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(REVIEW ARTICLE)

Functional foods and bioactive compounds: Roles in the prevention, treatment and management of neurodegenerative diseases

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Abstract

Neurodegenerative diseases are age related decline in the functionality of neurons and nerve cells hampering healthy ageing and associated with features such as learning shortfall, memory mishap, subjective decay and long term dementia. Biochemical underlying hallmarks include oxidative stress as a result of ROS generation and mitochondrial dysfunction, cholinesterase malfunction and inflammation of neurons. Neurodegenerative diseases represent a major threat to ageing population, as it is projected that in 2050, one in eighty-five individuals would have Alzheimer's disease. In this review, various functional foods were elucidated to possess bioactive compounds that exhibit neuroprotective activities via their: antioxidant, anti-amyloid aggregation, modification of monoamines and acetylcholinesterase inhibition amongst others. Lately, illuminating directions are towards frugal functional foods and bioactive compounds that would help the global populace as medicinal foods in the prevention, treatment and management of neurodegenerative diseases. This review attempts to evaluate the various functional foods, their bioactive compounds, their possible mechanism of action in the attempt to ensure healthy ageing, novel drug development and frugal neurodegenerative diseases management.

Keywords: Neurodegenerative diseases; Functional foods; Bioactive compounds; Alzheimer's disease; Parkinson's disease; Mechanism of action.

1. Introduction

It has been discovered that consumption of certain foods from plants and some other sources produce certain therapeutic effect, they possess bioactive compounds (such as polyphenols, alkaloids etc.), and their intake serve as a way of assessing their health benefits [1], such foods are referred to as functional foods. Many of these functional foods possess antioxidant activity and have been proposed to be beneficial in the management of Alzheimer's disease (AD) and Parkinson's disease, especially as cholinesterases, monoamine oxidase, and α-secretase inhibitors and prevention of α-amyloid aggregation [2,3].

Neurodegenerative diseases are characterized by loss of integrity of the neurons from the brain and spinal cord over a period of time and could lead to dementia [4,5]. The aging process originating from excess reactive oxygen species (ROS) production has been attributed to the global increase in neurodegeneration [6]. It is generally accepted that the brain is

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prone to oxidative stress because of the high level of fatty acids, high oxygen consumption, and low level of antioxidant defense [7,8,9].

Recently scientists and researchers have taken interest in foods with antioxidant-rich and health-promoting compounds as potential therapeutic agents [10,11]. Research evidences indicated that consumption of vegetables, fruits, teas, spices, and herbs is associated with reduced risk of several neurodegenerative ailments [12].

1.1. Functional foods

Functional foods, a general term used to refer to natural or processed foods containing bioactive compounds, can promote the health of a person beyond basic diets, or serve as a measure for prevention or treatment of chronic diseases.

In 2014, in the 17th international conference of functional food in health and diseases, functional food has been provided a new definition as natural or processed foods containing known or unknown bioactive components at the effective non-toxic dosage to execute clinically-proven or documented health benefit for the prevention, management or treatment of chronic diseases beyond the basic nourishments [13].

The increased research into the efficacy of functional foods is due to its health promoting activities as well as its reduced side effects. Thus, an increasing number of people have the high requirement for healthy foods or functional foods in many parts of the world [14]. Chinese medicinal foods have been favorited for thousands of years. Nowadays, the development in scientific research sustains the idea that the diet exerts a beneficial role in chronic diseases [15].

Healthy ageing is only made possible with preventive medicine of which diet is a critical factor. This simply means that food and its adjuncts can be of great importance to medicine. The use of functional foods is considered a cheap and practical approach to the management of neuronal diseases. Functional foods are mostly whole, fortified, enriched or enhanced foods that provides health benefits beyond the provision of essential nutrients [16]. Foods from plant sources are rich in bioactive phytochemicals such as polyphenols, alkaloid, etc. and their consumption present a passive mode of assessing their beneficial effects [3].

Bioactive compounds, the medicinal component in functional foods are not only essential and important, but also indispensable for health promotion, and the prevention or treatment of chronic diseases [17]. The bioactive components in functional foods usually have therapeutic effects, including antioxidant, anti-inflammatory, hypolipidemic, glycemic-regulating, cytoprotective, and neuroprotective functions [18].

1.1.1. Classification of functional foods

Functional foods have been considered as foods made up of nutrients that confer physiological or medical benefit to the consumers [19]. In fact, any healthy food confirmed to have a health promoting or disease preventing property beyond the basic functions of supplying nutrition is now regarded as a functional food [13]. Classification of functional foods as elucidated here serves as a generalized classification of foods with the essential bioactive compounds responsible for the therapeutic effects that birth their name.

Plants and herbs

There is growing requirement for antioxidants from plants and herbs in preventing and combating several chronic diseases. Several herbs and spices have been reported to exhibit antioxidant activity, including thyme, nutmeg, turmeric, white pepper, chili pepper, ginger, Indian medicinal plants and several Chinese medicinal plant extracts [20,21]. Medicinal plants often contain phenolic compounds, such as flavonoids, phenolic acids, tannins etc. These compounds have various therapeutic functions and antioxidant activities [22].

