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SHORT COMMUNICATION

Herbal efficacy of polyphenols used in the therapy of Alzheimer's disease

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Abstract: As a common cause of dementia, Alzheimer's disease has gained international attention due to its progressive nature. The primary causes of Alzheimer's disease are oxidative damage and aggregated protein buildup (tau and beta-amyloid proteins). Alzheimer's patients can lose their ability to remember things, learn new skills, or speak languages. As the condition progresses, they may also become depressed and aggressive. Current studies have focused on polyphenols, which are secondary metabolites found in plants and include flavonoids, tannic acid, resveratrol, curcumin, quercetin, rutin, genistein, daidzein, ellagitannins, and proanthocyanins. They could be able to lessen the rate at which Alzheimer's develops. Plant-based products contain polyphenols, which are the phenol groups generated from phytochemicals. Anti-oxidant, anti-inflammatory, anti-amyloidogenic, anti-viral/bacteria, and anti-carcinogenic qualities are displayed by polyphenols. Thus, every polyphenol has a role in the management of Alzheimer's. Through the modulation of signalling pathways, the polyphenols' mode of action in Alzheimer's disease includes the suppression of aggregated beta-amyloid plaque proteins, tau protein aggregation, oxidative stress, and inflammation. Consuming meals high in polyphenols may benefit the signalling pathways in neurons. Due to a significant biotransformation mediated by phase 1 and phase 2 reactions in the liver and gut bacteria, polyphenols have low bioavailability. By reducing the disease's toxicity, polyphenols aim to primarily slow the disease's progression and symptoms. In conclusion, In summary, the diverse array of polyphenols found in plant-based products holds promise in managing Alzheimer's disease by targeting oxidative stress, inflammation, and protein aggregation, offering a potential avenue to slow disease progression and alleviate symptoms

Keywords: Alzheimer's disease; Polyphenols; Tau aggregation; Dementia; Herbal remedies

1. Introduction

Alzheimer's disease is the irreversible neurodegenerative disease. It is the typical reason behind dementia. Alzheimer's patients may lose their ability to remember things, learn new things, speak languages, and so on. As the disease progresses, they may also become depressed and aggressive. The brain's neurons are mostly affected by this illness. The pathophysiological aetiology of Alzheimer's disease is the accumulation of tau protein in neurofibrillary tangles and extracellular plaques of β-amyloid peptide in the cytoplasm of neurons. There is a plethora of study being done on this illness. It is one of the most common and rapidly spreading diseases, primarily affecting the elderly and ageing population. It might have an impact on our healthcare system and society.

Although there isn't a full cure for this illness, we may manage its symptoms and slow down its advancement by eating a balanced diet, exercising, and consuming foods that are higher in nutrients, among other things. In addition, we can choose phytochemicals and nutraceuticals that have anti-inflammatory, antioxidative, and anti-amyloidogenic qualities, which may be beneficial for AD patients. Generally, polyphenols with antioxidant properties have a greater impact on AD by lowering the development of neuro fibrillary tangles, β-amyloid plaques, neuro inflammation, and oxidative stress [1].

Numerous plant foods include polyphenols, which are classified as flavonoids, phenolic acid, polyphenolic amides, and other polyphenols. They might aid with blood sugar regulation, brain function, lipid profiles, better digestion, and some types of cancer.

2. Polyphenols used in the treatment of Alzheimer's disease

The phenol groups generated from phytochemicals are known as polyphenols. They can be found in edible plant-based goods. Much more health advantages are associated with polyphenols. These have good medicinal qualities that may aid with a variety of illnesses, including brain function, digestion, cancer, and Alzheimer's. Due to a significant biotransformation mediated by phase 1 and phase 2 reactions in the gut microbiota and liver, polyphenols have a low oral bioavailability [2].

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The primary sources of polyphenols are a variety of fruits, vegetables and other plant materials. There are several subtypes of polyphenols, including flavonoids, hydroxy benzoic acid, hydroxy cinnamic acid, tannins, phenolic acids, and lignans. These particular polyphenols have a specific role in the pathophysiology of AD. These substances are frequently employed in the management of Alzheimer's disease because they lessen oxidative stress and the buildup of tau and β-amyloid proteins.

