destruction of rich forests in Degave. The species *Exacum tetragonum* was recorded in the flora of Degave.

Exacum bicolor is seen restricted to small pocket areas even in vast stretches of grassland. This unique feature accompanied by the drastic social changes leads to threating of the plants to extinction (Sreelatha *et al.,* 2007). Habitats of *Exacum bicolor* principally the dry grasslands are being exploited for laterite mining, quarrying and soil excavation for highways and for rubber and cashew planting. Grasslands are also utilized as industrial sites. Habitat destruction as a cause for population depletion has been reported in many studies (Sreelatha *et al.,* 2007).

Tissue culture

Being endemic to Western Ghat region, there is a need for mass production of *E. bicolor* to balance the overexploiting of the species for its medicinal importance (Sreelatha *et al*., 2007; Brilliant *et al*., 2010; Behera and Raina, 2012). Jeeshna and Paulsamy (2011a) reported that in *E. bicolor* the nodal explants were inoculated on MS media supplemented with BA and 2,4-D (1.5 and 0.9 mg/l) which produced callus. It was further subcultured on BA and NAA (1.0 and 0.2 mg/l) which resulted in shoot development. Varying degrees of shoot growth were observed in *E. bicolor* with different types and concentrations of phytohormones. BA was found to have greater influence than other phytohormones when cultured individually. In *E. bicolor* 10 µM BA produced the maximum number of shoots (10.0 ± 0.58) when compared to other phytohormones. The number of shoots per responsive explant in *E. bicolor* was significantly affected by the type and concentration of plant growth regulator. In *E. bicolor* to get higher number of shoots and biomass, *in vitro* propagated plants from agar medium were transferred to liquid culture, which improved the shoot number from 19.33 to 199.5 shoots per explant which showed 10 fold increment (Ashwini, 2016).

Genetic and molecular studies

Five *Exacum* species from Kolhapur district were morphometrically analyzed with the help of PCA, cluster analysis and CD by Anant (2012). All these tests revealed that *Exacum bicolor* was morphologically very distinct and *Exacum petiolare* Griseb. and *Exacum pedunculatum L.* were closely related with each other. The sequence of the species relationship is as per given succession *Exacum pedunculatum* L. p *Exacum petiolare* Griseb. (*E. pedunculatum* L. var. *petiolare* Trim.) *Exacum pumilum* Griseb. p *Exacum lawii* Cl. p *Exacum bicolor* Roxb. (*E. tetragonum* Roxb.).

Conclusion

The need of bicolour Persian violet is on the rise in order to meet the ever-increasing pharmaceutical requirements and consequently there is diminition in its populations in the natural habitat. In addition to over exploitation, the plant faces threats of changes in landscape ecology caused by climatic and anthropogenic factors. Due to increased demand, exploitation, improper cultivation practices, deforestation and habitat destruction, a large part of wild medicinal plants are hard to restore their populations, thus categorized into rare, endangered and threatened groups (Kumar and Sikarwar, 2002). It is crucial to manage the germplasm of these RET plants through conservation programmes (Rao and Hodgkin, 2002). Management should intend to boost the size of small populations to lessen further loss of genetic variation. Because a huge proportion of genetic variation is among populations, even small populations are worth preserving (Misra *et al.,* 2010).

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