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Nutritional and Medicinal Properties of *Marsilea quadrifolia*: A Comprehensive Review

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Abstract *Marsilea quadrifolia* is a semi-aquatic plant widely distributed in tropical and subtropical regions, known for its distinctive four-leaf appearance and rich nutritional content. Traditionally used in various medicinal practices, the plant exhibits significant antioxidant and anti-inflammatory properties. This study systematically reviews the existing literature to evaluate the nutritional and medicinal value of *Marsilea quadrifolia*, identify knowledge gaps, and propose future research directions. The study reveals that *Marsilea quadrifolia* contains various bioactive compounds, such as quercetin, tannins, and saponins, which not only help combat oxidative stress but also possess neuroprotective and antiepileptic potential. Additionally, its high carbohydrate and protein content make it a valuable dietary supplement. *Marsilea quadrifolia* holds great potential for applications in modern medicine and nutrition, though further clinical trials are necessary to support its potential therapeutic effects.
Keywords *Marsilea quadrifolia*; Nutritional content; Bioactive compounds; Medicinal value; Antioxidant; Dietary supplement

1 Introduction

Marsilea quadrifolia, commonly known as water clover, is a semi-aquatic plant belonging to the family Marsileaceae. It is widely distributed across tropical and subtropical regions, particularly in India, where it thrives in both aquatic and terrestrial environments (Bhanukiran et al., 2022). The plant is characterized by its four-leaf clover-like appearance, which has made it a subject of interest not only for its unique morphology but also for its potential health benefits.

Marsilea quadrifolia has been traditionally used in various medicinal practices due to its wide range of therapeutic properties. Recent studies have highlighted its significant antioxidant potential, which is attributed to the presence of bioactive compounds such as quercetin (Bhanukiran et al., 2022). Additionally, the plant is rich in essential nutrients, including carbohydrates, proteins, amino acids, flavonoids, saponins, and fats, making it a valuable source of nutrition (Kim et al., 2000; Agarwal et al., 2018). Despite its promising benefits, the plant remains under explored in scientific research, necessitating a comprehensive review of its nutritional and medicinal properties.

This study evaluates the nutritional and medicinal value of *Marsilea quadrifolia*, with a focus on exploring its bioactive compounds and potential health benefits. The study will consolidate existing findings, identify knowledge gaps, and define future research directions. Through a systematic analysis of current literature, the study aims to provide insights into the application of *Marsilea quadrifolia* in modern healthcare and nutrition, thereby promoting interest in plant-based therapies. Furthermore, this study seeks to raise awareness of the ecological significance of *Marsilea quadrifolia*, encouraging its sustainable use across various industries.

2 Nutritional Composition of *Marsilea quadrifolia*

2.1 Macronutrients (proteins, carbohydrates, and fats)

Marsilea quadrifolia, commonly known as water clover, is a rich source of macronutrients. The plant exhibits a high carbohydrate content, followed by significant amounts of proteins and fats. Quantitative analysis has shown that the total carbohydrate content is the highest among the macronutrients, making it a valuable energy source

(Agarwal et al., 2018). Additionally, the protein content is substantial, which is essential for various bodily functions, including muscle repair and enzyme production (Agarwal et al., 2018). The fat content, although lower compared to carbohydrates and proteins, still contributes to the overall nutritional profile of the plant (Agarwal et al., 2018).

2.2 Micronutrients (vitamins and minerals)

Marsilea quadrifolia also contains various micronutrients, including vitamins and minerals, which are crucial for maintaining overall health. The plant is known to have a diverse chemical composition that includes phenolic compounds, flavonoids, and other essential micronutrients (Subramanian et al., 2023). These compounds not only contribute to the plant's nutritional value but also offer antioxidant properties, which help in combating oxidative stress and maintaining cellular health (Zhang et al., 2016; Subramanian et al., 2023). However, specific details on the exact vitamins and minerals present in *Marsilea quadrifolia* are limited and warrant further investigation.

