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REVIEW ARTICLE **OPEN ACCESS**

Pharmacological potential of *Cyperus rotundus* in neurodegenerative disorders

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ABSTRACT
Cyperus rotundus Linn is considered as diuretic, astringent, analgesic, antispasmodic, aromatic, carminative, sedative, vermifuge, stimulant, antibacterial, stomachic and litholytic. Main chemical constituents responsible for exerting pharmacological actions include cyprotene, cyperene, isocyperol, aselinene, rotundene, cypera-2, 4-diene, valencene, γ-gurjunene, α-selinene, ylanga-2, 4-diene, trans-calamenene, cadalene, δ–cadinene, γ-calacorene, mustakone, epi-α-muurolene, γ-muurolene, nootkatene, cyperotundone, cyperol and α-cyperone . This review article focusses on geographical distribution of the plant identifies various phytoconstituents along with their structure present in plant part, their medicinal uses and various pharmacological properties exerted by *Cyperus rotundus* .
Keywords: *Cyperus rotundus, constituents, neuroprotection, pathophysiology.*

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INTRODUCTION

Cyperus rotundus Linn is a member of the Cyperaceae family. It is often referred to as purple nutsedge or nutgrass. It is a common perennial plant with tubers that are 1-3 cm tall and scaly, slender spreading rhizomes that emerge singly from the bulbous bases. The tubers have a distinctive odour and which are blackish in colour from outside and reddish white from inside. The linear, dark green leaves have grooves on the upper surface and stems that are around 25 cm tall. A few tiny blooms with a reddish-brown husk and 2-4 bracts are formed in small inflorescences. The nut is triangular, yellow in colour, oblong-ovate, and when ripe, turns black [1]. *Cyperus rotundus* can be found growing in cultivated fields, farmland, abandoned areas, grasslands, and wastelands along gravelly or sand riverbanks, roadside embankments and irrigation canal banks [2]. Practically every type of soil, as well as a wide variety of pH, elevation and soil moisture are favourable to purple nutsedge growth [3]. It grows best in damp, fertile soils and is promoted by frequent cultivation. It grows slowly, blossoms less, and produces fewer tubers in cool or wet soils [2].

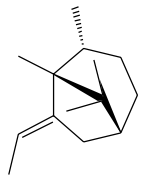
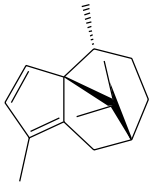
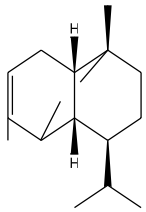
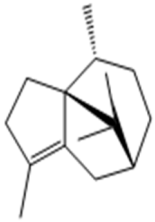
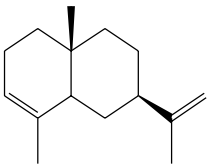
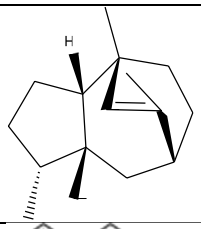
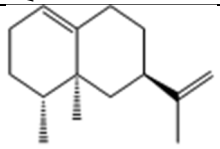
Distribution

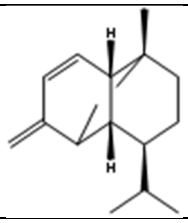
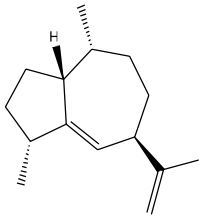
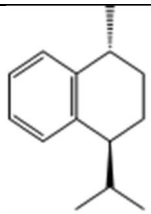
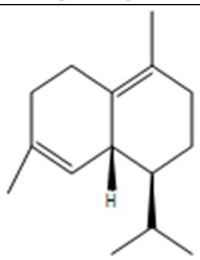
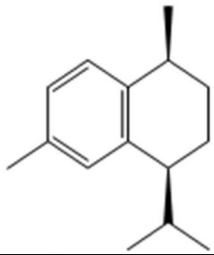
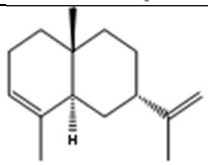
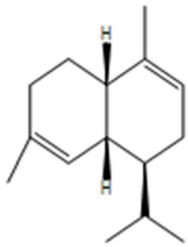
Cyperus rotundus is the worst invasive weed in the world and is a weed in more than 90 countries due to its distribution and effects on crops. Its ability to reproduce and survive in harsh environments is ensured by the basal bulbs, complex underground network of tubers, rhizomes and roots. Due to additional biological characteristics, such as its adaptability to solar radiation, high temperatures and humidity, this weed has become a serious problem in subtropical and even desert locations [4]. It is widely distributed in Eastern Asia **(**India, China, Japan, Taiwan, Korea, Myanmar, Nepal, Sri Lanka & Pakistan), Western Asia (Iraq, Afghanistan, Turkey, Syria, Yemen, Iran, Lebanon, Palestine & Saudi Arabia), Middle Asia (Uzbekistan, Kazakhstan, Turkmenistan, Kyrgyzstan), Caucasus (Armenia, Russian Federation & Azerbaijan), Western Indian Ocean (Comoros, Seychelles, Madagascar, Reunion & Mauritius), Africa (Swaziland, Algeria, South Africa, Egypt, Namibia, Libya, Botswana, Morocco, Zimbabwe, Tunisia, Zambia, Western Sahara, Mozambique, Chad, Malawi, Djibouti, Angola, Eritrea, Togo, Ethiopia, Sierra Leone, Somalia, Senegal, Sudan, Nigeria, Kenya, Niger, Kenya, Mauritania, Tanzania, Mali, Uganda, Guinea, Burundi, Ghana, Equatorial Guinea, Burkina Faso, Gabon, Benin, Rwanda & Zaire), North America (Mexico & USA), South America (Argentina, Brazil, Peru, Bolivia, Ecuador & Colombia), Pacific (Northern Mariana Islands, Marshall Islands & Micronesia) & Europe (Spain, Austria, Switzerland, Bulgaria, Greece, Albania, Croatia, Romania, Portugal, Serbia, France & Slovenia) [5].