Animal sources

These include calcium, probiotics and whey proteins from dairy products; n-3 fatty acids from fish; conjugated linoleic acid from beef and lamb meat; sphingolipids from eggs and the conditionally-essential nutrients L-carnitine, coenzyme Q, alpha-lipoic acid, choline and taurine, widely diffused in animal products. Even though functional food is a new and growing line of study, evidence has shown that these animal sources provides medicinal advantages.

Value added foods

Value added food are those that have been scientifically modified from the post-harvest stage of production to improve functionality [23]. They are sometimes termed ‘designer foods’ and the enhanced phytonutrients usually make them

more beneficial health wise [19]. They include foods that contain added nutrients which have therapeutic relevance and sometimes, they are foods which have been modified to remove constituents which may be harmful to the well-being of certain individuals.

1.2. Bioactive compounds in functional foods

Functional food bioactive compounds are extra-nutritional constituents that mostly occur naturally in plants and in other organisms as well and can exert biological effect [24]. The intake of natural dietary bioactive compounds is associated with low incidence of chronic diseases [25,26]. Epidemiological, clinical, and biochemical studies have revealed that these bioactive compounds through different mechanisms have various activities in the human body such as antioxidant, antidiabetic, antihypertensive, anti-alzhemic, anti-proliferative, anti-cancer and antimicrobial activities [27,28,29].

1.2.1. Phytochemicals

Polyphenols are one of the most studied phytochemicals and they comprise a wide family of molecules bearing one or more phenolic rings and are present in many food sources like wine, green tea, grapes, vegetables, red fruits, and coffee [30]. Several classes of phytochemicals have been proven to confer tremendous health benefits. The carotenoids and flavonoids have been especially implicated in the prevention, control and management of chronic diseases [19].

1.2.2. Vitamins

Vitamins are major constituents of foods and fruits, they are either fat soluble or water soluble, they are present in high amounts in some foods. They possess essential medicinal roles in tackling and managing various diseases. They are required in small amounts and are obtained from a correct diet [31].

They have been shown to possess diverse therapeutic effects, for example; Vitamin E is a fat-soluble vitamin with high antioxidant potency. Because it is fat-soluble, Vitamin E (specifically α-tocopherol) safeguards cell membranes from damage by free radicals. Its antioxidant function mainly resides in the protection against lipid peroxidation [32]. The dietary sources of vitamin E are vegetable oils, wheat germ oil, whole grains, nuts, cereals, fruits, eggs, poultry, meat [33].

1.2.3. Dietary minerals

Selenium (Se) is a trace mineral found in soil, water, vegetables (garlic, onion, grains, nuts, soybean), sea food, meat, liver and yeast [34]. At low dose, health benefits of Se are antioxidant, anti-carcinogenic and immunomodulator [35].

Calcium is another mineral with beneficial effects that includes the prevention and treatment of diseases such as osteoporosis (together with vitamin D), colorectal cancer [36], kidney stones, preeclampsia, and lead toxicity. These are a few of several minerals with health benefits found in foods.

1.2.4. Essential fatty acids

Omega-3 fatty acids are essential long-chain polyunsaturated fatty acids because human beings cannot produce them. Omega-3 fatty acids can be found in fishes such as salmon, sardines and tuna, it can also be found in walnut and flaxseed. Omega-3 fatty acids prevent chronic diseases such as cardiovascular diseases, dementia, depression, arthritis, stroke, cataract, cancer and neurodegenerative diseases.

1.2.5. Functional sugars

Trehalose, a natural sugar, is widely produced in non-mammals such as fungi, yeasts, and similar organisms. It can maintain cell integrity by preventing denaturation of proteins [37]. Functional fibers such as inulin, cellulose, and maltodextran isolated from foods where they occur naturally are often added to processed foods to help improve their nutritional profile. Dietary intake of fibers has many potential health benefits including prevention of chronic diseases [38].

2. Neurodegenerative diseases

Neurodegenerative diseases are for the most part age-related and irreversible diseases which are described by learning shortfall, memory decline, subjective decay and irregular conduct [39]. Morphological examinations have indicated that neurodegeneration is related with misfolding and accumulation of proteins which can prompt the deposition of senile

plaques and fibrils around the neurons [40]. Oxidative stress adds to neurodegeneration and assumes a significant role in the pathogenesis of neurodegenerative issue, for example, Alzheimer's disease (AD) and Parkinson's disease (PD) [7]. Trial examinations have demonstrated that oxidative stress and protein aggregation triggers a course of occasions which prompts neuronal death in various neurodegenerative disorder [40]. Beta amyloid aggregation promotes the creation of free radicals which could lead to oxidative harm to neurons, aggravation, neuronal inflammation and synaptic dysfunction [41]. The neurons are defenseless against oxidative stress due to their presentation to high level of oxygen and its by product [40]. The brain is rich in metal particles which could amass as a result of ageing and can be an agent of free radicals, lipid peroxidation and oxidative harm to the cerebrum tissue [27]. The cell reinforcement guarded instrument in the brain is poor and hence constrains its defensive mechanism against free radical assault. Under ordinary conditions, the cells can balance free extreme assault by means of the guideline of homeostatic equalization. Be that as it may, during the progression of neurodegenerative conditions, cell limit to keep up the redox balance diminishes, prompting the amassing of free radicals, and thus oxidative stress [42]. It is broadly acknowledged that oxidative stress is a significant factor to a few neurodegenerative diseases, for example, AD and PD [43]. The etiology of most neurodegenerative disease is ineffectively comprehended and has not been completely investigated. Nonetheless, a few reports have indicated that increment in the action of certain chemicals, for example, monoamine oxidase (MOA) and cholinesterases (ChEs) may prompt loss of dopaminergic and cholinergic synapses [44,45]. Acetylcholinesterase (AChE) is the key enzyme protein answerable for breakdown of acetylcholine. Inhibition of AChE is viewed as one of the objectives for the treatment of AD [46]. The most endorsed drugs for treatment of AD are the cholinesterase inhibitors [47]. This has prompted the persistent and complete quest for novel inhibitors from plant sources to find candidate for drug development [48]. Consideration has as of late been moved by food scientist researchers and analysts to tropical plant food sources with cell reinforcement rich and wellbeing advancing phytochemicals as potential therapeutic agents [10,11].

