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Review Article

Phytoflavonoids-A Future Perspective for the Therapeutic Potential of Alzheimer's Disease

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ABSTRACT

Millions of people suffer from the neurodegenerative diseases like Alzheimer's Disease (AD) worldwide. Due to their complex pathology, no effective pharmacological treatment has been found to date, despite extensive research. Developing new, effective therapeutic agents to cure these disease remains a major challenge. Although the cause of AD remains apparent, numerous studies indicates that oxidative stress and neuro-inflammation lead to neurodegeneration in the central nervous system and play vital role in AD morbidity and progression. Flavonoids, which are found widely in nature, exhibit anti-oxidative, anti-inflammatory, anti-mutative, anti-microbial, and neuroprotective properties, so have potential to treat these two kinds of disease. In this review, we focus on the anti-oxidative and neuroprotective action of flavonoids in attenuating Alzheimer's disease, and how they might be harnessed in the development of new pharmacological agents to treat these diseases. Some Flavonoids compounds Quercetin, Rutin, hesperidin, Naringinin, Epigallocatechin-3-gallate, displayed to be effective in AD. Considerable studies have demonstrated the anti-AD effects of flavonoids through various *in vitro* and *in vivo* models. However, more rigorous studies are needed to be done for flavonoids to develop into effective drugs and apply them to clinical practice.

Keywords: Alzheimer's disease, Flavonoids, Neuroprotective, Quercetin, Rutin.

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INTRODUCTION

Alzheimer's Disease (AD) is a continuous degenerative nervous disorder, that creates cognitive dysfunction and is indicated by loss of thinking ability leads to loss of personality changes including, reduced function of speech, impaired behavioral deterioration, impaired performance, slowness or delayed thoughts, and irregular gait movements.[1] AD is one of the greatest threats in the medical field, which is the main reason of causing dementia. This mostly occurs in elders above the age of 55 years. Around the world, overall 50 million individuals are approximated to be affected by dementia, and this count is expected two times increased each 20 years, until around 2050. Every 30 sec, another one new AD case is anticipated to evolve, or approximately a new million cases annually and the overall calculated occurance is anticipated to be 13.8 million.[2] Presently, many hypotheses take place a major part in etiology of AD. The first hypothesis is based on the cholinergic innervations, in this condition, the patient with AD showed a decreased level of acetylcholinesterase, choline acetyltransferase, and butyryl transferase which is more specifically in the cerebral cortex in the brain. Studies have reported that the postmortem brain tissue seperated from the patient with Alzheimer's disease showed cholinergic neuronal degeneration and loss of Ach transmission, such conditions lead to cognitive dysfunction. The second hypothesis proposed on Tubulin Associated Unit (TAU) protein. Tau proteins are majorly present in the neurons which contribute the neuronal microtubule network stabilization, when this process becomes over-phosphorylated, and form neurofibrillary tangles by the polymerization of tau proteins, these abnormalities lead to structural damage in the brain and altered function of synaptic cleft thus produces neurodegeneration.[3] The third hypothesis for AD is amyloid cascade.[4] This postulates that either over secretion or reduced clearance of amyloid beta peptides clearance results in high Aβ accumulation, which in turn causes neuronal damage. Two types of Aβ polymers plays important role that is Aβ40 and Aβ42 When they become oligomerizes, it will interfere with