2.3 Phytochemicals contributing to nutritional value

The phytochemical profile of *Marsilea quadrifolia* is extensive and includes a variety of bioactive compounds that enhance its nutritional and medicinal properties. Key phytochemicals identified in the plant include tannins, saponins, flavonoids, steroids, terpenoids, alkaloids, and phenolic compounds (Bhadra et al., 2012; Gopalakrishnan and Udayakumar, 2017). These compounds are known for their antioxidant, anti-inflammatory, and neuroprotective properties, which contribute to the plant's therapeutic potential (Bhadra et al., 2012; Gopalakrishnan and Udayakumar, 2017; Subramanian et al., 2023).

Tannins and Saponins: These compounds are present in both the leaf and stem extracts of *Marsilea quadrifolia* and are known for their antioxidant and anti-inflammatory properties (Gopalakrishnan and Udayakumar, 2017). Flavonoids and Phenolic Compounds: These are abundant in the plant and are primarily responsible for its strong antioxidant activities. Quercetin, a type of flavonoid found in *Marsilea quadrifolia*, has been shown to have significant antioxidant properties both in vitro and in vivo (Zhang et al., 2016; Subramanian et al., 2023). Alkaloids and Steroids: These phytochemicals contribute to the plant's medicinal properties, including its potential use in managing neurological disorders and diabetes (Bhadra et al., 2012; Bhanukiran et al., 2023; Subramanian et al., 2023).

Marsilea quadrifolia is a nutritionally rich plant with a diverse array of macronutrients, micronutrients, and phytochemicals. Its high carbohydrate and protein content, along with the presence of various bioactive compounds, make it a valuable addition to the diet and a potential source of therapeutic agents. Further research is needed to fully elucidate the specific vitamins and minerals present in the plant and to explore its full medicinal potential.

3 Medicinal Properties of *Marsilea quadrifolia*

3.1 Antioxidant properties

Marsilea quadrifolia has demonstrated significant antioxidant properties in various studies. The ethanolic extract of the whole plant has been shown to possess strong antioxidant potential, with IC50 values reported in multiple assays (Rawat et al., 2012; Bhanukiran et al., 2022). Additionally, the methanolic extracts of *Marsilea quadrifolia* leaves have been found to contain high levels of total phenolic content (16.48 ± 0.4 mg/g of gallic acid equivalent) and total flavonoid content (96.33 ± 4.4 mg/g of rutin equivalent), which contribute to its antioxidant activity. The IC50 value of the methanolic extract in the DPPH assay was found to be 258.55 µg/ml, indicating its efficacy in scavenging free radicals (Tripathy et al., 2023). Furthermore, silver nanoparticles synthesized using *Marsilea quadrifolia* extract exhibited strong antioxidant activities, surpassing those of the leaf extract alone (Figure 1) (Ashwini et al., 2012; Ishwarya et al., 2021).

3.2 Anti-inflammatory effects

While the provided data does not explicitly detail the anti-inflammatory effects of *Marsilea quadrifolia*, the presence of bioactive compounds such as flavonoids, phenolics, and terpenoids in the plant suggests potential anti-inflammatory properties. These compounds are known for their roles in reducing inflammation and oxidative

stress, which are often interlinked (Tripathy et al., 2023). Further research is needed to specifically elucidate the anti-inflammatory mechanisms and efficacy of *Marsilea quadrifolia*.

