Vol: 3, Pg: 34-45 Yr: 2023-AJABTR

Role of Plant Metabolites in Curing Neurodegenerative Disorders

Mainak Sarkar[1], Pratik Talukder[1]*

[1]Department of Biotechnology, University of Engineering and Management, Kolkata

*Corresponding: pratik.talukder@uem.edu.in

Abstract

Plant metabolites are the products produced during metabolism which occurs naturally in cells. Different types of secondary metabolites have their different therapeutic effects. Herbal medicines have been used for a long time to cure neurodegenerative disorders. Two of major types of neurodegenerative diseases which are of huge concern nowadays are- Parkinson's disease and Alzheimer's disease. During the past few decades, plant secondary metabolites have shown a large variety of beneficial effects against lots of neurodegenerative disorders including Parkinson's disease and Alzheimer's disease. More research is required to discover new bioactive compounds from plants which can be used to treat these neurodegenerative diseases.

Keywords

Plant metabolites, Secondary metabolites, Neurodegenerative disease, Parkinson's disease, Alzheimer's disease,

1. Introduction

. The term metabolites are usually used for small molecules. These metabolites participate in growth, development, reproduction, catalytic activity, defense, interactions with other organisms and various other kinds of cellular activities. There are two types of metabolites found in plants, primary and secondary.Primary metabolites are the chemical compounds produced during the growth and development processes. These chemical compounds are involved in the primary metabolic processes as growth, development, respiration and photosynthesis. They maintain the physiological functions of the body and are known as central metabolites. These are the intermediate products of anabolic metabolism. Carbohydrates, protein, lipids and organic acids are listed as primary metabolites.Secondary metabolites are considered to be the end products of primary metabolites as they are derived by the pathways in which the primary metabolites are used as substrates. Secondary metabolites do not play major role in growth, development, and reproduction like primary metabolites do, and are typically formed during the end or near the stationary phase of growth. Many of the identified secondary metabolites have a role in ecological function, including defense mechanism, by serving as antibiotics and by producing pigments.

2. Plants as source of secondary metabolites

Plant secondary metabolites can be divided into such groups - polyphenolic compounds, terpenoids, alkaloids, sulfur-containing compounds, nitrogen containing compounds etc [1]. These secondary metabolites are found in different parts of different plants.

Plant name	Part (culture)	Secondary metabolite present
Agastache rugosa	Hairy root	Rosmarinic acid
Brucea javanica	Suspension	Cathin
Camellia chinensis	Callus	Flavones
Fritillaria unibracteata	Multiple shoot	Alkaloids
Gentiana macrophylla	Hairy root	Glucoside
Mentha arvensis	Shoot	Terpenoid
Momordica charantia	Callus	Flavonoid
Gentianella austriaca	Multiple shoot	Xanthone
Adhatoda vasica	Shoot culture	Vasine
Catharanthus roseus	Suspension	Indole alkaloids
C. senna	Hairy root	Anthraquinone
Catharanthus roseus	Suspension	Catharathine

Reference- [2]

Plants are the most common sources of naturally active compounds. These bio-active compounds were used massively from the ancient time throughout the whole worldin herbal way and became the part of the health system. These bio-active compounds are none other than secondary metabolites of plants which came in our attention through some scientific research activities. As their production cost is almost nothing, they are highly economically affordable. Having a large range of chemical structure helps them to become widely active in the field of biology and therapy. As they are derived from pathways in which primary metabolites are involved, their production is very low in plant system, which makes them not so essential in plant's developmental process, but beneficial to humans. Alkaloids have antitumor, antimicrobial, antidiarrheal activities

which makes them useful in treatment of sleeping leg cramps, palpitation. They are also used for relaxing on psychotic and hypersensitive patients. Glycosides, another bio active compound is effective in suppressing and preventing dry coughs. These are also used as sedative and relaxing agents on muscle and heart in low doses. Moreover they have laxative, purgative and diuretic properties. Flavonoids belong to the phenolic family and show various medicinal activities. They primarily functions as phytoestrogens, has antioxidant and anti-cancer activities and can reduce the risk of coronary heart disease. Steroids are bioactive molecules that are useful in stress and cholesterol reduction, immune system activation, memory and learning enhancement and treatment of tumor cells. Terpenoids have significant medicinal properties like antiviral, antibacterial, antimalarial and anticancer etc. Saponins are a diverse category of plant substances that are present in many food and medicines derived from plants .Mainly there are two types of saponins - triterpenoids and steroidal saponins. They exhibit medicinal activities such as antihepatonic, wound healing, hypoglycemic, antibacterial, antiviral. Tanninbelongs to the chemical family of polyphenols and has analgesic and anti-inflammatoryproperties, in addition tannin helps in recovery of wounds and damaged mucous membranes. Phenolic compounds are one of the most common types of secondary metalloids present in plants. Phenols have antiseptic and anti inflammatory properties apart from this they also act as antioxidants preventing the growth of tumor promoting substances [3].