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synaptic signaling pathways and then polymerize into amyloid fibrils which is insoluble and accumulate as amyloid plaques, these plaques diffuse the entire brain and cause neuroglial cells activation and induced cytokines release, thus attributes inflammatory response and cerebral atrophy. Some of the genetic makeup also takes plays a part of the AD pathogenesis. APP (Amyloid Precursor Protein gene) was first identified as the causative gene for AD. In advanced research, two distinct forms of APP gene were identified as Familial AD and sporadic AD. According to some research, autosomal dominant mutations in APP, PSEN1, and PSEN2 cause familial AD. Sporadic AD is the result of the Appolipoprotein-E gene. This is approximately three-fold increased risk in the progression of AD.[5] Another mechanism includes oxidative stress, which is highly elevated in the aging brain. This free radical binds with proteins, nucleic acid, and lipid membranes and disturbs neuronal cellular function. Free radicals have high integrity to the brain tissue because of the increased amount of polyunsaturated fatty acids present in it, hence this causes a high risk of free radical binding, thus the neuronal cells undergo oxidative degradation due to increased levels of lipid peroxidation[6] results in the senile plaques formation and NFT accumulation, further cause the aberrant level of cytokines, as a result, pathogenesis of AD has been linked with the oxidative stress.

Another major cause of the progressive loss of neurons in AD is excitotoxicity, which is brought on by the increased risk of the neurotransmitter such as glutamate receptor like N-Methyl-D-Aspartate (NMDA).[7] It is quite likely that this process contributes to the death of cholinergic neurons, which causes an overabundance of calcium ions to enter the cells. Dementia brought on by disease Elevated Body Mass Index (BMI), blood pressure, and blood cholesterol are examples of vascular risk factors that have been associated with an increased chance of developing clinical AD.[8] According to studies, hypertension may increase the likelihood that neuropathological characteristics of AD, such as neurofibrillary tangles, will progress. Therefore, by either increasing the production of amyloid plaques or NFTs or decreasing their removal from the brain, vascular illness may have a direct impact on them.[9] Diabetes and AD have a long-standing relationship. Additionally, some research has indicated that individuals with AD had decreased insulin levels in their CSF (Cerebrospinal Fluid). Other important aspects include aberrant insulin metabolism in the CNS and insulin dysregulation.[10] Since insulin's function in the CNS is to regulate phosphorylation of tau and protect against Aβ buildup through the insulin-degrading enzyme (insulinase),[11,12] a plausible mechanism entails peripheral hyperinsulinemia decreasing insulin intake over the BBB because of the above oversaturation. A decreased amount of vitamin D (1, 25-dihydroxy vitamin D3) has also been connected to Alzheimer's disease, according to current research. The expression of neurotrophins, such as nerve growth factor, neurotrophin-3, and glial-derived neurotrophic factor, as well as the existence and functionality of brain cells, are regulated by 1, 25-dihydroxy vitamin D3, the active form of vitamin D.[13,14]

Thus, a multi-target approach is required to investigate the anti-Alzheimer effects because numerous pathways are associated in the AD pathogenesis. Patients undertaking AD treatment currently have access to two kinds of pharmacologic therapy. The first-generation cholinesterase inhibitor was tacrine, but its usage was constrained because of its harmful effects on the liver. Additional cholinesterase inhibitors, such as galantamine, rivastigmine, and donepezil. These medications serve as a delay may lessen the signs of moderate, severe, and mild AD.[15] Memantine is used as a dopaminergic medication and an NMDA receptor blocker to either delay or decrease the symptoms of moderate to severe AD. The most common side effects of galantamine, rivastigmine, and donepezil include fatigue, cramping in the muscles, and gastrointestinal problems. Because cholinesterase inhibitors can produce sinus node syndrome and other abnormalities in conductivity, every patient must have an ECG before beginning treatment. When starting a cholinesterase inhibitor, patients with a history of peptic or duodenal ulcer illness should be carefully monitored. A small percentage of patients may experience agitation or an acute decline in cognition very away after starting the medication; in this instance, it should be stopped right once. Although it can cause headache, dizziness, sleeplessness, constipation, and hypertension, memantine is usually well tolerated.[16] Initially, 5 mg of memantine per day is recommended; every week this quantity is then increased by 5 mg upto 20 mg. Though it causes headache, dizziness, insomnia, constipation, and hypertension, it is usually tolerated well and has lesser side effects compared to cholinesterase inhibitors.[17] Several AD medications are being developed, including: One medication called aducanumab targets a protein known as beta-amyloid. In Alzheimer's disease patients, this protein gathered as clusters surrounding brain cells. The symptoms of AD are brought on by these clusters, which halt communication between the cells. It has been demonstrated, though, that aducanumab breaks and dissolves beta-amyloid plaques. The FDA approved this medication in 2022, and in this year recently Lecanemab was approved for the treatment of primary stage of the disease symptoms.[18] Solanezumab: This is also targeting the beta-amyloid protein. Recently INDIANAPOLIS, declared that solanezumab did not deliberate the cognitive decline progression because of pathology of AD during started in amyloid plaque patients but there is lack of disease symptoms, known as the preclinical stage of AD. Solanezumab only targets soluble amyloid beta.[19] Research is being done on Nasal Insulin to fight against forgetfulness and target to improve memory function in AD patients.

