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NOVEL NUTRACEUTICAL COMPOUNDS IN THE TREATMENT OF ALZHEIMER'S DISEASE AND OTHER NEUROLOGICAL DISORDERS

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ABSTRACT

Alzheimer's disease (AD), which affects up to 50 million people globally today, is one of the biggest mysteries in medical science and public health systems. This complex brain condition is characterized by apathy, mood and neuropsychiatric abnormalities, as well as gradual cognitive impairment. Ageing is the primary risk factor for AD; it is a normal biologicalprocedure connected to a continuous dynamic that involves a progressive loss of people's physical capabilities, but with a reliable, lived-in perspective on life. According to studies, AD differs from healthy ageing in that it causes changes in the processes that safeguard neurons as well as their powerful functioning capabilities. Given the components of nutrition, regular exercise, and avoiding certain substances, a significant route has been created towards preventing AD in this environment. Avoiding harmful chemicals and narcotics, maintaining an active social life, engaging in meditation, and managing stress are all necessary for healthy ageing. Here, we examine how these elements are involved and how to reduce environmental risk factors for a higher standard of living. both proactive and creative, the use of trustworthy biomarkers in screening programs for early disease identification is becoming increasingly important for disease management.Additionally, the failure of conventional pharmaceutical therapies and the search for new medications have sparked the development of nutraceutical compounds in the context of "multi-target" therapy, as well as mindfulness techniques that are effective in the management of AD and ageing.All of these preventive measures combined with cutting-edge pharmaceutical techniques should form the basis of an integrated strategy for the eventual control of the illness. According to studies, AD is different from healthy ageing in that it causes alterations in the processes that safeguard neurons while maintaining their great functioning capabilities. Given that daily exercise, healthy eating, and avoiding harmful chemicals are all critical components of AD prevention, an important road has been opened in this regard.drugs, a bustling social life, meditation, and stress management are all necessary for good ageing. Here, we examine how these elements are involved and how to reduce risk factors from the environment for a higher standard of living. The control of the illness is increasingly dependent on prevention as well as cutting-edge screening programmes for early diagnosis of the disease utilizing accurate biomarkers. Additionally, the ineffectiveness of conventional pharmaceutical therapies and the quest for novel medicationshas sparked the development of nutraceutical substances in the framework of a "multitarget" therapy, as well as methods of mindfulness that have been shown useful for the management of ageing and AD. All of these protective factors coupled with an integrated strategy,The future management of the condition should be made possible by innovative pharmaceutical techniques.

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INTRODUCTION

Alzheimer's disease (AD) is a neurological condition that worsens with time and is marked by changes in mood, cognitive decline, and neuropsychiatric symptoms. According to the WHO's Alzheimer Report, AD affects more than 52 million individuals globally.

Pharmacological medicines only have a small number of palliative effects. In addition to the declining impacts of AD on human health and the quality of life for senior people, the disease also has a significant financial impact. The annual economic cost of AD is one billion dollars worldwide. AD is not only a medical problem and a challenge for society; it is also connected to public policies in the pursuit of patient quality of life and the protection of AD patients' carers. We are supporting integrative medicine in this situation. and defence of AD patients' caretakers. We are fostering integrative activity in this area, ranging from basic and translational research to the creation of cutting-edge technologies and initiatives in support of carers.

One of the main causes of Alzheimer's disease is neuroinflammation. The so-called "damage signals," which obstruct the cross-talks between neurons and glia, are the first step in the mechanisms by which the inflammatory process takes place in the human brain. As a result, NFkB is produced by activated microglia, which triggers the creation of proinflammatory mediators that eventually signal on neural receptors, reactivating the protein kinases that cause tau to form hyperphosphorylation.

Objective: We can discover compounds with tau antiaggregant activity, as well as compounds with antioxidative and anti-inflammatory activities when searching for nutraceutical bioactive principles.

As previously stated, the kind of food, particularly nutraceutical ingredients, and certain formulas are crucial components for avoiding the development of AD. Dietary adjustments, nutritional supplements, functional foods, and nutraceuticals are the foundation of one crucial method to prevent AD impairment. Chemicals in the diet known as nutraceuticals show certain disease-preventing qualities. Many of these substances have solid preclinical research published in prestigious medical journals and double-blind placebo-controlled clinical studies, and they are acquired through strict methods of extraction from earth's resources and Good Manufacturing Practices (GMP) laws. Structure, biochemical and metabolic effects, and other neuroprotective qualities of nutritional supplement substances all differ. They can alter the physiopathological processes in AD.

Nutraceuticals have the benefit of a multitarget approach with many pharmacological activities in the human brain, which is beneficial given that AD is a multifactorial illness. Among these objectives is the suppression of certain targets such as mitochondrial malfunction, oxidative stress, inflammatory pathways, acetylcholinesterase, tau protein aggregates, amyloid-senile plaques, etc. The study by Calfio et al., 2020 provides a thorough assessment and meta-analysis of the vast majority of the nutraceutical substances currently documented to potentially contribute to AD prevention.

The route to AD prevention appears to be a very promising avenue to control the spread of this disease in this context and considering the explosive rise in AD incidence. Clinical studies have shown that adopting a healthy lifestyle and taking several nonpharmacological measures can stop disease manifestations and even lessen symptoms in AD patients who have already been identified. These activities include mental and sensory stimulus, mindfulness, the use of Chinese and Ayurvedic medicine, and nutrition in particular. Utilizing nutraceuticals appears to be one of the most important and potent preventive measures in the latter group of actions.

However, these methods also require the use of early detection instruments, such as molecular biomarkers. Early recognition of cognitive impairment in individuals who are not displaying any symptoms isa cautionary bell to encourage the use of nutritional supplements. Functional foods are those that are thought to be good for the body and go beyond basic nutrition: some are foods in their natural state, like fish or vegetables; others are preparations, like pre-probiotics, that are crucial for defending the body against pathological or chronic diseases. Many bioactive substances are found in food but in small amounts, such as the flavonoids and anthocyanins found in fruits and veggies. However, if used in a concentrate preparation, these substances can be nutraceuticals that significantly improve people's overall health

Smart "drugs" enhance cognition rapidly. Four plant extracts—blueberries, rosemary, Curcuma, and garlic—improve brain processing speed, memory, and learning, alongside mental concentration for those seeking a natural strategy. A biopharmaceutical product made from natural components known to have consistently positive effects on human health is known as a nutraceutical. This includes pharmaceuticals created using natural components. The demand for functioning and nutraceutical foods that, in addition to their general nutritional functions, have properties for preserving longevity as well as health has increased as a result of new nutritional trends and a requirement to meet social and health demands. The lack of an all-encompassing definition and a set of laws governing nutraceutical foods is one of the most significant challenges confronting this revolution. Additionally, vitamins and compounds associated with them have neuroprotective properties that aid in reducing AD. Vitamins B6, 9, and B12 have neuroprotective effects against neuronal mortality, according to research. Niacin, a B3 component frequently referred to as nicotinamide riboside, is also efficacious. The cells transform nicotinamide riboside into nicotinamide adenine dinucleotide (NAD+), a coenzyme or helper molecule, just like they do with other types of vitamin B3. NAD+ appears to slow the progression of AD among those who are still in the infancy phase of the illness.

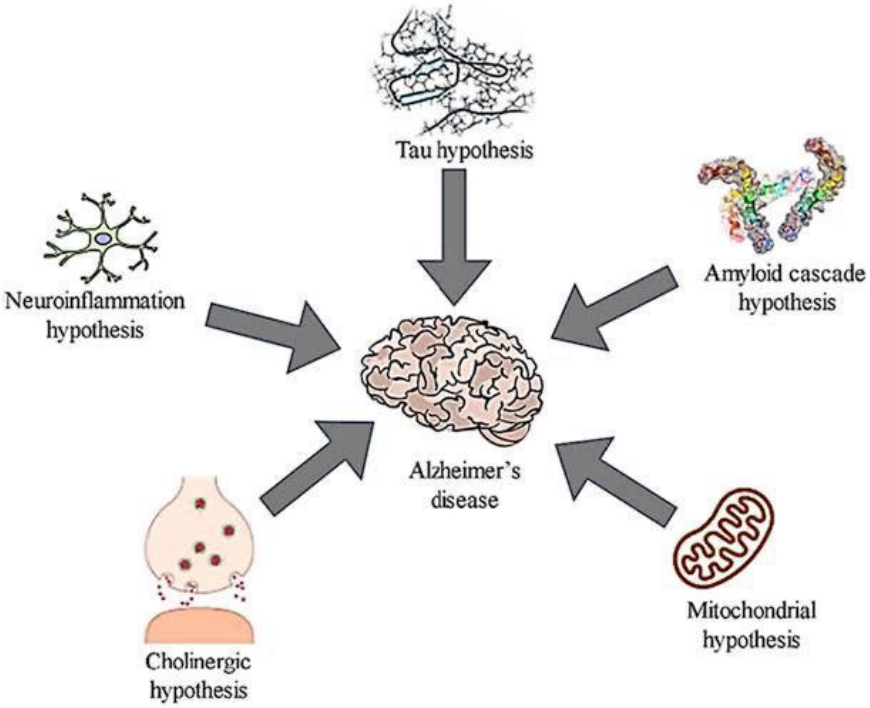


Figure 1: Proposed Alzheimer's Disease Hypothesis And The Mechanisms Involved.

MATERIALS AND METHODS

ADVANCEMENT OF NUTRACEUTICALS IN ALZHEIMER'S DISEASE

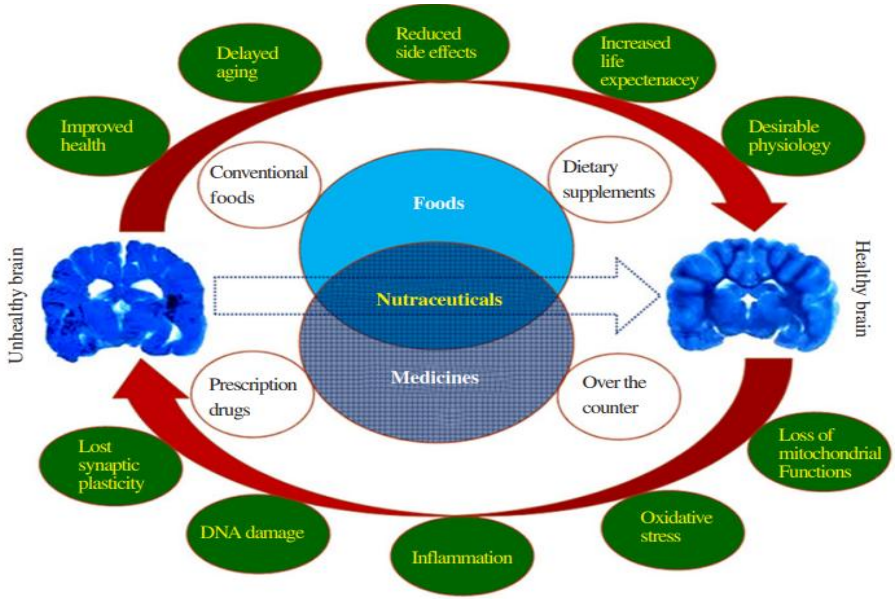
As previously stated, the kind of food, particularly nutraceutical ingredients, and particular formulae are crucial components for the prevention of AD. Dietary adjustments, nutritional supplements, functional foods, and nutraceuticals are the foundation of one essential method to prevent AD impairment. Nutraceuticals are chemical components of food that exhibit disorder qualities.

Several of these substances have solid preclinical research published in prestigious medical journals and double-blind placebo-controlled clinical studies, and they are obtained through strict extraction strategies from natural resources and Good Manufacturing Practices (GMP) laws. Nutraceutical substances have varied structural characteristics, engage in a variety of biochemical and metabolic processes, and exhibit a variety of neuroprotective effects. Nutraceutical substances have varied structural characteristics, engage in a variety of biochemical and metabolic processes, and exhibit a diversity of neuroprotective effects. attributes.

They can modify the physiopathological mechanisms causing neurodegeneration in AD and/or alter them to have pro-cognitive qualities. Nutraceuticals have the advantage of a multitarget strategy with various pharmacological activities in the human brain, which is advantageous given that AD is a multifactorial disease. The repression of particular targets includes acetylcholinesterase, tau protein aggregates, amyloid-senile plaques, mitochondrial dysfunction, oxidative stress, inflammatory pathways, and particular brain receptors (like NMDA), etc. are just one of these targets. The study by Calfio et al., 2020 provides a thorough assessment and meta-analysis of the majority of the nutraceutical compounds already reported to possibly contribute to AD prevention.

Polyphenols (curcumin, resveratrol, rosmarinic acid, and oleocanthal), flavonoids (delphinidin, quercetin, EGCG, luteolin, and cyanidin), and carotenoids are examples of bioactive substances in nutraceutical formulas. (astaxanthin, lutein, crocin), vitamins (B6, B9, B12), Perceptiv® (N-acetyl cysteine), AXONA \sAC-1200® (caprylic acid), BrainUp-10® (Andean \sshilajit, fulvic acid), plant extracts (Meganatural-az, \saged garlic, Ginkgo biloba), and other natural \smolecules (azaphilones, limonoids, huperzine A, \sS-allyl-L-cysteine, melatonin). They have demonstrated activity at many molecular locations associated with AD neuropathological alterations. Antioxidant, anti-inflammatory, anti-depressant, nootropic effect, anti-amyloid activity, anti-cholinesterase, anti-neurotoxic effect, neuritogenesis enhancer, and tau anti-aggregative (prevents tau hyperphosphorylation and promotes tau stabilisation) are the characteristics of this nutraceutical family of compounds.

Attributes can help maintain cognitive performance and have significant therapeutic potential for treating AD and other degenerative diseases. neurological disorders. Nutraceuticals for the treatment of AD have gained considerable interest recently from numerous scientists. These components are available in foods such as berries, peppermint, rosemary, olives, garlic, turmeric, apples, grapes, red wine, saffron, onion, celery, green tea, moss (Huperzia serrata), fungus (Aspergillus nidulans), and medicinal plants (Lemon Balm, Jatamansi, Maca, Ginseng, Moringa). They can also be obtained through diet directly. The knowledge above will help the general public choose better sources of nutraceuticals as a precautionary measure against AD because they undoubtedly pave the way for a healthy lifestyle.