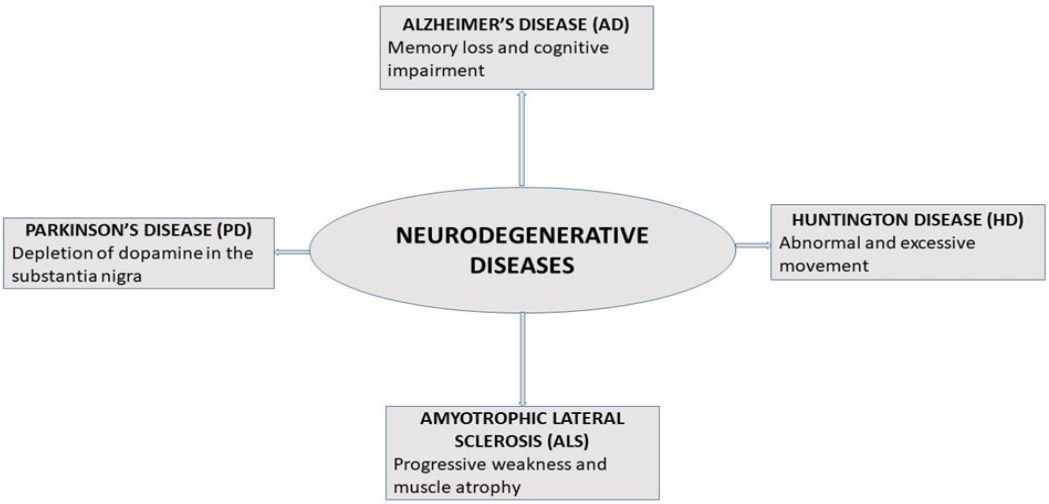

Figure 1 Overview of Neurodegenerative diseases

Both trial and epidemiological proof have shown that utilization of vegetables, natural products, teas, flavors, furthermore, herbs is related with the prevention of a few neurodegenerative diseases [49, 12, 50]. Acetylcholinesterase (AChE) is a compound bound to the membrane and hydrolyzes the synapse acetylcholine (ACh) into choline and acetic acid derivation after their capacity in cholinergic neural connections at the brain region [51,52]. The reaction of AChE to oxidative stress may prompt the occurrence and pathogenesis of an assortment of focal sensory system issue, for example, stroke, Alzheimer's sickness, and diabetes mellitus [53]. The examination on the conceivable effect of protocatechuic corrosive uncovered that protocatechuic modified Na+/K+-ATPase, cholinergic, and antioxidant markers in rodents. It was additionally detailed that alkaloid extricates from shea margarine and breadfruits had the ability to hinder monoamine oxidase, cholinesterase, and lipid peroxidation in an *in vitro* model [55].

2.1. Development stages of neurodegenerative diseases

The three developmental stages of neurodegenerative diseases (NDDs) and the symptoms.

2.1.1. Retrogenesis

The start of NDDs is the breaking down of the cholinergic arrangement of the basal forebrain, which elevates to the Entorhinal Cortex and the Hippocampus that are responsible for the short and the long haul memory. These alter the brain which for the most part begins 10-20 years ahead of time and the principal noticeable indication of NDDs is neglect or a few issues in present moment memory [55]. Side effects may incorporate improved memory mishaps, challenges in recognizing relatives. The disease with its movement begins influencing the cerebral cortex coming about in the type of a further abatement in cognition and balance. This stage is connected with the clinical finding of NDDs in patients which incorporate loss of recognizable spots, losing choice force, losing significant things, state of mind and character changes, whimsical activities in office, expanded uneasiness. Extra atrophy in the chosen portion of the cerebral cortex brings about the type of difficult issues with language, tangible neurons, and thinking [56].

2.1.2. Intellectual Dysfunction

There is an association among neurodegeneration and lethal proteins. This is associated with expanding obsessive neurofibrillary plaques and tangles in the entorhinal cortex (EC), caudate, substantia nigra. These proteins assume a pathogenic role in the progression of NDDs which prompts neurons degeneration and intellectual dysfunction. The Entorhinal Cortex (EC) is that portion which gets affected due to Alzheimer's. It has been archived that so as to keep the memory alive the correspondence between the Entorhinal Cortex (EC) and the hippocampus is extremely indispensable and any trouble between these two districts upsets the circuit and leads towards memory confusion and memory harm. It is reasoned that EC is the fundamental center which is increasingly powerless against NDDs and these diseases proliferate with the system of neurons [57].

