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Therapeutic Insights into α-Lipoic Acid and Thymoquinone for Neurodegenerative Diseases

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ABSTRACT

Exposure to toxicants like pesticides, heavy metals, aerosols, dyes, mutagens like UV rays is inevitable and produces a series of health hazards including neurodegeneration. There are limited or almost no treatments available currently to cure neuropathological conditions, such as Parkinson's disease, Alzheimer's disease and others. Although there may be an increasing range of therapeutic and supportive options that could be helpful yet early diagnosis is essential for treatment planning. If, supportive therapy measures are implemented prior to the onset of a disease, they are recognized as preventive methods. Current review is an attempt to designate the neuroprotective potential of some plant-based phytochemicals such as α-lipoic acid (α-LA) and thymoquinone present in edibles which have least probability of showing any of the side effects in target as well as other tissues so could be used as supportive therapeutics in neurodegenerative diseases. α-LA and thymoquinone both have anti-inflammatory, anti-tumoral, anti-microbial, anti-histaminic and immuno-modulatory effects. Study of current review will provide a research gap to investigators to pursue research against neurological disorders via use of plant-based phytochemicals such as α-LA and thymoquinone.

Keywords: Alzheimer's disease; Parkinson's diseases; α-Lipoic Acid; Thymoquinone; Neurodegeneration; Phytochemicals

1. INTRODUCTION

Neurodegenerative Diseases (NDDs) are gradually escalating chronic diseases of Central Nervous System (CNS) causing structural and functional degeneration of neurons such as Alzheimer's Disease (AD), Parkinson's Disease (PD), Amyotrophic Lateral Sclerosis (ALS), Multiple Sclerosis (MS), Spinocerebellar Ataxias (SCA) and dementia. These diseases are substantial threat to human health [1]. As elderly population is increasing, age-dependent neurodegenerative diseases are also increasing day by day. World Alzheimer's report 2023 states that Dementia is a leading cause of morbidity and 7th major cause of mortality worldwide. A new case of dementia arises every 3 seconds globally. As population grow older, the number of dementias globally is expected to rise from 55 million in 2019 to 139 million by 2050. By 2030. Globally 75% of people with dementia are undiagnosed (Alzheimer's Disease International). The annual costs due to dementia are anticipated to grow from US$1.3 trillion per year in 2019 to $2.8 trillion dollars (World Alzheimer's report 2023). It clearly indicates the cost of treatment society is bearing. Lack of sufficient therapeutic alternatives, serious

side effects of contemporary medications and extensive research in neurodegenerative diseases demand the development of new and safer treatments. There is substantial research suggesting that plant based natural phytochemicals are more potent to cure neurodegenerative disorders. Plant based natural medicine have captivated attention of scientific community in last few decades. Herbal or indigenous medicine are easy to obtain, have almost no or less toxic effects and cost effective also. Any damage to neurons affects their ability to communicate, leading to alteration in thinking, behaviour and feelings (Bist and Bhatt, 2022) [2].

Current review is an attempt to designate the neuroprotective potential of some plant-based phytochemicals such as α-Lipoic Acid (α-LA) and thymoquinone (TQ) present in edibles which have least probability of showing any of the side effects in target as well as other tissues. Thymoquinone (TQ), principal component of *Nigella sativa* extract and α-LA from vegetables both are plant based natural antioxidant and shows substantial curative properties against a wide range of health conditions in neurodegenerative diseases as well [3].

2. METHODOLOGY

We used "PUBMED" data base and screened over 200 research articles, and various international reports from authentic websites of W.H.O, Alzheimer's disease international and selected nearly 80 articles to write this review on the basis of question we are trying to address.

"PUBMED" data base displayed 1786 research articles for key word TQ and 4335 research articles for key word α-lipoic acid for year 2004 to 2024 (20 years) but when we search in combination for TQ and α-LA, "PUBMED" show only 4 research articles on nephrotoxicity [4], on Bio-active nano emulsion, [5], on role of some antioxidants [6]and on protective effects of natural compounds [7]. These results suggest that till date there have been no reports of comprehensive studies examining the effects and outcomes of TQ and α-LA combination in a NDDs mice model. we hypothesize to investigate the neuroprotective potential of TQ and α-LA combination in neurodegenerative diseases.

