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Phytochemical And Pharmacological Establishment Of Traditional Ethnomedicinal Plant 'Marsilea Minuta' - A Review

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Abstract

Marsilea minuta (Vernacular name-Sushni saag) is an aquatic and sub-aquatic fern distributed throughout India, widely used as a traditional or folk medicine in Asia. An alternative pathway, use of natural products or herbal medicine for the treatment of certain diseases to avoid the synthetic product because of their high cost, side effect, and drug resistance. From our ancient civilization natural remedies were used for the prevention of illness. Marsilea minuta is used by our indigenous people as a "sleep-induced vegetable''.The plant has an immense bio-active compound which is used as ''ethnomedicine'' for the prevention of various diseases. Marsilea minuta is an aquatic species developed in shallow water, freshwater ponds or mud, or damp soil. The whole plant is immersed with the green leaf lamina floating on the surface of the water when grown up in the water. The others species are Marsilea aegyptiaca (Amphibious), Marsilea. rajasthanensis Marsilea condensate and Marsilea hirsuta belongs to xerophytic.Marsilea minuta synonyms are Marsilea brasiliensis, Marsilea diffusa, Marsilea erosa wild, Marsilea coromandelica Burn. The plant consists of many Phyto compounds. This chemical compound obtained from the stem and leaf of Marsilea minuta and shows the different pharmacological actions. The present study gave an idea or knowledge and analyzed the adaptable medicinal value of Indian traditional herb, contributing authentication for phytochemical and pharmacological investigation presented in this plant.

Keywords: Marsilea minuta, Description, Phytoconstituents, Pharmacological activity.

1. Introduction

Marsilea minuta is commonly known as water clover, pepperwort, and small water clover, Gelid water layer, is an aquatic or sub-aquatic fern also highly soft and irregular pteridophyte belongs to family Marsileacae **Figure 1** and **2** [1], [2], [3]. Morphology of the plant was reported after measurement macroscopic evaluation, microscopic evaluation. Organoleptic characters are color, order, and taste. It has yellowish-green in color 1.5 to 2.5 cm four leaflets with smooth surface and astringent taste. T.S of the petiole of M. minuta Linn shows that epidermis, outer cortex, secretary cavity, proto and m, eta xylem. The microscopic character of leaf M. minuta Linn consisted of stomata, epidermal cells, and trichomes [4]. Accordingly, WHO (World Health Organization), all over the world 80 percent of people used natural products for primary health treatment. Juice of the fresh shoot and boiling leaves are used as a cough expectorant and treatment for respiratory disease [5], [6]. Greenish leaves eat as a potherb. A whole-plant extract is used as an antifertility treatment because it's aphrodisiac in nature [7], [8]. The plant is also suggested for the prevention of psychopathy, diarrhea, skin disease [9]. The plant also cured sedation and was used as an anticonvulsant agent [10]. The plant is recommended for the treatment of insomnia, also used for the prevention of epilepsy, migraine pain, and sleep disorder [11]. Leaves are used for the treatment of a gastrointestinal disorder, leaf extraction folk medicine practitioners are recommended as a nasal bleeding inhibitor. For treatment of swelling used the boiling leaf of Shorea robusta and leaves of Marsilea minuta.When it gives to gerbils for eating, leaves extract attenuates the cholesterol and triglyceride level in blood and liver. When fresh plant boiled and applied for the prevention of spasmodic muscle contraction of the urethra, leg, and bladder. For atopic dermatitis treatment used root extract of Marsilea minuta [12]. It also acts as an astringent, coolant, digestive, diuretic, hypnotic, and expectorant effects when it is taken as an entire plant. Many of its potent effects are reported in Ayurvedic treatment for the diseases such as psychopathy, diarrhea, cough, bronchitis, skin diseases, and fever. Fresh plant decoction is taken twice a day for 10-12 days for spasmodic muscular contraction of the urethra and bladder. Root paste is applied for atopic dermatitis.

