

# Phytochemicals in treatment of Alzheimer condition

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## Introduction

Alzheimer's disease is a neurodegenerative disorder that involves progressive impairment of cognitive function resulting in memory loss that severely affects daily life.

Until now only five drugs are available for the management of Alzheimer's disease and cholinesterase inhibitors class of drug are three of the five available medications approved.

Several scientific studies have shown the beneficial activities of the phytochemicals obtained by plants for treatment and prevention of Alzheimer's disease, like decreasing the cell damage caused by free radicals, neuroprotective effects, AchE, BchE, BACE-1 inhibitory activity, and  $\beta$ -amyloid aggregation and the side effect is much lower.

## Material and methods

Literature review has been done on different data from relevant scientific resources.

## Results and discussion

There are different groups of phytochemicals that have shown effects in Alzheimer's conditions:

Alkaloids are natural secondary metabolites that contains nitrogen in the structure and are mostly derived from amino acids. The most prominent examples from alkaloid group are galantamine, huperzine A and physostigmine. Galanthamine found in Amaryllidaceae family has shown to have a dual mechanism of action, modulates the nicotinic ACh receptors, and inhibits acetylcholinesterase (Castillo et al., 2020). Huperzine A is acquired from *Huperzia serrata* and has shown to have

AChE inhibitory activity, neuroprotective properties, majorly involves playing a role in protection against programmed cell death (Howes et al., 2016).

Terpenoids are natural products, that chemically are composed by two or more branches of five-carbon isoprene units. From this group we will mention *Rosmarinus officinalis* because many studies have shown promising results as a potential therapy in the treatment of Alzheimer's disease and the most important group of rosemary compounds are polyphenolic diterpenes. Diterpenes in rosemary have shown to have benefits in the treatment of Alzheimer's disease in many ways like A $\beta$  activity, AChE activity, antioxidant and anti-inflammatory properties. Some various types of diterpenes isolated from rosemary are carnosic acid, carnosol, rosmadial, isorosmanol, royleanonic acid, rosmariquinone, epirosmanol (Habtemariam, 2016).

Based on their chemical structure, phenolic phytochemicals can be classified into: (1) phenolic acids (2) flavonoids and (3) other phenolics.

(1) Phenolic acids - are classified in to hydroxybenzoic and hydroxycinnamic acids.

Main hydroxybenzoic acids found are vanillic, protocatechuic acids, gallic acid and ellagic acid.

From this group we will mention *Caesalpinia crista* from which are identified gallic acid, protocatechuic acid, catechin and has shown to have aggregation inhibitory property in addition to the cholinergic activity (Li et al., 2018). In addition to hydroxycinnamic acids includes caffeic acid, cholinergic acid, cinnamic acid, coumaric acid, ferulic acid, curcumin. Promising result for the treatment of Alzheimer's disease has been shown from ferulic acid, which is an antioxidant and anti-inflammatory compound derived from plants like *Nepeta* spp (Natarajan et al., 2013).

(2) Flavonoids - because of their potential AChE inhibitory activity allied to the well-known antioxidant

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activity and low toxicity are currently considered an important source of anti-Alzheimer's disease compounds. *Silybum marianum*, flavonoid silibinin has shown to inhibit AChE and A $\beta$  peptide aggregation at Alzheimer's disease treatment (Shi et al., 2016). *Camellia sinensis* or green tea is rich in flavonoids such as quercetin, gossypetin, myricetin, and rutin are known for antioxidant properties and are currently used for Alzheimer's disease therapy (Orhan et al., 2017).

(3) Other phenolics:

a) Lignans- *Cannabis sativa* is composed of lignans like cannabisin-M that exhibited a powerful radical-scavenging activity, while cannabisin-N exhibited weak acetylcholinesterase inhibitory activity (Singhal et al., 2012).

b) Stilbenes- Resveratrol, found in *Vitis vinifera*, has shown to have multiply pharmacological effects in neurodegenerative diseases (Phan et al., 2019).

c) Tannins- Gallotannins isolated from *Cornus officinalis* fruits have a protective role against Alzheimer's disease's progression and this is due to inhibition of A $\beta$  peptides accumulation (Hussain et al., 2019).

## Conclusion

Many natural molecules obtained from plants showed properties that are important in alleviating Alzheimer's disease, in this review, we have gathered plants rich in phytochemicals like alkaloids, terpenes, flavonoids, phenolic phytochemicals.

Alkaloids mainly due to AChE inhibitory activity are important in the treatment of Alzheimer's disease. The benefit of terpenes in Alzheimer's disease more commonly is due to antioxidant and anti-inflammatory activity especially from plants rich in monoterpenes, diterpenes, triterpenes, and sesquiterpenes.

Most polyphenols have shown good inhibit of A $\beta$  aggregation, BACE1 inhibition, antioxidant and anti-inflammatory activity, and more rarely AChE and BChE activity. Fewer studies were found regarding stilbenes, tannins, lignans, but these phytochemicals have shown powerful radical-scavenging activity which makes them strong antioxidants, inhibition of A $\beta$  peptides accumulation, BACE-1, and also AChE and BChE activity and can be seen as promising candidates in Alzheimer's.

As a conclusion, we can state that since Alzheimer's disease is multifactorial disease combination therapy using a mixture of phytochemicals in acting on several disease targets, could have the best result.

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