3. Neuropathology of NDDs

Neuropathology of different NDDs show specific neuronal susceptibility incorporated with the degradation of specific brain regions and an abnormal extracellular or intracellular protein deposition occurs in neurons or in glial cells. Neuropathology of all the conditions is quite different, yet all are correlated by nearly same symptoms like loss of memory, decline in cognitive function, and other detrimental effects including balance, walking, abnormal movements, breathing, swallowing, speech, behavioural changes, anxiety, time and place disorientation, misplacing articles etc. NDDs on the basis of protein conformational abnormalities can be classified as -amyloidosis, tauopathies, a-synucleinopathies, and transactivation response DNA binding protein 43 (TDP-43) proteinopathies.

3.1 Amyloidosis

Amyloids are β-sheet rich insoluble fibrous proteins. Amyloids aggregates mostly in the cytoplasm of neuronal and neuroglial cells. β-amyloid is a proteolytic product of the amyloid precursor protein [8]. Not only in AD but in other NDDs also β-amyloid depositions are found [9].

3.2 Tauopathies

Tau (τ) is a microtubule-associated phosphoprotein. In axons it is found plentiful and assist in polymerisation and stabilization of microtubules [10]. MAPT gene mutation at chromosome 17 is responsible for abnormal tau protein production in frontotemporal dementia and PD. 4R tau (4 conserved amino acid repeats) is associated with Progressive Supranuclear Palsy (PSP), corticobasal degeneration whereas 3R tauopathies include AD, CTE, Guam Parkinson dementia [11].

3.3 Synucleinopathies

Synucleinopathies type of ND is described by α-synuclein (140 amino acid presynaptic

protein) deposition in neuronal and oligodendroglia cells. α-synuclein was identified as a non-amyloid component of senile plaques in AD. Later it was associated with lewy bodies. Lewy body diseases like PD, PD with dementia have neuronal deposition of lewy body in neuronal cells whereas in Multiple System Atrophy (MSA) deposition is within oligodendrocytes. The actual reason behind abnormal conformation of α-synuclein is still obscure but it is likely to be intermingled with phosphorylation after translation or oxidative stress [12].

3.4 TDP-43 Proteinopathies

Transactivation response DNA binding protein or TAR DNA-binding protein-43(TDP-43) is a 43 kDa hnRNP protein having 414 amino acids encoded by TARDBP gene [13]. TDP-43 participate in many cellular functions including mRNA transport, RNA metabolism, mRNA splicing, transcriptional repression and stress granules [14,15]. Detailed pathology of TDP-43 is yet to be explained. Mouse model studies suggest that TDP-43 overexpression causes toxicity whereas inactivated TARDBP gene is embryonically lethal [16].

4. Mechanism of Neurodegeneration

NDDs disrupt or alter communication and their connectivity between sensory and motor neurons hence basic cognitive processes like perception, attention, memory, movement, hearing, speech, decision making, problem solving etc. are compromised. This disruption leads to continuous deterioration of synapses and axon that ends up with neuronal death [17]. CNS is an interacting system of billions of neuronal and glial cells making it most complex organ of human body [18]. Structural complexity leads to even more complex nature of pathologies to understand. Even after the breathtaking research work done in the past and extensive literature that has been available, still neuropathology of NDDs is not completely understood. Figure 1 describes some of the basic mechanisms that are involved in neurodegeneration.