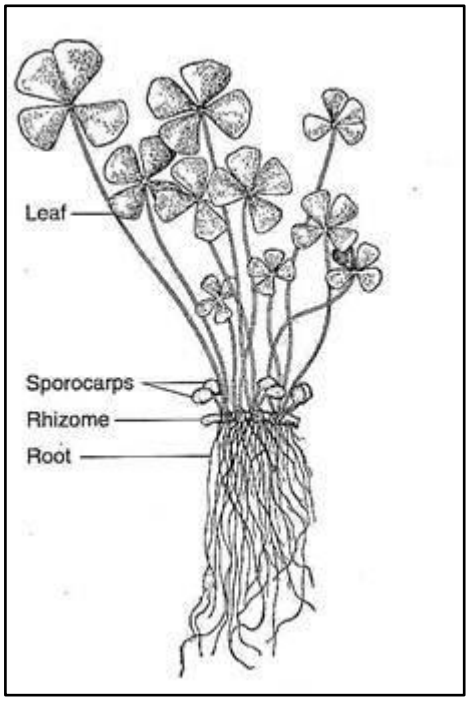


Figure 1. Structure of Marsilea.

Figure 2. Marsilea minuta plant

2. Taxonomic Classification.

M. minuta is thought to be closely related to Marsilea quadrifolia [13]. Molecular phylogenetic analysis of the genus Marsilea puts both in a widespread Old World subgroup also called "Marsilea" along with M. angustifolia, M. drummondii, M. crenata, and M. fadeniana and indicating that M. crenata is actually a synonym of M. minuta (**Table 1**).

Table 1. Taxonomy Classification

Sl no	Kingdom	Plantae
1.	Subkingdom	**Tracheobionta**
2.	Division	Pteridophyta
3.	Class	Polypodiopsida/Pteridopsia
4.	Order	Hydropteridales
5.	Family	Marsileaceae
6.	Genus	Marsilea L
7.	Species	M. minuta

3. Geographical distribution

Marsilea minuta is generally prevalent in almost all the states of India particularly tropical Africa and Asia. Generally, it grows freshwater or in brackish water (Trinidad) on sandy or clay substrates. It is also found in a swamp. The genus Marsilea is distributed all over the world and contains 10 fossil species and 53 well-defined living species which are identified in tropical Asia like India, Burma, Japan, China, also Australia, South America, South Africa. Hydrophytic and Xerophytic are two categories of Marsilea present in India's all-state [14], [15].

4. Other species of Marsila Minuta

Different species of Marsilea minuta are M. ancyclopoda, M .apposite , M. burchellii , M. aegyptica, M. coromandelina, M. crenata, M. crotophora, M. deflexa, M. distorata, M. drummondii, M. ephippiocarpa, M. farinose, M. quadrifolia, M. villifolia, M. villosa, M. vestita, M. macrocarpa, M.aminuta, M. vera, M. unicornis, M. mutica, M. nubicam, M. mollis, M. macropoda, M. macrocarpa, M. hirsute, M. aminuta L.

5. Material and methods

The bioactive molecule or Phyto-constituents isolated from the Marsilea minuta extract then identified or analyzed the pharmacological actions were searched across the Medline (National Library of Medicine) and Science Direct database. Updated data were searched by using the term Marsilea minuta, Phyto-constituents, bioactive compound, traditional uses, pharmacological properties as a keyword. In addition, all reference papers were identified and reviewed.

6. Phytochemical constituent

Searching for a new bioactive compound from the medicinal plant for drug development is a common trend in the pharmaceutical industry. Researchers are finding the new pharmacological active molecule which is analyzed or identified from the crude plant, it will help to treat or prevent disease. Identified or isolated the various types of phytoconstituents from Marsilea minuta like phenol, flavonoids, tannins, saponin, quinones, total sugar, terpenoids, coumarins, and anthraquinones [16], and also present Marsiline, Marsileagenin A [17]. Different types of flavonoids present like quercetin-3-o-glucoside, quercetin-3-o-galactoside, kaempferol-3-o-glucoside, chalcone-o-glucoside, also present hentriacontane, beta-sitosterol, quercetin-3-rutinoside (rutin), naringenin-7-o-glucoside [18], [19]. To perform the GC - MS analysis of a methanolic extract of leaf and stem of Marsilea minuta get the 36 Phyto compounds from leaf extract and stem extract show the presence of 27 Phyto compounds.

