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Morphological features, phytochemical and ethnopharmacological attributes of *Tabernaemontana divaricata* Linn.: A comprehensive review

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Abstract

Tabernaemontana divaricata Linn. is an ornamental, evergreen and highly useful ethno medicinal plant which is utilized for various traditional treatment purposes worldwide. The plant is commonly called Crepe Jasmine and it is belonging to the family of Apocynaceae. The plant is found in Asia, Australia, China, Japan, India and Myanmar. The plant is 1.5-2.5m in height with silvery grey bark; wrinkled and milky latex exudes when wounded, and has white colored flowers. The leaves are shiny deep green in color. According to the previous study the plant has diverse ranges of phytochemicals constituents such as alkaloids, steroids, flavonoids, phenolic acids and enzymes. The flowers of the plant contain epivoacangine, apparicine, isovoacristine, tabernaemontanine, voaphylline, and vobasine. It is ascribed with extensive series of useful pharmacological activities like anti-inflammatory, anti-cancer, analgesic, antioxidant, anti-diabetic, anti-convulsant, antimicrobial and anti-infertility activities. This plant is also used to treat various disorders like abdominal tumors, epilepsy, eye infections, fever, headache, inflammation, leprosy, asthma, diarrhea, paralysis, rheumatic pain, ulceration and vomiting. So, the review article briefly describes the morphological features, ethno medicinal uses, pharmacological properties and phytochemical composition of this medicinal plant. The present study is also an attempt to combine and document the important information of *Tabernaemontana divaricata* and highlights the future need for research and development.

Keywords: *Tabernaemontana divaricata*, phytochemistry, ethnobotany, pharmacology

Introduction

Nature is a resource of huge number of plants with medicinal properties. From these natural sources an impressive numbers of drugs are isolated and many varieties of traditionally used medicinal plants are distributed worldwide [1]. In Ayurveda, Homeopathy, Sidhha, and Folkloric medicine system the medicinal plants have a significant role to cure human physiological disorders [2]. The natural Phyto diversity of the earth is the ample source of medicinal plants and around 80% of the world population dependent on plant based medicines as traditional health care systems [3, 4]. Millions of people in the world are using medicinal plants for primary healthcare because of its least or no side effects in the mankind. All these medicinal plants has huge amount of phytochemical constituents. Depending on the presence of phytochemical constituents it is very easy to understand the medicinal importance of the plant [5]. To exploit against physical disorders the phytochemical substances are derived from different parts of the plants like flowers, leaves, stem, fruit and root. To specify the phytochemicals of this plant there are two forms as primary metabolites (amino acids, proteins, sugars and chlorophyll) and secondary metabolites (phenols, alkaloids, flavonoids, terpenoids, tannins, saponins and glycosides) [1].

Tabernaemontana divaricata is an ornamental plant as well as an evergreen shrub. It belongs to the family of Apocynaceae [1]. It is commonly known as Crepe Jasmine. In West Bengal it is known as Tagar or Kath Mallika. The plant is widely distributed in Asia, Australia, mangrove forest of China, Japan and in India. It generally occurs in upper Gangetic plain, Garhwal, Khasia Hills, Assam, Myanmar, Bangladesh, Vishakhapatnam, and West Bengal [6, 7].

It is found in the roadsides, lawns, gardens and human settled areas. This plant is very attractive because of its silvery grey bark, milky latex, shiny deep green leaves and white colored fragrant flowers. In traditional medicine it is very popular because this plant have huge amount of phytochemical compounds constituents such as alkaloids, terpenoids, steroids, flavonoids, phenylpropanoids, phenolic acids and several plant enzymes. The plant parts are used in curing various physiological disorders of human being like epilepsy, abdominal

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tumors, eye infections, fractures, fever, headache, inflammations, edema, leprosy, diarrhea etc [1, 8].