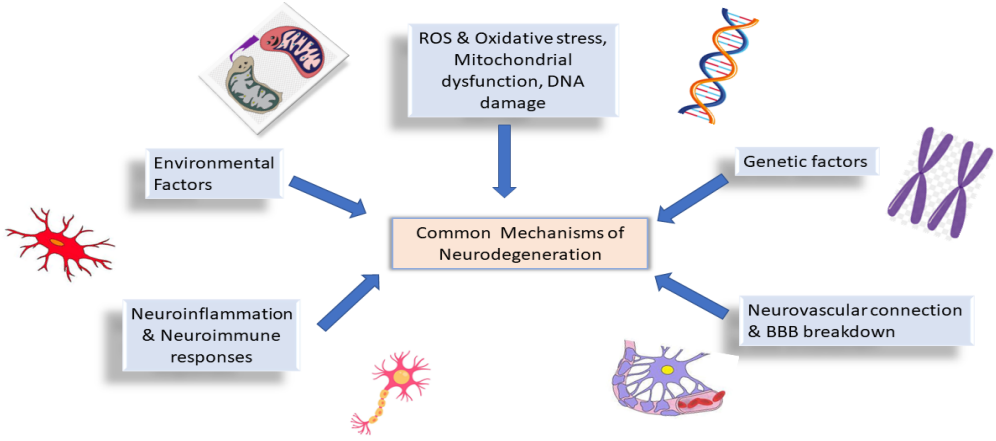

Fig. 1: Common Neurodegeneration Mechanism

4.1 Protein aggregation (Fig. 2)

Many NDDs are caused by intracellular and extracellular deposition of misfolded proteins assembled as insoluble neuro fibrils [19]. Amyloids are ~10nm wide fibrous quaternary protein structure with crossed β-pleated sheet [20]. Brain amyloidosis and NDDs are correlated, extracellular deposition of Aβ and hyperphosphorylated τ protein causes Alzheimer's, Intracellular deposition of α-synuclein (αSyn), PD and polyglutamine (polyQ) peptides causes polyQ diseases [21].

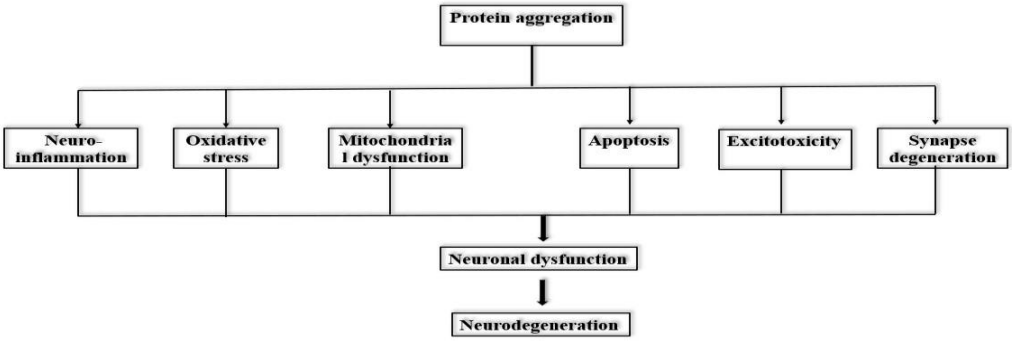

Fig. 2: Neurotoxic mechanism of protein aggregation leading to neurodegeneration

4.2 Mitochondrial dysfunction

Neuronal cells shows both excitability and conductivity. These activities require a lot of energy so mitochondria as center of cellular respiration are prone to mitochondrial damage. Mitochondria produce energy through tricarboxylic acid cycle (TCA cycle) and oxidative phosphorylation [22]. Mitochondria play a crucial role in neuronal membrane excitability, calcium equilibrium and nerve impulse propagation [23]. Mitochondria produce harmful ROS during cellular respiration. Mitochondria eliminate damaged organelles through mitophagy [24]. Damaged mitophagy pathway results in increased OS and iron-dependent a-synuclein oligomerization. It shows that mitochondrial dysfunction plays a central role in various neurodegenerative processes [25].

4.3 Neuroinflammation

Immune system protects brain by eliminating or hindering various types of pathogens through neuroinflammation process. Neuroinflammation encourage tissue repair and cleaning of cellular debris but prolonged neuroinflammation is pernicious to CNS [26]. Stimuli for neuroinflammation could be internal like protein aggregation, mutation or external like trauma, infection and drugs and prolonged inflammation include phagocytic cell microglia [27]. Microglia secrete proinflammatory cytokines Tumor Necrosis Factor (TNF- α), Interleukin -16 (IL-16), IL-1β and chemokine to engage subsidiary cells and eliminate pathogen. Under aging and long sustained stress microglial morphology is changed and it started secreting inflammatory responses excessively causing accelerated neurodegeneration [28,29]. The progression of neurodegeneration through microglia and astrocyte caused by neuroinflammation is demonstrated in figure 3.

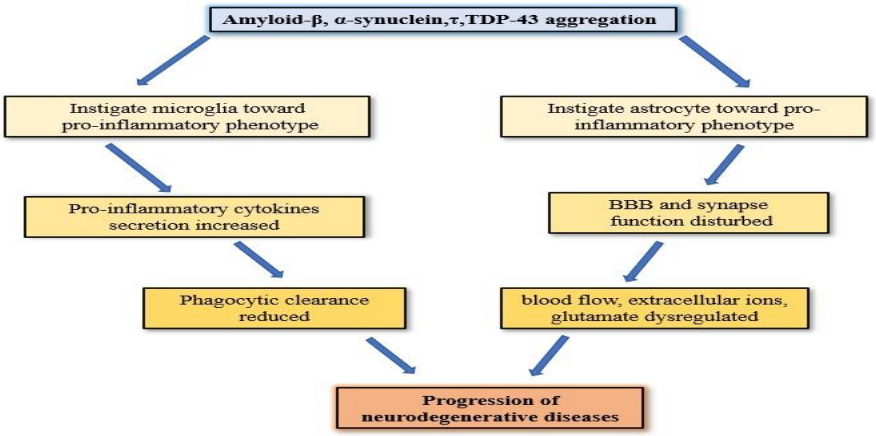

Fig. 3: Neuroinflammation causing neurodegeneration through microglia and astrocyte