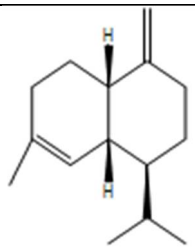
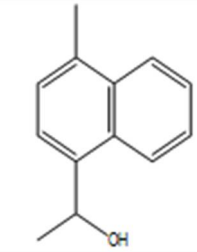
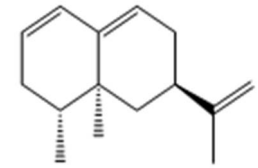
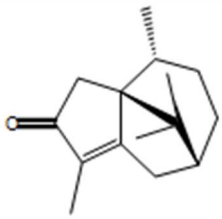
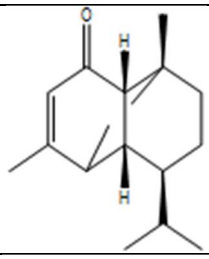
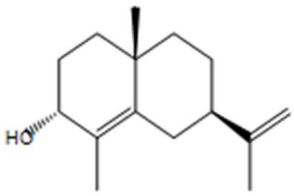
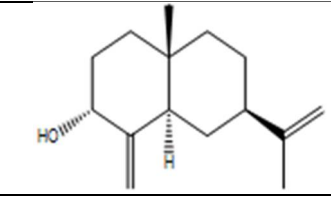
Phytochemistry

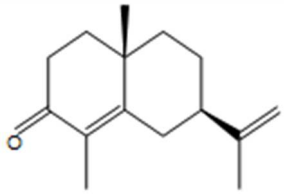
Major components of *Cyperus rotundus* according to various phytochemical studies are flavonoids, mono- and sesquiterpenes, essential oils, terpenoids [6,7]. Chemical constituents and their structures are shown in table 1.

Table 1: Chemical constituents and their structures

S.no	Chemical constituents	Structures
1.	Cyprotene	
2.	Cypera-2, 4-diene	
3.	α-copaene	
4.	Cyperene	
5.	Aselinene	
6.	Rotundene	
7.	Valencene	

8.	Ylanga-2, 4- diene	
9.	γ –gurjunene	
10.	Trans-calamenene	
11.	δ –cadinene	
12.	γ –calacorene	
13.	Epi- α –selinene	
14.	α –muurolene	

15.	γ –muurolene	
16.	Cadalene	
17.	Nootkatene	
18.	Cyperotundone	
19.	Mustakone	
20.	Cyperol	
21.	Isocyperol	

22.	α –cyperone	

Traditional uses of *Cyperus rotundus*

Cyperus rotundus was used traditionally for vomiting, stomach disorders, gastrointestinal spasms, indigestion, irritation of bowel and food poisoning. It has also been used for treating wounds, fevers, cervical cancer, malaria, bronchitis, infertility, cough, urinary tenesmus, dysmenorrhoea, insect bites, amenorrhoea, loss of memory, deficient lactation, dysuria, menstrual disorders [8,9,10,11,12]. Ayurveda claims that rhizomes of *Cyperus rotundus* are considered sedative, diaphoretic, antispasmodic, astringent, aromatic, antitussive, litholytic, carminative, analgesic, emmenagogue, vermifuge, stimulant, diuretic, antibacterial and stomachic [13].

1. Pathophysiology of neurodegenerative disorders

A) Alzheimer's disease

Alzheimer's disease (AD) often causes cognitive and behavioural deficits as well as a progressive and severe memory loss [14]. The main pathogenesis-related variables for AD are genetic, β-amyloid, and acetylcholine depletion [15]. A prominent neuropathological characteristic of Alzheimer's disease is cholinergic deficiency that is associated with memory loss and is closely related to the severity of cognitive dysfunction [16]. The main enzyme responsible for breaking down acetylcholine is acetylcholinesterase (AChE). Ataxia, myasthenia gravis, senile dementia, and AD are the neurological illnesses that are thought to be treated by inhibiting acetylcholinesterase [17,18]. Rhizomes of *Cyperus rotundus* are strong inhibitors of acetylcholinesterase [19]. Previous studies have linked Alzheimer's disease to inflammatory processes. Inflammation is brought on by reactive oxidative species (ROS), which have the power to harm cellular components and function as secondary messengers. In the treatment of AD, antioxidant usage may be beneficial [20]. The extract from *Cyperus rotundus* tubers demonstrated considerable antioxidant activity by regulating the levels of enzymes like CAT, SOD, and others [21].