3. Role of plant metabolites in the treatment of neural diseases

Secondary metabolites have shown both positive and negative effects on nervous system. As these are not chemically produced these shows less side effect on human health.

Group	Bioactive compound	Disease	Mechanism of action
Polyphenol	Caffeic acid	Alzheimer's disease	Reduces oxidative stress and calcium influx,
		Parkinson's disease	Reduces 5-S-cysteinyl-dopamine induced neurotoxicity
	Sinapic acid	Alzheimer's disease	Reduces the activity of enzyme caspase-3 and apoptosis
		Parkinson's disease	Reduces oxidative stress
Flavonoids	Isorhamnetin	Ischemic stroke	Reduces oxidative stress
	Catechin	brain ischemia	Reduces Interleukin 1-β and TNF α
Alkaloids	Skimmianine	Neurodegenerative disorder	Reduces TNF-α, Cyclooxygenase2 and Prostaglandin E2
	Evolitrine	Neurodegenerative disorder	Anti-inflammatory
Coumarins	Scopoletin	Alzheimer's disease	Antioxidant
Chromenes	Leptonol	Neurodegenerative disorder	Antioxidant and anti-inflammatory

Table 1: Role of different plant secondary metabolites in the treatment of neural diseases [4]

4. Role of plant metabolites in the treatment of Parkinson's disease

Parkinson's disease is defined by symptoms such as tremor, bradykinesia, rigidity, loss of balance, or facial dyskinesia. The other related problems are sleep disorders, cognitive impairment, depression, mood swings, psychosis, and dementia. Although the cause of neuronal cell death is still unknown, dopaminergic cell death has been linked to mitochondrial malfunction, oxidative stress, and consequent apoptotic cell death. Although the present medications used to treat this ailment provide symptomatic relief, preventive methods for the advancement of the disease is yet to be discovered. Many ethnobotanical researches have recently revealed that using a therapy based on medicinal plants can have better outcome than using synthetic drugs. On the other hand, medicinal herbs are used to cure both healthy and diseased people who suffer from memory loss. Asian countries like China and India utilized more than 20 medicinal plants to treat problems associated with the central nervous system. *Acorusc alamus, Allium sativum, Ginkgo biloba*, *Glycyrrhiza glabra,* and some other medicinal plants were highlighted by the Indian system of medicine as having the efficacy in the field of neuropharmacology [5]. Earlier, various cultures have established traditional methods of treating disease with medicinal plants. Some of these methods may appear odd and mystical, while others may seem logical and sensible. Many plants with medicinal benefits found all over the world, contain substances that shows pharmacological effects on humans. As the human brain is a particularly complicated organ, not all medications have been approved for the treatment of disorders linked with the brain. Parkinson's disease can be treated with levodopa, cycrimine, carbinoxamine, and carbidopa, according to regulatory authorities. Ayurveda has historically been used as an alternate kind of treatment for Parkinson's disease in

India. Levodopa is present in high concentrations in *Mucuna pruriens*, which has been shown to significantly improve the condition of a person suffering from Parkinson's disease. Powdered seeds were shown to have positive impact in clinical trials in PD patients without an accompanying increase in dyskinesia. Several classes of produced conventional synthetic neuroprotective agents and plant-based natural medicines have been identified. Synthetically produced neuroprotective compounds might cause some undesirable side effects in people; such as dry mouth, fatigue, sluggishness, drowsiness, anxiety or worry, balance issues, etc. Through research and initiatives at the national and international levels in the contemporary context, plant-based goods have gained widespread awareness. Several phytochemicals have biological activities that are connected to cognitive function, although neither the obtained results nor the mechanisms of action have been thoroughly described. The stimulation of cell stress-reaction pathways by phytoconstituents results in the modulation of neuroprotective effectiveness. The neuroprotective effects of the neurotrophic elements are primarily mediated by inhibiting the cell injury damage and the apoptosis pathways. Moreover, medicinal plants contain a variety of phytochemicals with different secondary metabolites, such as polyphenols (phenolic acids, anthocyanins, proanthocyanidins, flavonols, tannins), isoprenoids (sesquiterpenes, diterpenes, triterpenes, steroids, saponins), alkaloids (indole alkaloids, lysergic acid diethylamide, tropane alkaloids). Even while numerous medicinal plants have been used traditionally by many cultures to treat brain abnormalities, only a small number of them have undergone in-depth research to ascertain the pharmacological basis of their therapeutic actions. Researchers are particularly interested in a few of them because of their potential and

efficiency in the curing of cognitive impairment [6].