6.1 Name of the isolated compound from the methanolic extract of leaf of Marsilea minuta

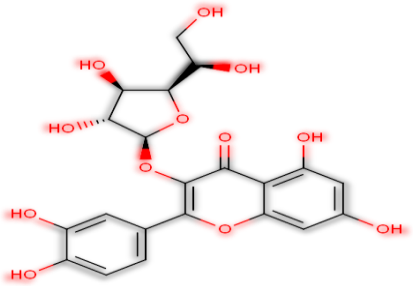
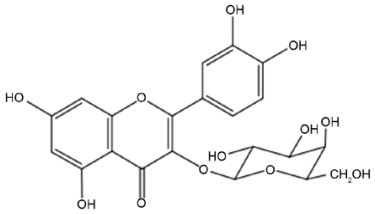
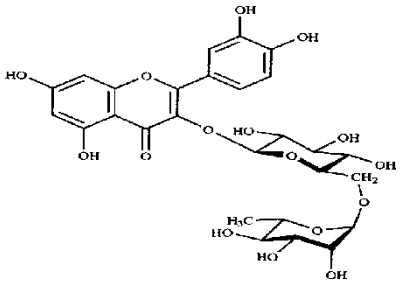
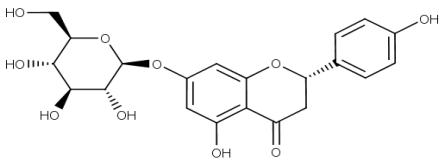
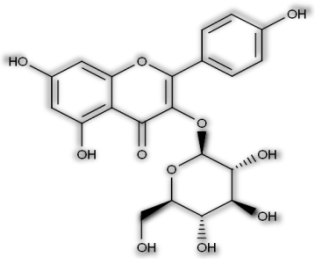
Hexanal, 3-amino-2-oxazolidinone, 1-butanamine, N-butylidene, hexanoic acid, phenylalanine, glycerine, benzenecarboxylic acid, benzofuran, 2-methoxy-4-vinylphenol, 5H-1-pyridine, benzene, 2-(1,3-butadienyl)-1,3,5-trimethyl-6-methyl-1,2,3,4-tetrahydroquinoline, L-proline, methyl ester,dodecanoic acid, 4-(2,6,6-trimethylcyclohex-1,3-dienyl)but-3-en-2-one, 3-oxo-a-ionone, tetradecanoic acid, 4-oxazole carboxylic acid, 4,5,-dihydro-2-phenyl, 11,14,17-eicosatrienoic acid, dioxabicyclo [5.1.0.0(2,4)]octane.

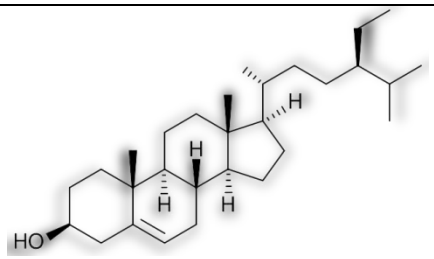
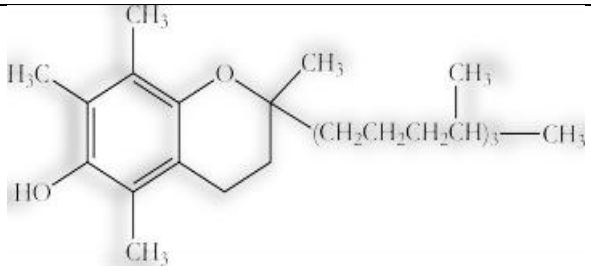
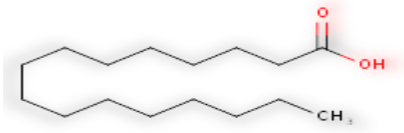
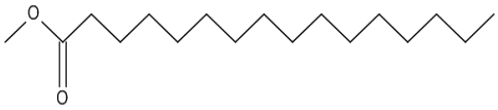
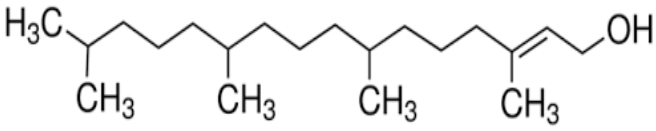
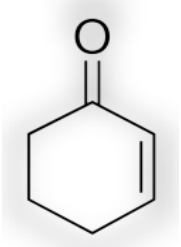
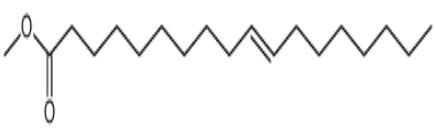
6.2 Name of the isolated compound from the methanolic extract of stem of Marsilea minuta