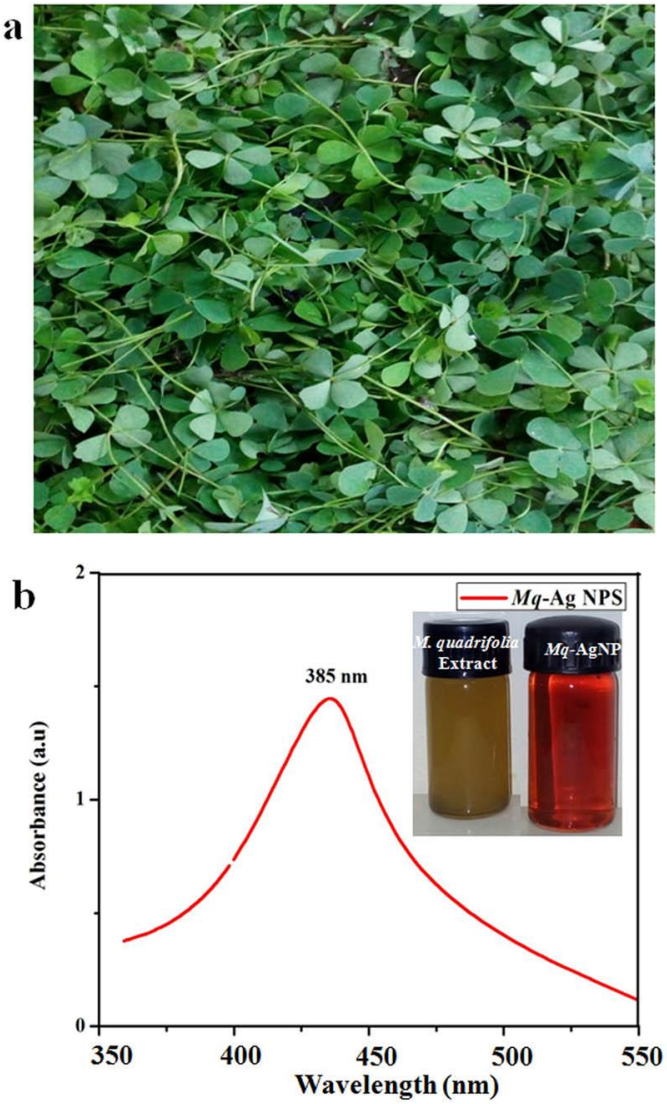

Figure 1 (a) Mq leaf and (b) UV-Vis spectrum of Mq-AgNPs (Adopted from Ishwarya et al., 2021)

3.3 Other medicinal benefits

Marsilea quadrifolia exhibits notable antimicrobial properties. The methanolic extract of its leaves has shown significant antibacterial activity against various uropathogenic bacteria, including *Enterococcus faecalis*, *Escherichia coli*, *Staphylococcus aureus*, and *Proteus vulgaris*. The extract demonstrated complementary or supplementary inhibitory effects when combined with certain antibiotics, enhancing their efficacy against these pathogens (Tripathy et al., 2023). Additionally, silver nanoparticles synthesized using *Marsilea quadrifolia* extract displayed superior growth inhibition effects against tested bacteria, highlighting its potential as an antimicrobial agent (Hsu et al., 2001; Gopalakrishnan, 2014; Ishwarya et al., 2021).

Although the provided data does not include specific studies on the anticancer properties of *Marsilea quadrifolia*, the presence of bioactive compounds such as flavonoids and phenolics suggests potential anticancer benefits. These compounds are known for their roles in inhibiting cancer cell proliferation and inducing apoptosis. Further research is required to confirm and detail the anticancer properties of *Marsilea quadrifolia* (Snehunsu et al., 2013; Chowdhury et al., 2017).

4 Bioactive Compounds in *Marsilea quadrifolia*

4.1 Identification of key bioactive compounds

Marsilea quadrifolia is a rich source of various bioactive compounds, which contribute to its medicinal properties. High-performance thin-layer chromatography (HPTLC) analysis has identified quercetin and its derivatives as major constituents in the chloroform extract of *M. quadrifolia* (Subramanian et al., 2023). Additionally, several new polyphenols, including kaempferol derivatives and other known compounds, have been isolated from the ethanol extract of the plant (Zhang et al., 2016). Another significant compound identified is 1-Triacontanol cerotate (1TAC), which was isolated from the petroleum ether fraction of the methanolic extract (Snehunsu et al., 2015). The hydroalcoholic extract of *M. quadrifolia* has also been found to contain a high total phenolic content, which is likely responsible for its therapeutic effects (Bhanukiran et al., 2023).

