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Trewia nudiflora: A potential source of new drugs

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ABSTRACT

Medicinal plants have long history of being using as traditional medicines in almost every corner of the earth. Various chemical constituents of the plant are responsible for the activities. The plant *Trewia nudiflora*, belongs to the Euphorbiaceae family and is found abundantly in South Asia and Eastern Australia. Almost all parts of the plant such as root, stem bark, leaf, fruit and seed possess bioactive chemical constituents. The major chemical constituents are taraxerone, betasitosterol, nudiflorine, trewiasine, dehydrotrewiasine and maytanbutine. Although various parts of the plant have potential activity against cancer, tuberculosis, anti-inflammatory, antiulcer and antimicrobial activities, but many activities like diabetes, arthritis, analgesic, anticoagulant has not yet been studied. So, this plant could be a potential source for the future research.

Keywords: *T. nudiflora*, Chemical constituents, Anticancer, Anti-inflammatory, Antimicrobial.

INTRODUCTION

Normally the plants that possess therapeutic properties or exert really useful pharmacological outcomes on the human body are specified as medicinal plants. Some secondary metabolites, like alkaloids, sterols, terpenes, flavonoids, saponins, glycosides, cyanogens, tannins, resins, lactones, quinines, volatile oils etc are naturally synthesized and accumulated by medicinal flora [1].

Notable opportunities with alternative treatments are provided by medicinal plant life. They not only provide access and low-cost remedy to poor people but also, they can generate income, employment and foreign exchange for developing countries. Many common recuperation herbs and plant components have been proven to have pharmacological value, mainly in the rural areas and that these can be used to prevent, alleviate or treat a number of human diseases [2].

The medicinal plant life has been used for the remedy of ailments and diseases since ancient time. Ancient Chinese scriptures and Egyptian papyrus hieroglyphics describe medicinal uses for plants. Indigenous cultures (e.g., African and Native American) used herbs in their recovery rituals, while others developed typical medical systems (e.g., Ayurvedic and Traditional Chinese Medicine) in which natural therapies had been used. Researchers have observed that humans in distinct parts of the world have a tendency to use identical or similar flora for treating identical illnesses [1].

It was estimated by the WHO that above 80% of the world's population depend either entirely or mostly on traditional remedies for health benefits [2].

A tropical plant named *Trewia nudiflora* L. (Euphorbiaceae), typically disbursed in India and its neighboring countries, Malaysia and the south of China, enjoys notable popularity in traditional herbal medicine [3]. Resinous matter and carbohydrate are enclosed in the root of *Trewia nudiflora*. Various plants parts of *T. nuliflora* such as whole plant, fruit, leaves, and seeds have been mentioned for pharmacological activities [4]. It carries a pyridine alkaloid, N-methyl-5-carboxamide-2-pyridone, nudiflorine. Bark yields taraxerone and betasitosterol. Seeds include a maytansinoid compound named, trewiasine and additionally include an alkaloid ricinidine [5].

PLANT DESCRIPTION

Geographical source

Eastern Australia, Malaysia, the Indian subcontinent, Southern Asia, the south of China and some islands of the western Pacific etc are enriched with most of its species. These are plentiful in areas on river, pond and canal bank.

Vernacular names

This plant is known as

English: Gutel, False white teak

Bengali: Latim, Lattu, Pitali, Gotagamar (Sylhet)

Hindi: Pindar, Gori, Gambhara

Urdu: Pindara

Malyalam: Nevkumizhu

Tribal name: Bolno-khap (Garo), Chagalla-dibhangor (Chakma), Rinmoro (Marma).

Taxonomy
The taxonomy of this plant is:

Kingdom:	Plantae
Division:	Angiosperma
Class:	Eudicots
Unranked:	Rosids
Order:	Malpighiales
Family:	Euphorbiaceae
Subfamily:	Acalyphoideae
Tribe:	Acalypheae
Subtribe:	Rottlerinae
Genus:	*Trewia*
Species:	*nudiflora*[6]

Figure 1: *Trewia nudiflora* buds and flowers

Figure 2: *Trewia nudiflora* fruits and tree

General description

Trewia nudiflora Linn. (Euphorbiaceae) is a hastily growing, smooth wooded versatile dioecious tree. It grows within the semi-evergreen and moist tropical forests as well as distinct non-forest areas of tropical districts of Bangladesh, India, China and Malaysia. *T. nudiflora* is a branchless tree and leaves long pointed, reverse, furry underneath when young, ovate 11-20 cm by 7-12 cm, stalks 2-7.5 cm long. Fully grown male flowers are yellow in long lax drooping inflorescences while females are green, solitary or 2-3 together in the leaf axis. Male and female flowers appear on separate trees [7].