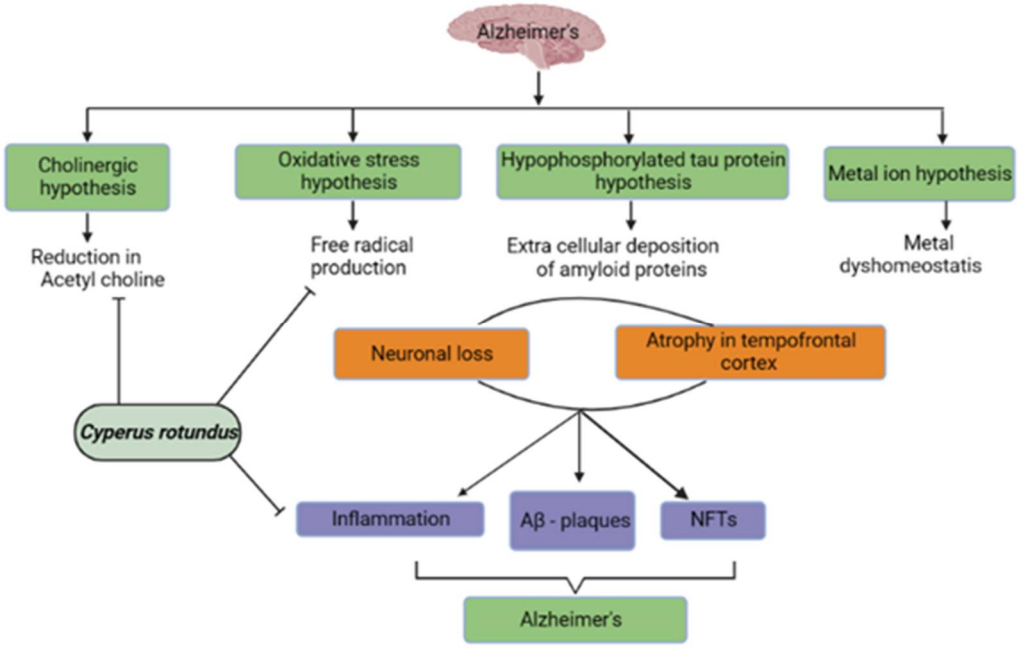


Fig. 1: Pathophysiology of Alzheimer's disease

B) Parkinson's disease

Protein misfolding, disturbed protein handling, mitochondrial dysfunction, oxidative stress, poor calcium handling, and neuroinflammation are some of the neuropathological pathways involved in the pathogenesis of Parkinson's disease (PD) [22]. Major Dopaminergic nuclei located in the

midbrain and responsible for the majority of the brain's essential functions include the substantia nigra (SN) and ventral tegmental area (VTA). The primary feature of motor symptoms of PD is the gradual death of dopaminergic neurons in SN pars compacta and dopaminergic denervation in forebrain regions [23]. *Cyperus rotundus* decreases calcium overloading and inhibits mitochondrial dysfunction which provides neuroprotection in Parkinson's disease [24].

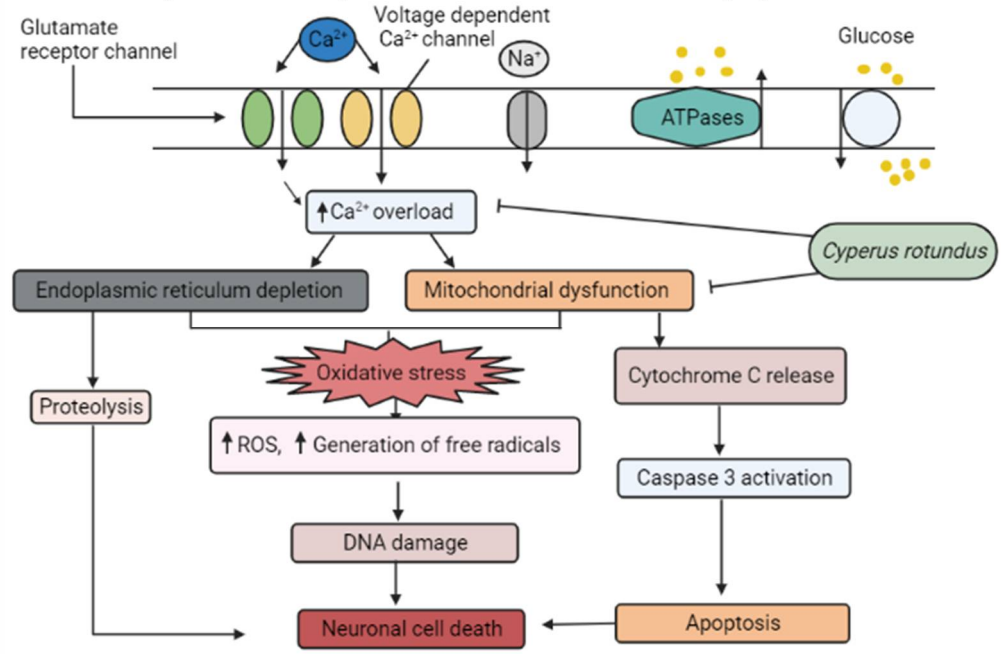


Fig.2: Pathophysiology of Parkinson's disease

C) Epilepsy

A sudden and excessive neural discharge known as an epileptic seizure results from an uncontrolled depolarization of the neural membrane. Impaired mechanisms that control this transmission, such as the harmony between inhibitory (γ-aminobutyric acid, GABA) and excitatory (glutamic and aspartic acid) neurotransmitters, cause the seizure to spread [25]. Genetic susceptibility, head injuries, various metabolic disorders and neurodegenerative diseases can cause epilepsy [26]. *Cyperus rotundus* provides neuroprotection in epilepsy via decreasing glutamate and increasing GABA neurotransmitter levels [27].

