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A review on phyto-pharmacological significance of *Marsdenia tenacissima Wight & Arn*

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Abstract
Medicinal plants are a renewable source of cheaper medicines. In India, drugs of herbal origin have been used in the traditional systems of medicines such as Unani, Ayurveda and, Siddha. The herbal formula containing a selective combination of individual herbal ingredients that are formulated for a specific ailment or group of disease conditions. When the herbals are using combined which are more potent and effective within the body than individual herbs due to their activating or catalyzing influence over one another. *Marsdenia tenacissima* is a genus of plant and the family Apocynaceae and the genus described in 1810. The plants are found in the tropical regions in Asia, Africa, Australia, and the Americas.
This review aims to provide extensive information on the pharmacological activities of various parts of *Marsdenia tenacissima*. This is a contribution that provides an extensive review of the ethnomedicinal uses, chemical composition, and pharmacological profile of *Marsdenia tenacissima* as a prime medicinal plant.

Keywords: *Marsdenia tenacissima* wight & arn, traditional uses, phytochemistry, pharmacology, review

Introduction
Herbal and products containing herb(s) have been in trade and commerce and are currently used for a variety of purposes. The WHO defined the herb as being fresh (or) dried, fragmented (or) powdered plant material, which can be used in this order state (or) further processed and formulated to become the final herbal product. Treatment of herbs by squeezing, steaming, roasting, detecting (or) infusing in water. They are cheap, not harmful and they are more effective than any synthetic drug. Extracting with alcohol and baking with honey can create an herbal product such as juices, tinctures, decoctions, infusions, gums, fixed oil, essential oil, and resins. They are using medical (or) starting material for additional processing and as food ingredients. Herbal drugs, which are manufactured from plant materials are prone to contamination, deterioration, and variation in composition. Quality control of herbal medicine provides a host of problems.

Materials and Methods
The plant is a perennial climber containing grey bark. Leaves are 7 to15 cm long and 7 to10 cm wide, broadly ovate, acuminate, deeply cordate at the base with rounded lobes; both surfaces are densely velvety tomentose when young, but almost glabrous above when old. Petioles are pubertal and about 5–10 cm long.

Floral characteristics [1, 2, 3, 4]
Flowers of Murva is a greenish-yellow, arranged in much-branched, corymbose cymes. The calyx is deeply divided; lobes 3–4 cm in diameter, hairy outside. Corolla lobes are acute. The fruit is a follicle, about 10–15 cm long, paired, ovoid, lanceolate, and longitudinally wrinkled, seed is about 1–2 cm long, flattened, and ovate-oblong shape. Flowers are occurring in March and April, while fruits mature in May and June. The seeds are scattered very frequently by the splitting of fruits.

Table 1: Classification [1, 2]

Kingdom	**:**	**Plantae**
Order	:	Gentianales
Family	:	Apocynaceae
Genus	:	*Marsdenia*
Species	:	*Marsdenia tenacissima*

Fig 1: Whole Plant of *Marsdenia tenacissima*

Fig 2: Roots of *Marsdenia tenacissima*

Traditional Uses [1, 2, 3, 4]

In Ayurveda, it is used in the treatment of a variety of diseases such as Fungal infection of the skin, Leprosy, Fever, itching, obesity, urinary disorder, intestinal parasites, piles, excessive thirst. purgative, alterative, and given in colic and gonorrhea, heart diseases, and neuroprotection. Vata conditions such as (nervousness, anxiety, tremors, constipation, light and interrupted sleep), skin diseases, Sushruta (An ancient Indian physician, known as the main author of Treatise the compendium of Sushruta), and the plant is used for vomiting indigestion, colic pain, and fever.

Table 2: Chemical Constitutions of Parts of *Marsdenia Tenacissima* [3, 4, 5]

S.No	Parts	Chemical Constituents
1.	Root	17β-Marsdenin, 17α-Marsdenin, D-cymerose, β-D-glucosyl-L-thevetose, Cinnamic acid, acetic acid, and more in pregnane glycosides of 3-oxy sugars, Marstenacissides A1-A7, Marstenacissides A8-A12, Marstenacissides B1-B9, Marstenacissides B10-B17, Marsdenisides M.
2.	Stem	Polyoxypregnane glycosides such as Tenacigenoside, Tenacissocide-C, H, Tenacigenosides-K, G Marsdenoside B, H, and 11α-O-2-Methylbutyryl-12, β-O-Acetyltenacigenin B.
3.	Seed	pregnane glycosides of 3-oxy sugars
4.	Whole plant	Two steroidal glycosides