With a diameter of 3.5 cm by 3 cm, *Trewia nudiflora* Linn. (Euphorbiaceae) fruits are fleshy, grayish green and depressed globose [7]. The fruits are large, hard green, and dull, turn out to be colored upon ripening. Fruits are a capsule 2-3 cm across, woody, extensively cuneate to rounded, 3-4 locule, the pericarp of the fruit is very thick; the seeds are globose and ovoid [4]. During the monsoon season (June-October), the hard fruit of *Trewia nudiflora* that is green in colour fall to the ground in a great amount. It is observed wild in Forest areas. The flowering takes place from March to April and simply after flowering the fruiting takes place between May to June [4].

Noticeable natural restoration of *T. nudiflora* is observed in moist and coarse-textured soil. The seedlings of the species are normally sensitive to drought and get killed at the uncovered upland sites. The moisture and light regimes are the common elements that influence the relative abundance and distribution of male and female individuals [8].

CHEMICAL CONSTITUENTS

Kang Q et al isolates three new compounds, namely, (+)-dihydrodehydro diconiferyl alcohol 4-O-β-(6″-O-galloyl)-glucopyranoside, 4,4′-O-dimethylellagic acid 3-(2″-O-acetyl)-α-rhamnopyranoside, and ethyl O-β-(6′-galloyl)-glucopyranoside, from the stem bark of *Trewia nudiflora* [9]. Three new ent-atisane diterpenes, namely, 17-hydroxy-ent-atisan-19-oic acid, 17-hydroxy-ent-atisan-19-oic acid methyl ester, and 16α,17-dihydroxy-ent-atisan-19-al, had been isolated from the pericarp of *Trewia nudiflora* collected from this plant with five recognized phenolic compounds, *i.e.,* gallic acid, ethyl gallate, protocatechuic acid, 3,4,4′-tri-O-methylellagic acid, and α-tocopherol, and two different known compounds, *i.e.,* trans-cinnamic acid and taraxerone. Trace quantities of maytansinoids had been isolated via antifungal-activity-guided fractionation [10].

It was also found that the bark of *Trewia nudiflora* consists of taraxerone and betasitosterol. The plant yields a pyridine alkaloid, N-methyl-5-carboxamide-2-pyridone, and the leaves consist of an alkaloid, nudiflorine. The seeds additionally have a maytansinoid compound, trewiasine [5]. Three maytansinoids, namely, dehydrotrewiasine, maytanbutine, and trewiasine, had been isolated and identified from *Trewia nudiflora* having robust cytotoxic activity. It was the first time that maytanbutine was obtained from this plant [11]. Another two maytansinoids namely N-methyltreflorine and methyltrewiasine, discovered in the dried fruits of Trewia nudiflora [12].

Shilpi JA *et al.,* extracted new cardenolides namely trewianin and trewioside along with scopoletin and indole-3-carboxylic acid from the stem bark of the plant [5]. Some preliminary phytochemical screening confirmed the presence of a number of phytochemicals along with steroids, phenolic compounds, alkaloids, glycosides, flavonoids and tannins [13]. Glyceride oil, pyridinone alkaloids mainly ricinidine was reported in seeds also [14]. In addition to the phytochemicals, presence of antioxidant compounds was also reported and evaluated by DPPH radical scavenging assay [15].

PHARMACOLOGICAL ACTIVITY

Ceberoprotective Activity: Cerebroprotective activity of Trewia nudiflora was reported against ischemic rat models. In their study Kumar and Kumar (2012) mentioned that ethanol extracts of the leaf have significant cerebroprotective effects. The animal was treated with the extract for 7 days at 200mg/kg and 400mg/kg dose and significant improvement on behavior pattern and spatial learning were reported [16].

Antitumor Activity: A dose dependent anti-tumor activity was reported on ethanolic plant extracts against crown gall tumors on potato discs, KB cell culture and leukemic mice [17]. The seed contains large amount of maytansinoids which has been reported the presence of anti-tumor activities [18-19]. It was also reported that the seeds are rich in anti-tumor compounds such as trewiasine, dehydrotrewiasune and demethytrewiasine [19-20].

Anti-tubercular Activity: In their study Li et al (2004) found that, the seed endotheliums of *Trewia nudiflora* shows activity against *Mycobacterium tuberculosis* where minimum inhibitory concentrations (MIC) is100 µg/mL. The antitubercular activity is responsible due to the presence of the two compounds name 9'-butyl americanol A and americanin [21].