5. Diagnosis

Biggest hurdle in NDDs diagnosis is that degeneration of neuronal cells starts way before symptoms of disease appear [30]. Timely diagnosis of NDDs is pivotal for treatment to avert further advancement of the neurodegeneration which takes millions of lives every year globally [31]. Diagnostic techniques such as Positron Emission Tomography (PET), Computed Tomography (CT), Single Photon Emission Computed Tomography (SPECT), Region of Interest (ROI), Voxel-based Morphology (VBM), brain mapping, structural and functional Magnetic Resonance Imaging (sMRI and fMRI), Cerebrospinal Fluid (CSF) from lumber puncture, Arterial Spin Labelling (ASL), Diffusion Tensor Imaging (DTI) and graph theory [32].

PET can detect Aβ and can also be detected by CSF via lumbar puncture. PET tracer like [18F]-2-fluoro-2-deoxy-D-glucose (FDG), [11c] Pittsburgh compound B (PiB), Florbetaben, Flortaucipir, THK, RO848, GtP1, PM-PBB3, UCB-j, UCB-H etc. are used extensively in neuroimaging [32]. Multimodal machine learning is an emerging approach using more than one imaging technique for better diagnosis [33]. Saliva and blood-based biomarkers are future of NDDs diagnostics [34]. World Health Organisation predicts that in 20 years, NDDs will overtake cancer to become the second most prevalent cause of death, after cardiovascular diseases.

6. Therapy

There are many therapeutic approaches available like Ayurveda, Unani, Homeopathy and allopathy to treat neurodegenerative diseases. Ayurveda focus on brain tonic called as "Medhya" herbs like Shankhpushpi, Brahmi etc. While Unani focuses diet and removal of toxins. In homeopathy customized very diluted substances for each patient, but its efficacy lacks substantial scientific evidences, modern allopathy using medication, gene therapy, stem cell therapy, deep brain stimulation but currently no permanent treatment is available for neurodegenerative diseases. Plant based phytochemicals like α-lipoic acid and thymoquinone may play a big role to develop supportive therapeutics as its easy availability in our diet and lack of any side effects.

6.1 Drugs currently used in NDDs treatment

Drug such as donepezil, curcumin, rivastigmine, quercetin, resveratrol, levodopa are used with *in vivo* models of study of liposomal based carriers like Wistar rats, rabbit etc. NDDs such as AD, PD and ALS with their drug class, drugs and their mode of actions are discussed in table1. Noteworthy thing is that all of these drugs either interfere with some other pathway or produce any kind of side effect so none of the mentioned drug in the table 1 is completely safe.

Table1: Current therapeutic approaches in neurodegenerative diseases treatment

Neurodegenerative diseases	drugs	Name of drug class	Mode of action
Alzheimer disease	Donepezil, galantamine, rivastigmine	Cholinesterase Inhibitors	Increases acetylcholine levels in the brain
	Memantine	NMDA Receptor Antagonists	Block the N-methyl-D-aspartate (NMDA) receptor, reducing the effects of excess glutamate, which can be neurotoxic
	Aducanumab	Amyloid-directed monoclonal antibody	Binds with amyloid-beta plaques and helps in removing plaques
Parkinson disease	Levodopa	Dopamine Precursors	Increase dopamine levels and alleviate motor symptoms.
	Apomorphine hydrochloride, pergolide, ropinirole,	Dopamine agonist	Mimics the effects of dopamine and improve motor symptoms.
	Carbidopa	Decarboxylase inhibitors	Stop the peripheral breakdown of levodopa
	Selegiline, Rasagiline	MAO-B Inhibitors	Increase dopamine levels in the brain and improve motor symptoms.
	Entacapone, Tolcapone	COMT Inhibitors	Increase dopamine levels in the brain and improve motor symptoms.