Fig 1: Natural Habitat of *Tabernaemontana divaricata*

Taxonomical Position

Kingdom:	Plantae
Phylum:	Tracheophyta
Class:	Magnoliopsida
Order:	Gentianales
Family:	Apocynaceae
Genus:	<i>Tabernaemontana</i>
Species:	<i>divaricata</i>
Botanical Name:	<i>Tabernaemontana divaricata</i> (L.) R. Br. ex Roem. & Schult.

Vernacular Names

English:	Crepe Jasmine, Pinwheel Flower
Sanskrit:	Nandivarksha
Hindi:	Chandni, Tagar, Tagari
Assamese:	Kathanda
Bengali:	Tagar, Kath Mallika
Kannada:	Nandi battalu, Nanjubattalu, Nandyaavarta
Mizo:	Par-arsi, Kelte-bengbehBattalu
Tamil:	Nandiarvattai
Gujarati:	Sagar
Marathi:	Ananta, Tagar
Malayalam:	Kutampale
Bangladesh:	Dudhful/ Kath-Mallika

Botanical Features

Tabernaemontana divaricata (Figure 1) is an evergreen medicinal shrub and moderately fast-growing. It can grow as a garden plant, and also found on roadsides, lawns, and human settled areas. The plant is a glabrous, 1.5-2.5m in height with silvery grey bark, wrinkled and milky latex exudes when wounded, and has snow white colored fragrant flowers. The leaves are shiny deep green in color [6].



Fig 2: Leaves and Stems



Fig 3: Flower

Leaves: The leaves (Figure 2) of the plants are oval in shape, simple, entire, opposite/sub-opposite, pinnate venation, lanceolate or elliptic-oblong, cuneate at base, acuminate and wavy margins, dark green in color, glossy leathery texture [6].

Stem: The stem (Figure 2) of the plant is woody, smooth-no hairs, dichotomously branched, dark brownish, hard, erect, branched, solid, tuber-like and thick, silvery grey bark and milky latex, multi-trunked or clumping stems [6].

Root: The root of the plant is tap root system. The root is silvery brownish, hard, branched; with no odor and taste.

Flowers: The flowers (Figure 3) are small, trumpet-shaped, milky white in color, actinomorphic, sweetly fragrant, solitary or few-flowered cymes in axils or terminal, pin-wheel arrangement of petals, calyx lobes 5, imbricate, campanulate, corolla salver-shaped, tube dilated below the top, lobes 5, ovate; Stamens 5, included in the dilated portion of the tube, filaments short, anthers linear; Carpel's 2, distinct, style long, stigma ob-ovoid and ovules many [6].

Fruits: The fruits are rare but pod or pod-like, ribbed and curved, dry or hard, follicles 2, green outside, orange-red within narrowed into a slender curved beak.

Seeds: The plant has many seeds, dull brown in color, minutely pitted, and irregular, enclosed in a red pulpy aril.

Flowering and Fruiting Time: Throughout the year, specially the month of July-September.

Phytochemical Components

Phytochemical study of the plant revealed that the plant parts contains high amount of various phytochemicals, and bioactive substances. These are alkaloids, terpenoids, steroids, flavonoids, phenylpropanoids, phenolic acids, saponins, tannins, proteins, cardiac glycosidase, carbohydrates and several plant enzymes [9]. The plant ethanolic extracts showed the rich amount of flavonoids and protein presence. As well as in leaves amount of phenols were observed very high. In leaves total flavonoids was assessed as 19.6 mg quercetin equivalents/g (mg QE/g), total phenols was estimated 47.1mg Gallic acid equivalents/g (mg GAE/g) and total protein level was estimated 18 mg/g. In flower flavonoids was assessed 15.4 mg QE/g, total phenols was estimated 6.2 mg Gallic acid equivalents/g (mg GAE/g) and total protein level was estimated 2 mg/g [1]. The flowers of the plant contain apicarine, isovoacangine, isovoacristine, 11-methoxy-N-methyl dihydro-Pericyclivine, tabernaemontanine,

tabersonine, voaphylline, N-1-methyl-Voaphylline and vobasine. Huge amount of both primary (amino acids, proteins, sugars and chlorophyll) and secondary metabolites (phenols, alkaloids, flavonoids, terpenoids, tannins, saponins and glycosides) are present in the plant parts of *Tabernaemontana divaricata* [10-17].