Nutraceuticals and their various categories

To avoid the onset of minor signs of chronic diseases and to promote health, nutritional supplements are used in non-specific biological treatments. Improvement and encouraging a person's well-being. It is widely recognised that nutritional supplements play a beneficial function in promoting brain health and preventing neurodegenerative diseases like dementia and AD. Following are the classification standards for nutraceuticals. The table outlines the mechanisms of action of some dietary supplements for AD.

Table No:1.

B vitamin Family: Vitamin B6, B12, B9	Vitamins B6, B9, and B12 are important for maintaining healthy brain function, which includes controlling thought, memory, emotion, motor abilities, vision, and respiration. These vitamins are also helpful in the production of several neurochemicals, DNA/RNA synthesis, and RNA repair.
Alpha-lipoic acid (ALA)	Alpha-lipoic acid's anti-inflammatory and antioxidant properties help the CNS produce more cellular energy.
Antioxidant vitamins: C, and E	Ascorbic acid, a type of vitamin C, is essential for the production of dopamine and noradrenaline, two well-known neurotransmitters involved in the regulation of tyrosine metabolism. Vitamin E, a potent antioxidant, is also required.
Ginkgo biloba	Ginkgo biloba reduces oedema and lipid peroxidation in cell membranes in response to bromethalin-induced cerebral lipid peroxidation, which lessens neuronal damage.
Isoflavones: soybeans	By replicating the effects of oestrogen on the brain's oestrogen receptor, isoflavones appear to enhance cognitive performance and boost the brain's antioxidant capacity.
Garlic (Allium sativum)	Allicin, an organosulfur substance found in Allium sativum, reduces the activity of cholinesterase enzymes and raises acetylcholine levels in the brain.
Caffeine	It has been demonstrated that caffeine, a xanthine alkaloid, can reduce the development of amyloid-beta by squelching hydroxyl radicals.
Flavanols: catechin, epicatechin, epigallocatechin, epigallocatechin gallate, isorhamnetin, kaempferol, myricetin and quercetin	The biological components of flavanols have the power to reduce inflammation, scavenge free radicals (oxidative stress) in the blood and gut, and guard against cellular damage.
Polyphenols (non-flavonoid): curcumin and resveratrol	Resveratrol exerts decrease inflammation and minimizes neuronal toxicity.
Sesquiterpene alkaloid (Huperzine A)	A sesquiterpene alkaloid called huperzine A has the potential to be a reversible inhibitor of acetylcholinesterase.
Carotenoids	Antioxidant properties of carotenoids are responsible for neuroprotection.
Fish oil: omega-3 fatty acids	By displacing arachidonic acid from membranes that catalyse the formation of thromboxane, prostaglandins, and leukotrienes, omega-3 fatty acids found in fish oil have a direct impact on the metabolism of arachidonic acid.
Cyanide (anthocyanidins)	Cyanide (anthocyanidins) blocks the body's production of pro-inflammatory cytokines and the promotion of brain cell deterioration.
Flavonoids	Flavonoids as memory and learning modulators: molecular interactions with behavioural consequences.

Antioxidants

Oxidative stress in AD: It is believed that oxidative stress plays a role in the aetiology of AD. When the body's antioxidant defence systems and the production of reactive oxygen species (ROS) are out of equilibrium, oxidative stress results. ROS can harm lipids, proteins, and DNA in cells, which can cause cell loss and tissue injury. ROS are believed to play a role in the development of tau protein tangles and amyloid-beta (A) plaques, which are markers of AD.

Because the majority of chronic illnesses are accompanied by a significant amount of oxidative stress, antioxidants are crucial in the therapy of all disorders. Parkinson's disease, Huntington's disease, Alzheimer's disease, and amyotrophic lateral sclerosis (ALS).

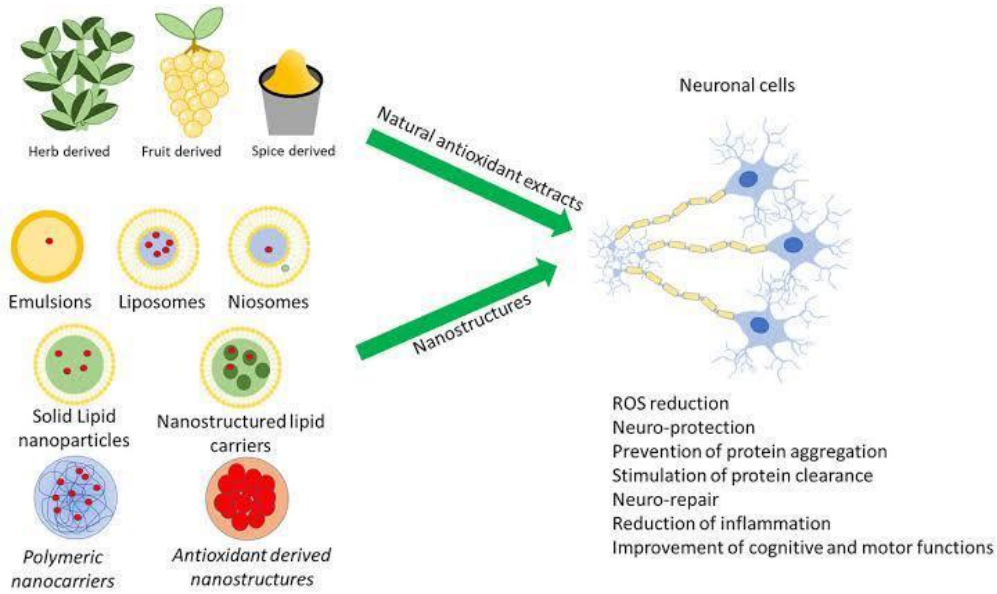


Figure 3: Association between Food Insecurity and Procurement Methods among People Living with HIV in a High Resource Setting.

These are the main brain diseases. (Katsuno et al., 2018) . All of these neurological conditions involve significant involvement of oxidative stress. Oxidative stress is brought on by both ageing and a deficiency in nutritional antioxidants. High dietary antioxidant intake and a lessened likelihood of AD have been linked in numerous research. It is crucial because curing an illness is much more challenging than avoiding it. Antioxidant therapy is a potential strategy for reducing the progression of diseases. harm from oxidation brought on by beta-amyloidConsuming foods high in antioxidant potential can help to some degree decrease inflammation, altered antioxidant defences, and mitochondrial abnormalities caused by beta-amyloid-induced free radicals.

Intervention studies, however, have produced a range of outcomes. The issue with most vitamin E research is that they use synthetic vitamin E, as in the study described above where patients were administered 1000 IU of vitamin E. However, there could be many issues with that. First, dl-alpha tocopherol, a synthetic form of vitamin E, only has about an eighth of the action of its native counterpart. The manufactured vitamin E is the other factor that could obstruct the uptake of additional tocopherols, including gamma tocopherol, tocotrienol, and other vitamin E family substances. so using both natural and manufactured

There are numerous issues with vitamin E in studies. Another issue is the dosage. (Cristina et al., 2014). Vitamin C and E levels in individuals with AD's cerebral spinal fluid are low. In 2004 (Zandi et al.). The cerebrospinal fluid and plasma lipoproteins' vulnerability to oxidation was greatly reduced by the mixture of vitamins C and E. Because vitamin C regenerates vitamin E in the organism when vitamin E and C are combined. It is ideal to administer antioxidants before serious harm takes place. Even minor harm can be repaired. antioxidants defend against

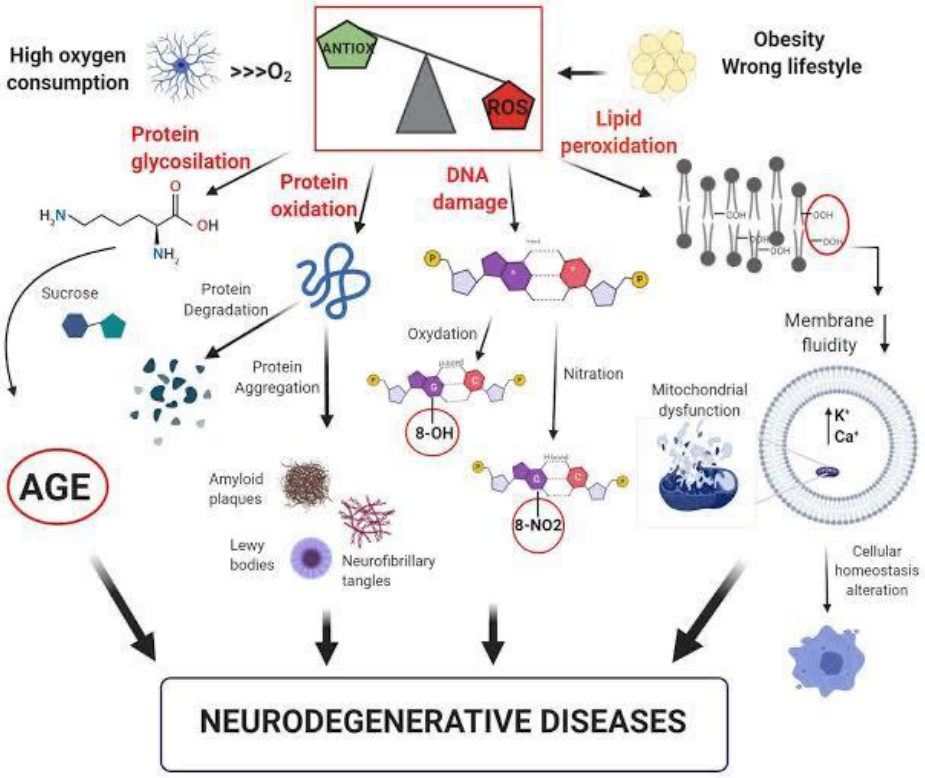


Figure 4: Neurodegenerative Diseases Cascade.

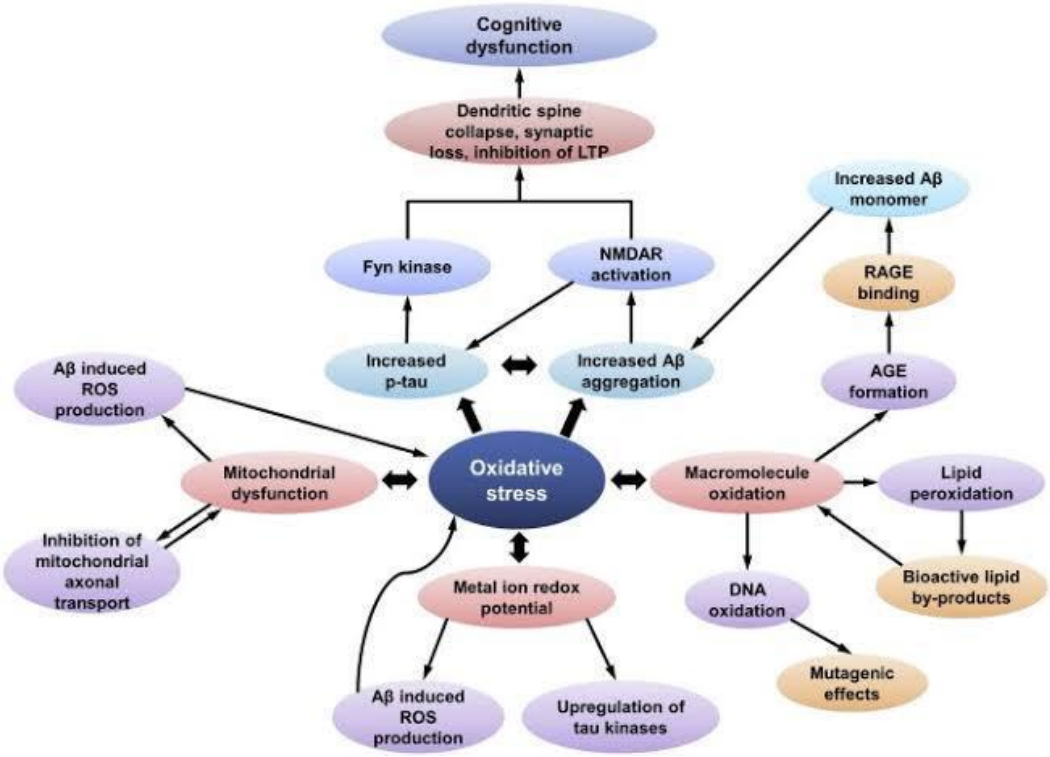


Figure 5: Oxidative Stress Cascade.

Prebiotics

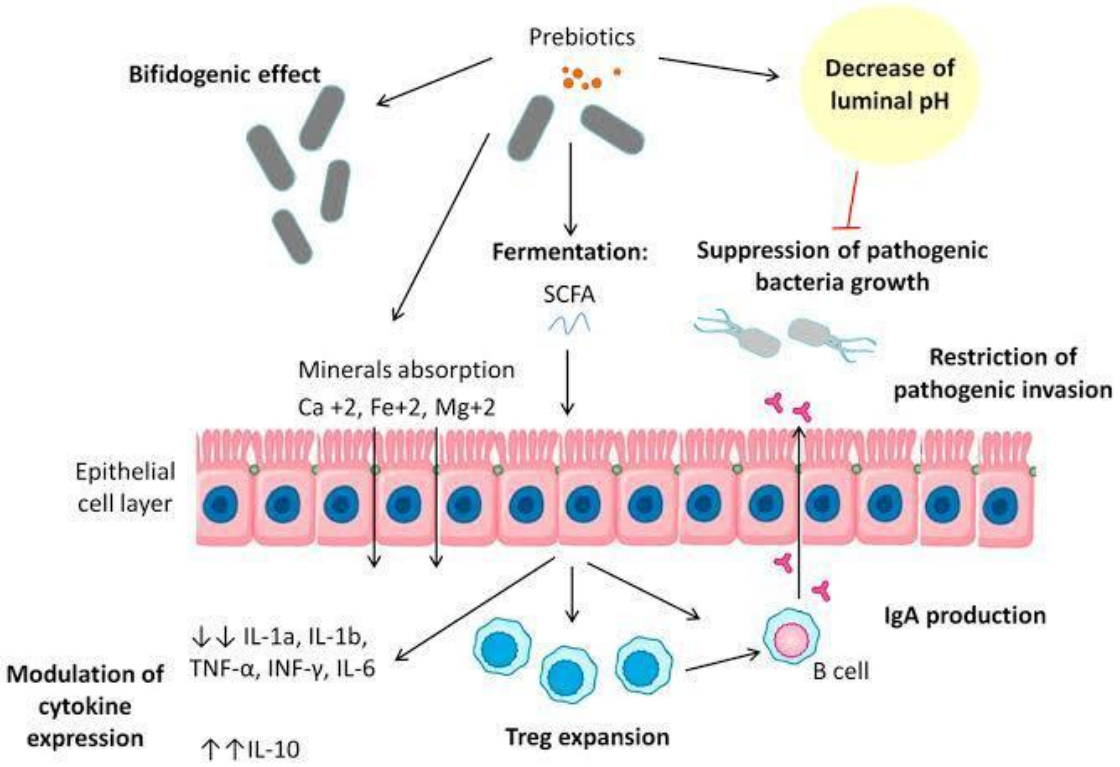


Figure 5:Action of prebiotics: mechanism.