Table 3: Biological Activities of Parts Of *Marsedenia Tenacissima* [3, 4, 5]

S.No	Parts	Biological Activities
1.	Stem	Analgesic activity, anti-inflammatory activity, anti-arthritic, and antioxidant activities
2.	Roots	Cytotoxic, and anti-HIV activity, anticancer activity
3.	Leaves	Flatulence and a remedy for gonorrhea, cough, fever, and vomiting
4.	Flowers	Cough, fever, and vomiting

Results and Discussion

Phyto-Pharmacology

Anti-Tumor activity [7, 49, 55, 57]

Anti-tumor activities are evaluated by the MTT method. *Marsdenia tenacissima* ethanolic extract was isolated and purified by silica, macroporous adsorption resin, Sephadex LH-20, and ODS column using chloroform, ethyl acetate, and n-butyl alcohol fractions. Ten compounds are isolated and identified as1.betulinic acid, 2. tenacissoside H, 3. tenacissoside G, 4.
tenacissoside I, 5. chlorogenic acid, 6.scutellarein-4-methyl ether,7.kaempferol-4-methyl ether, 8.kaempferol, 9. daucosterol, 10.sitosterol. The 8th compound showed inhibitory effects on gastric cancer cells MKN-45 and SGC-7901 and the IC-(50) values of 48.87 mugs/ml & 54.71 mug/ml.

Anti-Cancer Activity [8, 56]

Axl-and c-Met, and related molecular mechanisms need to be elucidated and assessed by the ability of *Marsdenia tenacissima* extract to restore erlotinib or gefitinib sensitivity in tyrosine kinase inhibitors resistant HCC827/ER cells and xenograft mice models. *Marsdenia tenacissima* extract is a high efficient at restoring resistance to erlotinib than gefitinib. *Marsdenia tenacissima* extract treatment may be a potential therapeutic strategy for overcoming erlotinib and gefitinib cross-resistance in non-small cell lung cancer, especially for erlotinib resistance.

Anti-Hiv Activity [9]

Isolation and identification of the 13 new poly-oxy-pregnane glycosides from the *Marsdenia tenacissima* root extract, such as Marstenacissides B10-B17 (1,2,4,7,8,11,12 and 14) and Marstenacissides A8-A12 (3,9,10,13 and 15) also besides of 2 known poly-oxy-pregnane glycosides Marsdenosides M and L (5 and 6). This structure is established by spectroscopic techniques and comparison with the reported data in the literature. Previously isolated Marstenacissides and anti-HIV activities, such as A1 to A7 and B1 to B9 are assessed, some of which is exhibited slight or negligible effects against HIV-1

Anti-Angiogenic Activity [10]

In the traditional Chinese medicine *Marsdenia tenacissima* plant is mainly used as an anticancer drug, has been shown to possess anticancer activities. Human umbilical vein endothelial cell proliferation and capillary-like tube formations were investigated by the in-vitro and used the chick embryo chorioallantoic membrane (CAM) assayed by the in-vivo method using the *Marsdenatenacissima* extract. The result revealed that *Marsdenia tenacissima* extract inhibited the proliferation of human umbilical vein epithelial cells by the HUVECs. *Marsdenia tenacissima* extract decreases the VEGF-A expression in the human hepatoma cell expressions of VEGF-A and VEGF receptor-2 in the HUVECs. Chorioallantoic membrane was able to reduce the formation of blood vessels in chick embryos. Present data described that the extracts of *Marsdenia tenacissima* may serve as the potential anti-angiogenesis agents.

Antipyretic Activity [11]

Marsdenia tenacissima aqueous and ethanolic root extracts are used for the phytochemical investigation to identify the phytoconstituents and further assessed for antipyretic activity by the yeast-induced pyrexia in experimental rats and compared with the standard drug, paracetamol. Results of the evaluation of antipyretic activity on experimental animals, and the ethanol or aqueous extract at the dose (100mg/kg and 200mg/kg p.o.) exposure significant ($p \leq 0.01$) antipyretic activity as observed from the evaluation parameter. The ethanol and aqueous extract revealed the presence of steroid glycosides, alkaloids, saponins on qualitative chemical tests. Results observed that the ethanol and aqueous extracts of roots of *Marsdenia tenacissima* are to develop the bioactive principles for antipyretic activity.