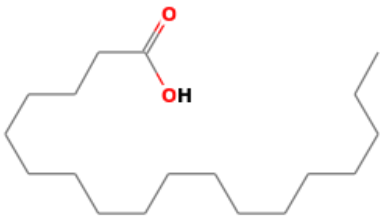
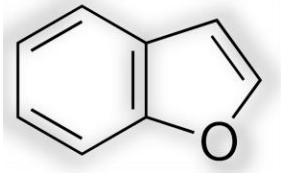
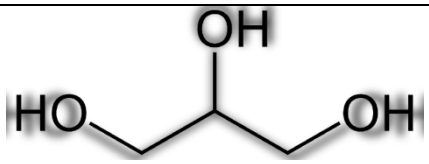
Butanal, 4-hydroxy-3-methyl-acetohydroxamic acid, 2-octene, glycerine, heptanoic acid, 2,5-diamino-2-methylpentanoic acid, octanoic acid, phenol, 2,4-dichloro-, dianhydro mannitol, dodecanoic acid, 1-dodecanol, 1,19-eicosadiene, methyl ester, phytol,8-hexadecenal,14-methyl-,(Z) [20]. **Table 2** has described the isolated phyto-compounds from Marsilea minuta.

Table 2. Some significant chemical structures of phytoconstituents

Phytoconstituents name	Chemical structure

Qercetin-3-o-glucoside	
Quercetin-3-o-galactoside	
Quercetin-3-rutinoside	
Naringenin-7-O-glucoside	
Kaempferol-3-O-glucoside	

Beta-sitosterol	
Hentriacontane	
Hexadecanoic acid	
n-Hexadecanoic acid methyl ester	
Phytol	
2-Cyclohexane-1-one	
10-Octadecanoic acid methyl ester	

Octadecanoic acid	
Benzofuran	
Glycerin	

7. Pharmacological activity

Marsilea minuta possesses many pharmacological activities such as antipyretic and analgesic, antidiabetic, antitussive, expectorant, antiamnesic, anti-aggressive, antimicrobial, hepatoprotective, antifertility, anti-tumor, antioxidant activity. This study was aimed to present an overview of traditional use, phytochemical and pharmacological investigations present in this plant.

7.1 Antiproliferative activity

Benzofuran, 2,3 dihydro, n-hexadecanoic acid-like compounds have antiproliferative activity, which comes from the methanolic extract of Marsile minuta stem and leaf. From these aspects, there is a chance to get a new active compound that inhibits proliferation. But proper evidence or research articles are not present for this.

7.2 Antitumor activity:

Whole plant Ethanolic extracts (Plant extract used in a range of 10, 100, and 1000 ppm) shows that the Marsilea minuta inhibits the crown gall tumor. The potato disc method is a useful process to observe inhibition of crown gall tumors. Compared to the positive control camptothecin, at (10,100,1000) ppm concentrations of Marsilea minuta ethanolic extract inhibition the tumor 82.2 percentage, where T. prolifera and S. ciliaris inhibition 75.68 percentage and 80 percentage [21], [22].

7.3 Antimicrobial activity:

The whole plant extract of Marsilea minuta shows the activity against the Gram-positive (-ve) and Gram-negative (-ve) bacteria. Petroleum ether, chloroform, ethyl acetate, water, alcohol are used as solvents for extraction. Agar well diffusion method was used to observe the extract activity against bacterial strain. Different concentrations of extract 100 to 500 mcg/ml were used to check the effectiveness against the bacterial strain [23] which is described in **Table 3**.