These methods include the creation of microbial metabolic products, taking note of short-chain fatty acids (SCFAs), promoting the absorption of ions and trace elements (such as calcium, iron, and magnesium), a drop in luminal pH, and immune system control (increasing IgA production and modulating cytokine production)

The microbiota's function concerning neurodegenerative diseases has lately been studied. Additionally, the gut-brain pathway is now recognised as a crucial factor in the emergence of neurodegenerative conditions. Thus, among the novel substances that might be used in AD prevention are prebiotics and probiotics, which are essential for the preservation of healthy microbiota.

The prebiotics

According to a definition first used in 1995, a prebiotic is "a non-digestible food ingredient that beneficially affects the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon, and thereby improves host health." They primarily comprise carbohydrates that are immune to digestive enzymes and secretions.

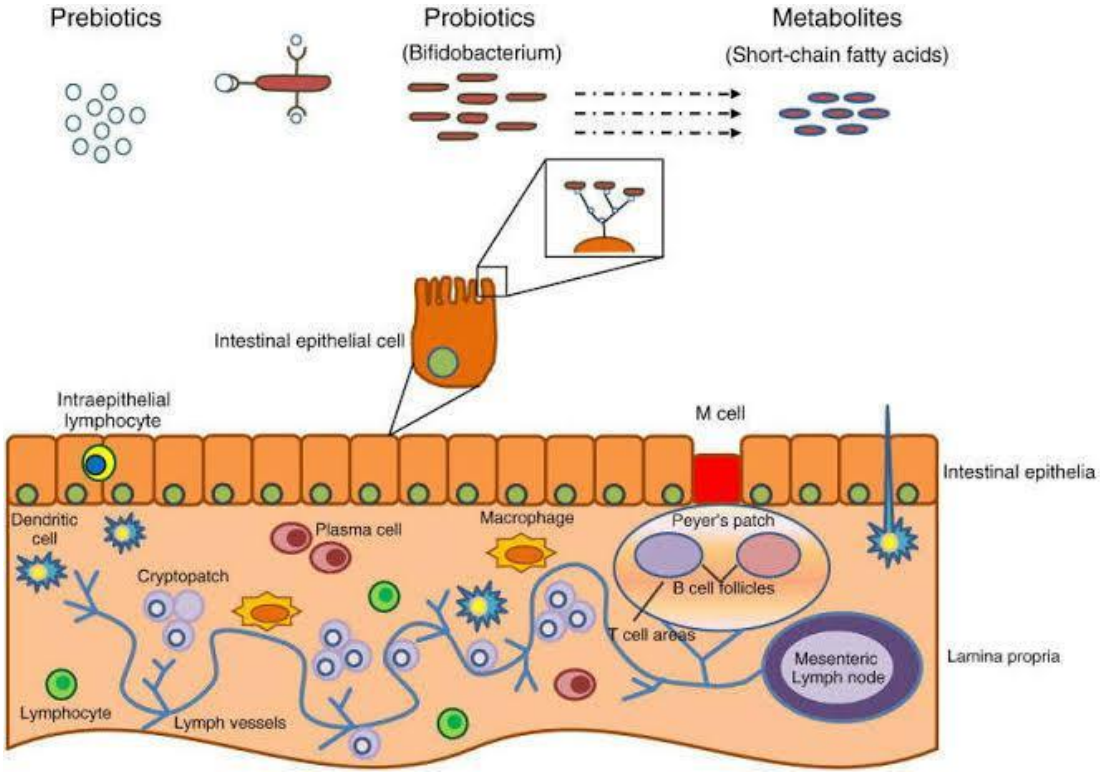


Figure 6: The Putative Effects of Prebiotics as Immunomodulatory Agents.

Like -glucan and resistant carbohydrates. The microflora in the gut ferments them once they get to the colon, which encourages the development of commensal strains while inhibiting the growth of pathogenic bacteria. Fructooligosaccharide is one of the most researched prebiotics. (FOS). This substance, which is present in many fruits and veggies and is derived from the degradation of inulin, serves as a substrate for the growth of the microflora Lactobacillus and Bifidobacterium. Regarding cognitive impairment, FOS supplementation to transgenic AD mice raised Glucagon-like peptide-1 (GLP-1), a protein that easily penetrates the blood-brain barrier (BBB) and promotes satiety, insulin secretion from the pancreas, and a slowing of gastric emptying

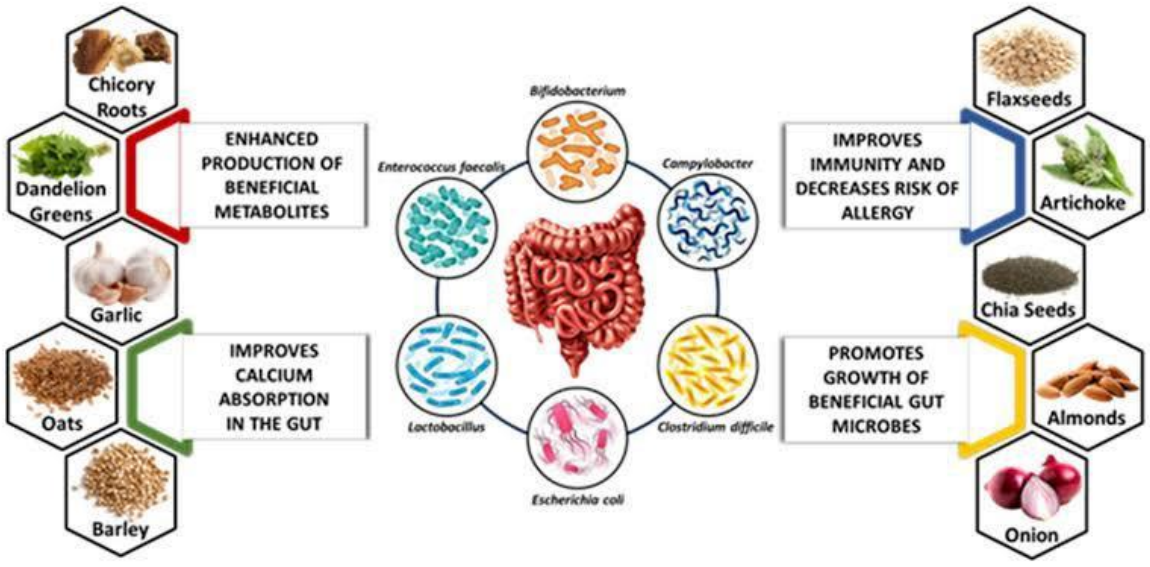


Figure 7: Plant Prebiotics and Their Role in the Amelioration Of Diseases.

Since cerebral GLP-1 rises, it enhances insulin resistance in the central nervous system (CNS), which reduces neuronal cell loss brought on by the impaired glucose metabolism seen in AD. Through the expression of synapsin-1, which covers synaptic vesicles and is used as a measure of neuronal activity, FOS supplementation also affects neuroplasticity. Synapsin-1 levels sharply decline in AD individuals.

In contrast to the controls, however, FOS supplementation in AD rodents resulted in the restoration of physiologically normal synapsin-1 levels. Additionally, it was shown that B. longum combined with FOS substantially reduced levels of C- reactive protein (CRP), TNF-, serum AST, serum endotoxin, steatosis, HOMA-IR, and the nonalcoholic steatohepatitis activity index.

Xylooligosaccharides are another prebiotic that has undergone significant research with positive outcomes. (XOS). This substance is the most prevalent biopolymer in the plant world and is produced from oligomers of xylan. XOS was a great choice to test for cognitive impairment due to its accessibility and anti-inflammatory properties. The administration of XOS supplements to APP/PS1 mice with POCD, a frequent comorbidity of AD caused by hepatectomy, enhanced their cognition. Memory loss, poor equilibrium, and executive dysfunction are the most frequent symptoms seen following a POCD intervention. These symptoms are brought on by neuroinflammation and a decline in BBB integrity. Supplementing the operated mice with XOS reduced the fluctuations in the microbiota, particularly in the genera Lactobacillus and Bacteroidetes, to mention a couple.

The latter reduced intestinal inflammation by enhancing the diversity of the gut bacteria. The amounts of the immunosuppressive cytokine IL-10 as well as the proinflammatory cytokines IL-1 and IL-6 dropped. Following surgery, AD mice's BBB and epithelium barrier weakened as a result of a drop in the tight junction protein zonulin-1. (ZO-1). ZO-1 was elevated in both epithelial and hypothalamic tissue after XOS administration, indicating a connection between a "leaky gut" and a more permeable BBB. BBB images obtained using Transmission Electron Microscopy (TEM) revealed that supplemented AD mice had BBBs that were similar in composition and structure to those of control subjects.

Probiotics

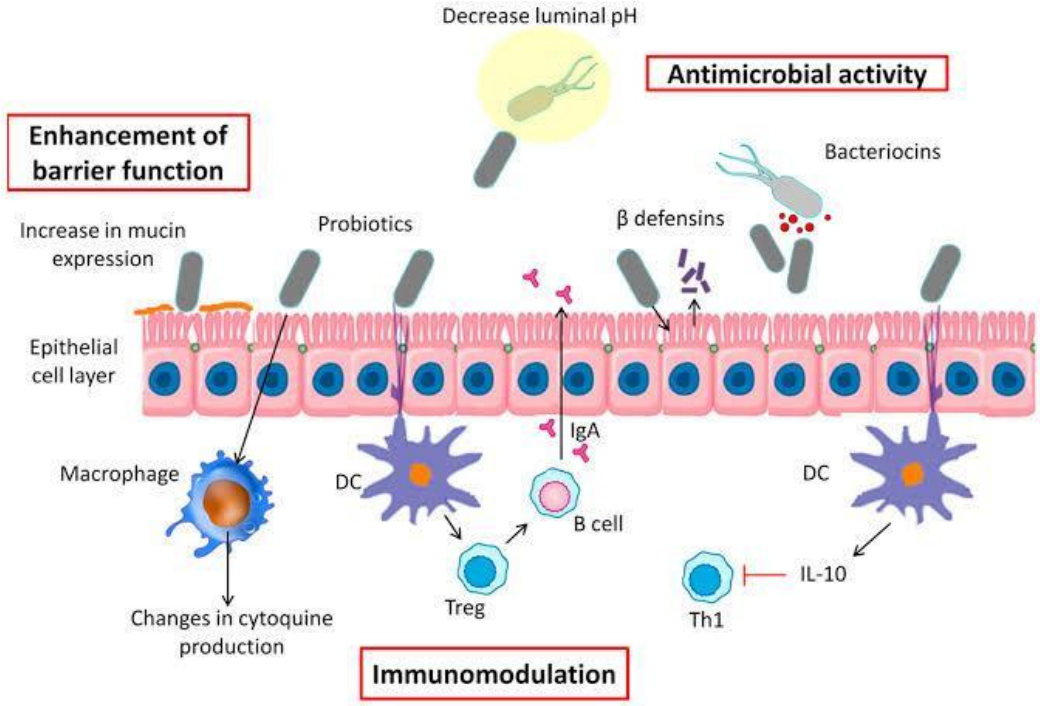


Figure 8: Diagram illustrating several pathways for how probiotic bacteria could function in the colon.

These processes include the regulation of the human immune system, antagonistic effects on diverse bacteria, competitive adhesion to the mucosa and epithelium (antimicrobial activity), increased mucus production, improved barrier integrity, and enhancement of barrier function (immunomodulation).

According to the most recent definition of probiotics, they are "live bacteria that, when given to a host in sufficient proportions, offer a health benefit". One of the most crucial

Ones that come under the category of "functional foods" include Lactobacilli (such as L. acidophilus, L. rhamnosus) and Bifidobacteria (such as B. bifidum, B. infantis). This commensal bacteria can have a variety of effects on AD and other neurodegenerative illnesses.

Due to the effect on the levels of many important regulators, such as Brain-Derived Neurotrophic Factor (BDNF), G-Aminobutyric Acid (GABA), Dopamine (DA), and serotonin (5 hydroxytryptamine; 5 HT), they directly alter the CNS biochemistry, which in turn affects mind and behaviour. The gut-brain axis link, in which there is bidirectional communication between the gut and the brain, might help to explain this in part brain d.