2.1.3. Stride Abnormality

Predicting an unsettling influence in step action shows an unsettling influence in intellectual capacities. A term has been proposed, " Last-in-First-out" which alludes to the marvel in which the neural circuits develop late in the formative life cycle are progressively powerless against neuro-degeneration and this idea helps in early expectation of any sort of dementia (neurodegenerative diseases) expressed that a solid movement pattern need input not just from the neurological framework connected to motor and tangible neurons yet additionally from cortical procedures for example to judge, plan and a spatial mindfulness [58]. Unsettling influences in psychological work have an immediate connection with more elevated level step aggravations and it is one of the significant side effects of cerebrum disorder [59].

2.2. Mitochondria dysfunction in neurodegenerative disease

The mitochondrion gets most affirmation for its role in creating vitality for cells in the body and they are known as the powerhouse. Inconceivably, the mitochondria in our cells has drawn a lot of attention from scientists, the most in the ongoing decade for its role in various life forms [60, 61]. Mitochondrial dysfunctions are ascribed to either innate or changes in mitochondria DNA or nuclear DNA which lead to altered proteins or on the other hand mitochondria RNAs. Despite when tissue-explicit isoforms of mitochondrial proteins are placed into thought, it is hard to explain the variable examples of impacted organ systems in the mitochondrial disorders. Since brain and muscle cells require a critical sum of energy, they contain high thickness of mitochondria to help their energy demand [62]. Lately, it is recommended that mitochondrial dysfunction may be significant in a wide scope of wellbeing conditions, for example, Parkinson's disease, bipolar disorder, schizophrenia, autism, diabetes, asthma, incessant exhaustion disorder, Alzheimer's disease, a variety of gastrointestinal diseases [63,64,65]. Various triggers can prompt mitochondrial dysfunction coming about into the side effects of NDD. A portion of the triggers incorporate; hereditary varieties, deficiencies of fundamental nutrients and minerals, xenobiotic, certain microscopic organisms and infections and stress [66]. Loss of efficiency in mitochondria is inclined to a few signs including impaired vision, visual debilitation and other ordinarily experienced indications of diseases. According to the structure and elements of the powerhouse, consumption of capacity emerges from the failure to keep up the transmembrane potential and electrical signs of its inward film. This at that point influence the progression of electron and additionally metabolic response/pathways. Bringing about decrease in energy [67,68].

Mitochondrial dysfunction is portrayed by aging, and basically, of every incessant chronic disease including NDDs [69,70]. One of the results of mitochondria dysfunction is the generation of ROS, created as a metabolite of oxidative phosphorylation. The basic starting point of ROS and the related reactive nitrogen species (RNS) are mitochondria, and these free radicals can harm biomolecules. Be that as it may, antioxidant agents and superoxide dismutase proteins (SOD) have the capacity to hinder the activities of ROS/RNS [71,72]. Responses of the electron transport chain can likewise start uncoupling proteins, which could result in a hole of protons back over the proton slope of the matrix of the mitochondrial into the framework [73,74].

Neurons in a general sense depend on mitochondrial capacities with regards to long distance stream of mitochondria to the neurotransmitter, confinement, and evacuation of flawed mitochondria from synaptic locales and metabolic requests that require high vitality stream yields and consistently associated with the age of ROS. Steady development of ROS prompts oxidative harm and hindered proteostasis inside mitochondrial compartments [75, 76] (Jaiswal, 2013; Jaiswal, 2014). This thusly changed the equalization of mitochondria elements driving to pathogenesis. This is the premise of the mechanism by which mitochondria dysfunction causes neurodegenerative diseases.

A few examinations have called attention to the contribution of mitochondrial dysfunction and its stressors in NDDs most particularly in Parkinson's disease and related issues [77,78]. Mitochondrial dysfunction is an amazing reason for degeneration contrasted with oxidative harm in some of Parkinson's and related illness model [79]. Mitochondrial stressors which are lately studied to cause Parkinson's disease however, presumed that more data is basic to adequately grasp the capacity in Parkinson's disease pathogenesis. Any cancer prevention agent most particularly plant-based cell reinforcement that can target mitochondria will be an ideal treatment for neurodegenerative diseases. Various investigations are in progress most particularly the potentiation of energy creation, preventing oxidative stress by scavenging reactive oxygen species [80].

2.3. Alzheimer's Disease (AD)

AD is the commonest perceived NDDs [81]. Fruitful discovery in medicine have expanded the normal life expectancy, bringing about a maturing populace. Since AD and most NDDs are maladies of ageing, the pervasiveness is attempted to keep on expanding later on and the disease is suggested to affect 1 out of 85 individuals on the planet by 2050 [82].