Nowadays some other drugs being developed like verubecestat, AADvac1, CSP-1103, and intepirdine. It appears that AD and the

problems associated to it will not be treated by a single medication. Future research may incline more towards the prevention and treatment of the causes of AD.[20]

Moreover, few treatments for AD have been approved, and those that have meant to control symptoms instead change the outbreak of the disease. This poses serious public health concerns. Consequently, our focus is on dormant disease-modifying therapies that have typically been used in the clinically discernible disease patients and involve plant extracts. This will be a difficult but exciting role in the fight against AD. The function of medicinal plants in AD prevention. Herbal medicine is the traditional treatment in India. To treat a so many diseases, many Ayurvedic formulations have been developed. The majority of scientific evidence highlights the significance of medicinal plants that enhance or extend nervous system function. Consequently, plant-derived substances can be used as an alternative to suppressing or modifying the symptoms and reducing the progression of AD. Phytocompounds like polyphenols, flavonoids, sterols, triterpenes, and alkaloids present in various plant sources showed a positive role against various diseases.[21] Among these phytocompounds, the ongoing analysis demonstrated that the compounds rich in flavonoids can improve cognitive dysfunction and control disease progression.

Flavonoids

Flavonoids are the chief compounds obtained from natural sources specifically, it can be found in a wide range of fruits, vegetables, leaves, and vegetation. Flavonoids are classified as polyphenolic secondary metabolites. From various natural resources like vegetables, plants, and other organic products, above 10,000 flavonoids have been isolated. It interacts with various proteins in the body and modify the transporters, enzymes, hormones, and free radical scavenging properties.[21] Flavonoids have a wide range of biochemical and antioxidant characteristics that make them effective disease inhibitors, preventing diseases including cancer, Alzheimer's Disease (AD), atherosclerosis, and others.[22] Flavonoids are associated with a multitude of health-promoting effects and are essential components in a wide range of nutraceutical, pharmaceutical, medicinal, and cosmetic applications because of their anti-inflammatory, anti-mutagenic, anti-carcinogenic, and antioxidant properties. They can also modulate important cellular enzyme functions. They are also known to efficiently block a number of other enzymes, such as phosphoinositide 3-kinase, lipoxygenase, cyclo-oxygenase, and Xanthine Oxidase (XO).[23]

Numerous flavonoids have been found to have excellent therapeutic potential. Based on their molecular makeup, flavonoids are categorized.[24]

a) Rutin, quercetin, galangin, and kaempherol are examples of flavonols.

b) Catechin, epicatechin, and epigallocatechin are examples of flavanols.

c) Genistin, daidzein, glycetin, and formanantine are isoflavones.

d) The anthocyanidins are cyanidin, malvidin, and delphinidin;

e) The flavanones are naringin, hesperetin, and naringenin

f) The flavones are apigenin, diosmin, and luteolin.