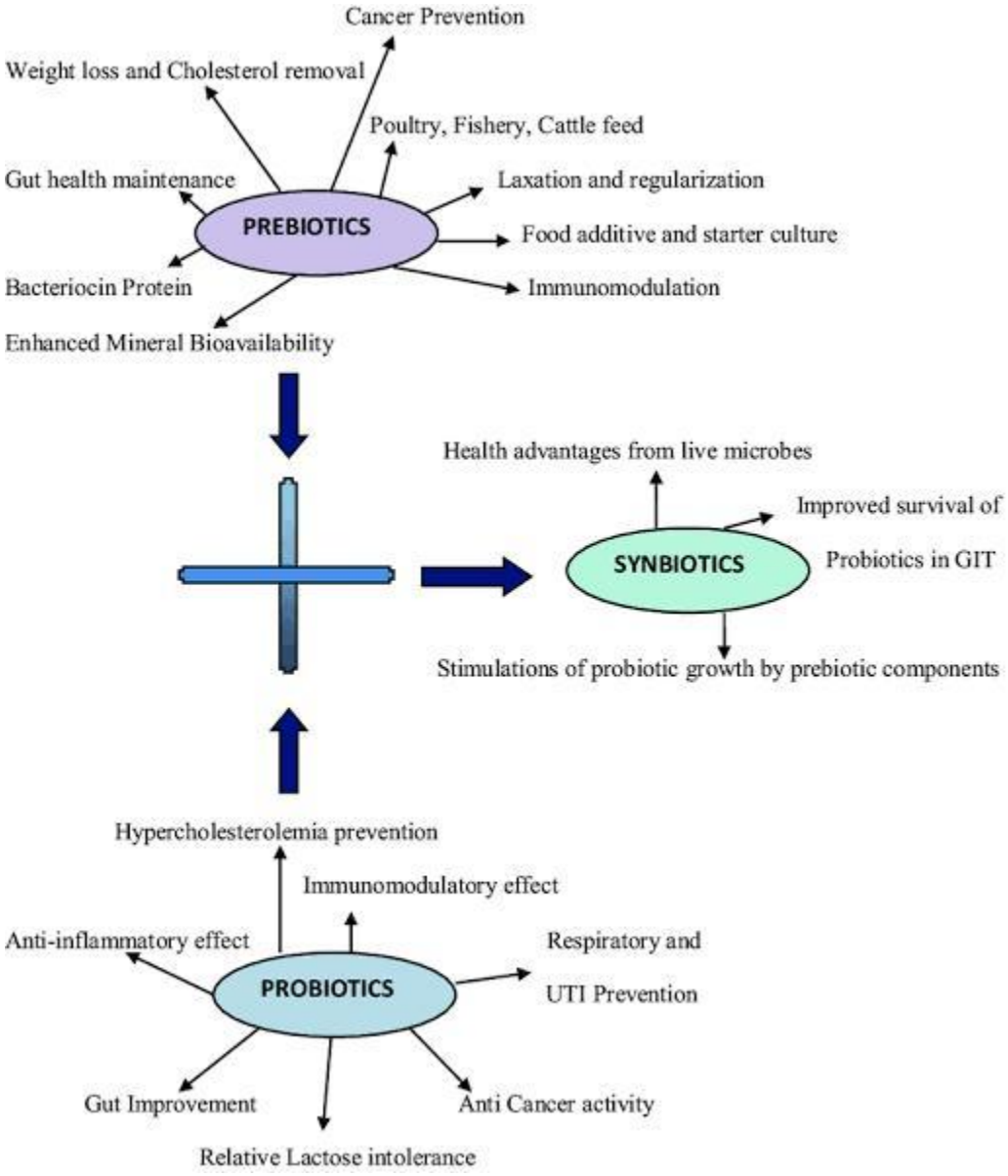


Figure 9: Pictorial summary of Prebiotics, Probiotics And Synbiotics.

In this sense, probiotic bacteria that generate short-chain fatty acids and tryptophan both indirectly influence CNS function. They also influence the immune system, reducing the generation of pro-inflammatory cytokines and swelling. Certainly, with tryptophanas well as short-chain fatty acids, the immune system can work together to control cellular immunological reactivity.

In research by Cattaneo et al. (2017) on brain amyloidosis, the bacteria studied were chosen based on their anti- or pro-inflammatory profiles (Escherichia/Shigella, Pseudomonas aeruginosa, Eubacterium rectangle, Eubacterium hallii, Faecalibacterium prausnitzii, and Bacteroides fragilis). Therefore, IL-4, IL-10, and IL-13 cytokine expression was assessed and shown to be associated with the makeup of the gut microbiota. In this instance, a rise in Escherichia coli/Shigella and a reduction in.

Changes in the cytokine profiles of the cognitively impaired and amyloid-positive individuals were associated with an increase in Escherichia/Shigella and a reduction in Eubacterium rectal, resulting in a proinflammatory condition. seen in people with AD. This is consistent with an increase in the proinflammatory markers IL-6, CXCL2, NLRP3, and IL-1 as well as a reduction in IL-10 (anti-inflammatory cytokine). The latter supports the idea that the gut microbiome modulates inflammation.

Ferulic Acid's potential to produce substantial amounts has been established by a few probiotic species from the Lactobacillus and Bifidum families. Moreover, preclinical investigations revealed that pretreatment with FA reversed neuroinflammation in transgenic AD mice and reduced A fibril levels in the hippocampus and cortical lobes when compared to controls. missing the phenolic molecule that the probiotic generated.

By cutting-edge fermentation technology, one intriguing probiotic reaction is achieved. Kefiris a dairy product that is made by fermentation as a result of the action of many yeasts (fungi) and bacteria (lactobacilli). It is similar to liquid yoghurt. Kefir's positive benefits on AD have recently been investigated, and it has been found that it improves cognitive impairment in rats that have AD caused by streptozotocin.

The regulation and amplification of the insulin/PI3K/Akt pathway by the gut microbiota, as was shown in another model of sporadic AD, might help to explain the latter, at least in part. All of the latter demonstrates how crucial the gut-brain axis is for AD growth and progression.

Ginko Biloba

Concerning its potential benefit for improving memory, cognitive function, overall brain performance, activities of daily living, and global clinical assessment in patients with mild cognitive impairment or AD G. biloba is probably regarded as the herb that has been the most thoroughly studied.

In the 3- to 6 months following the administration of the herbal supplements, patients with AD treated with 120 to 240 mg of G. biloba extract of objective measures of cognitive function were shown to have a minor but substantial benefit, according to the study by Yang G et al. In formal clinical studies, no substantial side effects of the medicine were discovered, however, two instances of bleeding problems were reported. There was not enough concrete evidence to support treatment. Many minerals, fibres, proteins, and oligosaccharides are also present in soybeans. It has been demonstrated that soybean isoflavones have an agonistic impact on oestrogen receptors.

Soybean supplementation was shown to improve memory in patients, and this was later determined to be the cause. By imitating the actions of oestrogen, namely through the brain's oestrogen receptor, isoflavones appear to enhance cognitive function. According to research by Gabor et al., oestrogen replacement treatment increases choline absorption and potassium-stimulated acetylcholine release, which is thought to enhance cholinergic function. Another investigation by Bansal et al. showed that prolonged soy supplementation enhances cognitive function, reduces thiobarbituric acid reactive compounds, and raises plasma glutathione peroxidase levels in both young and old mice.

Garlic

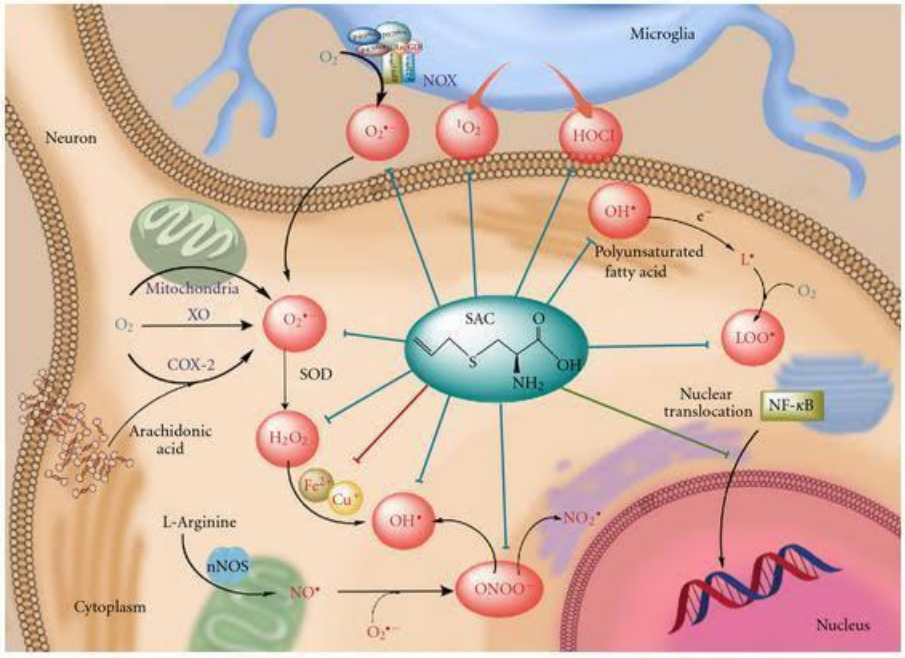


Figure 10: S-allyl cysteine-associated antioxidant pathway (SAC).

SAC can remove superoxide anion (O2•), hydrogen peroxide (H2O2), hydroxyl (OH•), peroxynitrite (ONOO), and peroxyl (LOO•) radicals produced in neuronal cells, as well as hypochlorous acid (HOCl), singlet oxygen (HOCl), and peroxynitrite (ONOO) and peroxyl (LOO•) radicals produced in microglial cells (blue lines).

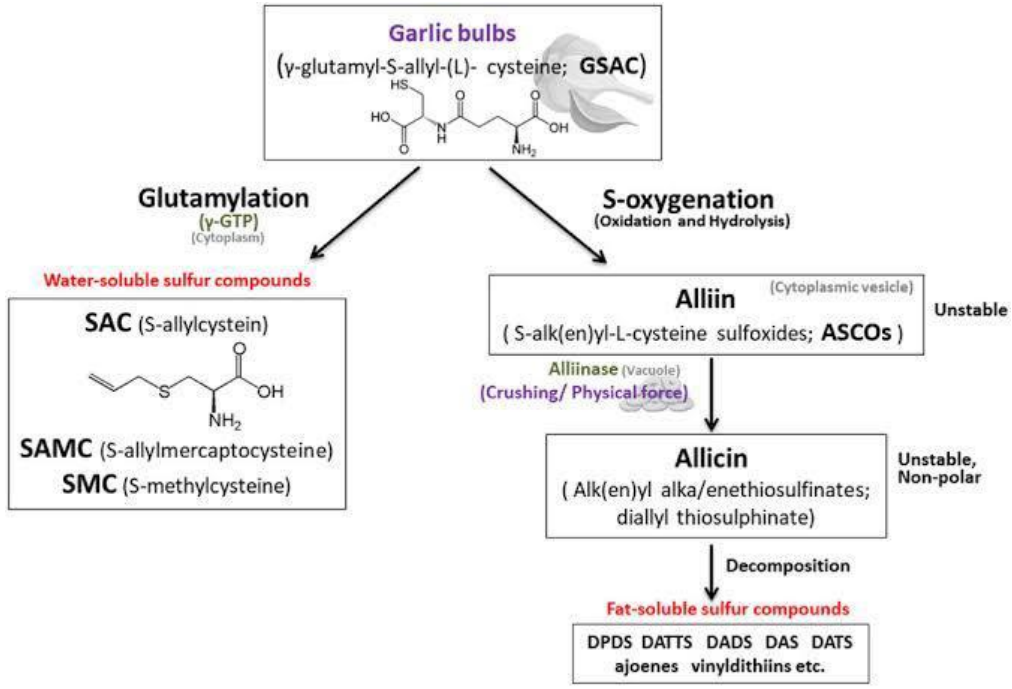


Figure 11:Garlic's (Allium sativum) S-Allyl cysteine: Formation, Biofunction, and Food Processing Resistance for Value-Added Product Development.

Allicin and several of its components in garlic extracts have been demonstrated to have antioxidant properties and to protect against neurotoxicity (caused by amyloid-beta) in both cells and animals.

Animal testing. According to research by Jeong et al., allicin, an organosulfur component of Allium(A.) sativum, inhibits cholinesterase enzymes and increases levels of acetylcholine in the brain, suggesting a potential use in the treatment of AD. Another study, similar to the Doetinchem Cohort Study, found that higher consumption of allium (onion, garlic, and leek) was linked to lower scores on the speed of cognitive processes and cognitive flexibility in participants. This finding was made after administering garlic extracts to 2613 participants aged 43 to 70 years for cognitive function (in a 5-year interval and dietary assessment).cross-sectional investigations. Nevertheless, when comparable research was done, the consumption of A. sativum was not linked in longitudinal analysis. and a loss of cognitive.

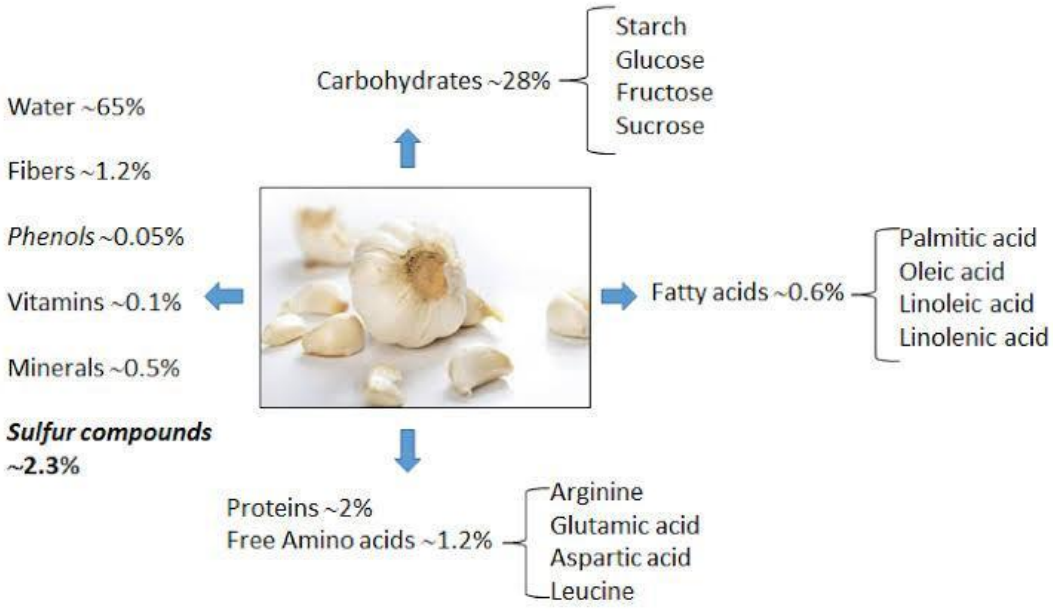


Figure 12: Garlic Nutraceutical Constituent.