Amyotrophic lateral sclerosis	Riluzole	Glutamate-receptor antagonist	Inhibit glutamate release and/or enhancing glutamate uptake, which may help protect motor neurons from excitotoxicity.
	Edaravone	Free-radical scavengers	reducing oxidative stress and potentially slowing the progression of ALS by protecting motor neurons from damage.
Huntington's Disease	Tetrabenazine	Tetrabenazine	Inhibit vesicular monoamine transporter 2 (VMAT2), reducing the uptake of monoamines such as dopamine and serotonin, which can help reduce chorea and other hyperkinetic movements.
	Deutetrabenazine	Deutetrabenazine	A newer VMAT2 inhibitor with improved pharmacokinetic properties and potentially reduced side effects compared to tetrabenazine.
Multiple Sclerosis	Interferon beta-1a, Interferon beta-1b	Interferon Beta	reducing inflammation and the formation of inflammatory lesions in the central nervous system, which can help slow the progression of MS.
	Glatiramer acetate	Glatiramer Acetate	Modulate the immune response, acting as a decoy for myelin basic protein and shifting the immune response away from inflammation,
	Natalizumab	Natalizumab	Bind to α4-integrin on the surface of immune cells, preventing their migration across the B.B.B into CNS reducing inflammation in MS.
	Fingolimod	Fingolimod	Modulate the immune response by sequestering lymphocytes in lymph nodes
	Ocrelizumab	Ocrelizumab	reduces numbers of CD20-positive B Target cells, and the immune response in the CNS

ALS: Amyotrophic lateral sclerosis; COMT: Catechol O-methyltransferase; NMDA: N-methyl-D-aspartate (NMDA); CD20: cluster of differentiation 20; CNS: Central nervous system; MAOB: Monoamine oxidase type B; MS: Multiple Sclerosis; VMAT2: Vesicular monoamine transporter type 2; B.B.B: Blood brain barrier;

6.2 Nanoparticles based therapies

Blood Brain Barrier (BBB) and various drawbacks of available therapies like reduced drugs availability for transportation to the brain due to trapping of drug by plasma proteins [35]. Nanoparticles as new therapeutics could be used for safe and targeted drug delivery [36]. Smaller size makes nanoparticles more efficient to interact at subcellular molecular level [37]. Use of nanoparticles for NDDs treatment have many advantages such as low toxicity, more precise delivery of drug to target organ, high capacity of drug loading and better chemical and physical stability [38]. Apart from size, polarity and surface chemistry of nanoparticles is also important factor to reach at CNS across BBB. Liposomal based nanoparticles have been most utilised due to its easy modification [39]. Nanoparticles based therapies are efficient because it can deliver drugs to targeted site and works at subcellular level.

6.3 Diets and Phytochemicals as supportive therapeutics

Healthy diet is very crucial in averting NDDs. Studies suggest that vitamin B9, B12, C, A and E have a neuroprotective effect on NDDs. Polyphenols (curcumin, lignans, lignin, stilbenes, flavonoids, coumarins, cinnamic acid, benzoic acid etc. are secondary metabolites having antioxidant properties, aromatic compound [40]. Various studies suggest that dietary polyphenols could reduce OS and enhance synaptic plasticity so may be used as neuroprotective agents in NDDs [41,42].

6.3.1 Neuroprotective potential of α-lipoic acid

α-LA provides antioxidant protection to the body [43] and it is found to be neuroprotective in combination of other antioxidants like vitamin C [44]. It may also facilitate the production of energy for cells and enhance the effectiveness of other antioxidants. Lipoic acid may reduce the toxicity from toxic metals such as mercury [45], cadmium [46], lead [47], copper, manganese and zinc ions [48].

In the past, lipoic acid has been administered to patients and test animals as therapy for diabetic neuropathy and in various intoxications [49]. α-LA has been identified as a powerful antioxidant found naturally in our diets, but appears to have increased functional capacity when given as

a supplement in the form of a natural or synthetic isolate. α-LA is a cofactor for mitochondrial α-keto dehydrogenase complexes and participates in S-O transfer reactions.