Hepatic Disease Activity [12]

Acute liver injury was induced by the N-acetyl-p-aminophenol (APAP) in mice. The mice were divided into 5 groups: normal group, model group, saponins of *Marsdenia tenacissima* (SMT) dose groups are (15, 30, and 60mg per kg). The serum activities of the alanine aminotransferase (ALT) and aspartase aminotransferase (AST) are determined by ultraviolet spectroscopy. Liver tissue sections are examined after HE staining. The results observed in mice with APAP-induced acute liver injury, SMT dose (30mg and 60mg per kg) markedly decreased the elevated serum levels of ALT and AST. SMT has significantly increased superoxide dismutase activities and decreased the malondialdehyde content in liver homogenates. Saponins of

Marsdenia tenacissima has a protective effect on acute liver injury induced by the APAP in mice.

Induced Apoptosis Activity [13]

This study, assessed the antitumor activity and related mechanisms of *Marsdenia tenacissima* extract by the various biotechnological methods. MG63 osteosarcoma cells treated with the *Marsdenia tenacissima* extract and doxorubicin survival rates are measured, individually or jointly, and changes in the cellular shape, apoptotic rates, and Fas expressions are observed. Results revealed that the combination of the MTE and doxorubicin up-regulated Fas expression and induced apoptosis, The survival rate of the combined application of 50mg per ml MTE and 1 mug/ml doxorubicin was significantly lower than the individual application (P≤ 0.01). The results explained that the MTE may promote the effects of doxorubicin chemotherapy, may be related to the up-regulation of Fas expression in the tumor cells.

Biological Character of The Seeds Of Marsdenia Tenacissima [14]

Studied the morphological characteristics, water content, viability, and germination through seeds of *Marsdenia tenacissima* handled with the different hormones and different concentrations to analyze the biological characteristics of the seeds to lay the foundation for cultivating high-quality seedlings. The results observed that the fruit of *Marsdenia tenacissima* follicles was contained (24.03 0.29) grains. The longitudinal diameter and transverse diameter are (80.84 2.07) mm and (11.22 0.29) mm. The thousand seeds weight was (22.82 0.024) g and seed moisture content 7.93%. There had no dormancy characteristic that belonged to the normal type seed. 150mg/L GA3 could improve the germination rate of the seed significantly, other hormone treatment is not done.

Pharmacological Effects and Clinical Application [15]

Marsdenia tenacissima is Chinese medicine, it contains an antitumor effect. The chemical composition of *Marsdenia tenacissima* includes triterpenoids, steroids, organic acids, and so on. The main active constituents of C21 steroids have been studied more than the others. Modern pharmacological studies showed strong biological activity and a significant role of antitumors, blood pressure, asthma, and so on. Nowadays *Marsdenia tenacissima* preparation has extensive application in the clinic.

Five New Pregnane Glycosides from The Seeds Of *Marsdenia Tenassima* [16, 27, 28, 32]

Isolation of five new pregnane glycosides from the stem extract of Marsdeniatenacis

sima, namely Marstenacissides E (1), F (2), G (3), H (4), I(5). And the structures are determined based on IH and 13C NMR, COSY, TOCSY, ROESY, and FABMS experiments.

Hplc Determination of Tenacissoside G and I [17, 31, 41, 42]

HPLC determination method was established by using Ecosil C_(18) column (4.6mm*150mm, 5 mm). Using mobile phase was acetonitrile: water and the ratio are (48:52), flow rate was 1.0 ml. min~(-1), the detection of wavelength was 230 nm, and the maintained column temperature was 300 C. From the results indicated that the calibration curves of Tenacissosides G and I. The linear ranges of 0.4124-4.1240 mugs(r=0.999 7), respectively. The average percentage of Tenacissosides G and I were 99. 5% (RSD=2.4%) and 100% (RSD=2.4%), respectively. This method can be applied to the quality control of Tenacissosides G and I in the caulis of *Marsdenia tenacissima.*

Chemo-Resistance Reversal Activity [18]

Polyoxypregnane steroids and sugar moieties are isolated from the *Marsdenia tenacissima* extract with a disaccharide derivatives. These structures were elucidated by the extensive spectroscopic analysis, and the absolute configurations were determined by the X-ray crystallographic analysis. Naturally occurring poly-oxy-pregnane glycosides bearing a sugar moiety. These two exhibites a wide spectrum of chemoresistance reversal activity, and potential mechanisms are studied accordingly.