4.2 Mechanisms of action

The bioactive compounds in *M. quadrifolia* exhibit various mechanisms of action that contribute to its medicinal properties. Quercetin, a major constituent, has shown strong antioxidant activities in both in vitro and in vivo assays, significantly attenuating oxidative stress markers in a restraint-induced oxidative stress model in mice (Zhang et al., 2016). The neuroprotective effects of quercetin and its derivatives are attributed to their ability to bind effectively to protein targets, such as the NMDA receptor, thereby exhibiting NMDA antagonistic properties (Subramanian et al, 2023).

1-Triacontanol cerotate (1TAC) has demonstrated the ability to reduce reactive oxidative damage in the brain, particularly in the frontal cortex and hippocampus, by normalizing malondialdehyde (MDA) and glutathione (GSH) levels in chronic epileptic rats (Snehunsu et al., 2015). The hydroalcoholic extract of *M. quadrifolia* has shown significant antidiabetic potential by reducing blood glucose levels and improving biochemical parameters in streptozotocin-induced diabetic rats, likely due to its high phenolic content (Bhanukiran et al., 2023).

4.3 Potential therapeutic applications

The diverse bioactive compounds in *M. quadrifolia* offer a wide range of therapeutic applications. The neuroprotective properties of quercetin and its derivatives make *M. quadrifolia* a potential candidate for the treatment of neurological disorders, such as excitotoxicity-induced neuronal damage (Subramanian et al, 2023). The strong antioxidant activities of the polyphenols, particularly quercetin, suggest that *M. quadrifolia* could be developed into products for relieving oxidative stress (Zhang et al., 2016).

The antiepileptic properties of 1-Triacontanol cerotate (1TAC) highlight its potential use in managing epilepsy and related disorders by minimizing oxidative damage in the brain (Snehunsu et al., 2015). The antidiabetic effects of the hydroalcoholic extract of *M. quadrifolia* validate its traditional use in treating diabetes, offering a natural alternative for managing blood glucose levels and improving overall metabolic health (Bhanukiran et al., 2023). Additionally, the plant's anticonvulsant effects, as demonstrated in behavioral and EEG studies, further support its use in traditional medicine for epilepsy (Sahu et al., 2012).

The bioactive compounds in *Marsilea quadrifolia* exhibit significant antioxidant, neuroprotective, antiepileptic, and antidiabetic properties, making it a valuable medicinal plant with diverse therapeutic applications. Further research is warranted to fully elucidate the mechanisms of action and optimize the use of these compounds in clinical settings.

5 Traditional Uses of *Marsilea quadrifolia*

5.1 Historical usage in traditional medicine

Marsilea quadrifolia (MQ) has been utilized in traditional medicine for centuries. In Indian traditional medicine, MQ has been employed for its sedative and antiepileptic properties (Sahu et al., 2012). The plant has also been used to treat insomnia and various neurological disorders, highlighting its significance in ethnopharmacology (Li et al., 2002; Snehunsu et al., 2015). The diverse chemical composition of MQ, including phenolic compounds, tannins, saponins, flavonoids, and alkaloids, contributes to its wide range of therapeutic benefits (Subramanian et al., 2023).

5.2 Cultural significance in different regions

In Asia, particularly in India, MQ holds cultural importance as a traditional health food and medicinal plant. It is widely distributed in the state of West Bengal, where it is valued not only for its medicinal properties but also as a dietary supplement (Agarwal et al., 2018). The plant's use in traditional health practices underscores its cultural significance, as it is integrated into daily life for its health benefits. The presence of bioactive compounds such as polyphenols and flavonoids further enhances its reputation as a beneficial plant in various cultural contexts (Zhang et al., 2016; Jiang et al., 2018).