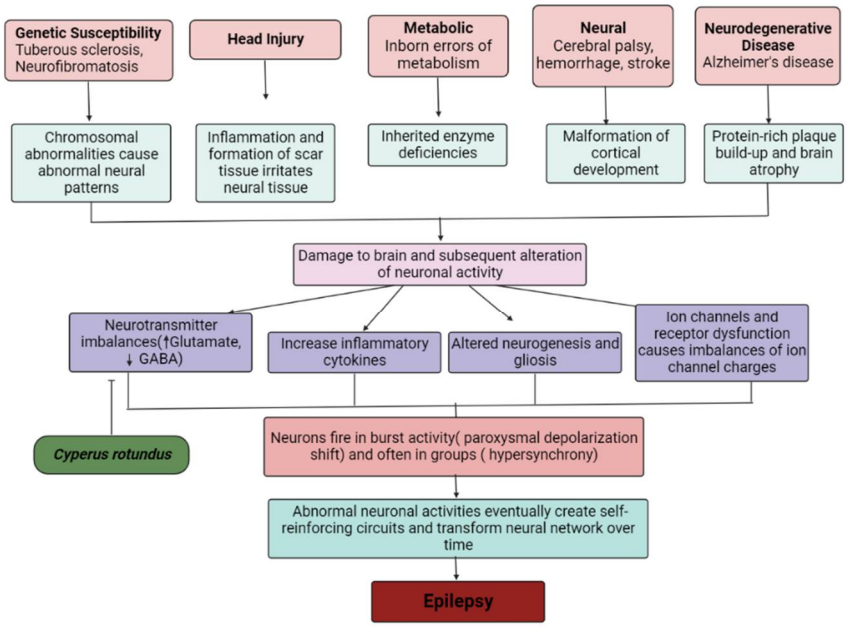


Fig.3: Pathophysiology of epilepsy

D) Depression

The monoamine hypothesis of depression suggests that the underlying pathophysiologic basis of depression is a decrease in serotonin, norepinephrine, and/or dopamine levels in the central nervous system. Noradrenaline, dopamine, and 5-hydroxytryptamine are few of the many monoamine neurotransmitters that are processed by the MAO enzyme [28, 29, 30]. There are two types of MAO: A and B. When it comes to the metabolism of the main neurotransmitter monoamines, MAO A is more crucial than MAO B. Clinical studies have suggested that MAO A inhibitors can be used to treat depression [31, 32, 33]. *Cyperus rotundus* is a well-known herbal remedy for the treatment of depression; it significantly inhibits MAO A activity [34].

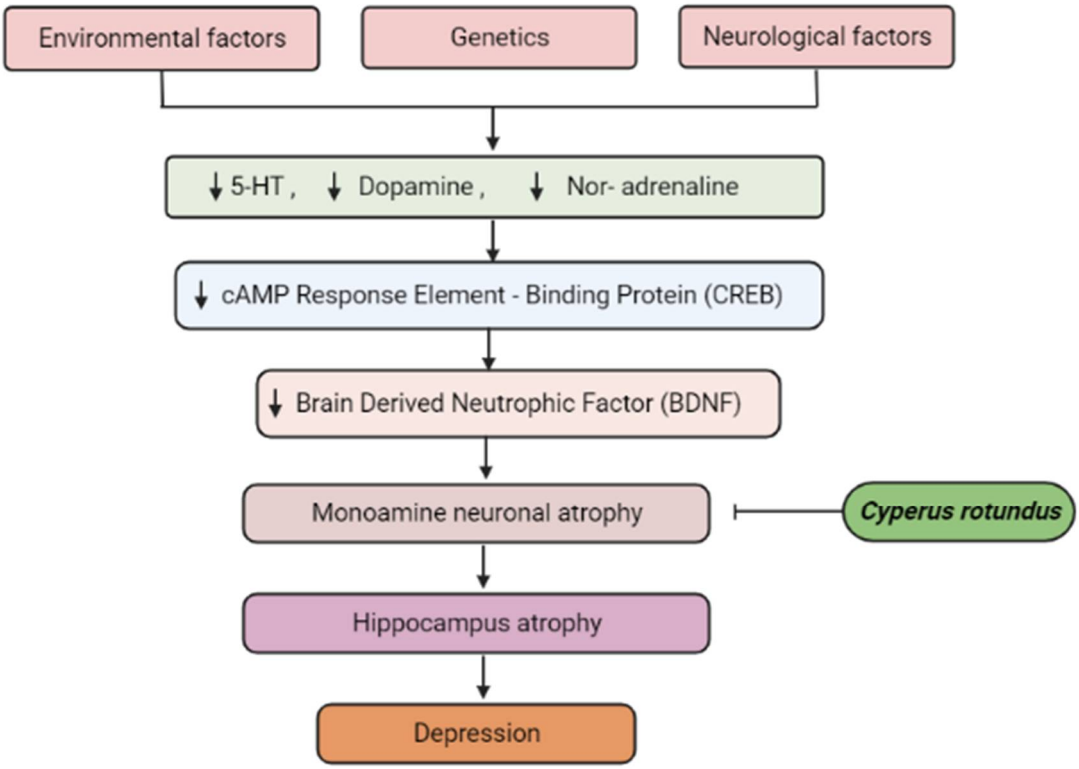


Fig.4: Pathophysiology of depression

2. Therapeutic effects of *Cyperus rotundus*

A) Neuroprotection

1. Mitochondrial dysfunction and oxidative stress

The clustering of metabolic abnormalities is associated with oxidative stress, inflammation, and atherosclerosis development. Since antioxidants are reducing agents that prevent other biomolecules from oxidising, they contribute to abnormal function and pathological physiology. Low levels of reduced glutathione, antioxidant enzymes, and mitochondrial dysfunction are thought to be the causes of the increased ROS generation. The essential oil from the CR and the extract have both shown strong antioxidant potential [35]; in addition to its ability to reduce and chelate metals, it also scavenges superoxide radicals, hydroxyl radicals, and gas radicle peroxide [36].