Table 3. Antimicrobial activity of M.minuta plant extract

Microorganism	Effect	Plant extract
E . coli (-ve)	Positive	Ethyl acetate, chloroform, Water.
S. aureus (+ve)	Positive	
P. aeruginosa (-ve)	Positive	
S. pneumonia (+ve)	Positive	

At a concentration of 500 mcg/ml, ethyl acetate extract was notably active against E.coli and S. Aeruginosa also noticed alcoholic fraction against these bacteria at the same concentration. Another study has been done for investigating antimicrobial activity, acetone, chloroform, DMSO, ethanol, petroleum ether extract of rhizome of Marsilea minuta. At a dose of 100 microgram/ml concentration to show the inhibition of bacterial growth in agar media.DMSO and ethanol extract show high effectiveness against bacterial strains like B.subtilis. Antibacterial assay results showed M. minuta leaves extract exhibited a good inhibitory effect against all of the test strains. Among the tested pathogens, P. aeruginosa exhibited the maximum inhibition zone

7.4 Antipyretic and analgesic activity:

Ethanolic leaf extract of Marsilea minuta shows the antipyretic action were Brewer's yeast induced pyrexia as the pathogen. Paracetamol was used as a standard drug for analyzing pyretic activity with compare extract. Ethanolic extract dose 200 mg/k and 400 mg/kg applied and observed it reduces the temperature by inhibition of prostaglandin receptors. A dose of 200 mg/kg and 400 mg/kg of ethanolic extract show analgesic effect, compared with the diclofenac as a standard drug. This study followed the hot plate method and tail immersion method. Analgesic activity may be the inhibition of the prostaglandin receptor or leukotriene receptor [24].

7.5 Antidiabetic agent:

Ethanolic leaf extract of Marsilea minuta reveals that dose 100 mg/kg, 250 mg/kg, and 500 mg /kg increased glucose tolerance in our body (OGTT), and reduced the glucose level in alloxan-induced diabetic mice. Glibenclamide 3 mg/kg/p.o is used as a standard drug. 500 mg/kg of the ethanolic extract showed a significant rise in blood glucose level compared to untreated diabetic rats [25].

7.6 Hepatoprotective activity:

Methanolic extract of Marsilea minuta shows anti hepatotoxicity and hepatoprotective agent. Assessment of Hepatoprotective Activity, Determination of Serum Biochemical Parameters, Assessment of AntiHepatotoxic Activity were checked. The methanolic extract reduced the carbon tetrachloride-induced liver injury in mice. Including dose 100 mg/kg,200 mg/kg,400 mg/kg extract, 200 mg/kg extract reduced the alanine transaminase (ALT), Aspartate aminotransferase (AST), Serum protein (PRO), serum albumin (ALB) , serum bilirubin (BILT), serum alkaline phosphatase (ALP) level [26]. MMME at dose 200 mg/ kg shows a good hepatoprotective effect.

7.7 Antitussive and expectorant:

Methanolic, ethyl acetate, and petroleum leaves extract of Marsilea minuta inhibit the sulfur dioxide and ammonium liquor induced cough in mice. The volume of phenol red in mice's tracheas estimate or evaluate the expectorant activity. Methanolic extract 250 and 500 mg/kg, ethanolic extract 250 and 500 mg/kg, petroleum ether extract 250 and 500 mg/kg dose of Marsilea minuta used. At dose 500 mg/kg decreased the number of coughing. Methanolic extract 500 mg/kg shows an expectorant effect. M. mimuta demonstrated significant antitussive and expectorant effects. These effects are important evidence for the traditional use of M. mimuta in the treatment of cough, respiratory disorders. The isolation of bioactive constituents and the mechanism of action explained for the observed activities have not been established, and thus further investigations need to be conducted [27].

7.8 Anti-amnesic activity:

Ethanolic extract of Marsilea minuta (whole plant) used as an anti-amnesic agent. It shows a positive effect on amnesic rats, 200 and 400 mg/kg concentration of ethanolic extract used for scopolamine (1 mg/kg) and electroconvulsive shock-induced amnesia. The experiment was evaluated by assay of acetylcholinesterase (AChE) activity in rat brain and radio-ligand binding assay. 400 mg/kg dose of ethanolic extract inhibited the activity of AChE in the hippocampus region of the brain, 400 mg/kg showed better Antiamnesic activity [28].