Anthocyanins

The largest subclass of flavonoids is called flavonols. They contain OH group in C-3 position, that may be glycosylated, and a ketone group attached to the flavonoid structure. Many different fruits and vegetables contain flavonols. Chief among the flavonols is myricetin, fisetin, kaempferol, and quercetin. Apples, berries, kale, tomatoes, onions, and grapes are just a few of the foods high in flavonols. Flavonols Consumption is associated with a different role of antioxidant, which lowers the risk factors for vascular disease.[25] The other flavonoids category is flavanones. Not as with flavones, however, because the double bond between positions 2 and 3 is saturated they are also known as dihydroflavones. It is the only structural distinction among the two flavonoids subclass. Oranges, lemons, and grapes are just a few examples of the citrus fruits that commonly contain flavanones. Some examples of flavanones are Hesperitin, naringenin, and eriodictyol. Flavonones are incorporated with several health benefits through their pharmacological properties like free radical-scavenging properties, agents that decrease cholesterol, blood lipids, and inflammation.[25]

Isoflavonoids are the considerable and very typical subclass of flavonoids. This is distributed in limited sources and is mostly present in soybeans and other leguminous plants. Some of the studies reported that there is a presence of microbes.[26]

Flavonoids have amazing potential against various diseases. Since they have been shown to have oestrogenic activity in certain animal models, isoflavones such as genistein and daidzein are often considered phytoestrogens.[27] Catechins, flavan-3-ols, or flavanols Flavanonols are sometimes referred to as 3-hydroxy derivatives of flavanones or dihydroflavonol catechins. In flavanols, the hydroxyl group is situated at position 3 on the C ring. Positions 2 and 3 not have a double bond, in contrast to many flavonoids. Bananas, apples, blueberries, peaches, and pears all contain high levels of flavanols.[28] A large range of plants, flowers, and fruits contain pigments known as anthocyanins that are vibrant in color. Algae-derived pigments include anthocyanins such as cyanidin, peonidin, delphinidin, and malvidin. They can be found in large quantities in the outer layers of a wide variety of fruits, such as raspberries, strawberries, blueberries, bilberries, blackberries, red grapes, black currants, and cranberries. To

facilitate their beneficial effects on health, they are utilized in the food industry for different applications Flavonoids Fight against neurodegenerative diseases,[29] Studies have reported that the research conducted on various plant metabolites, among metabolites, flavonoids takes plays a major part in enzymes and receptor action of the brain and employ remarkable CNS effects for averting illnesses caused by neurons, such as Alzheimer's and Parkinson's. They have the potential to inhibit enzymes like xanthine oxidase, aldose reductase, and phosphodiesterase. Ca^{2+} ATPase, cyclooxygenase, and lipoxigenase to avert the neurodegenerative diseases.[30] By using the molecular docking technique, significant work has also been done to look for new flavonoids with potential medical applications in AD.[31] They have evaluated and created a new series of flavonoids based on this research. Most of them demonstrated stronger AChE inhibitory activities than the AD medication rivastigmine. The isoflavone skeleton was also mentioned as a potential structural model for the creation of new AChE inhibitors. The effect of inhibitory activity of flavonoid derived AChE and BChE lik rutin, kaempferol galactoside, quercetin and macluraxanthone have been the focus of some studies. AChE and BChE were among those that macluraxanthone showed a concentration-dependent inhibition.[32] By using molecular docking studies, several studies have shown that flavonoids and their derivatives can reduce the production of Aβ. According to reports, flavonoids and the inhibition of NF-B-related mechanisms are closely related. Additionally, it has been proposed that flavonoids interact with the BACE-1 catalytic center to significantly reduce BACE-1 activity.[33]

METHODOLOGY

In this review, to collect the data by different combinations of keywords like Alzheimer's disease, medicinal plants, pharmacological activities, phytochemistry, ethno-medicinal uses were entered into databases consisting of international databases of Web of Science, PubMed, and Scopus. Then, the articles on application of medicinal plants for prevention and treatment of AD were selected, and those demonstrating potent effects of these plants and/or their compounds were reported. Their detailed information of the various plants containing phytocompounds responsible for the antialzheimer activity against various neurotoxicity is mentioned in the Table 1.