Isoflavones in soybeans

To clarify the function of coffee in the development of cognitive impairment, dementia, and AD, further research on soy, which is a rich source of phytoestrogens, particularly isoflavones, which has been examined as a potential estrogenic replacement, is necessary.

Caffeine

It has been demonstrated that a xanthine alkaloid can reduce the development of amyloid-beta in animal models of AD and also has an anti-oxidative function, by quenching caffeine-containing hydroxyl radicals. It has structural similarities to adenosine, for which related research has defined caffeine's mechanism as being rather complicated. It is a non-selective antagonist of adenosine receptors (mostly A1 and A2A). Coffee and caffeine stimulate the central nervous system temporarily, but it is less apparent how they affect cognition over the long term. In an experimental mouse model of AD, the reduction in amyloid plaques was associated with high levels of phosphor-CREB, low levels of phosphor-JNK and phosphorus expression, and activation of protein kinase A activity. Other comparable research has shown that caffeine use is linked to better cognitive function, alertness, healthy brain functioning, and a slower rate of cognitive ageing. a case-control investigation by

Increased blood levels of caffeine (1200 ng/mL) were linked to a decreased risk of progression to dementia in individuals with mild cognitive impairment, according to research by Cao C et al., and 3 to 5 cups of coffee per day was associated with a 65% reduction in the incidence of AD and dementia, according to other studies. Also, it emerges from several research that, in certain cases, drinking or administering coffee has been linked to a lower risk of dementia and cognitive decline, but this doesn't always turn out to be the case. These assertions.

The varying and inconsistent nature of the evidence that is currently available (i.e., confounding, survival bias resulting from cohort age, the timing of conclusions on the function and advantages of coffee in the prevention of neurodegenerative diseases like dementia and AD are not included in the study (exposure). To clarify the function of caffeine in the emergence of cognitive impairment, dementia, and AD, recommendations for more research are necessary.

Quercetin

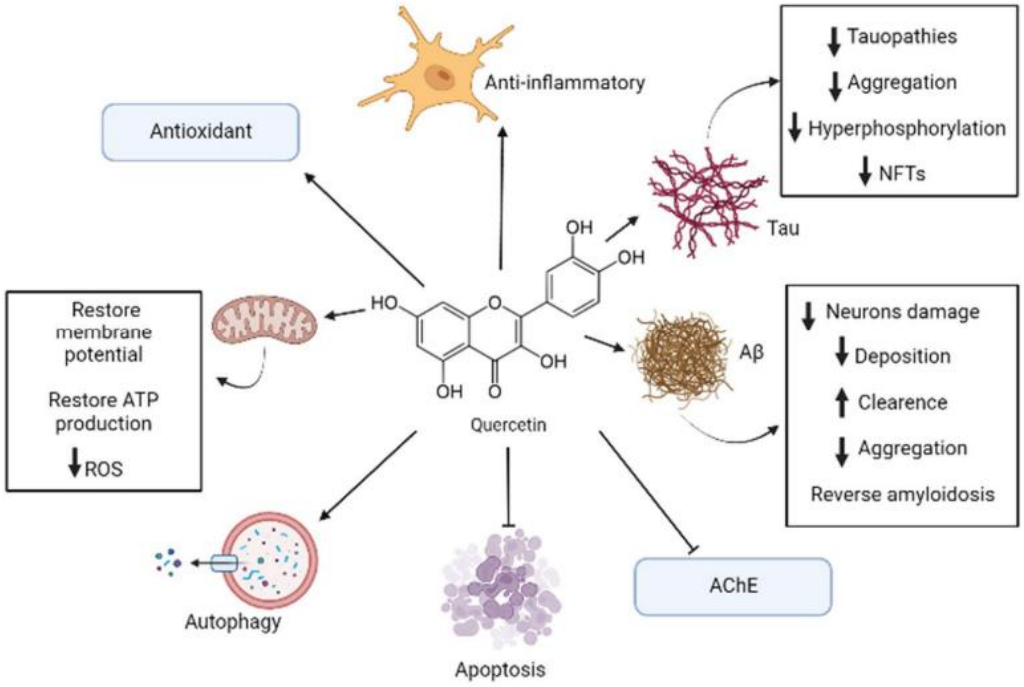


Figure 13: Quercetin as a nutraceutical.

With a daily average intake of 5 to 40 mg, quercetin, which is a member of the flavanols subclass of flavonoids, is one of the most consumed molecules in the human diet. The constituents of quercetin's chemical structure include.

5 hydroxyl groups and 3 ring configurations. It can pass the blood-brain barrier, which is crucial in the setting of neurodegenerative illness. Many qualities of quercetin, such as its anti-inflammatory and antioxidant abilities, are advantageous to human health. Because of the brain's high content of unsaturated fatty acids, high oxygen consumption, and low antioxidant capacity, the latter is particularly significant in the context of neurodegenerative disorders.

Of those in this group, quercetin is one of the most significant. Quercetin can be isolated from the entire fruit, however, apple peel has higher concentrations of this compound than apple meat. According to estimates, apples contain 2.1 to 7.2 mg/100 g of quercetin, the majority of which is present in the water-soluble glycoside form. Figures provide a summary of all the aforementioned impacts, with quercetin being one of the most significant effects in this categorization.

Quercetin can be isolated from the entire fruit, however, apple peel has higher concentrations of this compound than apple meat. According to estimates, apples contain 2.1 to 7.2 mg of quercetin per 100 g.

According to certain research, quercetin can prevent cell mortality and damage produced by treatments with H2O2 and A in primary neuronal cultures and PC12 cell models, respectively, when applied in low doses of 5 to 10 M. Moreover, research in treatment with quercetin can considerably reverse pathogenic processes, such as -amyloidosis, tauopathies, astrogliosis, and microgliosis, as demonstrated by the murine triple-transgenic Alzheimer's models. The learning and recall abilities of the test animals also improved. Also, it was demonstrated that administering quercetin (0.5 to 50 mg/kg) to animals in vivo tests had
the harm brought on by several neurotoxic substances.

Quercetin has a better AChE inhibitory activity than traditional AD medications, according to in silico studies. This is because quercetin (particularly in its comparison to traditional medications used in clinical practise, biomolecules 2022, 12, and 249 (4 of 16 methylated form azaleatin) exhibit a greater union with the active site of this enzyme. Quercetin's antioxidant capabilities are primarily provided by its ability to scavenge free radicals, chelate metals, and shield neurons from Metal toxicity. Nitric oxide synthase and nuclear factor erythroid 2-related factor 2 (Nrf-2) are transcriptional factors and enzymatic systems that quercetin can influence to stimulate genes that code for antioxidants and detoxifying enzymes.

Amino acids. Moreover, quercetin can influence the activity of pathways such as PI3K/Akt, tyrosine kinases, Protein Kinase C (PKC), and mitogen-activated protein kinase (MAPK) that are crucial for neurogenesis, cognition, and neuronal survival. New research even reveals that this system might control the production and clearance of misfolded protein aggregates prevalent in neurodegenerative illnesses like AD. The Nrf2-ARE pathway defends neurons against oxidative stress-induced damage and cell death.

Reactive oxygen species (ROS) generation is decreased, the potential of the mitochondrial membrane is restored, and ATP synthesis is raised as a consequence of quercetin's action on the mitochondria. Furthermore, quercetin controls AMP-activated protein kinase (AMPK) expression, which is crucial for controlling energy metabolism and lowering ROS generation. Yet another crucial

In the context of AD, the AMPK has the feature that these proteins inhibit A deposition, promote A clearance, and control the processing of A's precursor protein, APP. Due to its ability to scavenge free radicals and ROS in this situation, quercetin also has an anti-inflammatory impact. Furthermore, it has been shown that quercetin can reduce the production of TNF- by modulating the activity of

Quercetin can decrease the mRNA levels of TNF- and IL-1 in glial cell models produced by lipopolysaccharide (LPS), and it can also decrease the apoptotic rate in the cocultures of neurons and microglia.

Microglial stimulation causes neuronal death. Furthermore, quercetin has a neuroprotective impact and is implicated in inducing autophagy, a critical mechanism in preserving the integrity of the central nervous system. Furthermore, quercetin can activate the SIRT1 protein, which in turn can decrease proapoptotic transcriptional factors and prevent Bax-dependent apoptosis.

By stabilising the oligomeric forms of these misfolded proteins and so limiting fibril growth, quercetin has been shown in in vitro tests to be beneficial in preventing protein aggregation of A, tau protein, and -synuclein in the setting of AD.

Due to its chemical makeup and interactions with substances like BACE-1 and NF-, quercetin can also prevent the development of A oligomers and weaken its fibrils, which lessens the neurotoxic consequences of these protein aggregates. Another investigation used

The pretreatment of HT22 hippocampal neurons with quercetin has been shown to decrease tau hyperphosphorylation. Moreover, the CDK5 enzyme, a crucial player in the control of tau, can be inhibited by this substance. Quercetin can also lessen the amounts of NFTs, A, and cognitive impairment in the triple-transgenic animal models of Alzheimer's disease, according to research on these mice.

Anthocyanins/berries

Fruits and Vegetables	Anthocyanin Content	Administrated as
Blackberry (*Rubus fruticosus*)	820–1800 mg/kg	Fresh fruit
Black mulberry (*Morus nigra*)	42.4 mg/100 g	Fresh fruit
Bilberry (*Vaccinium myrtillus*)	1,610-5,963 mg/L	Juice 100%
Black carrots (*Daucus carota* ssp. *sativus* var. *atrorubens*)	1,750 mg/kg	Fresh vegetable
Black chokeberries (*Aronia melanocarpa*)	1,480 mg/100 g	Fresh fruit
Black soybean (*Glycine max*)	0.1-23.04 mg/g	Seed coat
Black currant (*Ribes nigrum*)	176-1,298 mg/L	Juice 100%
Blood orange (*Citrus sinensis*)	4.6 ± 0.7; 72.4 ± 0.6 mg/L	Fresh fruit
Blueberry (*Vaccinium virgatum* and *Vaccinium corymbosum*)	134 mg/kg	Fresh fruit
Cherry (*Prunus cerasus*)	22 mg/100 g	Fresh fruit
Cornelian cherry (*Cornus mas*)	128.45 ± 5.14 mg/L C3G 226.78 ± 8.61 mg/L	
Cowpea (*Vigna unguiculata*)	1.7-3.9 mg/g	Seeds
Cranberry (*Vaccinium macrocarpon*)	460–2,000 mg/kg	Fresh fruit
Eggplant (*Solanum melongena L.*)	11.53 g/100 g DW delphinidin, 0.55 g/100 g DW of petunidin	Fruit
Grape (*Vitis vinifera*)	300–7,500 mg/kg	Fresh fruit
Kiwi (*Actinidia melanandra*)	478 µg/g in skin, 81 µg/g in flesh	Fresh fruit
Mahaleb cherries (*Prunus mahaleb*) (g/kg DW)	7.80±1.10; 15.60±3.10; 17.70±3.50; 18.90±0.90	Fresh fruit
Pepper (*Capsicum annuum L.*)	0.96 mg anthocyanin/100 g fresh weight	
Pomegranate (*Punica granatum*)	43 mg/L	Juice
Purple maize (*Zea mays indurate*)	4.3 to 117-mg C3G/g	dark-colored purple corncob
Purple sweet potato (*Ipomoea batatas L.*)	0.94- 1.75 g/kg	Fresh weight
Strawberry (*Fragaria × ananassa*)	232 mg/100 g	Fresh fruit

C3G = cyanidin 3-glucoside; P3OG = pelargonidin-3-O-glucoside; DW = dry weight.

Berries are known for having a high concentration of vitamins, minerals, dietary fibre, phenolic compounds, and organic acids. Nevertheless, the primary bioactive substances regarded as a water-soluble dyes are anthocyanins (ANT). blueberry, bilberry, and red wine

Natural dietary anthocyanins are abundant in cranberries, elderberries, raspberries, strawberries, maqui, and Calafate (an indigenous Patagonian fruit). Berry extracts have been linked to the prevention of AD and other diseases.

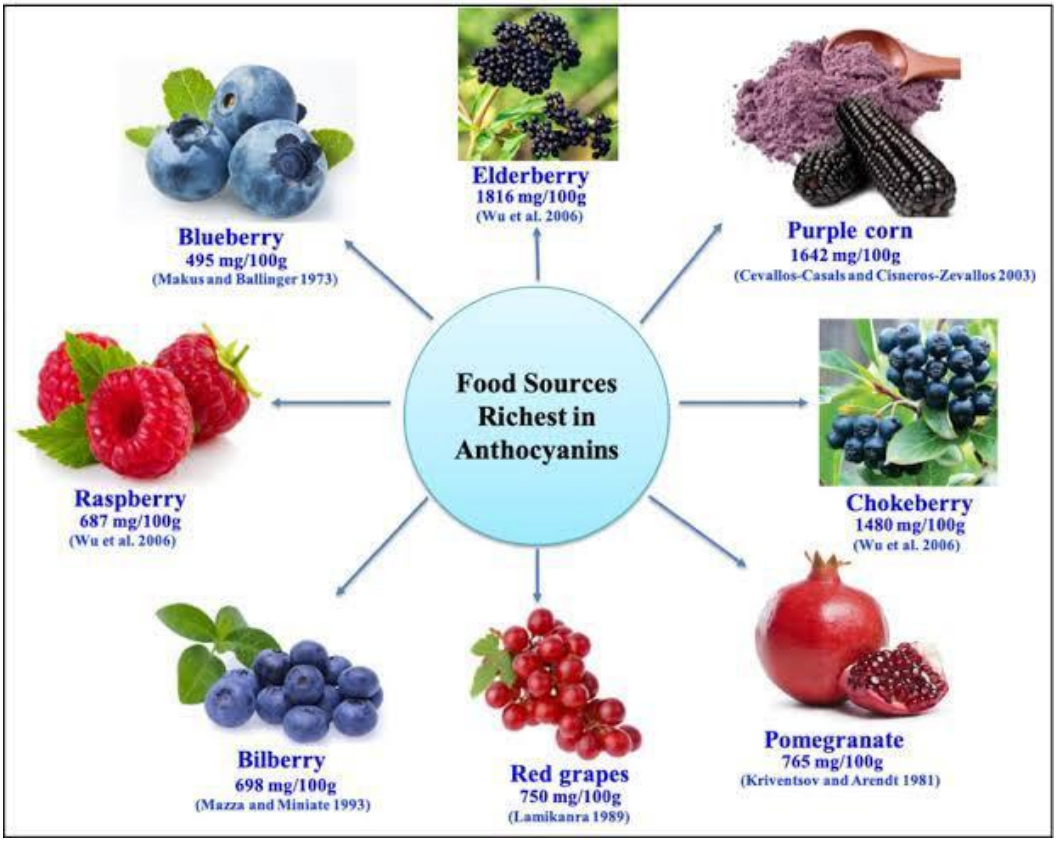


Figure 14: Food sources richest in Anthocyanins.