2. Effect on neurotransmitter levels

Neurotransmitters are chemical messengers that your body requires in order to function. They carry chemical "messages" from one neuron to the following target cell. A muscle, gland or different type of nerve cell could be the next target cell [37]. More than 40 neurotransmitters are found in the human nervous system, with glutamate, acetylcholine, dopamine, norepinephrine, gamma-aminobutyric acid (GABA), histamine and serotoninb eing the most important ones [38]. Imbalance between excitatory and inhibitory neurotransmitters leads to neurodegenerative diseases like Parkinson's, Alzheimer's and Epilepsy etc. [39]. According to various research studies *Cyperus rotundus* have potential to alter various neurotransmitter levels like decrease in glutamate level [40], increase in dopamine [41], GABA, serotonin [42] and acetylcholine levels [41] etc.

3. Apoptotic cell death

The brain is more susceptible to oxidative stress than other organs because it consumes more oxygen, produces more fatty acids, has less capacity to regenerate cells, and has lower levels of antioxidant enzymes [43]. It is believed that oxidative stress-induced neuronal damage is the root cause of many neurodegenerative disorders including Parkinson's disease, Alzheimer's disease, amyotrophic lateral sclerosis, Huntington's disease [44]. The anti-apoptotic activity of *Cyperus rotundus* is responsible for the neuroprotective effects. The plant extract's high concentration of flavonoids, phenolics, and other active ingredients may be explained by its anti-oxidant and anti-apoptotic properties [21].

4. Neuronal inflammation

Neuroinflammation is the medical term for an inflammatory reaction that occurs in the brain or spinal cord. Inflammation is mediated by the synthesis of chemokines, cytokines, secondary messengers and reactive oxygen species. These, ediators are produced by resident CNS glia (microglia and astrocytes), peripherally derived immune cells and endothelial cells. These neuro-inflammatory responses have immunological, biochemical, psychological and physiological effects. Immune cell recruitment, edema, tissue damage, and possibly cell death are all consequences of inflammation [45]. Various pharmacological studies have shown that *Cyperus rotundus* possesses anti-inflammatory activity and reduces neuronal inflammation [46,47].

B) Other therapeutic action

Cyperus rotundus also possess anti-pyretic [48], anti-emetic, spasmolytic [49], anti-diarrhoeal [1], anti-hyperlipidaemic [50], hepatoprotective [51], antidiabetic activity [52,53]. Anti-dysmenorrhoea effect [54] and also used in cerebral ischemia [55] and peptic ulcers [56].

Table 2: Uses of *Cyperus rotundus* in various diseases and their outcomes

S.n.	Disease	Plant part	Animal	Model	Results	References
1.	Alzheimer's	Rhizomes	Wistar rats	Aβ rats' model	Spatial memory impairment was repaired using *Cyperus rotundus* extract in Aβ rat model	[57]
		Rhizomes	Wistar rats	NBM-lesioned rats with stereotaxic apparatus.	Treatment with *Cyperus rotundus* tubers extract might dramatically reduce cognitive impairments after NBM (Nucleus Basalis of Meynert) injury, implying that this extract has therapeutic potential in ageing and age-related neurodegenerative diseases.	[58]
		Rhizomes	Wistar rats	Aβ rats' model	*Cyperus rotundus* almost recovered spatial memory deficit, as well as an increase in mitochondrial distribution in CA1 and neurogenesis in the SGZ (subgranolar zone)of the rats' dentate gyrus.	[47]
		Rhizomes	Wistar rats	Aβ rats' model	Following Aβ treatment, *Cyperus rotundus* may enhance learning impairment and may lead to an improvement in AD-induced cognitive dysfunction.	[59]

		Rhizomes	Wistar rats	Streptozotocin (STZ)-induced rat model	Memory and learning significantly decreased after STZ injection. Treatment with an extract of *Cyperus rotundus* may improve recall and consolidation abilities.	[60]
2.	Epilepsy	Rhizomes	Albino mice	Pentylentetrazole (PTZ)	Anticonculsant effect is shown by extract of *Cyperus rotundus* in PTZ induced kindling in mice.	[27]
		Rhizomes	Albino rats	Pentylentetrazole (PTZ)	The *Cyperus rotundus* rhizomes' ethanol extract is valuable for creating a powerful phytoconstituent for treating epilepsy, and the flavonoids in the extract may have anticonvulsant properties.	[61]
3.	Depression	Rhizomes	Wistar rats	Rat model of depression.	The findings imply that *Cyperus rotundus* extract has a substantial antidepressant effect in rats and may be effective in treating depression.	[34]
4.	Pyrexia	Rhizomes	Albino rats	Dried Brewer's yeast	Antipyretic effect was observed in *Cyperus rotundus* administered rats	[48]
5.	Emesis	Rhizomes	Dogs	Apomorphine	Extract of *Cyperus rotundus* protects 50% dogs against apomorphine induced vomiting.	[62]
6.	Spasms	Rhizomes	Rabbits	Acetylcholine, 5-hydroxytryptamine, barium chloride	A direct relaxing effect on the smooth muscle was demonstrated by the extract of *Cyperus Rotundus.*	[49]
7.	Diarrhoea	Rhizomes	Albino mice	Castor oil	A significant antidiarrheal activity was shown by extract of *Cyperus rotundus*.	[1]
8.	Hyperlipidaemia	Rhizomes	Wistar rats	High fat diet	A significant decrease in Hyperlipidaemia was observed using extract of *Cyperus rotundus*.	[50]
9.	Hepatic disease	Rhizomes	Wistar rats	Carbon tetrachloride	Hepatoprotective action was observed by administration of extract of *Cyperus rotundus* in rats.	[51]
10.	Diabetes	Rhizomes	Wistar rats	Alloxan-induced diabetes	In a model of fructose-mediated protein glycoxidation, *Cyperus rotundus* has the ability to inhibit AGE production and protein oxidation. Targeting diabetic problems might	[52,53]