Ethnomedicinal Uses

Tabernaemontana divaricata is a useful and remarkable medicinal shrub which is used as a traditional medicinal plant in ayurvedic, homeopathy and folkloric treatment system for different human ailments healing purposes in various parts of the world. Many parts of this medicinal plant are applied in the treatment of multiple diseases such as asthma, diarrhea, epilepsy, abdominal tumors, eye infections, fever, fractures, headache, inflammation, leprosy, edema, paralysis, piles, rabies, rheumatic pain, ulceration and skin diseases [6]. Also the plant is used as anti-hypertensive, aphrodisiac, diuretic, anthelmintic, hair growth promoter, purgative, and remedy against poisons and tonic for brain, liver and spleen [6].

In Thai, Ayurvedic and Chinese traditional medicines system the plant is used for fever, pain, dysentery [18, 19]. While, in Africa, from the roots extraction, latex from fruits or crushed leaves are used as remedy for headache, constipation, flatulence and stomach ache [18, 20]. Also the mixture of leaf powder with other species is soaked in water and used to cure bewitched persons or consumed daily to revive appetite [11]. In Malaysia, decoction of bark from the plant is used to treat syphilis, whilst the steam from boiled juice is inhaled to treat ulceration of the nose [19].

The roots are prepared as decoction and used orally for treatment of fever as well as the plant paste applied to cure orchitis [18, 21]. In Bangladesh, the leaves of the plant are used to treat tumors [22]. The leaves extracts is applied in the treatment of sores [18]. As the plant *Tabernaemontana divaricata* is found throughout the temperate and tropical regions of India, America, Thailand and so many places in the world, the different plant parts are used different traditional way to cure several disease.

Pharmacological Activities

Antioxidant Activity

Various scientists reported the antioxidant effects of *Tabernaemontana divaricata* by using the carbon tetrachloride (CCl₄)-induced hepato-toxicity model [23-25]. The hepato-toxicity is because of the metabolite of CCl₄, a free extreme that causes the per-oxidation of lipids in the endoplasmic reticulum that prompts cell passing [26].

In an *in vivo* study, Gupta *et al.* reported that methanolic leaves extract of *Tabernaemontana divaricata* showed a significant hepato-protective effect. Where lipid per-oxidation is decreasing and significantly the level of anti-oxidant agents were increasing in a dose dependent manner such as glutathione (GSH), superoxide dismutase (SOD) and catalase (CAT) [23, 24].

In another investigation, Mandal and Mukherji demonstrated that the plant is one of the best scavenging system to fight against the effects of air pollution. Their result concluded that the plant *Tabernaemontana divaricata* have a high range of activity of antioxidant agents such as CAT, SOD, GSH, phenolic peroxidase and ascorbate peroxidase [24].

Anti-analgesic Activity

In folk medicine, the analgesic properties of *Tabernaemontana divaricata* are previously reported by using roots. The anti-nociceptive effect is confirmed by the

experiment of Henriques *et al.* They showed that mice treated either orally or intraperitoneally with 150 mg/kg of *Tabernaemontana divaricata* and 30 min before it is placed on a heated plate (50-55 °C). Then the result showed significantly greater response times to the heat stimulus than the control that is without plant extracts treatment. But this analgesic effect has not been verified for this mechanism [27].