Alzheimer's affiliation evaluated that one of every eight Americans above age of 65 years and half of the Americans above age of 85 years have been directly experiencing this devastative neurodegenerative disorder [83]. According to this estimation, the quantity of patients may arrive at 16 million by 2050 [84,85] subsequently expanding the monetary expense of Alzheimer's disease (AD) social insurance framework, which is 80-100 billion dollars presently [83]. Loss of cholinergic neurotransmitters in hippocampus and neocortex has been a reliable finding in AD, along these lines complementing the need to utilize a significant system that manages the AChE capacity to battle this defect. Tacrine, donepezil, and rivastigmine are a couple of AChE inhibitors endorsed by U.S. Food and Drug Administration for the modulation of AD symptoms [86]. Although new set of such inhibitors has been compelling in work yet there has been expanding need to search for new drugs.

Alzheimer issue are particularly portrayed by dynamic intellectual degeneration, and pathologically by the nearness of decrepit plaques (amyloid-β peptide (Aβ)) and neurofibrillary tangles made out of hyperphosphorylated tau. Around 5–10% of cases are familial, happening in a beginning stage, autosomal-prevailing example. These proteins (amyloid precursor protein, presenilins 1 and 2) are identified with the commonplace instances of AD [87]. The risk components of AD incorporate ecological and hereditary variables. Apolipoprotein E quality has been identified with the pervasiveness of non-familial, sporadic Alzheimer's [88].

Alzheimer's Disease (AD) is portrayed as a ceaseless and dynamic neurodegenerative disease with well-defined pathophysiological mechanism, for the most part affecting average temporal lobe and associative neocortical structures [89]. Since its revelation a few hundred years ago, AD continues to present issues for affected families and society, particularly in developing nations [90]. AD starts bit by bit; propels; and inevitably prompts disarray, character and conduct changes, and impeded judgment. Lost autonomy, confused eating conduct, and weight reduction may go with different side effects [91]. Manifestations of AD bring about a dynamic dementia, with expanding loss of memory, scholarly function, and unsettling influences in discourse. People with poor physical function have appeared to be at a higher hazard for developing dementia and AD [92].

Diminishes in the endogenous degrees of neurotrophic factors have been appeared to increment the vulnerability of neurons to oxidative stress, what's more, have been credited to brought down synaptic thickness. As is the situation with other neurodegenerative diseases, the nearness of DNA fragmentation, caspase initiation, and the declaration of different apoptosis-related qualities has been portrayed [93] Be that as it may, especially in Alzheimer's disease, the present information are opposing. For instance, it is as yet hazy whether the apoptotic procedure is legitimately answerable for the passing of neurons. Despite the fact that apoptosis may not be the essential driver of neuronal degeneration in Alzheimer's ailment, customized cell demise may add to the proceeded with movement of malady pathology [94].

In the light of this reality, polyphenolic mixes from foods grown from the ground have been explored in view of their potential antioxidative properties. [95, 96]. There has been developing spotlight on conventional natural medications

directly since the disappointment of existing treatments. [97]. The first neurotransmiter saw as associated with AD is acetylcholine [98]. Therefore, there have been complex studies to utilize AChE inhibitors. Plants give abundance of bioactive mixes, which apply a considerable system for the treatment of neurological diseases, for example, Alzheimer's disease. [99]. It has been as of late demonstrated that a Chinese herb, Yizhi Jiannao Granules is compelling in improving AD side effects, what's more, it additionally disturbs such improvement when consolidated with acupuncture [100]. Zeatin has been found to have a defensive role against Aβ-prompted neurotoxicity in PC12 cells and enhance scopolamine-incited amnesia in ICR mice [101].

2.4. Parkinson's Disease (PD)

PD, positioned second most basic NDD succeeding AD, is depicted clinically by dynamic inflexibility, bradykinesia, and tremor, and by loss of pigmented neurons in the substantia nigra in the midbrain and the existences of Lewy bodies pathologically [94]. Internationally as at 2006, more than 4 million individuals of a normal age of 60 years are living with PD furthermore, this occurrence is higher in male contrasted with female [102]. The lower impact in females might be most likely because of higher estrogen focus. A few bits of proof from after death inquire about showed that numerous procedures are related with apoptosis or necrosis, including oxidative stress, mitochondrial dysfunction, neuroinflammation, excitotoxicity and collection of misfolded proteins due to proteasomal and autophagic disarranges [103].

2.5. Huntington's disease or Huntington's chorea (HD)

It is a dynamic neurodegenerative (autosomal predominant) ailment situated in the basal ganglia described by choreiform development, dystonia, dementia, mental issue, and enlargement of the ventricle. This ailment is connected with the precarious development of a trinucleotide cytosine, adenine, guanine (CAG) repeats in the Huntington gene [104]. Glutamine (Q) encoded from this CAG rehash is communicated in the HTT protein as a Poly-Q stretch close to its N terminal [105]. Commonly, healthy individuals acknowledge under 26 CAG repeats in their HTT gene bringing about typical HTT working in vesicle movement and endocytosis [106]. These misfolded and atypical mHTT protein can't exercise its survival roles. The features incorporates cleavage and conglomeration arrangement of misfolded mHTT in the core of cell, cytoplasm, and neurites [107]. Strangely, notwithstanding the set up association of the capacity of ROS and oxidative stress in Huntington disease, preliminaries endeavoring to treat the illness utilizing great cell reinforcements have to a great extent been insufficient [108].