5.3 Comparison with modern medicinal uses

Modern scientific research has validated many of the traditional uses of MQ. Studies have demonstrated its neuroprotective potential against excitotoxicity induced by monosodium glutamate, suggesting its role in managing neurological disorders (Subramanian et al., 2023). Additionally, MQ has shown anticonvulsant effects in pentylenetetrazole-induced seizure models, supporting its traditional use as an antiepileptic agent (Sahu et al., 2012). The isolation of active components like 1-Triacontanol cerotate, which ameliorates oxidative damage in the brain, further corroborates its efficacy in treating epilepsy (Snehunsu et al., 2015). These findings align with historical uses and provide a scientific basis for the continued use of MQ in modern medicine.

The traditional uses of *Marsilea quadrifolia* are deeply rooted in cultural practices, particularly in India, where it has been used to treat neurological conditions and as a health food. Modern research supports these traditional applications, demonstrating the plant's potential in neuroprotection and seizure management, thereby bridging the gap between historical knowledge and contemporary scientific validation.

6 Case Studies on the Medicinal Applications of *Marsilea quadrifolia*

6.1 Case study: use in treating specific diseases

One notable case study investigated the neuroprotective potential of *Marsilea quadrifolia* (*M. quadrifolia*) against monosodium glutamate (MSG)-induced excitotoxicity in rats. Excitotoxicity, a condition where neurons are damaged due to the over-activation of glutamate receptors, is implicated in several neurological diseases. The study utilized a chloroform extract of *M. quadrifolia* (CEMQ) and identified quercetin and its derivatives as major constituents through high-performance thin-layer chromatography (HPTLC). The results demonstrated that CEMQ significantly improved locomotor activity, memory, and learning in MSG-treated rats, suggesting its potential in ameliorating neurotoxicity. The neuroprotective effects were attributed to the N-methyl-D-aspartate (NMDA) antagonistic properties of the extract (Figure 2) (Mishra et al., 2008; Subramanian et al., 2023).

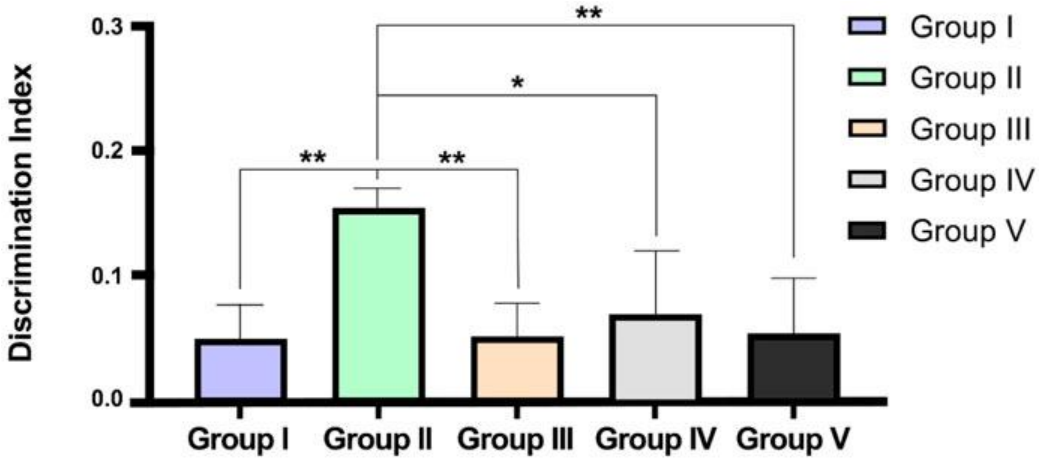

Figure 2 Effect on CEMQ on discrimination index using object recognition test. The data represents significance at *$p < 0.003$ and **$p < 0.002$ (Adopted from Subramanian et al., 2023)