FUTURE PERSPECTIVES

Herbal medicines emerged as an alternative to improve recovery and management of neurodegenerative diseases especially alzheimer's disease. Traditional herbal medicines have been used from ancient times and provided promising effect as an adjuvant to neurotoxicity. The plants and their phytocompounds like flavonoids such as flavonols, flavanones, isoflavones have shown promising effect in improving neuroprotective against various animal model of Alzheimer disease. Such effects occur by

Table 1: The various characteristics of flavonoids as a Neuroprotectants for anti-alzheimer's activity

Plant/family	Parts used	Reported flavanoids	Types of extract	Screening model/ animal used	Inference	Reference
Gingo biloba	Leaves	Quercein, Kaempherol, Isorhaemnetins	Standardized extract of Ginkgo biloba leaves (EGb)	Rats and gerbils Against oxidative stress *In vitro*, 25–100 μg/ml; *in vivo*, 40–100 mg/kg	*Research conducted in-vitro demonstrated that GBE shielded cultured neurons from amyloid-β-induced apoptosis.* It has also been demonstrated that neuroprotective effects are enhanced by the flavonoid fraction, which ranges from 25–100 μg/ml *in-vitro* and 40–100 mg/kg *in-vivo*.	[34]
Melissa officinalis L. (Labiatae)	Leaves	Quercitrin, rhamnocitrin, luteolin	Ethanol 80% (1:10) over four days through the maceration process.	Male albino Wistar rats weighing between 180 and 220 g 50, 100, 200, and 400 mg/kg of M. officinalis extract	Flavanoids present in this extract could improve the memory via the cholinergic system and the potent antioxidant activity in rats and scopolamine-induced memory impairment.	[35][36]
Salvia officinalis	Aerial parts of plant	Hispidulin, kaempferol, quercetin, luteolin, and apigenin	Oxhlet apparatus 0.6L and was exhaustively extracted with solvents of increasing polarity (petroleum ether, dichloromethane, and methanol)	Cell culture: Human SH-SY5Y cells	Significant neuroprotective activity against Aβ toxicity.	[37] [38]