					be possible using *Cyperus rotundus*.	
11.	Peptic ulcers	Rhizomes	Wistar rats	Ethanol	Extract of *Cyperus rotundus* provides cytoprotective action against ethanol induced gastric damage.	[56]
12.	Dysmenorrhea	Rhizomes	Albino mice	Diethylstilbestrol	Anti-dysmenorrhea effect was shown by extract of *Cyperus rotundus* in diethylstilbestrol induced dysmenorrhea.	[54]
13.	Cerebral Ischemia	Rhizomes	Male Sprague Dawley rats	Occlusion of the two common carotid arteries or two-vessel occlusion (2VO)	Total oligomeric flavonoids (TOFs), produced from *Cyperus rotundus*, and were investigated for their neuroprotective potential in a rat model of brain ischemia and reperfusion. Rats receiving TOFs had their neurological impairments greatly reduced, and their anxiogenic behaviour was turned around.	[55]

CONCLUSION

Traditional applications of natural substances, especially those of plant origin, have received a great deal of interest since they have undergone extensive efficacy testing and are generally considered safe for human use. A thorough examination of the literature on *Cyperus rotundus* shows that it is commonly utilised traditional and Ayurvedic medicine remedy for treating ailments among various ethnic groups. This plant has demonstrated significant neuroprotective properties, making it a possible treatment for a variety of illnesses of the central nervous system (CNS). The chemical makeup and medicinal benefits of *Cyperus rotundus* are covered in this article. The therapeutic potential of this plant is being investigated by researchers because it may possess other, undiscovered therapeutic characteristics.

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Competing Interests: None

Authors Contribution:
Nikita Yadav: Writing of the manuscript
Dr. Abhilasha Ahlawat: Study design and Proof reading
Dr. Govind Singh: Supervision and Proof reading

REFERENCES

1. Uddin, S. J., Mondal, K., Shilpi, J. A., & Rahman, M. T. (2006). Antidiarrhoeal activity of Cyperus rotundus. *Fitoterapia*, *77*(2), 134-136.
2. Holm, L. G., Plucknett, D. L., Pancho, J. V., & Herberger, J. P. (1977). The world's worst weeds. *The world's worst weeds.*
3. Swarbrick, J. T. (1997). Weeds of the Pacific islands. *Technical Paper-South Pacific Commission*, (209).
4. Bendixen, L. E., & Nandihalli, U. B. (1987). Worldwide distribution of purple and yellow nutsedge (Cyperus rotundus and C. esculentus). *Weed Technology*, *1*(1), 61-65.
5. Al-Snafi, A. E. (2016). A review on Cyperus rotundus A potential medicinal plant. *IOSR Journal Of Pharmacy*, *6*(7), 32-48.