6.2 Case study: integration into modern herbal formulations

In another study, the active component 1-Triacontanol cerotate (1TAC) was isolated from the methanolic extract of *M. quadrifolia* and evaluated for its antiepileptic properties. The study focused on the ability of 1TAC to

minimize reactive oxidative damage in the brain due to chronic epilepsy in rats. The results indicated that 1TAC normalized malondialdehyde (MDA) and reduced glutathione (GSH) concentrations in the frontal cortex and hippocampus of pentylenetetrazole (PTZ)-induced epileptic rats. The efficacy of 1TAC was found to be dose-dependent, with higher doses showing better results than the standard drug sodium valproate. This study highlights the potential of integrating 1TAC into modern herbal formulations for treating epilepsy (Snehunsu et al., 2015).

6.3 Case study: clinical trials and research findings

While clinical trials specifically involving *M. quadrifolia* are limited, the existing preclinical research provides a strong foundation for future investigations. The neuroprotective and antiepileptic properties demonstrated in animal models suggest that *M. quadrifolia* could be a promising candidate for clinical trials aimed at treating neurological disorders (Kao and Lin, 2010). The studies reviewed indicate that the plant's diverse chemical composition, including phenolic compounds, flavonoids, and saponins, contributes to its medicinal properties. Further clinical research is necessary to validate these findings and explore the therapeutic potential of *M. quadrifolia* in human subjects (Snehunsu et al., 2015; Subramanian et al., 2023).

7 Potential Risks and Safety Concerns

7.1 Toxicological studies

Marsilea quadrifolia has been traditionally used for various medicinal purposes, but its safety profile needs thorough evaluation. Toxicological studies have been conducted to assess the safety of its active components. For instance, 1-Triacontanol cerotate (1TAC), an isolated compound from *M. quadrifolia*, was subjected to acute oral toxicity studies. The results indicated that 1TAC did not exhibit any significant toxic effects at the tested doses, suggesting a favorable safety profile for this compound (Snehunsu et al., 2015). Additionally, the neuroprotective potential of *M. quadrifolia* was evaluated in a study where rats were treated with chloroform extract of *M. quadrifolia* (CEMQ). The study did not report any adverse effects at the administered doses, further supporting the plant's safety (Subramanian et al., 2023).

7.2 Side effects and contraindications

While *M. quadrifolia* shows promise in therapeutic applications, potential side effects and contraindications must be considered. The studies reviewed did not report significant side effects at therapeutic doses. However, it is crucial to note that the absence of reported side effects in these studies does not guarantee the absence of adverse effects in broader populations or at higher doses. Therefore, caution is advised, especially for individuals with pre-existing health conditions or those taking other medications. Further research is needed to comprehensively understand the side effects and contraindications associated with *M. quadrifolia*.

7.3 Safe usage guidelines

Based on the available studies, *M. quadrifolia* appears to be safe when used within the tested dosage ranges. For instance, 1TAC was found to be effective and safe at doses of 40 and 80 mg/kg body weight in reducing oxidative damage in epileptic rats (Snehunsu et al., 2015). Similarly, CEMQ was administered at doses of 200 and 400 mg/kg in neuroprotective studies without adverse effects (Subramanian et al., 2023). These findings suggest that *M. quadrifolia* can be safely used within these dosage ranges. However, it is essential to conduct further studies to establish comprehensive safe usage guidelines, including long-term safety and potential interactions with other drugs. While preliminary toxicological studies indicate that *M. quadrifolia* and its components are relatively safe, further research is necessary to fully elucidate its safety profile, potential side effects, and safe usage guidelines.

8 Future Research Directions

8.1 Gaps in current knowledge

Despite the promising medicinal properties of *Marsilea quadrifolia*, several gaps in the current knowledge need to be addressed. While the plant's antioxidant properties have been well-documented, the specific mechanisms through which these antioxidants exert their effects remain unclear (Zhang et al., 2016; Bhanukiran et al., 2022). The neuroprotective potential of *Marsilea quadrifolia* has been demonstrated in animal models, but the exact

pathways and molecular targets involved in this neuroprotection are not fully understood (Subramanian et al., 2023). Furthermore, the pharmacokinetics and bioavailability of the active compounds in *Marsilea quadrifolia* have not been extensively studied, which is crucial for developing effective therapeutic applications (Zhang et al., 2016; Agarwal et al., 2018).