5. Role of plant metabolites in the treatment of Alzheimer's disease

One of the most common neurodegenerative disorders, Alzheimer's disease causes a persistent loss of memory, learning, and other cognitive abilities. It also results in widespread neuronal death and the production of disoriented plaques and neurofibrillary masses. The major component of senile plaques that is primarily engaged in the formation of Alzheimer's disease is beta-amyloid peptide (APβ). Aggregation of APβ causes energy loss, oxidative stress, inflammation, and apoptosis, which all contribute to the death of neurons. Brain sections containing plaques typically show a lower number of synapses, and the neurites around the plaques are frequently scraped, indicating that APβ harms both neurites and synapses. Glutamatergic or acetylcholinergic neurons appear to be primarily effected. It is significant to note that amyloid precursor protein (APP) causes the development and accumulation of neurotoxic types of APβ. Gamma-secretase-mediated sequential cleavages of APP and -secretase (beta-site amyloid precursor protein cleaving enzyme, BACE) produce APβ. Because to its capacity to reduce the APβ, studies have suggested that berberine may have clinical importance for AD. As the APP cleaving enzyme BACE-1 starts the synthesis of APβ, by halting hippocampus deterioration and decreasing BACE-1 activity, berberine alleviated behavioural impairment. It is significant because it also has AChE and monoamine oxidase (MAO) inhibitory properties because both play a role in the progression of AD. Moreover, it was demonstrated in further research that berberine inhibits the production of BACE-1 and lessens the deposition of APβ plaques. It has been discovered that decreased cholinergic transmission in AD causes cognitive function loss, which can be addressed by AChE inhibitors.

Salsoline has the ability to prevent the AChE enzyme from working. The effectiveness of AChE and BuChE inhibitors in the management of AD has been established. For the first time, research has shown that three salsola species are AChE and BuChE inhibitors. Salsoline targets a novel method of treating AD due to its targeted activity against BuChE. As a result, more has to be done in this area. According to reports, GSP enhances cholinergic transmission by decreasing AChE. One study showed that some constraining modes between specific groups of AChE residues and GSP were displayed upon GSP docking into the dynamic location of AChE. Hydrogen bonds and hydrophobic interactions, among other possible ligand/protein interactions, were found in the aforementioned complex. It was discovered that His440 and Ser200 held hydrogen-holding collaborations that could suggest the impact of a catalytic triad for the AChE suppressing mechanism through GSP, which would aid in the development of new potential Damage preventers important for the treatment of AD [7].

Extracts of *G. biloba* leaf contain a number of Flavonoids. The cooperative actions of these phytochemicals results in interactions with certain regions of brain, which are predicted to lessen neurocognitive decline. Among these include an increase in cerebral blood flow brought on by an increase in the vasorelaxant neurotransmitter nitric oxide, a decrease in the enzymatic deamination of monoaminergic neurotransmitters, free radical scavenging, and neuroprotection, which includes decreased amyloid-β-toxicity. These interactions support the use of ginkgo, which has been prescribed for centuries in traditional Eastern forms of medicine for illnesses of old age, including AD, and which is frequently mentioned as offering protection against amyloid-β-induced oxidative stress. Modern, carefully supervised intervention trials on humans have also produced some encouraging