Antifungal Activity: Du et al. reported antifungal activity of the ethanolic extract of pericarp against fungus against *Penicillium avellaneum* [10].

Antibacterial Activity: The plant is rich source of antibacterial diterpenoids. The major diterpenoids are neo-lignans, cardenolides and ent-atisane [10,22-23]. The methanolic extract of *T. nudiflora* exhibit antibacterial activity against four Gram positive bacteria (*Staphylococcus gallinarum, S. sciuri, Streptococcus iniae* & *S. constellatus*) and eight Gram negative bacteria (*Xanthomonas axonopodies, X. campestris, Edwardsiella anguillarum, Siccibacter colletis, Aeromonas cavernicala, A. diversa, Vibro rotiferianus* & *Enterobacter xiangfangensis*). The inhibition zone ranges from 15-20 mm for 15 µl/disc. The MIC values of the extract was ranging between 100-200 µg/ml [24]. The antibacterial activity of *T. nudiflora* leaf was also evaluated by Begum Y. She has found that the extract was strongly effective against *Shigella dysenteriae* having zone of inhibition (ZOI) 37.5 mm and effective against *Pseudomonas aeroginosa* with 16.5 mm ZOI. In addition, the fruit extract has potential against Shigella boydii with ZOI 22.5 mm [25]. Beside the other parts, the seed also exerts antibacterial activity. It was found that the seed extract shows activity against *Pseudomonas aeroginosa* with ZOI of 20 mm [8].

Anti-inflammatory Activity: Alcoholic extract of *T. nudiflora* roots shows considerable anti-inflammatory activity against rats. The anti-inflammatory activity is due to scavenging of free radicals by the action of antioxidant enzyme superoxide dismutase and glutathione peroxidase [26].

Anti-ulcerogenic effect: Ralakshimi et al., (2012) reported dose dependent anti-ulcerogenic effect of the ethanolic extracts of leaves on indomethacin and cold restraint stress-induced gastric mucosal damage on albino rats [27].

DISCUSSION

Herbal medicine is the foundation for various conventional medicines in the world. At present, these drugs share 25% of all crude drugs in the market and another 25% used after chemical modification, and day by days herbal drugs are gaining popularity [28-29]. The main reason behind the popularity of herbal drug is reasonable cost, natural origin, less side effects, more safety and easy availability [30].

Trewia nudiflora has long history of being using as a medicinal plant in many regions of the world. The various parts of the plant have pharmacological activities like cerebroprotective, anticancer, anti-tubercular, antimicrobial, antiulcer and so on. The phytochemical present in the leaf, root and fruit is responsible for giving pharmacological activity [31]. Although no research data has been found on other pharmacological activities like anticoagulant, antidiabetic, antidiarrheal, analgesic, immunomodulatory, hypolipidemic, anti-asthmatic, hepatoprotective, anthelmintic and many more. Some new chemically active compounds have already been discovered from various parts of the plant but many new compounds could still be discovered from these plants by selecting different plant parts and using various types of solvents.

This review only comprising very few scientific works because too many works has not been done yet on this plant. But this study compiles all the available scientific data on this plant. This study could offer some authentic scientific evidence to the traditional practitioners as they are prescribing these drugs without proper scientific investigation. This effort could link together the modern scientific approach with ethnomedicinal use of herbal drugs.

At present microbial disease is one of the promising diseases and resistance are developing rapidly on available antimicrobial compounds because of the irrational use. So, the demand for new antimicrobial compounds is very high. The isolated new antimicrobial compounds from this plant like 9"-butyl americanol A, americanin, trewiasine, treflorine, dehydrotrewiasune and demethyltrewiasine has potential for using as a new source. Further steps should be taken on these compounds to make the available as an established pharmaceutical drug with proper formulation and dosage forms. In addition, focus should be made to discover new drugs having different pharmacological activity. Beside the bioactive drugs, the plant is also a good source of nutritional compounds. The fatty acids such as elaeostearic acid (38.50%), oleic acid (34.35%), linoleic acid (26.15%) and arachidic acid (1%) could be used as nutritional supplements [32].

CONCLUSION

Reviewing this plant, it can be concluded that this plant has potential of being using as a solution for many diseases. In addition, focus should be done on other pharmacological areas which is still untouched. More research work also needed to investigate the mechanism of potential activity of the various isolated compounds of the plant.

Conflict of Interest

None declared.

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