Morinda citrifolia L. (Rubiaceae, Noni)	Fruit	Quercetin, kaempferol, nicotifloroside, narcissoside, and rutin	Not mentioned	Male adult New Zealand rabbits hydrocephalus animal model. Memantine (20 mg/kg, intraperitoneally; memantine-treated group) or noni (5 ml/kg, intragastrically;	According to research, noni has more pronounced inhibitory effects on neurodegenerative diseases brought on by hydrocephalus. than memantine in fourth p ventricle periventricular tissue.	[39], [40]
Withania somnifera (Solanaceae)	Root, fruit and leaves	Catechin, kaempferol, and naringenin	*In vitro*: methanol–chloroform (3 : 1) extract of plant *In-vivo:* alcoholic extract-leaves	Against the toxicity in cultured human neuroblastoma SK-N-MC cells caused by Aβ1-42. Effects of the Ashwagandha leaves Extract on scopolamine- induced damages of cell were studied	Conceivable treatments and preventative measures for neurodegenerative illnesses, and thus WS is considered as ethnopharmacological uses in traditional medicine for cognitive disorders, still warrant further molecular analyses.	[41-44]
Commiphora wightii	Oleo-gum resin obtained as an exudate from the tapping of stem and branches of *Commiphora wightii*	Muscanone naringenin The substances quercetin-3-O-α-L-arabinose, quercetin-3-O-β-D-glucuronide, quercetin-3-O-β-D-galactoside, and quercetin-3-O-α-L-rhamnoside	Ethyl acetate extract of the resin of plant Commiphora whighitii	Scopolamine- induced deficits streptozotocin (STZ) model of dementia in mice. gugulipid : 50 mg/kg, p.o	Gugulipid has significant protective affect against streptozotocin-induced memory deficits model of dementia that can be attributed to anti-oxidant and anti-AChE activity of gugulipid.	[45, [46]]
Glycyrrhiza glabra (Gg) (Leguminosae)	Roots	Liquiritigenin (4′,7-dihydroxyflavanone) and isoliquiritigenin (2′,4,4′-trihydroxychalcone), licuraside, liquiritin, isoliquiritin, and liquiritin apioside.From dried roots, five new flavonoids have been identified: 1-methoxyphaseolin, glucoliquiritin apioside, shinflavanone, shinpterocarpin, and prenyllicoflavone A. Additionally, licoflavanone and pinocembrin were extracted from the leaves.	Aqueous extract of Gg was prepared by macerating the dried powdered root with the respective solvent for 24 h. The macerated powdered roots were then extracted by using soxhlet extractor for 36 h, 1-2 cycles per hour.	Diazepam-induced amnesia served as the interoceptive behavioral model.	Findings suggest that the roots extract of *Glycyrrhiza glabra* appears to be a promising drug for improving memory in the management of impaired learning, dementia, Alzheimer's disease, and other neurodegenerative disorders which might be mediated by its antioxidant and anti-inflammatory activities.	[47], [48]
Tinospora Cordifolia (Menispermaceae)	Leaves, stem, seeds	Quercetin Kaempferol Luteolin	50% aqueous ethanolic extract was prepared by percolating 1.5 kg dry stem powder in a percolator with 5 L capacity for 4 times.	*Inslico* model *Invitro* model:Primary cerebellar and neuronal cultures were obtained from 6-day old albino Wistar rat pups.	Compounds from *Tinospora cordifolia* are a possible lead for the development of drugs that may be useful in the management of AD. From the *in vitro* studies Plant extract suggest as safe and effective non-palliative therapeutics against neurodegenerative diseases.	[49-51]
Convolvulus pluricaulis Convolvulaceae	Plant	Kaempferol	Aqueous extact	Human microtubule-associated protein tau (hMAPτ) induced neurotoxicity in Alzheimer's disease (AD) Drosophila model.	Supplementation of C. pluricaulis along with the regular standard food ameliorate the neurotoxic effect of hMAPτ in AD Drosophila model and also reveals that it is a potent neuroprotective agent.	[52], [53]

Emblica officinalis	Fruits	Fruits-apigenin, luteolin, and myricetin Leaves- Myricetin 3-O-rhamnoside flavanones and flavan-3-ols: flavanones were eriodictyol, naringenin, and their derivatives epigallocatechin 3-O-gallate, and gallocatechin.	Unripe fruit extract 98% ethanol (maceration)	Adult male, Swiss albino rats	According to the current study, EEPE fruit is a great source of a natural cognitive enhancer that may be used to treat AD and other neurodegenerative illnesses. shows unequivocally that EEPE fruits have significant positive effects on memory, learning, and antioxidant capacity. Unripe fruit showed notable effects on cognitive enhancement that were comparable to the standard when compared to ripe fruit.	[54-57]

Listed Various Phytocompounds isolated from the various plant sources, their extraction methods against Alzheimer,s disease by using different animal models.

modulation of various mechanism including inhibited amyloid beta protein aggregation, antioxidant, anti-inflammatory, modulation of neurotransmitters activity like Dopamine, GABA Acetyl Cholinesterase (AchE) and Butyryl Cholinesterase (BchE).