7.9 Antifertility activity:

Marsilea minuta methanolic plant extract at 250 mg/kg concentration shows an antifertility activity mechanism followed by inhibition of gonadal steroids-genesis. The antifertility activity of methanol extract of Marsilea minuta (F. Marsileacae) was studied on female Swiss albino mice. The extract was found to produce a significant elevation of the level of total cholesterol and ascorbic acid content of the ovaries of the treated mice. It also produced a significant reduction in the activities of glucose-6-phosphate dehydrogenase. These observations indicate that the methanol extract produced antifertility activity in mice, which may be due to inhibition of gonadal steroidogenesis [29].

7.10 Anti-aggressive activity:

Plant extract of Marsilea minuta shows anti-aggressive activity by applying Footshock-induced aggression, Isolationinduced aggression, and resident-intruder aggression methods. At concentration 100 mg/kg, 200 mg/kg, and 400 mg/kg dose given for 14 days and also given diazepam 2.5 mg/kg as a standard drug. To perform the anti-aggressive activity using these validated models, foot shock-induced aggression, isolation-induced aggression, and resident-intruder aggression. Different doses of Marsilea minuta extract show different anti-aggressive actions [30].

7.11 Antidepressant activity:

Marsiline isolated from Marsilea minuta was reported to have sedative and anticonvulsant property. The ethanol extract of Marsilea minuta was standardized for marsiline (1.15%, w/w) and studied for its antidepressant activity. Ethanolic extract of Marsilea minuta shows a significant role as an antidepressant agent. At a dose of 400 mg/kg, p.o concentration decreased immobility time, forced swimming test (FST) and tail suspension test (TST) also reduced the number of escape failures learned helplessness, imipramine used as a standard drug. Immobility time in FST and TST was significantly ($P < 0.05$) reduced by ethanol extract of Marsilea minuta treated animals. A decrease in the number of escape failures in LHT was also observed in Marsilea minuta treated rats. The

antidepressant effect exhibited by Marsilea minuta extract may be due to its effect on 5-HT2A density in the rat frontal cortex. [31].

7.12 Chemo Convulsion:

At a dose concentration of 800 mg/kg leaves extract and 400 mg/kg alcoholic extract of Marsilea minuta give benefits to Metrazol-induced seizures [32].

7.13 Sedative:

Aqueous and alcoholic extract of Marsilea minuta show sedative effect at a dose concentration 400-600 mg/kg.

7.14 Antioxidant activity:

Methanolic extract of leaves of Marsilea minuta show at dose 25 ug/ml, 50 ug/ml, 100 ug/ml, 150, 200 ug/ml concentration DPPH radical scavenging activity and hydrogen peroxide activity. 200 micrograms per liter dose concentration more free radical scavenging and high hydrogen peroxide scavenging concentration sensitive with was at 100 micrograms per liter [33].

7.15 Gold nanoparticle:

Distilled water leaves extract of Marsilea minuta used for the preparation of gold nanoparticles by using Agar well diffusion method, at dose concentration 50-400 microlitre nanoparticle formulation inhibits bacterial growth and shows effectiveness against E.coli, S. aureus. Methanolic extract of Marsilea minuta is used as a hepatoprotective agent [34].

Conclusion

Herbal drugs play an important role in the treatment of several disease conditions. The plant has tremendous biological effects and is applied in the different systems of traditional medication for the treatment of various diseases. Marsilea minuta is an aquatic pteridophyte, it has a lot of phytoconstituents that have been isolated and identified. For folk medicine, it's used for the treatment of a mental disorder or insomnia condition. Researchers are finding a new pharmacological action that makes it easier for us to prepare new drugs for the prevention of chronic disease. The benefit of the vital nature of Marsilea minuta L. and its wide geographical distribution might offer an opportunity to develop many formulations by the usage of this plant. Thus, this article offers an excellent accessible source for a study on active compounds for traditional medicine and allied applications for future researchers and makes it useful for society.

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Conflict of Interest

None

Funding

Not applicable

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