Functional human research linked berry consumption to slower rates of cognitive deterioration in aged adults, indicating the protective effects of ANT on so many cognitive processes. In healthy older people, the 30 mL blueberry supplement (387 mg ANT) significantly increased brain activity in locations related to cognitive performance (Brodmann areas, precuneus, anterior cingulate, and insula/thalamus).

In a randomised, double-blind, placebo-controlled study, older persons with cognitive problems showed enhanced cognition following a long-term (24-week) blueberry supplementation. This demonstrates that supplementing with ANT-rich berries has cognition benefits in this dementia-at-risk cohort. The preventative impact, however, will rely upon the quantity and ANTarchitecture (aglycone or its glucoside conjugated).

Berries that contain anthocyanins have intriguing pharmacological properties, such as antioxidant and anti-inflammatory properties, which enhance neuronal and cognitive brain function. According to the postulated mechanism of action, ANT prevents tau hyperphosphorylation and GSK-3 activation brought on by A in PC12 cells.

To prevent tau protein filament formation caused by heparin, anthocyanins' planar aromatic ring is crucial. Inhibiting oxidative stress and neuroinflammation are two essential ways through which ANT generate protective benefits, according to other research.

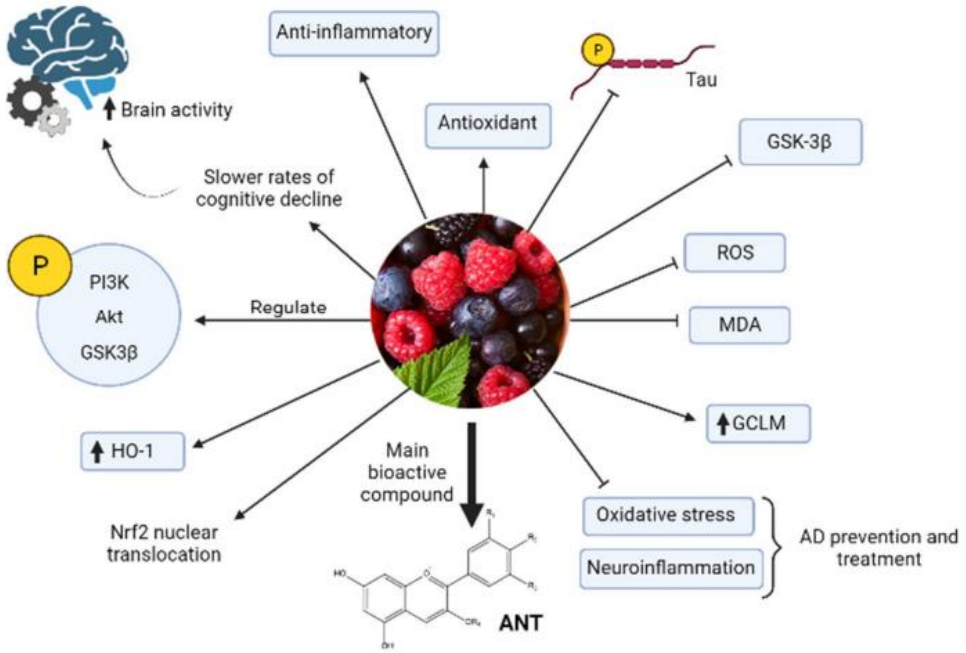


Figure 15: Functional Benefits of Nutraceuticals in Quercetin-rich foods.

In the management or prevention of AD. Long-term Nrf2 nuclear translocation, glutathione cysteine ligase modulatory subunit (GCLM) and HO-1 expression, as well as upregulation of p-PI3K, p-Akt, and p-GSK-3 expression, reduction of ROS and Malonaldehyde (MDA), and upregulation of p-PI3K, p-Akt, and p-GSK-3 expression, are all effects of the ANT.

Boswellia acid

Boswellic Acid, a pentacyclic terpenoid found in Indian herbal medicine and made by plants in the genus Boswellia, is another intriguing substance. Specifically, it was shown that 3-Acetyl-11-Keto-Beta-Boswellic Acid (AKBA) by the manipulation of miRNA 155, has neuroprotective effects against LPS-induced neuroinflammation. It has been shown that co-administration of celecoxib and 3-Acetyl-11-Keto-Beta-Boswellic Acid increases the protection against LPS-induced cognitive impairment in mice, which is consistent with this anti-inflammatory activity. Subsequent research revealed that pre-treatment with Acetyl-11-Keto-Beta-Boswellic Acid had an impact on brain cytokines, which ultimately resulted in a decrease in proinflammatory cytokines like TNF-a and an increase in cognitive function in rats with LPS-induced memory impairment. Eventually, it was shown that AKBA had strong anti-inflammatory and neuroprotective properties in AD. Acetylcholinesterase (AChE) inhibition, which increases acetylcholine levels, potentiates this.

Carotenoids

40 different varieties of the carotenoid family have been detected in blood and human tissues, as has been reported in multiple review studies, and there are over 700 different members in total. The main carotenoids found in humans are lutein, lycopene, -cryptoxanthin, and zeaxanthin, including carotenes. Based on their structural arrangements and experimental evidence, the carotenoids are designated as having known antioxidant action. These chemicals are frequently found in orange, deep yellow, and red fruits and vegetables because they are naturally occurring fat-soluble pigments. Astaxanthin, a carotenoid produced from seafood, has been extensively investigated for its anti-inflammatory and antioxidant properties in both in-vivo and in-vitro animal models. Due to its protective effects on the mitochondria and the microcirculatory system, astaxanthin was also thought to be a strong neuroprotective substance.

When compared to people with mild AD, the results showed that patients with serious or medium AD do not have enough of the main carotenoids lutein and beta carotene.

The control group or AD. Lycopene was the only one of the six carotenoids studied to have an inverse correlation with the level of cognitive performance and enhancement as measured by the MMSE and DemTect (Dementia Detection Test) in healthy individuals from the age range of 45 to 102. This relationship was also supported by the Clock Drawing Test that was administered to the study group.

AlphaLipoic Acid

The body naturally produces lipoic acid (LA), which is similar to a vitamin. Synthetic lipoic acid is referred to as ALA.ALA can reduce inflammation and has anti-inflammatory properties.

Showed antioxidant capabilities that are necessary for cellular energy production. Other advantages of ALA were discovered in the research by Packer et al. and Maczurek et al., which demonstrated that ALA had a variety of properties that could obstruct the pathogenesis or progression of AD as it plays a crucial role in brain operation by preventing it from developing or slowing the disease's progression. Several evaluations emphasised that mitochondrial failure and oxidative stress, which are both linked to energy depletion, were to blame for the biochemical symptoms of AD. The mechanism of action appears to increase the acetylcholine production in the body via turning on choline acetyltransferase and boosting glucose absorption, which in turn increases the amount of acetyl-CoA available for the synthesis of ACh. redox-active compounds chelated.

Another method of action included transition metals, which stopped the formation of hydroxyl radicals and scavenged reactive oxygen species, raising the amount of reduced glutathione. According to Hager et al., ALA has produced a range of outcomes in individuals who have mild to moderate AD. In open research with nine individuals with AD and similar dementias, 600 mg of ALA every day was given to those who were also receiving conventional ACh inhibitors for around 337 days. Those who received ALA demonstrated the stability of their cognitive performance as measured by the following measures: shown by the consistent scores on the MMSE and AD assessment measures, from which he deduced a successful outcome for the aforementioned nutraceuticals.

Based on the results of the clinical trials, it is believed that ALA is relatively safe for healthy people, however, it was noted that one research trial occasionally experienced slight stomach pain at large dosages. Other mild adverse effects that have been observed include nausea and skin irritation. Both allergic responses and a possible blood sugar decrease are possible. Red meat, spinach, carrots, beets, potatoes, plus broccoli are among the typical foods that contain ALA, but only in trace levels.

Moreover, it is commonly accessible like an OTC supplement. There are no established dosages for ALA supplements, however, doses between 600 and 900 mg/day are common. clinical studies with Alzheimer's provided for 4 years to a research group of 815 people aged 65 to 94 years to examine if they will develop AD used daily for up to two years. When compared to people who don't consume fish or have been eating it infrequently, the results showed a 60% lower risk of AD for those who ate fish once a week or more. The overall amount of omega-3 and DHA consumed was then linked to a lower risk of AD. As a result, it is determined that weekly fish eating and dietary intake of omega-3 fatty acids are both beneficial in reducing the risk of AD.

Omega 3 fatty acids

Another comprehensive evaluation conducted by Hooijmans et al. revealed that omega-3 fatty acids decreased the quantity of amyloid- in experimental animals used to study AD. A dietary addition was used for a long time, proving that it may also enhance cognitive abilities including learning, thinking, reasoning, memorizing, problem-solving, and decision-making. Nevertheless, the impact seemed to be more pronounced in bigger rats than mice, and in males than females.

Omega-3 fatty acid supplementation also supports epidemiological observational research suggesting its effects may be advantageous in illness beginning, with minimal impairment of brain function like AD, Parkinson's disease, and amyotrophic lateral sclerosis. amyotrophic lateral sclerosis, among others. Omega-3 fatty acid treatment also reduced the amount of neuronal death, particularly in female rats. This comprehensive review

Positive findings suggest that long-term usage of omega-3 FA supplementation in Patients with ad may warrant additional clinical trials.

In another trial, 815 people between the ages of 65 and 94 were given omega-3 fatty acids daily for four years to examine if AD would develop in them. When compared to people who don't consume fish or have been eating it infrequently, the results showed a 60% lower risk of AD for those who ate once a week or more. The overall amount of both omega-3 and DHA consumption was then linked to a decrease in AD.

Polyphenol/Honey

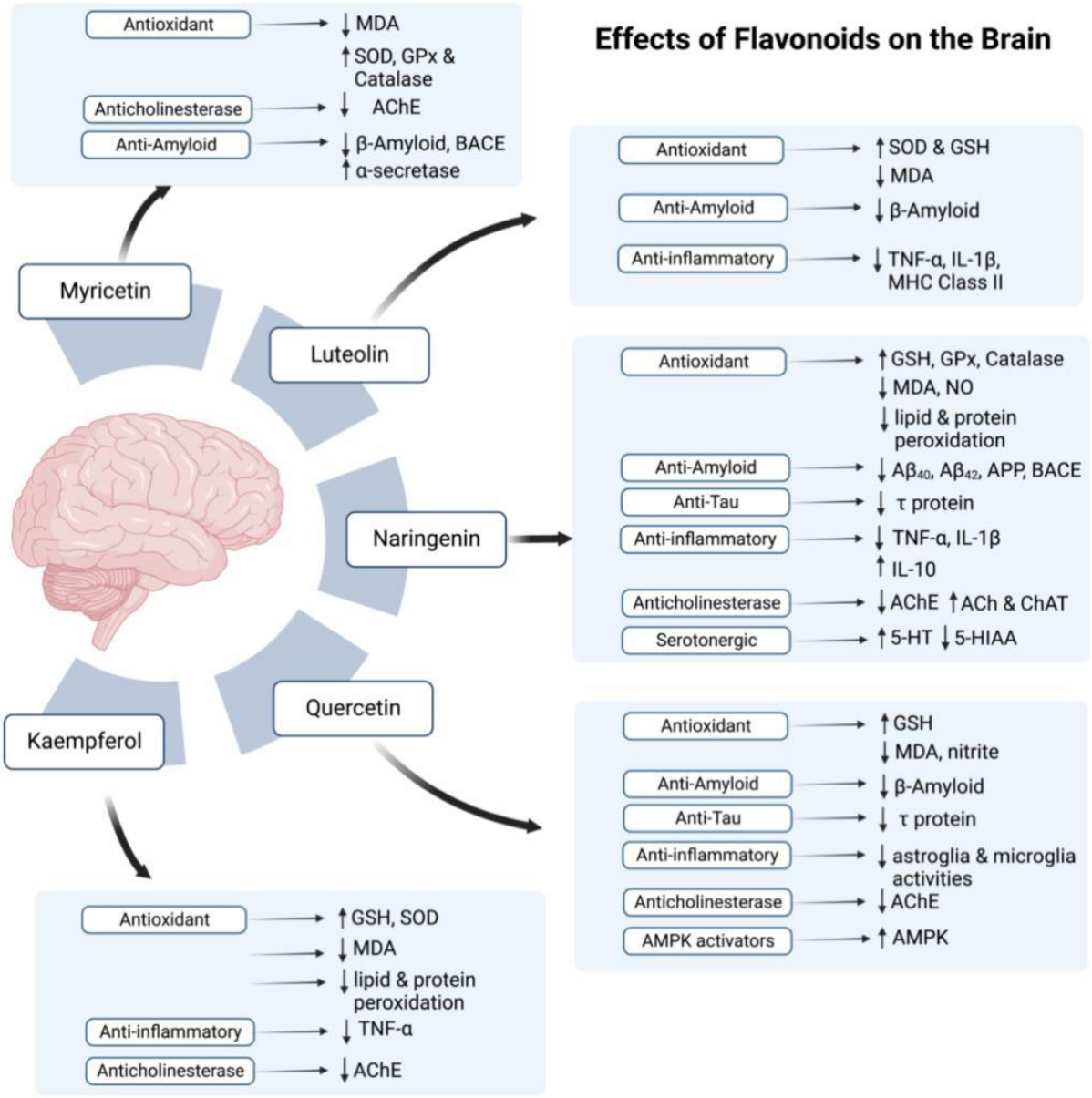


Figure 16: Effects of flavonoids on the brain.