Anti-inflammatory Activity

In case of rats, the anti-inflammatory effect of *Tabernaemontana divaricata* was showed in carageenin-induced paw edema [28-31]. In this experiment, male rats were treated by injecting 0.1 ml of carageenin into one of the hind paws. The plant decoctions (150-200 mg/kg) were executed either orally or intra-peritoneally 1 h before the sub-plantar infusion of carageenin. After carageenin injection, by using a modified the edema measurements were done in 1, 2 and 4h. This experiment reported that compared to animals without extract administration, the plant extracts had significant anti-inflammatory effect on carageenin-induced paw oedema and this anti-inflammatory effect was dose dependent [26]. *Tabernaemontana divaricata* has very potent for the anti-inflammatory mechanism because the presence of the chemical agent, phenolic acid that has a potential anti-inflammatory benefits [32].

Anti-microbial Activity

The anti-microbial effect of *Tabernaemontana divaricata* shows against various infectious diseases such as syphilis, leprosy, gonorrhoea, dysentery, diarrhea, and malaria. An *in vitro* study reported that at the concentration of 250 µg/ml of apparicine, an alkaloid can inhibit the activity of *Polio III virus* [33, 34]. Also, in an *in vitro* study it was shown that apparicine at a concentration of 1.2 percent can exhibited antimicrobial activity against *Salmonella*, *Shigella*, *Pseudomonas*, *Escherichia*, *Proteus*, *Staphylococcus* and *Corynebacterium*. Moreover, apparicine, acts as an opioid agonist to opioid receptors in an *in vitro* study [35, 36].

Another experiment demonstrated that voacamine has a strong antimicrobial activity against Gram-positive bacteria such as *Staphylococcus aureus* and *Bacillus subtilis*. It also has moderate activity against Gram-negative bacteria such as *Escherichia coli* and *Pseudomonas aeruginosa* [23].

Gastro-protective Effect

The methanolic (TDFME 500 mg/kg, p.o) extracts of the flower of *Tabernaemontana divaricata* plant showed anti-ulcer property or gastro-protective effect in Wistar rats by pyloric ligation induced gastric ulceration model using Omeprazole (8mg/kg, p.o) as a standard drug. There are five parameters volume of gastric juice, pH, free and total acidities and ulcer index were evaluated. In this experiment the test extract diminished volume of gastric juice, free and absolute acidities and ulcer file. Also the raised pH of gastric acid increased, like standard. The tests were 89.84% and 79.53%, respectively and the observed percentage protection for standard. Therefore in case of TDFME 500 mg/kg all the parameters had positive effect and the standard also shows similar result. In the present study it was concluded *Tabernaemontana divaricata* flower methanolic extract possesses ulcer preventive properties that means the plant had significant gastro-protective effect at a dose of 500 mg/kg. In this scenario further experimental operations are also recommended to know the mechanism of action [6].

Antifungal Activity

To evaluate the antifungal activity *Tabernaemontana divaricata* petroleum ether, chloroform and ethanolic extracts of the plant were tested by the cup plate method. In this case different concentrations of the extracts (5%, 10%, 15%, and 20%) were arranged for test. With nutrient agar medium, all the petriplates were poured and keep the petriplates for solidification. For this test *Aspergillus niger* and *Candida albicans* microorganisms were used and swabbed on the petriplate containing media. Using cork borer the four wells were prepared. Different concentrations of the sample were filled in these wells. Then at 280°C for 48 h all the plates' standard and control Flucanazole and DMF were incubated. As a result, against *Aspergillus niger* and *Candida albicans* the plant extracts carried out the antifungal activity. So in all the concentration the ethanol extract showed maximum inhibition zone, where the chloroform and petroleum ether extract resulted potent antifungal activity [37].

Anti-diabetic Activity

The present experiment was demonstrated to evaluate the anti-diabetic activity of the methanolic extract of leaves of *Tabernaemontana divaricata* on alloxan induced diabetic mouse model. The variant doses like 300 and 400 mg/kg of body weight the extract was allowed to pass intraperitoneally and the blood glucose levels were measured at 0, 2, 6, 12 and 16 hours of time interval. With a standard drug metformin, the anti-hyperglycemic effect of the extract was compared. At 12th hour of the treatment period the extract of 400 mg/kg decreased maximum blood glucose level from 14.19±0.47 to 6.86±0.41 mmol/L. Also the extract was subjected to Brine shrimp lethality bioassay. Then the LC₅₀ value of the extract was 27.87µg/ml. So, the present results demonstrated that the leaves of *Tabernaemontana divaricata* has potential anti-diabetic, compared to standard drugs [38].