8.2 Emerging research trends

Recent studies have begun to explore the neuroprotective effects of *Marsilea quadrifolia*, particularly its potential to mitigate excitotoxicity induced by monosodium glutamate (Subramanian et al., 2023). This line of research is promising and suggests that *Marsilea quadrifolia* could be developed into a therapeutic agent for neurological disorders. Additionally, there is a growing interest in the plant's polyphenolic compounds, such as quercetin, which have shown significant antioxidant activities both in vitro and in vivo (Zhang et al., 2016). The use of advanced analytical techniques like HPTLC and HPLC for the standardization and quality control of *Marsilea quadrifolia* extracts is also an emerging trend, ensuring the consistency and efficacy of its medicinal preparations (Bhanukiran et al., 2022).

8.3 Recommendations for future studies

Future research should focus on elucidating the molecular mechanisms underlying the antioxidant and neuroprotective effects of *Marsilea quadrifolia*. Detailed studies on the pharmacokinetics and bioavailability of its active compounds are essential to understand how these compounds are absorbed, distributed, metabolized, and excreted in the body (Zhang et al., 2016; Agarwal et al., 2018). Additionally, clinical trials are necessary to validate the therapeutic potential of *Marsilea quadrifolia* in humans, particularly for the treatment of neurological disorders (Subramanian et al., 2023). Researchers should also explore the synergistic effects of the various bioactive compounds present in the plant to develop more effective multi-target therapies. Finally, standardization of extraction methods and quality control measures should be prioritized to ensure the safety and efficacy of *Marsilea quadrifolia*-based products (Rai, 2009; Bhanukiran et al., 2022).

9 Concluding Remarks

Marsilea quadrifolia, an aquatic medicinal plant, has been extensively studied for its nutritional and medicinal properties. The plant is rich in carbohydrates, proteins, amino acids, flavonoids, saponins, and fats, with carbohydrates being the most abundant. Additionally, *M. quadrifolia* contains a variety of polyphenols, including new compounds such as kaempferol derivatives and quercetin, which exhibit strong antioxidant activities both in vitro and in vivo. The neuroprotective potential of *M. quadrifolia* has also been demonstrated, particularly against monosodium glutamate-induced excitotoxicity in rats, suggesting its efficacy in improving locomotor activity, memory, and learning, likely due to its NMDA antagonistic properties.

The high nutritional content of *M. quadrifolia*, particularly its rich carbohydrate and protein profile, makes it a valuable dietary supplement. Its significant antioxidant properties, attributed to polyphenols like quercetin, suggest that *M. quadrifolia* can be developed into functional foods or nutraceuticals aimed at reducing oxidative stress and related conditions. The neuroprotective effects observed in animal models indicate potential therapeutic applications in the management of neurological disorders such as Alzheimer's disease and other forms of neurodegeneration. These findings underscore the plant's dual role in both nutrition and medicine, offering a natural alternative for health maintenance and disease prevention.

In conclusion, *Marsilea quadrifolia* stands out as a plant of significant nutritional and medicinal value. Its rich composition of essential nutrients and bioactive compounds provides a strong foundation for its use in health-promoting applications. The antioxidant and neuroprotective properties further enhance its potential as a therapeutic agent. Future research should focus on clinical trials to validate these findings in humans and explore the underlying mechanisms of its bioactive compounds. The integration of *M. quadrifolia* into dietary and medicinal practices could offer a natural and effective approach to improving overall health and managing various diseases.

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Conflict of Interest Disclosure

The authors affirm that this research was conducted without any commercial or financial relationships that could be construed as a potential conflict of interest.

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