6. Kilani, S., Abdelwahed, A., Ammar, R. B., Hayder, N., Ghedira, K., Chraief, I., ... & Chekir-Ghedira, L. (2005). Chemical composition, antibacterial and antimutagenic activities of essential oil from (Tunisian) Cyperus rotundus. *Journal of Essential Oil Research*, *17*(6), 695-700.
7. Ohira, S., Hasegawa, T., Hayashi, K. I., Hoshino, T., Takaoka, D., & Nozaki, H. (1998). Sesquiterpenoids from Cyperus rotundus. *Phytochemistry*, *47*(8), 1577-1581.
8. Talukdar, A. D., Tarafdar, R. G., Choudhury, M. D., Nath, D., & Choudhury, S. (2011). A review on pteridophyte antioxidants and their potential role in discovery of new drugs. *Assam University Journal of Science and Technology*, *7*(1), 151-155.
9. Him-Che, Y. (1985). Handbook of Chinese herbs and formulas. *Institute of Chinese Medicine, Los Angeles*, *1*, S219-S24.
10. Duke, J. A., & Ayensu, E. S. (1985). *Medicinal plants of China* (Vol. 4). Reference publications.
11. Bown, D. (1995). *The Royal Horticultural Society encyclopedia of herbs & their uses*. Dorling Kindersley Limited.
12. Chopra, R. N. (1956). Glossary of Indian medicinal plants.
13. Sivapalan, S. R. (2013). Medicinal uses and pharmacological activities of Cyperus rotundus Linn-A Review. *International Journal of Scientific and Research Publications*, *3*(5), 1-8.
14. McKhann, G., Drachman, D., Folstein, M., Katzman, R., Price, D., & Stadlan, E. M. (1984). Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. *Neurology*, *34*(7), 939–944.
15. Safahani, M., Amani, R., Aligholi, H., Sarkaki, A., Badavi, M., Moghaddam, A. Z., & Haghighizadeh, M. (2011). Effect of different doses of soy isoflavones on spatial learning and memory in ovariectomized rats. *Basic and Clinical Neuroscience*, *2*(4), 12.
16. Hasselmo, M. E. (2006). The role of acetylcholine in learning and memory. *Current opinion in neurobiology*, *16*(6), 710-715.
17. Mukherjee, P. K., Kumar, V., Mal, M., & Houghton, P. J. (2007). Acetylcholinesterase inhibitors from plants. *Phytomedicine*, *14*(4), 289-300.
18. Orhan, I., Şener, B., Choudhary, M. I., & Khalid, A. (2004). Acetylcholinesterase and butyrylcholinesterase inhibitory activity of some Turkish medicinal plants. *Journal of ethnopharmacology*, *91*(1), 57-60.
19. Sharma, R., & Gupta, R. (2007). Cyperus rotundus extract inhibits acetylcholinesterase activity from animal and plants as well as inhibits germination and seedling growth in wheat and tomato. *Life Sciences*, *80*(24-25), 2389-2392.
20. Gilgun-Sherki, Y., Melamed, E., & Offen, D. (2003). Antioxidant treatment in Alzheimer's disease. *Journal of Molecular Neuroscience*, *21*(1), 1-11.
21. Kumar, K. H., & Khanum, F. (2013). Hydroalcoholic extract of Cyperus rotundus ameliorates H2O2-induced human neuronal cell damage via its anti-oxidative and anti-apoptotic machinery. *Cellular and molecular neurobiology*, *33*(1), 5-17.
22. Brundin, P., & Melki, R. (2017). Prying into the prion hypothesis for Parkinson's disease. *Journal of Neuroscience*, *37*(41), 9808-9818.
23. Jovanovic, V. M., Salti, A., Tilleman, H., Zega, K., Jukic, M. M., Zou, H., ... & Brodski, C. (2018). BMP/SMAD pathway promotes neurogenesis of midbrain dopaminergic neurons in vivo and in human induced pluripotent and neural stem cells. *Journal of Neuroscience*, *38*(7), 1662-1676.
24. Jia, H., Liu, Y., Yu, M., Shang, H., Zhang, H., Ma, L., Zhang, T., & Zou, Z. (2019). Neuroprotective Effect of *Cyperi rhizome* against Corticosterone-Induced PC12 Cell Injury via Suppression of Ca^{2+} Overloading. *Metabolites*, *9*(11), 244.
25. Wesół-Kucharska, D., Rokicki, D., & Jezela-Stanek, A. (2021). Epilepsy in Mitochondrial Diseases—Current State of Knowledge on Aetiology and Treatment. *Children*, *8*(7), 532.
26. Engelborghs, S., D'hooge, R., & De Deyn, P. P. (2000). Pathophysiology of epilepsy. *Acta neurologica belgica*, *100*(4), 201-213.
27. Mohsen, K., Zahra, K., Mehrdad, R., & Yaser, A. (2011). Anticonvulsant and antioxidant effect of hydro-alcoholic extract of Cyperus rotundus rhizome on pentylentetrazole-induced kindling model in male mice. *Journal of Medicinal Plants Research*, *5*(7), 1140-1146.
28. Knoll, J. (1997). History of deprenyl--the first selective inhibitor of monoamine oxidase type B. *Voprosy meditsinskoi khimii*, *43*(6), 482-493.
29. Lim, D. W., Jung, J. W., Park, J. H., Baek, N. I., Kim, Y. T., Kim, I. H., & Han, D. (2015). Antidepressant-like effects of sanggenon G, isolated from the root bark of Morus alba, in rats: involvement of the serotonergic system. *Biological and Pharmaceutical Bulletin*, b15-00471.
30. Ago, Y., Arikawa, S., Yata, M., Yano, K., Abe, M., Takuma, K., & Matsuda, T. (2008). Antidepressant-like effects of the glucocorticoid receptor antagonist RU-43044 are associated with changes in prefrontal dopamine in mouse models of depression. *Neuropharmacology*, *55*(8), 1355-1363.
31. Seckl, J. R., & Fink, G. (1992). Antidepressants increase glucocorticoid and mineralocorticoid receptor mRNA expression in rat hippocampus in vivo. *Neuroendocrinology*, *55*(6), 621-626.
32. McArthur, R., & Borsini, F. (2006). Animal models of depression in drug discovery: a historical perspective. *Pharmacology Biochemistry and Behavior*, *84*(3), 436-452.
33. Pariante, C. M., & Miller, A. H. (2001). Glucocorticoid receptors in major depression: relevance to pathophysiology and treatment. *Biological psychiatry*, *49*(5), 391-404.