Anti-cancer Activity

Hydro alcoholic decoction of flowers of the plant was tested for anticancer activity. By soxhlet extraction method, the extract was prepared. Here the solvent petroleum ether and hydroalcohol were used. In the *in vitro* study against human cancer cell line (HeLa) the experiment was performed. Also to analyze the cell growth inhibition MTT assay was used. The results of hydro alcoholic decoction of flowers of *Tabernaemontana divaricata* showed a moderate amount of anticancer activity and the IC₅₀ value was greater than 100 µg/ml. The further research is needed to clarify the anticancer activity of the plant [39].

Hepato-protective Activity

Hepato-protective effects of *Tabernaemontana divaricata* was evaluated in rats against DEN and Fe NTA induced liver necrosis. Ethanolic decoction of *Tabernaemontana divaricata* was used at doses of 200 and 400mg/kg bodyweight and standard drug was 5-fluorouracil. Sample and standard was orally executed to male Wistar Albino rats once daily for 24 weeks. Simultaneously, they were treated with the carcinogen DEN and Fe NTA. In case of simultaneously treated rats the plant extract notably reduces uric acid, bilirubin, AST; ALT and ALP parameters in blood as well as it increased marker enzymes levels in liver. Comparison with the treated group, the treatment with the extracts showed a significant increase in the levels of antioxidant components and reduces the levels of malondialdehyde. But the results showed better in all the parameters when, comparing with 200mg/kg body weight

rats, 400 mg/kg body weight rats and 5-fluorouracil treated rats. So the protective effect of the extract was confirmed against induced liver necrosis by this histopathological study. Thus the plant has a very good hepato-protective effect against liver cell necrosis [38, 40].

Antinociceptive Activity

In mice, the crude ethanolic extract of the leaves of *Tabernaemontana divaricata* showed antinociceptive activity by using the model of acetic acid induced writhing. The extract resulted significant inhibition of writhing in acetic acid induced mice at the oral 250 and 500 mg/kg body weight of the respective dose. That was compared to the standard drug diclofenac sodium at the dose of 25 mg/kg of body weight. The experiment demonstrated that produced serious antinociceptive activity [38, 41].

Toxicity Assessment

Tabernaemontana divaricata carried out a huge number of pharmacological activities so it is very essential to know the toxicological evaluation of the plant. According to Henriques and colleagues investigation of mice, the toxicity of the plant using the behavior screening test treated with alcoholic or aqueous extracts of the plant sample at doses of 150- 200 mg/kg body weight. By this test it was reported, at these concentrations the results were almost identical from control animals that indicate no toxicity [27]. On the other hand, according to Melo and Colleagues demonstration of the major alkaloids of the plant 'voacristine' which introduced on cultures of yeast the dose-dependent cytostatic and cytotoxic effects. In case of toxicity assay of *Tabernaemontana divaricata*, there were only a few experiments have done. It is highly important to make out the adverse toxicity effects and to continue the further investigations for toxicity of the plant [23].

Conclusion

The current review article highlighted that the *Tabernaemontana divaricata* Linn. Has the immense potentiality for morphological, phytochemical, nutritional, ethno botanical parameters as well as prominent medicinal properties. Through this review article, it can be said that the plant has been used as an important remedial agent for several physiological disorders in different parts of the world. Also the review cited the important biological or biochemical properties of *Tabernaemontana divaricata* as well as it highlights the researchers are actively working with this plant to know the ethno biological potentiality. Therefore, considering its entire aspects it can be concluded that there is an ample scope for future research on *Tabernaemontana divaricata* [42-46].

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Conflict of Interest

The author declares no conflict of interest.

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