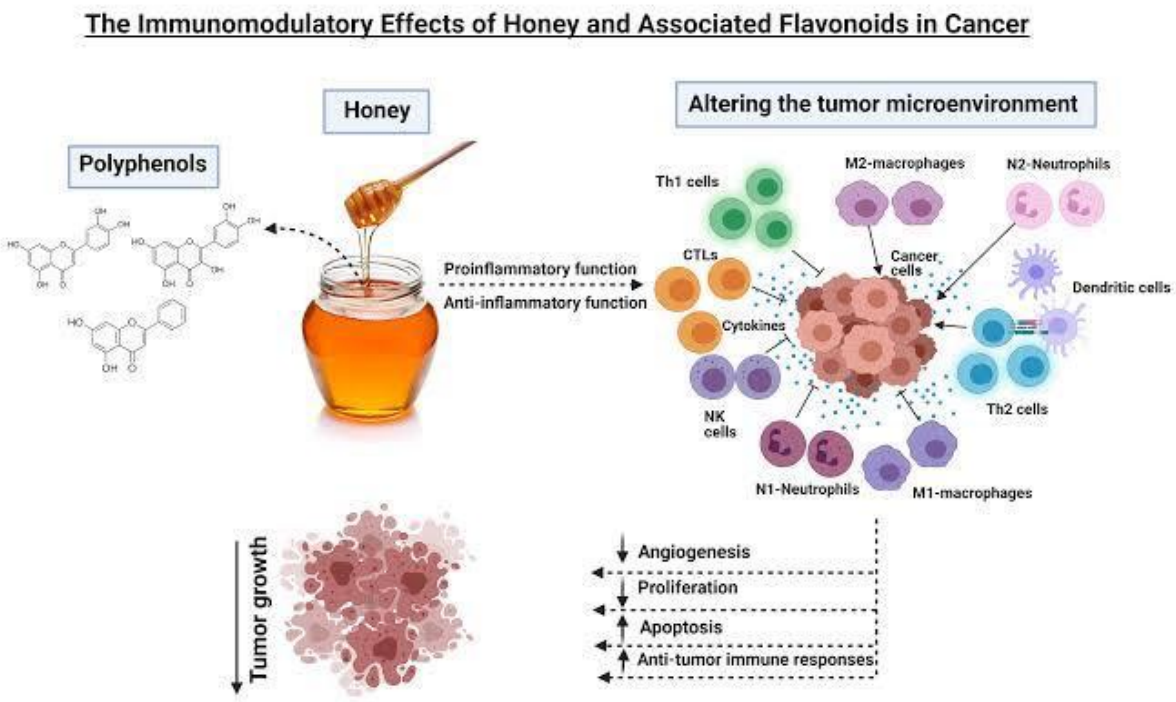


Figure 17: Benefits of Honey as a Nutraceutical.

Due to its nutraceutical qualities, which include antibacterial, bacteriostatic, anti-inflammatory, and wound and sunburn healing activities, honey has been investigated since the early 1970s. Many antioxidant and non-peroxide-dependent capabilities were also shown by recent investigations, in addition to those previously mentioned. The presence of polyphenols in it is one of the primary causes of these qualities, which can also offer highlights.

Considering the plant sources of the honey.

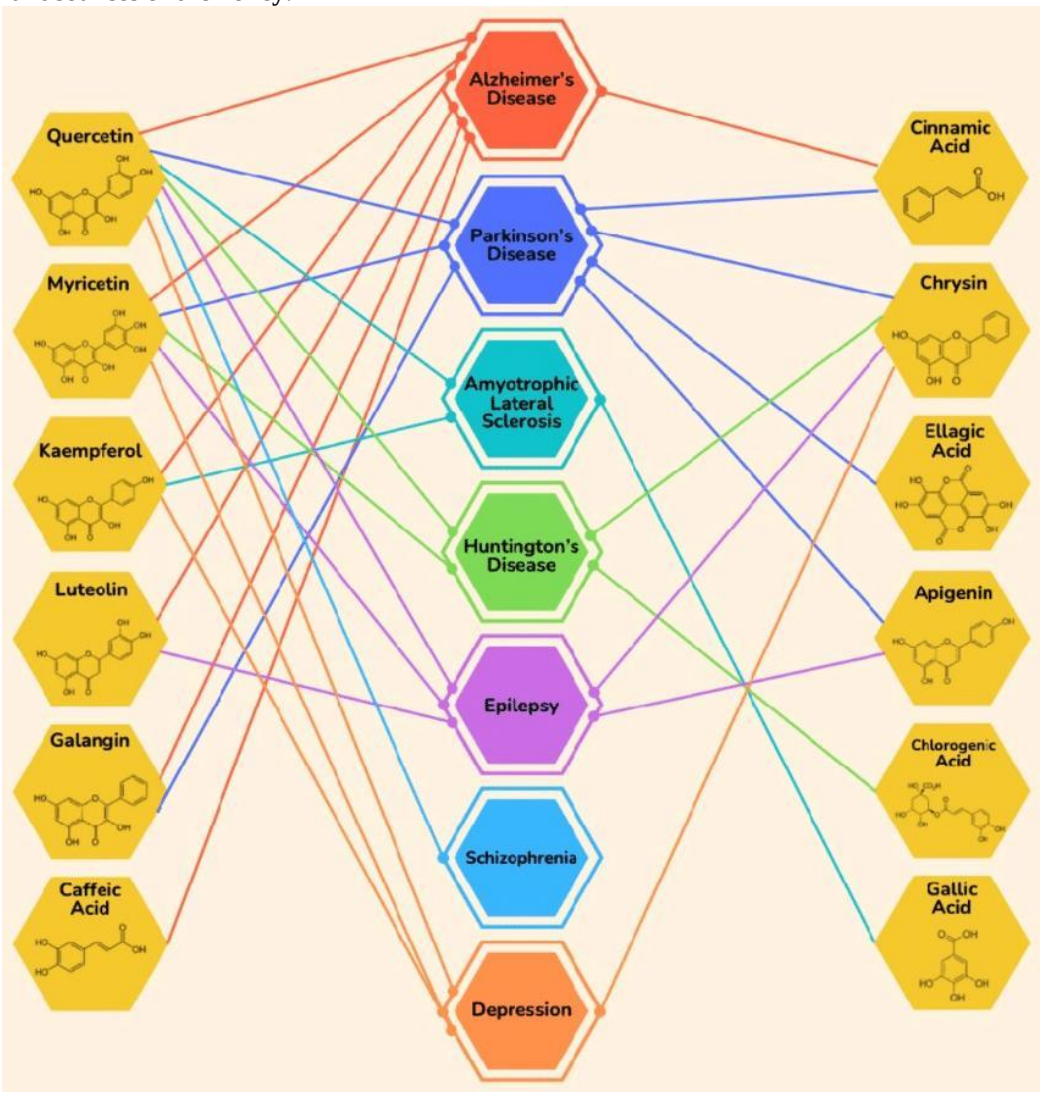


Figure 18:varied honey polyphenols' medicinal potential for treating various neurological diseases.

These essential polyphenols are present in a wide variety of honey varieties, indicating that honey may be an effective supplementary and alternative medicine for the management and treatment of a wide spectrum of neurological illnesses.
In neurodegenerative illnesses including Alzheimer's disease (AD), Parkinson's disease (PD), Huntington's disease (HD), and multiple sclerosis, the latter is crucial (MS). Increased oxidative stress brought on by reduced antioxidant levels, neuro-inflammation, prions, protein and mitochondrial malfunction, glutamatergic excitotoxicity, and genetic changes results in all of these conditions.
Nerve cell malfunction or death. As a result, honey's polyphenols can prevent neurodegenerative diseases in many ways.
(I) antioxidant effect in neurons
(ii) improvement of neuronal function and regeneration
(iii) defence against A-induced neurotoxicity
(iv) Defence against nitric oxide-induced neurotoxicity in hippocampal cells
(v) regulation of neuronal and glial cell signalling pathways Luteolin is one flavonoid found in honey.

This bioactive substance has a neuroprotective effect towards microglia-induced neuronal cell death that improves spatial working memory in old rats by preventing inflammation linked to microglia in the hippocampus. Another investigation found that luteolin improved baseline synaptic transmission, although

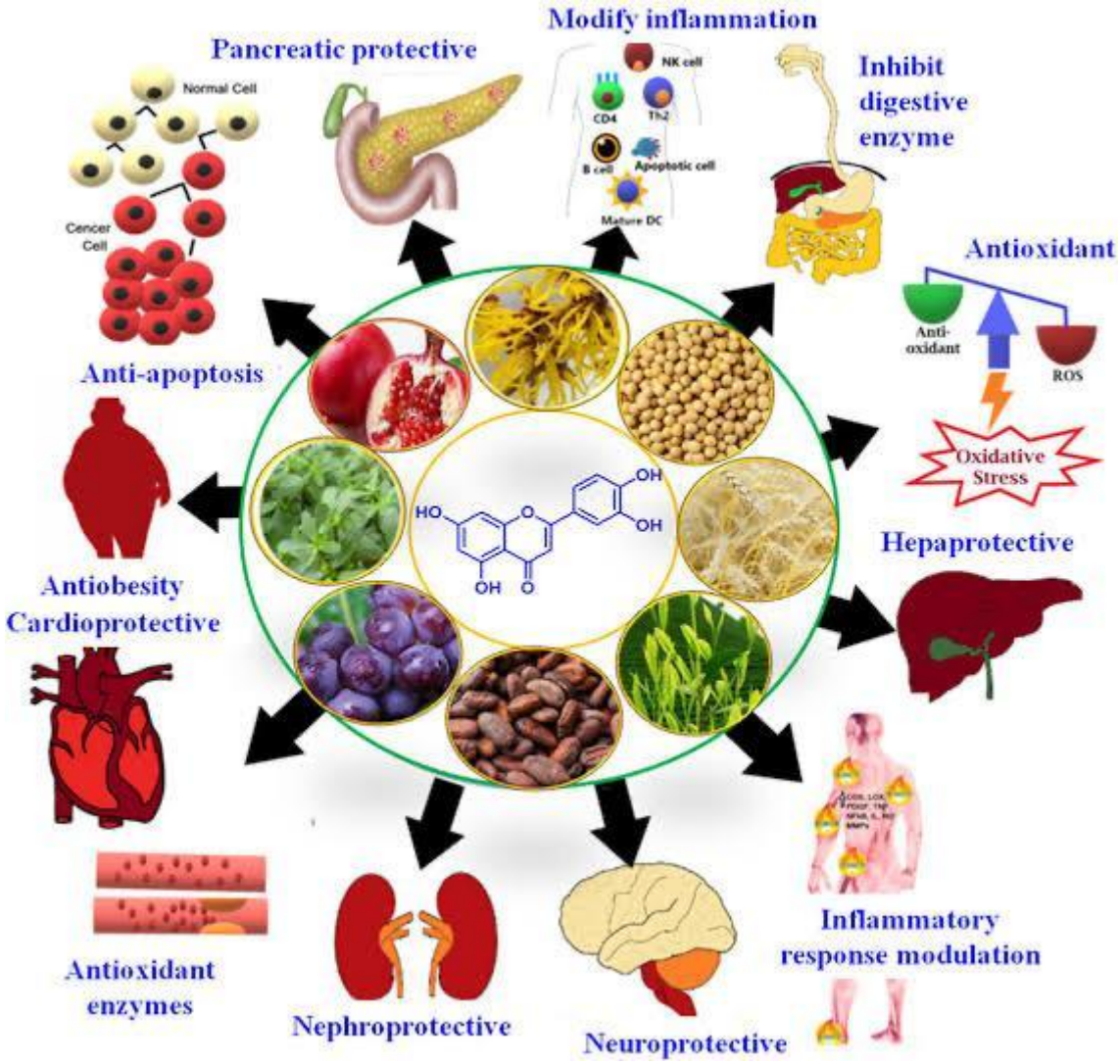


Figure 19: Dietary phenols as nutraceutical agents.

By both the activation of cAMP response element-binding protein (CREB), high-frequency stimulation induces long-term potentiation (LTP) in the oral gyrus of the rat hippocampus, protecting synaptic function and restoring memory in neurodegenerative illnesses. Lutein also protects against -amyloid-induced toxicity in rat-cultured cortical neurons, which is consistent with its neuroprotective function.

A flavonoid found in honey is Kaempferol. In Parkinson's disease mouse models brought on by the neurotoxin 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine, this chemical has a neuroprotective effect (MPTP). The latter causes behavioural and biochemical changes that are comparable to those seen in Parkinson's disease (PD), including behavioural abnormalities, a decrease in dopamine and its metabolites, a decrease in SOD and glutathione peroxidase (GSH-PX) activity, and an increase in

MDA concentrations in mice's substantia nigra. When mice were given kaempferol every 24 hours for 14 days in a row, the behavioural and biochemical changes significantly improved. The histochemical results showed that kaempferol reduced the loss of TH-positive neurons brought on by MPTP, providing further evidence of neuroprotection.

As phosphor-PDK1, phospho-Akt, and phospho-Bad levels fall and caspase-3 levels do not rise following a middle cerebral artery blockage, another polyphenol found in honey, ferulic acid, supports a neuroprotective action. Ferulic.

During brain ischemia/reperfusion damage in rats, the acid also had a neuroprotective effect against oxidative stress-related apoptosis by inhibiting ICAM-1 mRNA expression and by reducing the number of microglia and macrophages. Also, after transient-focal ischemia in rats, its anti-inflammatory and antioxidant capabilities were established.