34. Hao, G. F., Tang, M. Q., Wei, Y. J., Che, F. Y., & Qian, L. J. (2017). Determination of antidepressant activity of Cyperus rotundus L extract in rats. *Tropical Journal of Pharmaceutical Research*, *16*(4), 867-871.
35. Hu, Q. P., Cao, X. M., Hao, D. L., & Zhang, L. L. (2017). Chemical composition, antioxidant, DNA damage protective, cytotoxic and antibacterial activities of Cyperus rotundus rhizomes essential oil against foodborne pathogens. *Scientific reports*, *7*(1), 1-9.
36. Kakarla, L., Katragadda, S. B., Tiwari, A. K., Kotamraju, K. S., Madhusudana, K., Kumar, D. A., & Botlagunta, M. (2016). Free radical scavenging, α-glucosidase inhibitory and anti-inflammatory constituents from Indian sedges, Cyperus scariosus R. Br and Cyperus rotundus L. *Pharmacognosy Magazine*, *12*(Suppl 4), S488.
37. Sheffler, Z. M., Reddy, V., & Pillarisetty, L. S. (2022). Physiology, Neurotransmitters. In *StatPearls*. StatPearls Publishing.
38. Axelrod, J. (1974). Neurotransmitters. *Scientific American*, *230*(6), 58-71.
39. Teleanu, R. I., Niculescu, A. G., Roza, E., Vladâcenco, O., Grumezescu, A. M., & Teleanu, D. M. (2022). Neurotransmitters-Key Factors in Neurological and Neurodegenerative Disorders of the Central Nervous System. *International journal of molecular sciences*, *23*(11), 5954.
40. Sunil, A. G., Kesavanarayanan, K. S., Kalaivani, P., Sathiya, S., Ranju, V., Priya, R. J., ... & Babu, C. S. (2011). Total oligomeric flavonoids of Cyperus rotundus ameliorates neurological deficits, excitotoxicity and behavioral alterations induced by cerebral ischemic–reperfusion injury in rats. *Brain Research Bulletin*, *84*(6), 394-405.
41. Sutalangka, C., & Wattanathorn, J. (2017). Neuroprotective and cognitive-enhancing effects of the combined extract of Cyperus rotundus and Zingiber officinale. *BMC Complementary and Alternative Medicine*, *17*(1), 1-11.
42. Pal, D., Dutta, S., & Sarkar, A. (2009). Evaluation of CNS activities of ethanol extract of roots and rhizomes of Cyperus rotundus in mice. *Acta Pol Pharm*, *66*(5), 535-541.
43. Friedman, J. (2011). Why is the nervous system vulnerable to oxidative stress?. In *Oxidative stress and free radical damage in neurology* (pp. 19-27). Humana Press.
44. Andersen, J. K. (2004). Oxidative stress in neurodegeneration: cause or consequence?. *Nature medicine*, *10*(7), S18-S25.
45. DiSabato, D. J., Quan, N., & Godbout, J. P. (2016). Neuroinflammation: the devil is in the details. *Journal of neurochemistry*, *139 Suppl 2*(Suppl 2), 136–153.
46. Ahmad, M., Rookh, M., Rehman, A. B., Muhammad, N., Younus, M., & Wazir, A. (2014). Assessment of anti-inflammatory, anti-ulcer and neuropharmacological activities of Cyperus rotundus Linn. *Pakistan Journal of Pharmaceutical Sciences*, *27*(6).
47. Shakerin, Z., Esfandiari, E., Ghanadian, M., Razavi, S., Alaei, H., & Dashti, G. (2020). Therapeutic effects of Cyperus rotundus rhizome extract on memory impairment, neurogenesis and mitochondria in beta-amyloid rat model of Alzheimer's disease. *Metabolic Brain Disease*, *35*(3), 451-461.
48. Gupta, M. B., Palit, T. K., Singh, N., & Bhargava, K. P. (1971). Pharmacological studies to isolate the active constituents from Cyperus rotundus possessing anti-inflammatory, anti-pyretic and analgesic activities. *The Indian journal of medical research*, *59*(1), 76-82.
49. Singh, N., Kulshrestha, V. K., Gupta, M. B., & Bhargava, K. P. (1970). A pharmacological study of Cyperus rotundus. *The Indian journal of medical research*, *58*(1), 103-109.
50. Friedewald, W. T., Levy, R. I., & Fredrickson, D. S. (1972). Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clinical chemistry*, *18*(6), 499-502.
51. Kumar, S. S., & Mishra, S. H. (2005). Hepatoprotective activity of rhizomes of Cyperus rotundus Linn against carbon tetrachloride-induced hepatotoxicity. *Indian journal of pharmaceutical sciences*, *67*(1), 84.
52. Raut, N. A., & Gaikwad, N. J. (2006). Antidiabetic activity of hydro-ethanolic extract of Cyperus rotundus in alloxan induced diabetes in rats. *Fitoterapia*, *77*(7-8), 585-588.
53. Ardestani, A., & Yazdanparast, R. (2007). Cyperus rotundus suppresses AGE formation and protein oxidation in a model of fructose-mediated protein glycoxidation. *International journal of biological macromolecules*, *41*(5), 572-578.
54. Chen, Y., Wang, X., Liu, J., & Huang, L. (2011). *Anti-dysmenorrhea components from the rhizomes of Cyperus rotundus Linn.(Cyperaceae)* (Doctoral dissertation, 027-oaps-2011;).
55. Jebasingh, D., Devavaram Jackson, D., Venkataraman, S., Adeghate, E., & Starling Emerald, B. (2014). The protective effects of Cyperus rotundus on behavior and cognitive function in a rat model of hypoxia injury. *Pharmaceutical Biology*, *52*(12), 1558-1569.
56. Zhu, M., Luk, H. H., Fung, H. S., & Luk, C. T. (1997). Cytoprotective effects of Cyperus rotundus against ethanol induced gastric ulceration in rats. *Phytotherapy Research: An International Journal Devoted to Medical and Scientific Research on Plants and Plant Products*, *11*(5), 392-394.
57. Shakerin, Z., Esfandiari, E., Razavi, S., Alaei, H., Ghanadian, M., & Dashti, G. (2020). Effects of *Cyperus rotundus* Extract on Spatial Memory Impairment and Neuronal Differentiation in Rat Model of Alzheimer's Disease. *Advanced biomedical research*, *9*, 17.
58. Rabiei, Z., Hojjati, M., Rafieian-Kopaeia, M., & Alibabaei, Z. (2013). Effect of Cyperus rotundus tubers ethanolic extract on learning and memory in animal model of Alzheimer. *Biomedicine & Aging Pathology*, *3*(4), 185-191.
59. Mehdizadeh, M., Dabaghian, F. H., Shojaee, A., Molavi, N., Taslimi, Z., Shabani, R., & Asl, S. S. (2017). Protective effects of Cyperus rotundus extract on amyloid β-peptide (1-40)-induced memory impairment in male rats: A behavioral study. *Basic and Clinical Neuroscience*, *8*(3), 249.

60. Nasri, S., Naseri, M., & Piri, M. (2018). The effect of hydroalcoholic extract of Cyperus rotundus rhizome on memory and learning in Streptozotocin-induced rat model of Alzheimer's disease.
61. Shivakumar, S. I., Suresh, H. M., Hallikeri, C. S., Hatapakki, B. C., Handiganur, J. S., Sankh, K., & Shivakumar, B. (2009). Anticonvulsant effect of Cyperus rotundus Linn rhizomes in rats. *Journal of Natural Remedies*, 192-196.
62. Singh, N., Pandey, B. R., Verma, P., Bhalla, M., & Gilca, M. (2012). Phyto-pharmacotherapeutics of Cyperus rotundus Linn.(Motha): an overview.

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