A few perceptions pinpoint apoptotic neuronal passing in the striatum over the span of Huntington's sickness. They were first to appear DNA strand breaks in these neurons [73]. Be that as it may, DNA strand breaks ended up being a vague marker for apoptosis. Furthermore, transformed huntingtin was appeared to activate the JNK flagging pathway prompting consequent neuronal apoptosis [109]. Excitotoxicity is considered a pathogenetic factor in Huntington's ailment.

Besides, huntingtin has been exhibited to be a substrate for the effector caspase-3, with the polyglutamine succession in the transformed protein being supported for cleavage by caspases eventually coming about in cut particles with expanded neurotoxicity [77]. With respect to caspases, the restraint of caspase-1 end up being of advantage during the course of the illness in a mouse Huntington model. As of late, it has been demonstrated that transformed huntingtin has a diminished proclivity for its coupling accomplice Hip-1 (Huntingtin interfacing protein-1 [110]. Free Hip-1 associates with HIPPI (Hip-1 protein interactor) by means of its pseudo-DED area and moreover ties the DED protein caspase- 8 of a complex, whereby the apoptotic course is perhaps started [79]. Since there is no causal treatment for Huntington's sickness up until this point, regulation of the apoptotic course is viewed as a promising remedial intercession.

2.6. Amyotrophic sidelong sclerosis (ALS) or Lou Gehrig's illness

ALS additionally was known as motor neuron illness is described by dynamic loss of engine neurons in the front horn of the spinal string [111]. In familial ALS, about 20% of the cases came about because of transformations in SOD1. The elements of SOD1 are assorted and incorporate searching extreme superoxide radical subsequently adjusting cell breath, vitality digestion, and posttranslational adjustment. ALS disorders can be deadly when delayed leads to wasting of respiratory and motor neurons [112].

Similar to the case in other neurodegenerative disease, oxidative pressure, the overactivation of glutamate receptors, also, calcium over-burden are viewed as conceivable causative systems. In autosomal-prevailing acquired cases (around 5% of all ALS patients) a change in the quality coding for superoxide dismutase could be distinguished. This compound physiologically applies hostile to oxidative and cytoprotective impacts going about as free extreme scrounger. There are four unique theories, how superoxide dismutase can act neurotoxic [113]: (1) the development of hydroxyl radicals; (2)

the nitrosylation of tyrosine buildups in proteins by peroxynitrite derivates; (3) copper and zinc poisonous quality, also, (4) obsessive protein accumulation with the arrangement of incorporation bodies. In any case, these present speculations all point to expanded oxidative pressure, prompting mitochondrial dysfunction and the initiation of the characteristic apoptosis course in the separate neurons. Expande articulation of the expert apoptotic protein Bax, with a simultaneous decline in the statement of Bcl-2, just as DNA fracture have been found in transgenic mouse models of ALS [114,115]. Besides, expanded caspase-1 and - 3 movement has been found in the engine cortex and spinal strings of patients. Moreover, dynamic caspase-3 was distinguished specifically in ventral horn neurons of those people [116].

ALS is additionally underscored by discoveries that caspase inhibitors were neuroprotective both in animal and tissue culture models of the diseases [113]. At last, a commitment of the p53 tumor silencer quality to the degeneration of motor neurons has been proposed; in any case, this idea is disputable.

3. Mechanism of action of functional foods on neurodegenerative diseases

The various mechanism of actions of functional foods in the prevention, treatment and management of neurodegenerative diseases are elucidated below.

3.1. Cholinesterase Inhibition

Developing lines of proof recommends that among 73 local and naturalized plants gathered from the focal district of Argentina, natural divisions got from concentrates of Achyrocline tomentosa (Marcela) (Asteraceae), Eupatorium viscidum (Common boneset) (Asteraceae), Ruprechtia apetala (manzano del campo) (Polygonaceae), Trichocline reptans (arnica) (Asteraceae), and Zanthoxylum coco (cochucho, coco) (Rutaceae) exhibited significant restraint of AChE (higher than 80%) [99] Poncirus (Trifoliate Orange) extricate has been appeared to repress AchE considerably[83]. Methoxsalen disconnected from restorative herbs Treculia obovoidea (Caterall) and Angelica archangelica (Garden Angelica), shows antimicrobial and hostile to AchE activities in vitro. [117,118]. Studies on the seeds of Cassia obtisufolia demonstrated their neuroprotective role in mice by means of attenuation of optional Ca2+ dysregulation and mitochondrial toxin 3-NP. Moreover, they can improve memory debilitation through AChE inhibition. [97] Flavonoids, a gathering of phenolic mixes which show antimutagenic, anticarcinogenic, and antiageing properties [119,120] might be liable for neuroprotective role of Cassia obtusifolia extracts. Dried ginger has been appeared to incite Ca2+ hostile movement and butylcholinesterase inhibitory action which are compelling in AD treatment [121].

3.2. Change of Monoamines Activity

Moringa oleifera (MO) which has a place with the family Moringaceae, is pervasive practically everywhere throughout the Asian and African nations. Its products of the soil which show calming and hypotensive impact are expended as nourishment by the people. [122]. It has been found as of late that Moringa oleifera leaf extract which is not harmful even at higher fixation levels, improves memory through nootropics movement and gives considerable cell reinforcements like nutrient C and E to battle oxidative worry in AD. [123,124] Wealth of studies proved that monoamines involved in the memory decline are modified by Moringa oleifera leaf extricates [125]. Several lines of proof additionally propose that colchicines-prompted AD can be enhanced by ethanolic concentrate of Moringa oleifera by altering the mind monoamines (norepinephrine, dopamine, and serotonin) and electrical action in a rodent model.