Eating foods high in polyphenols can protect neuronal cells from neurodegeneration and influence neuronal signalling pathways. One of their main advantages is that they may chelate metals and reduce free radicals. Additionally, the following polyphenols are implicated in the pathophysiology of Alzheimer's disease: quercetin, kaempferol, hesperidin, resveratrol, curcumin, and catechin [3].

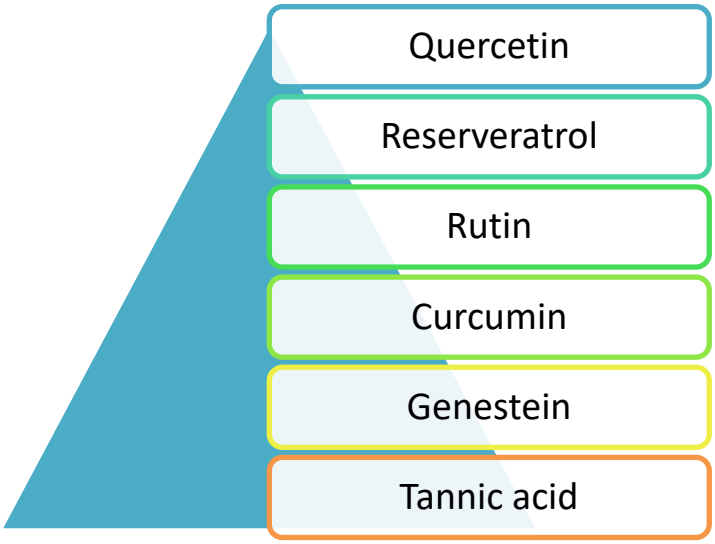

Figure 1: Various Polyphenols used in the treatment of Alzheimer's disease

2.1. Flavonoids

One might think of flavonoids as a symptomatic anti-Alzheimer drug. Flavonoids' antioxidative, anti-inflammatory, and anti-amyloidogenic qualities may provide them a unique role in the cause of Alzheimer's disease. Because flavonoids have anti-oxidative properties, they may be able to slow down the symptoms and course of disease. They support the reduction of oxidative stress associated with Alzheimer's disease. Certain flavonoids have the ability to block the synthesis and accumulation of amyloid-β peptides, and by reducing tau aggregation, they can facilitate the removal of Ab peptides and prevent tau phosphorylation through the mTOR/autophagy signalling pathway [4]. Flavonoids may be able to slow down the pathophysiological course of AD. Flavonoids interact with several signalling pathways to increase their activity and therapeutic potential.

The primary way that flavonoids contribute to the pathophysiology of AD is by blocking signalling pathways like ERK (extracellular signal-regulated kinase), p13-kinase, NFKB (nuclear factor kappa-light-chain-enhancer of activated B cell), MAPKS (mitogen-activated protein kinases), and endogenous antioxidant enzyme systems [5].

2.2. Resveratrol

Another name for resveratrol is 3,4,5-trihydroxystilbene. It is a kind of naturally occurring polyphenol. It can be found in peanuts, chocolate, berries, and grapes. Resveratrol has anti-inflammatory, antiviral, antioxidant, and anti-cancer effects. It was initially found in 1940. It demonstrates a unique therapeutic promise for lowering Alzheimer's disease risk. It helps to facilitate AD models both in vivo and in vitro. Owing to its anti-inflammatory and antioxidant qualities, it is specifically utilised in the pathophysiology of AD and may slow the disease's progression. By activating NAD(+) dependent histone deacetylase enzymes, it specifically reduces or removes neurotoxic β-amyloid peptides and reduces neuronal cell damages [7].

Because of resveratrol's low bioavailability, biotransformation, and other dietary factors, it is an effective monotherapy for AD. Studies reveal that resveratrol may lessen the generation of inflammatory markers, alleviate oxidative stress, scavenge free radicals, limit platelet aggregation, suppress activation of astrocytes and microglia, and lessen the death of neurons.

2.3. Curcumin

Alzheimer's disease is treated with curcumin, a polyphenol derived from the turmeric herb and a member of the Zingiberaceae family. Numerous studies are conducted on curcumin's mechanism of action in vivo and in vitro to treat AD. They might conclude that curcumin holds a great deal of promise for treating AD. Owing to its antioxidant qualities, curcumin prevents the formation of disaggregated amyloid-β plaques. It also lowers cholesterol, alters microglial activity, attenuates tau hyperphosphorylation and facilitates tau clearance, and inhibits acetylcholinesterase by interfering with signalling pathways [8].