Human Hematologic Neoplasm Activity [19]

Marsdenia tenacissima is a traditional medicinal plant, it is widely used to treat cough, asthma, expectorant, esophageal cancer, gastric cancer, lung cancer, and hepatocellular carcinoma. In-vivo and in-vitro anti-hematologic neoplasm activity of the ethanolic extract of *Marsdenia tenacissima* herb by using different assays to elucidate the possible mechanism of action. Materials and methods: The cytotoxicity of CME on tumor cells and peripheral blood mononuclear cells was evaluated by using MIT apoptosis assays. The protein expressions of Cyclin DI, Bax, Bcl-2, caspase-3, and caspase-9 are detected by Western blotting. The in-vivo anti-tumor effect was evaluated by measuring tumor volume changes and measuring tumor weight. *Marsdenia tenacissima* ethanolic extract showed the effects of proliferation inhibition and induction of apoptosis on human hematologic neoplasm tumor cells in-vitro as well as hematologic neoplasm growth in-vivo.

Five New C-21 Steroidal Glycosides from the Stems of *Marsdenia Tenacissima* [20, 36, 58, 59]

Isolation of five new C-21 steroidal glycosides (1-5) is isolated from the stems of *Marsdenia tenacissima*. Both chemical structures and relative configurations of the new compounds are elucidated by mass spectrometry and NMR spectroscopy. Cellular assay of these compounds exhibited that they are week cytotoxic to the various cell lines.

Phyto-Pharmacognostic Investigation [21]

Herbal drugs were habitually considered to have less toxic and almost free of the side effects of synthetic ones. The plant *Marsdenia tenacissima* was traditionally used in various diseases. The study revealed that the pharmacognostical, phytochemical, and pharmacological investigations of *Marsdenia tenacissima*. The roots are extracted for soxhlet by using petroleum ether, alcohol, water. The obtained extract was studied for the preliminary phytochemical screening for detection of the presence of the various classes of chemical principles namely, carbohydrates, proteins, steroids, glycosides, alkaloids, tannins, saponins, flavonoids, lignin, and its anti-oxidant activity.

Ftir Fingerprint Spectrograms of Marsdenia Tenacissima [22, 30]

Marsdenia tenacissima extract was used to develop a reliable method of tracing the geographical origins by FTIR

finger print analysis. Full-spectrum peaks and characteristic peaks are analyzed and characterized by the fingerprints then the principal component analysis and the cluster analysis are carried out. The identification of results and the actual location showed a high degree of consistency, namely lower the space distance, and greater the similarity of different samples.

Effects of Drought Stress and Re-Watering of Marsdenia Tenacissima [23]

Four experimental treatment groups are designed to analyze the physiological changes under different degrees of drought stress and rewatering. The results exhibited that proline and soluble sugar contents quickly increased to the peak 8 days after the drought treatment, decreased along with an increase of the drought stress. The contents of proline and soluble sugar are significantly higher than the control during the stress period. SOD and POD enzymes exhibited a higher activity during the drought stress period compared to control. The MDA content revealed a pattern of increase to decrease and decrease to increase. All physiological stresses are relieved after rewatering. It is described that *Marsdenia tenacissima* could tolerate drought and has a strong ability to recover from the drought stress.

Physiological Indexes To Salt Stress Activity [24]

To explain the salt tolerance of *Marsdenia tenacissima* was used a material to analyze the variation of 5 physiological indexes under various concentrations of salt stress. The results revealed that *Marsdenia tenacissima* could accumulate a certain amount of proline and soluble sugar to adjust the osmotic potential of cells and induce antioxidant enzyme that is (SOD and POD) activity to increase under different concentrations of salt stress. But below 300 mmol L~(-1) salt stress, SOD, and POD activity decline suddenly on the 5th and 9th day of treatment, indicating the 300 mmol? L~(-1) salt stress had surpassed the tolerance range of *Marsdenia tenacissima*. So it is recommended that the soil salt content should be lower than 0.47% for planting.

Conclusion

Marsdenia tenacissima is a traditionally used and much more potent medicinal herb among the thousands of medicinal plants. The pharmacological activity was revealed in the present review confirmed that the therapeutic effect of *Marsdenia tenacissima* is high. The presence of phytochemical constituents and pharmacological activities are proved that the plant has the potential development of new good therapeutic effects of drugs in the future.

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