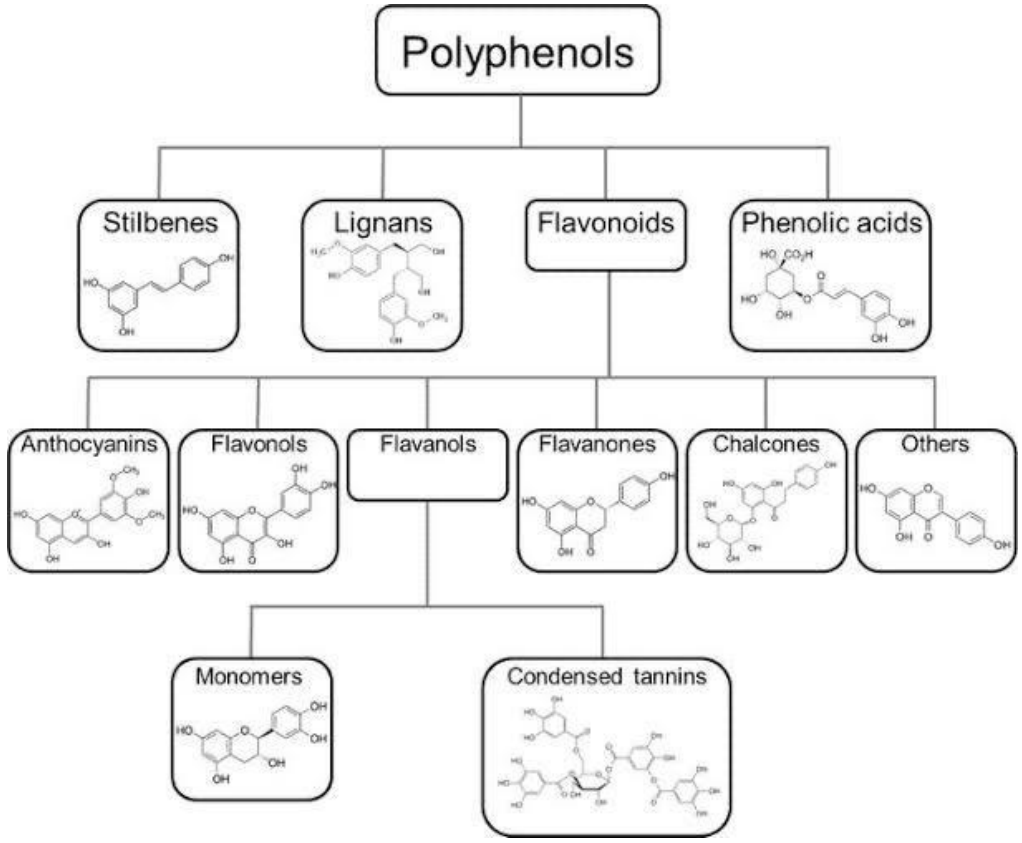
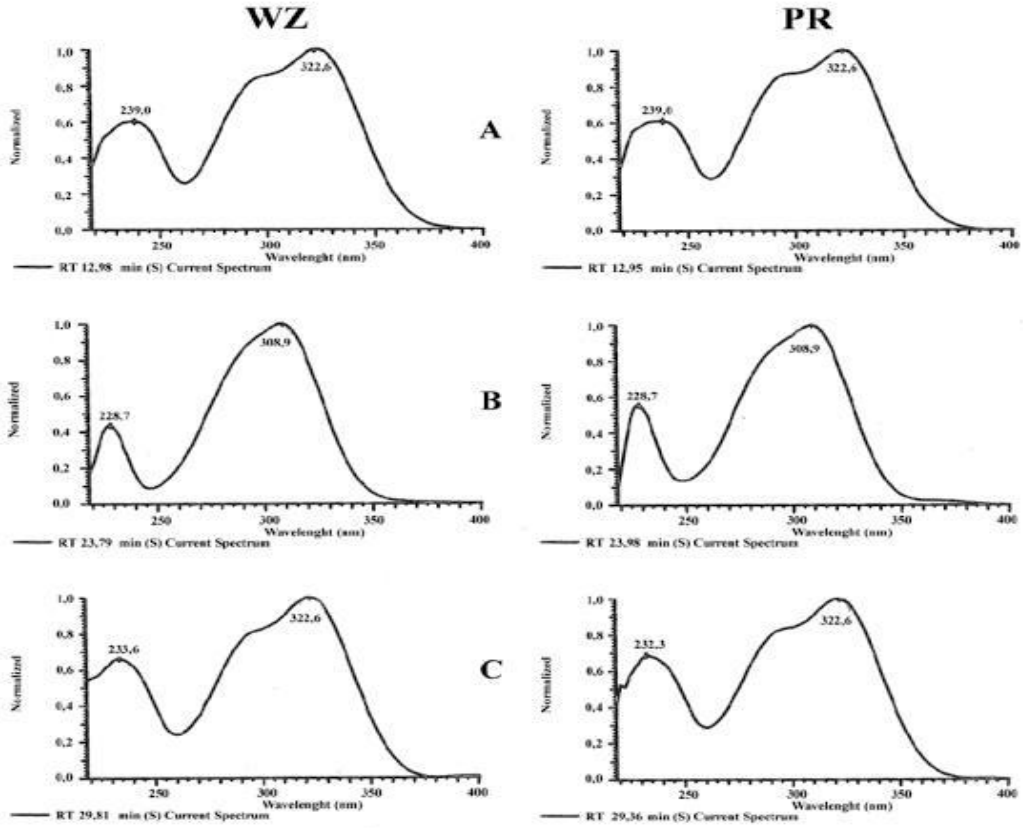


Figure 20: Classification of phenols.



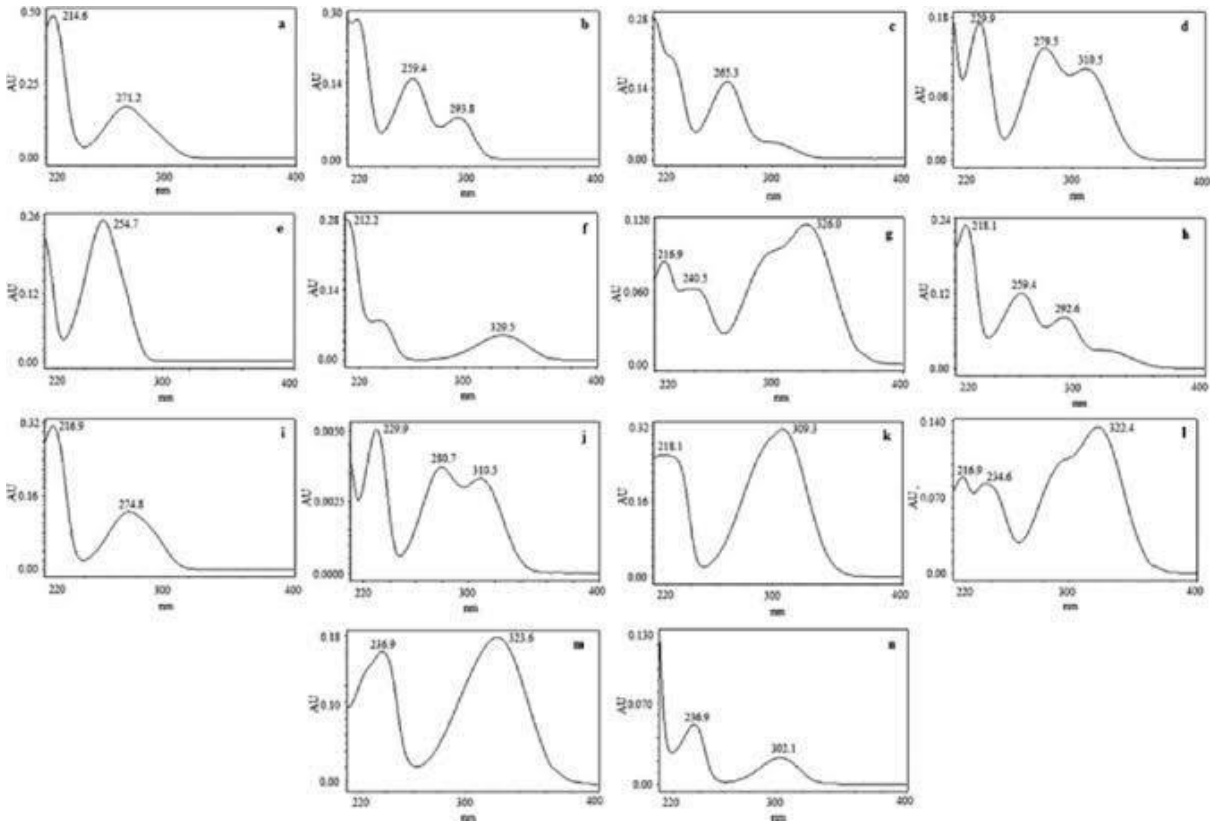


Figure 21:UV spectra (220-400 nm) of standard phenolic acids (WZ) isolated from Silphium perfoliatum L. (PR): Phenolic acids: A – caffeic, B – p-coumaric, C – ferulic, D – protocatechuic, E – p-hydroxybenzoic, F – vanillic, G – chlorogenicflava

On the other hand, pheochromocytoma-12 (PC12) cell lines are protected by chlorogenic acid, which is also found in honey, against methylmercury-induced apoptosis. Chlorogenic acid was used in this investigation to stop the production of reactive oxygen species.

(ROS), inhibiting glutathione peroxidase's (GPx) and glutathione's (GSH) lowering effect and attenuating apoptosis via activating caspase-3. By decreasing the activities of acetylcholine esterase and MDA in the hippocampus in addition to the frontal cortex in mice, it also exhibits neuroprotective benefits in scopolamine-induced learning and memory impairment, as reported by Kwon et al.

DISCUSSION

As of right now, despite the numerous studies and comprehensive evaluations conducted on dietary regimens and herbal supplementation for delaying or halting the progression of neurodegenerative disorders including.

AD, the available scientific data is still insufficient. Studies looking for possible nutraceutical therapies to either prevent or postpone cognitive decline and reduce the progression of AD have been quickly expanding, with several clinical studies having recently been completed or being planned. A combination of a healthy diet and regular exercise, for example, may help postpone the progression and risk of brain degeneration in AD, according to many important pieces of research. Since that researches are still underway today to determine the cause of AD, guidelines for its prevention and treatment should be changed accordingly. The study of neuro-nutraceuticals is still in its exploratory stages, and many doctors, neuroscientists, and other researchers are still thinking about it. With today's incredible advancements in neuroscience to uncover therapeutic advantages for degenerative disorders like AD, there has been a significant development in the identification of compounds, pharmacophores, and phytochemicals in the twenty-first century. Certainly, target molecule identification utilising high throughput technology is now being done. The various dietary supplements discussed in this review, such as the B vitamin group, the antioxidant vitamins C and E, Gingko Biloba, garlic, isoflavones, flavanols, curcumin, and resveratrol, Huperzine A, ALA, carotenoids, fish oil, and cyanidin, represent significant developments and show that found naturally bioactive compounds can be advantageous to the ageing brain. and have potential effects that might be used to help ameliorate crippling brain disease as well as cognition. The authors recommend more studies as a result.is required to investigate the usage of various neuro nutraceuticals in bigger populations of elderly people to obtain a verified result of its influence on whether it is a preventative or a cure for AD.

CONCLUSION

We have updated the main categories of dietary supplements with effects demonstrated in both the prevention and the therapy of Alzheimer's disease (AD). a huge expansion of bioactive substances in the treatment and prevention of this disease. In addition, we described the key data in favour of a unique multitarget Alzheimer's disease strategy. The mono-target strategies used now are insufficient for treating AD patients effectively. Nutraceuticals are now a beneficial alternative in this regard since they can affect many targets connected to the onset/development of AD. They can alter the gut microbiota, which affects the biochemistry of the central nervous system (CNS), the anti-aggregation characteristics of A and tau, and other aspects that are connected to AD.

Functional declines with age are partly determined by hereditary factors, and epigenetic variables also play a significant role. hence, the activity of these genes that cause vulnerability to AD can be minimized by leading a healthy lifestyle, practising physical activity, eating a balanced diet, avoiding drugs and other potentially dangerous substances, participating in social activities, and ageing actively throughout one's life cycle. Elderly people who are confined for an extended period may experience cognitive impairment. Our results imply that AD is a striking discontinuity with normal ageing. Understanding this process demands a systems biology-based approach.

Concerning all the research that is done until now, has helped reduce AD symptoms and research in the field of novel nutraceuticals should be continued to find and develop new compounds that can eventually find a new pathway for acting on tau&amylolid protein and finding a permanent cure for Alzheimer's disease and other neurological disorder.

Abbreviation

Alzheimer's disease **(AD**),
Parkinson's disease **(PD**),
Huntington's disease **(HD**),
lipoic acid **(LA),**
DemTect (Dementia Detection Test),
3-Acetyl-11-Keto-Beta-Boswellic Acid (**AKBA**),
Acetylcholinesterase (**AChE)**,
glutathione cysteine ligase modulatory subunit (**GCLM**),
Malonaldehyde (**MDA**),
anthocyanins (**ANT**),
controls AMP-activated protein kinase (**AMPK**),
Reactive oxygen species **(ROS),**
mitogen-activated protein kinase **(MAPK**),
Brain-Derived Neurotrophic Factor **(BDNF**),
G-Aminobutyric Acid (**GABA**),
Dopamine (**DA**),
and serotonin (5 hydroxytryptamines; 5 HT), Transmission Electron Microscopy (**TEM**),
Xylooligosaccharides(xos), C- reactive protein (**CRP**),
Blood-brain barrier**(BBB**),
Fructooligosaccharides**(FOS**),
Glucagon-like peptide-1 (**GLP-1)**

Author's contribution

Muhammad fahaam javidakhtar shaikh (Doctor of Pharmacy), is responsible for writing—original drafts and manuscript preparation, linguistic aspects, visualization, supervision and project administration.

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Conflict of interest

The author declares no conflict of interest.

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