2.4. Quercetin

Quercetin is a flavonoid. It may be therapeutically useful in the management of AD. Quercetin is frequently found in everyday foods, fruits, and vegetables. Quercetin has been the subject of numerous in vitro studies to determine its potential in the pathophysiology of AD. In addition to reducing or inhibiting the development of amyloid-β proteins and inflammatory cascade pathways, quercetin also inhibits the oxidative damage of neurons. The bark of the plant quercetin tinctoria, which is a kind of pigment present in practically all fruits, vegetables, and herbs, contains quercetin. Acid hydrolysis splits the substance into two components: glycone and aglycone [9].

2.5. Rutin

Rutin is a naturally occurring flavonoid glycoside that is also known as (quercetin-3-0-rutinaside) and is present in plants and vegetables. It works therapeutically on a number of cellular processes that are compromised by diseased diseases. Because rutin can pass through the blood-brain barrier, it helps lessen the symptoms of a number of neurodegenerative illnesses. It possesses antioxidant, anticancer, antibacterial, and anti-inflammatory qualities. Rutin's antioxidant and anti-inflammatory qualities also help to lessen the signs and progression of Alzheimer's disease [10].

Rutin is able to prevent the aggregation of β-amyloid. It can eliminate inflammation and neurofibrillary tangles that contribute to dementia. It can also alert the oxidant-antioxidant balance linked to the loss of neuronal cells. Its physiological and chemical characteristics are linked to both its bioavailability and certain actions such as metal chelation. Through its ability to lower β-amyloid plaque and mitigate oxidative stress, rutin enhances spatial memory in individuals with Alzheimer's disease [11].

2.6. Genistein

One kind of polyphenol that is frequently used to treat Alzheimer's disease is genistein, which can slow the disease's progression and symptoms. Numerous studies have confirmed that genistein is a selective oestrogen receptor modulator (SERMS) that can enhance brain function by crossing the blood-brain barrier [12]. By preventing β-amyloid protein from aggregating and causing neurotoxicity, genistein aids in slowing down the progression of AD. Recent in vitro research reveals that although oestrogen is effective in treating AD. Genistein supplementation may be able to reduce the risk of breast cancer and endometrial cancer brought on by oestrogen therapy.

3. Challenges of using polyphenols in Alzheimer's disease

Enhancing Bioavailability of Polyphenols: Overcoming the challenge of low bioavailability associated with polyphenols through innovative delivery methods or formulations to ensure their effective therapeutic concentration in the brain, thereby maximizing their impact on Alzheimer's disease [11].

3.1. **Clinical Translation:** Moving beyond preclinical studies to conduct extensive clinical trials that assess the safety, efficacy, and long-term effects of polyphenol interventions in diverse populations with Alzheimer's disease, establishing a solid foundation for their clinical application.

3.2. Identification of Optimal Polyphenol Combinations: Investigating synergistic effects and optimal combinations of various polyphenols to maximize therapeutic benefits, considering the complex multifactorial nature of Alzheimer's disease and the potential additive or synergistic effects of different polyphenolic compounds [12].

3.3 Understanding Mechanistic Insights: Further elucidating the detailed molecular mechanisms underlying the beneficial effects of polyphenols on Alzheimer's pathology, exploring their interactions with specific signaling pathways, and identifying key targets for more precise therapeutic interventions.

3.4 Personalized Treatment Approaches: Developing personalized treatment strategies based on individual variations in polyphenol metabolism, considering factors such as genetic makeup, gut microbiota composition, and lifestyle, to tailor interventions for maximum efficacy and minimal side effects in Alzheimer's patients.

4. Conclusion

This work illustrates the use of plants in the treatment of AD. Polyphenols are the chemical constituents which are having high therapeutic efficacy in the treatment of various ailments. Alzheimer's disease is one of the leading neurodegenerative disorder in the world. Dementia is the major symptom of AD. Medicinal plants will exhibit their beneficial role in the management of Dementia. The world is again revolutionizing in to using plants for better health outputs.

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Author's short biography

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I am Hymavathi Panthagani studying B.Pharm 3rd year in Narayana Pharmacy College, Nellore.