DISCUSSION

Several investigations have reported that the flavonoids reverse cognitive impairment and inhibit their progression by the AChE inhibitory effects[58] anti-amyloid property [59,60] and also exert its neuroprotective role by suppressing neuroinflammation.[61] Study has also reported that flavonoids possess antioxidant and hydrogen donating capacity, By this mechanism; flavonoids protect the neurons against oxidative stress, thereby suppressing the damage of neurons and potentiating cognitive function.[62] Flavonoids also affect the gene expression and interaction with mitochondria, which modulates the signals of the intercellular cascade that will prevent neuronal cell death.[63]

Flavonoids are revealed as a very precious class of secondary metabolites that have possibilities for the treatment of Alzheimer's. Flavonoids are vast and present in almost all natural resources. As the investigation continues, this class may manifest to be a rich source of new molecules for the development of new therapeutic agents for the treatment of Alzheimer's. From our literature review, we observed the balanced role of flavonoids in inhibiting Aβ-accumulation, and ACHE activity and also exhibit antioxidant action by inhibiting lipid peroxidation, one or more of these mechanisms are involved in enhancing memory function.

Abundant studies about the Antialzheimer effect of crude extract containing flavonoids and flavonoid-rich fractions containing uncharacterized flavonoids have been carried out. Consequently, it is tough to reproduce the results and find out the bioactive flavonoids. For this reason, there is a need for phytochemical standardization and bioactivity-guided identification of bioactive flavonoids. Besides, it is looking forward to the bioactive fractionation of extracts and the rich fractions will yield new flavonoid molecules.

Present treatment of Alzheimer's disease includes the use of multiple doses for prolonged periods causes serious side effects and adverse events bound to happen to the patients. By use of natural compounds rich in flavonoids are free from side effects, which will be commonly associated with clinically used anti-Alzheimer drugs. Hence, in the future, these flavonoid-rich compounds can be supplemented as anti-alzheimer drugs to reduce the side effects. Flavonoids not only activate the neurogenic pathways in treating amnesia but are also effective against epilepsy and depressive patients.

CONCLUSION

From this review, we gain an insight idea about the pathogenesis of Alzheimer's disease and the possible role of natural flavonoids against Alzheimer's disease. This will motivate the researcher to update the rational design of flavonoid-based pharmaceutical drugs for Alzheimer's disease. Flavonoids are present in all natural sources with a span of concentration. Numerous preclinical and clinical studies stated that flavonoids have potential against various neurological diseases including Alzheimer's. Moreover, advanced research is needed to standardize the dose, bioavailability, and adverse events of flavonoids in Alzheimer's disease patients.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

AD: Alzheimer's disease; **Aβ:** Amyloid Beta; **Aβ40 and Aβ42:** Amyloid-β 1-40 and Amyloid-β 1-42; **APP:** Amyloid precursor protein gene; **PSEN1:** Presenilin 1; **PSEN2:** Presenilin 2; **NFTs:** Neurofibrillary tangles; **NMDA:** N-methyl-D-aspartate; **BMI:** Body Mass Index; **CSF:** Cerebrospinal Fluid; **CNS:** Central Nervous system; **BBB:** Blood Brain Barrier; **ECG:** Electro Cardio Gram; **FDA:** Food and Drug Administration; **AADvac1:** active immunotherapy vaccine targeting pathological tau protein; **OH group:** Hydroxyl group; **AChE:** Acetyl cholinesterase; **BChE:** Butyryl cholinesterase; **NF-κB:** Nuclear factor kappa-light-chain-enhancer of activated B cells; **BACE-1:** Beta-site amyloid precursor protein cleaving enzyme 1; **GABA:** Gamma-Aminobutyric Acid.

SUMMARY

During the last decade, flavonoids received much attention and a variety of beneficial effects have been elucidated against a myriad of neurodegenerative disorders. Various flavonoid compounds found in the plant sources (mentioned in Table 1) hold significant potential in preventing and mitigating AD by reducing oxidative stress, promoting neurogenesis, and regulating key processes involved in the development of AD. Further research and clinical studies are needed to fully understand and harness the therapeutic benefits of these bioactive compounds. This review highlights the promising benefits of certain flavonoid compounds. These compounds hold great promise in promoting brain health and may contribute to reducing the risk of Alzheimer's disease.

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