3.3. Anti-amyloid Aggregation Effect

Ginkgo biloba being a potential storage facility of cell reinforcements offers plentiful of medical advantages to AD patients like antiamyloid accumulation impact. Extensive examinations on Ginkgo biloba uncovered that 240 mg of Ginkgo biloba every day can diminish the rate of AD. Although there are a couple of considerable investigations on Ginkgo biloba to improve AD indications and overall deals of it surpass $249 million yearly in the United States, [126] yet there has been enlarging need to start all the more encouraging clinical preliminaries right now. It has been discovered that the Ginkgo biloba removes enhance subjective imperfections in a mouse model of AD (Tg2576). Manifold clinical preliminaries demonstrated enhancement of AD symptoms [127] and the clinical assessment of EGb 761 that is generally utilized for dementia in numerous nations and a broadly utilized dietary enhancement in the United States for memory enhancement is by and by in progress. [128].

3.4. Antioxidant agents

Desmodium gangeticum for the most part known as Salparni, is pervasive in India and has huge therapeutic use as a harsh tonic, febrifuge, stomach related, anticatarrhal, antiemetic, and mitigating conditions. Moreover, it has been broadly utilized in ayurveda for the enhancement of neurological symptoms. Its concentrates utilized in mice to assess the viability in improvement of AD side effects by means of nootropic action and disintegration of AChE movement

yielded extensive outcome. [129]. It likewise has antioxidative property [130]. Rosmarinic acid detached from Salvia officinalis, attenuates various occasions incited by Aβ-like responsive oxygen species arrangement, lipid peroxidation, DNA discontinuity, caspase-3 activation, furthermore, tau protein hyperphosphorylation [131]. Despite a couple of pharmacological activity of prudent features attributed to AD incorporate cancer prevention agent activity, mitigating effects [132] and cholinesterase inhibition. Rosmarinic acid has been known to start cell reinforcement, calming, antimutagen, antibacterial, and antiviral properties. Rosmarinic acid viably represses corridor mark occasions of AD-like arrangement of fibrils from Aβ, destabilization preformed Aβ fibrils in vitro and tau hyperphosphorylation [133].

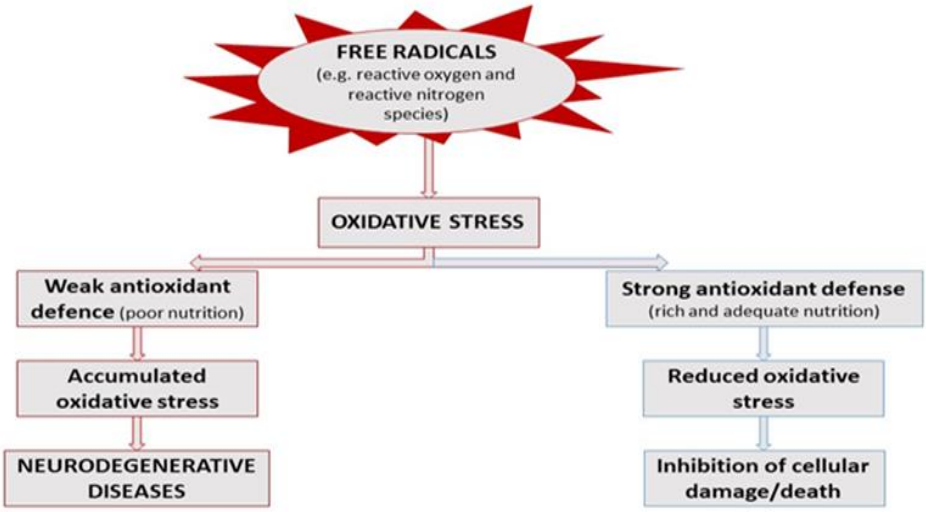

Figure 2 Role of Antioxidants in Neuroprotection

4. Some functional foods bioactive compounds and their role in neurodegenerative diseases

Some bioactive compounds would be examined and discussed further on their role in the prevention, treatment and management of neurodegenerative diseases.

4.1. Polyphenols

Most polyphenols are potent antioxidants [134] and may also possess anti-inflammatory properties [135,136] and several novel works show that polyphenols are also able to modulate several cell-signaling pathways in a wide range of human diseases.

In AD animal models, curcumin reduced proinflammatory cytokines, oxidative damage, and beta-amyloid production, ameliorating cognitive deficits [137]. Curcumin decreases senile plaques by binding with the Aβ oligomers, destabilizing them and preventing their extension [133]. Resveratrol displays its neuroprotective effect by decreasing microglia-induced neuroinflammation, protecting the brain against hypoxic–ischemic damage and ameliorating cognitive function in the Alzheimer's disease model [138]. It should be noted however, that the beneficial roles of polyphenols are not all equal in intensity and vary among different food sources. Several flavonoids have been shown to be useful in prevention of neurodegenerative diseases, like Alzheimer's or Parkinson's [59]. Flavonoid supplementations can modulate specific signaling kinases like CaMKII and ERK, controlling the activation of CREB and the increased expression of Brained Derived Neurotrophic Factor (BDNF) and NGF at the brain level [139, 140].