findings. Terpenoids show effectiveness in interacting with several physiological systems, including the immune system, the central nervous system, and CVD prevention. Terpenoids operate as an antioxidant, stimulate the formation of nitric oxide, and bind to androgen and glucocorticoid receptors. Particular neurocognitive connections with neurotransmitter function, the processes of neurogenesis, and long-term potentiation have also been observed to improve memory in damaged rodents and have anti-stress, antidepressant, and anxiolytic effects. Research on young, healthy subjects remains at its infancy and is supported by a variety of methodologies. But, as a whole, it shows potential for improving cognition. Animal and in vitro research suggests that ginseng may be especially helpful for AD related cognitive loss since ginsenosides have been shown to reduce the amyloid-β inhibitory protein's influence on cholinergic transmission. Resveratrol is found in few sources, including grapes, and comes from a subclass of polyphenols known as stilbenes. With its potential to help with a variety of disease conditions, including cancer, cardiovascular disease, and possibly life extension, resveratrol has attracted a lot of study attention. The numerous biological targets that resveratrol interacts with are likely the basis for the many and various health effects that have been attributed to it. They comprise, but are not limited to, sirtuins, several kinases, DNA/RNA, and lipoproteins, as well as cyclooxygenase 1 and 2. Resveratrol's ability to perform anti-inflammatory effects, to directly engage with cell signaling, and to have connections to cardiovascular health are all explained by these particular interactions. Resveratrol's interactions with these targets, as well as others like the stimulation of cerebral blood flow and its capacity to reduce amyloid-β induced cell death in vitro, imply that it has the potential to be a helpful treatment agent

for AD. Likewise, findings from animal models suggest the role of resveratrol in this context with decreased pathological indicators, such as amyloid-β plaques and behavioural impairments, such as better learning and memory, in response to resveratrol exposure and consumption [8].

6. Future aspects

During the last decade, secondary metabolites haveshown a large variety of beneficial effects against lots of neurodegenerative disorders. More research is required to discover new bioactive compounds from plants so that it may replace usage of synthetic drugs which are harmful to the body.Nowadays, the consumption of fruit, greens, and drinks containing flavonoids, alkaloids, terpenoids and other secondary metabolites is recommended. More studies are needed, especially accurate clinical trials to ensure the clinical effectiveness of bioactive compounds in neurodegeneration so that it might be used as a better prophylactic agent to improve human health. Another issue that needs to be settled in the research is to identify the amount of metabolites absorbed; either they work in a synergistic way or individually in improvement of human health [9]

7. Conclusion

Many scientific studies have shown that herbal drugs like polyphenols, coumarins, and alkaloids offer therapeutic effects when used to treat nervous diseases. The use of phytochemicals as bio-active agents for the treatment of neurodegerative disorder has become a matter of great importance because plant-based natural compounds outperform synthetic drugs in terms of efficacy and negative effects.

References

1. Teoh, Eng Soon, and Eng Soon Teoh. "Secondary metabolites of plants." Medicinal orchids of Asia (2016): 59-73.

2. Pagare, S., Bhatia, M., Tripathi, N., Pagare, S., & Bansal, Y. K. (2015). Secondary metabolites of plants and their

role: Overview. Current Trends in Biotechnology and Pharmacy, 9(3), 293-304.

3. Das, Kuntal, and SevgiGezici. "Secondary plant metabolites, their separation and identification, and role in human disease prevention." Ann. Phytomedicine 7 (2018): 13-24.

4. Abdulwanis Mohamed, Z.; Mohamed Eliaser, E.; Mazzon, E.; Rollin, P.; Cheng LianEe, G.; AbdullRazis, A.F. Neuroprotective Potential of Secondary Metabolites from Melicopelunu-ankenda (Rutaceae). Molecules 2019, 24, 3109

5. Grizzell JA, Patel S, Barreto GE, Echeverria V. Cotinine improves visual recognition memory and decreases cortical Tau phosphorylation in the Tg6799 mice. ProgNeuro-Psychopharmacology Biol Psychiatry. 2017; 78:75–81.

6. Vijayakumar, S., S. Prabhu, S. Rajalakhsmi, and P. Manogar. "Review on potential phytocompounds in drug development for Parkinson disease: a pharmacoinformatic approach." Informatics in Medicine Unlocked 5 (2016): 15-25. https://doi.org/10.1016/j.imu.2016.09.002

7. Hussain G, Rasul A, Anwar H, Aziz N, Razzaq A, Wei W, Ali M, Li J, Li X. Role of Plant Derived Alkaloids and Their Mechanism in Neurodegenerative Disorders. Int J BiolSci 2018; 14(3):341-357. doi:10.7150/ijbs.23247.

8. Wightman, E. (2017). Potential benefits of phytochemicals against Alzheimer's disease. Proceedings of the Nutrition Society, 76(2), 106-112. doi:10.1017/S0029665116002962

9. Minocha, Tarun, Hareram Birla, Ahmad A. Obaid, VipinRai, P. Sushma, ChandanShivamallu, Mahmoud Moustafa et al. "Flavonoids as Promising Neuroprotectants and Their Therapeutic Potential against Alzheimer’s Disease." Oxidative Medicine and Cellular Longevity 2022 (2022).