4.2. Turmeric

Curcuminoids are the major phytochemicals of turmeric that are responsible for the characteristic yellow color [141]. In AD animal models, curcumin reduced proinflammatory cytokines, oxidative damage, and beta-amyloid production, ameliorating cognitive deficits [137]. Curcumin decreases senile plaques by binding with the Aβ oligomers, destabilising them and preventing their extension [133].

4.3. Pepper

The neurological effects of pepper is attributed to capsaicin. Capsaicin works as a chemical signal, activating the peripheral terminals of the sensory neurons by increasing membrane permeability to cations such as calcium and sodium. A recent study conducted by Ogunruku et al [3] revealed the inhibitory effects of phenolic extracts from ripe and unripe bell pepper fruits (C.annum var grossum) on â-secretase activity and â-amyloid aggregation.

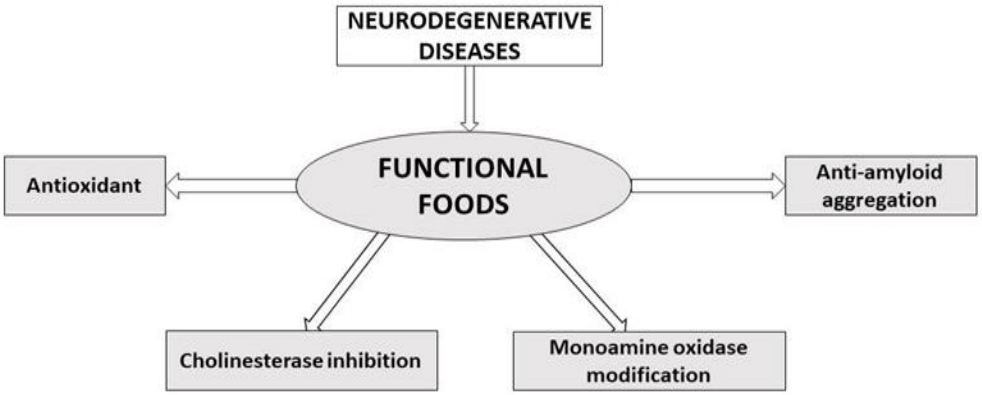

Figure 3 Mechanism of Action of Functional foods and Bioactive compounds in Neuroprotection.

4.4. Red wine

Resveratrol is a stilbenoid polyphenol and a natural phytoalexin. It is produced by several plants in response to injury, it can be found in red wines. Resveratrol displays its neuroprotective effect by decreasing microglia-induced neuroinflammation, protecting the brain against hypoxic–ischemic damage and ameliorating cognitive function in the Alzheimer's disease model [138]. It should be noted however, that the beneficial roles of polyphenols are not all equal in intensity and vary among different food sources.

4.5. Green and black tea

Teas are rich in flavonoids with much attention drawn to green tea because of its higher presence of epigallocatechin-3-gallate (EGCG) which is a potent antioxidant and anti-inflammatory agent. Several flavonoids have been shown to be useful in prevention of neurodegenerative diseases, like Alzheimer's or Parkinson's [59].

4.6. Fish

Some human studies suggest that higher intakes of omega-3 fatty acids from dietary sources are related to reduced risk of dementia and AD [142]. The neuroprotective effect of fish intake was mainly attributed to its high content in long-chain omega-3 fatty acids, in particular Docosahexaenoic acid (DHA) [143].

4.7. Fruits and Green leafy vegetables

Fruits and green leafy vegetables are rich in polyphenols, minerals and vitamins which have neuroprotective effects. Vitamin C and E have demonstrated neuroprotective effects due to their confirmed antioxidant properties and are able to protect the brain from damage due to oxidative stress thereby preventing and slowing the occurrence of neurodegenerative diseases [144]. Low levels of vitamin A are a risk factor for AD and a major problem in the aging population because a number of genes implicated in AD are maintained in the immune system by vitamin A [145]. The B-vitamins have also shown promising roles in the management of neurodegenerative diseases due to the roles of folate, homocysteine, thiamine and nicotinamide in nutrient and energy metabolism [144].

5. Conclusion

Natural compounds or naturally-derived compounds have the potential to serve as the main neurodegenerative therapeutics, representing a significant of the available modalities in treatment. Apparently, nature provides a wide range of bioactive compounds with tremendous potential in the prevention and management of neurodegenerative diseases. Moreover, many of these compounds are part of the daily diet, creating the opportunity to use food as with the concept of functional foods, an effective prevention strategy, especially in the early stages of the disease conferring

neuroprotection. A number of proposed mechanism identified have been elucidated in these functional foods action viz a viz; antioxidant effect, acetylcholinesterase inhibition, anti-amyloid aggregation, modification of monoamines etc. Research into functional foods would overall enhance the development of novel drugs and therapies that would be effective in the prevention, treatment and management of various neurodegenerative diseases so as to ensure healthy ageing amongst the global populace.

Compliance with ethical standards

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Disclosure of conflict of interest

There is no conflict of interest amongst the author.

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