α-LA administration to animals has been shown to protect tissue against oxidative damage. α-LA and its active reduced counterpart, dihydrolipoic acid (DHLA), have been shown to protect against hemolysis and neurological disorders and it is used clinically to treat patients with diabetic polyneuropathy [50]. Because this molecule is soluble in both aqueous and lipid portions of the cell, its biological functions are not limited solely to one compartment. In addition to ROS scavenging, α-LA has been shown to be involved in the recycling of other antioxidants in the body including vitamins C and E and glutathione. Not only the antioxidant qualities of this molecule been studied, but there are also several reports pertaining to its blood lipid modulating characteristics, protection against LDL oxidation and modulation of hypertension. Therefore, α-LA represents a possible protective agent against risk factors of cardiovascular disease [51]. Lipoic acid can be administered orally since it is easily absorbed in the stomach. It crosses BBB and does not show toxic actions at doses used for prophylactic and therapeutic purposes.

α-LA is found in whole grains, vegetables having green leaves, potatoes, tomatoes, carrot, broccoli, cauliflower etc. and meats contain some amount of α-LA [52]. Easy availability makes it a good natural supplement to improve NDDs. α-LA shows its health benefits at 600–1800 mg/day, and 600–2400 mg/day is reported as safe dose.

α-LA is an organo-sulfur compound [53] which was discovered by Snell and colleagues in 1937, and its characteristics were further defined by Reed and associates in 1951. Both hydrophilic and lipophilic nature [54], absorption in Alimentary canal and consistent uptake all over the central nervous system [55], ability to cross blood brain barrier, having anti-inflammatory effects [56], nontoxic in nature as remedial doses [57], reduces cognitive deterioration and alleviates neurodegeneration related complications [58,59] make α-LA a convincing neuroprotective agent for NDDs. α-LA is also known as thioctic acid. Dithiolane ring is the reason of chemical reactivity of α-LA. Presence of Sulphur atoms gives it a high electron density and make it a good antioxidant. As an antioxidant it donates electron to Reactive Oxygen Species (ROS) and stabilize them but don't become free radical itself. α-LA serves as a cofactor in the Krebs cycle and in the production of cellular energy [60,61]. α-LA converts to dihydrolipoic acid (DHLA) in our body, which acts as more powerful antioxidant. Both α-LA and DHLA can scavenge ROS and Reactive Nitrogen Species (RNS) in test tube [62]. Preclinical studies have shown that α-LA supplementation can reduce oxidative stress, improve mitochondrial function, and protect against neuronal damage. Clinical trials have also suggested potential benefits of α-LA in improving cognitive function and reducing oxidative stress markers in AD patients [63]. After significant research, α-LA is now considered as a therapeutic agent in NDDs including PD, AD, multiple sclerosis, dementia etc. Prior studies support α-LA protective potential in disease's budding stage on mitochondrial dysfunction. α-LA enhances mitochondrial biogenesis and improves antioxidation [64]. As a pleiotropic agent it regulates genes encoding Nrf-2 and NF-kB by activating signal transduction pathways [65]. α-LA and its reduced form DHLA both as antioxidants remove free radicals, check monocytes and T-lymphocytes to enter CNS [66]. α-LA in PD alter monoamine concentrations across the brain [67]. Noradrenaline and dopamine secretion is restored by α-LA through reducing monoamine metabolism rate and enhancing its secretion and amount of Acetylcholine is adjusted by increasing acetylcholinesterase activity. A good number of studies suggest that α-LA reduces OS and increases serotonin,

dopamine and norepinephrine neurotransmitters in brain [68].

6.3.2 Neuroprotective potential of Thymoquinone

TQ is a principal medicinal component of *Nigella sativa* [69,70]. It is a volatile organic oil. Chemically TQ is a low molecular weight monoterpene. Low molecular weight and lipophilic nature make it suitable to cross blood brain barrier. TQ enhance memory and cognition in various NDDs, reduces depression, anxiety, hallucinations, delusions, agitation etc., avoid seizures and drug deaddiction [71,72]. *Nigella sativa* is an annual flowering plant species of family Ranunculaceae. *N. sativa* seeds and oil has been used to cure various types of sickness [73]. from centuries people of India, China, Saudi Arabia, Iran, Syria, Turkey was using *Nigella sativa* for ailments like Asthma, Bronchitis, Cough, fever, digestive tract problems, headache, seizures, Liver disorders, Kidney problems, Inflammation [74,75]. *N. sativa* shows antioxidant properties, reduces inflammation, antibacterial, protect liver, chemo preventive and chemotherapeutic activities [76]. *N. sativa* is known as kalonji, black seeds, Kala Jira, black cumin etc. also. *N. sativa* contains TQ (28-45%), apinene, sesquiterpene longifolene (1-8%), tanethol (1-4%), carvacrol (6-12%), p-cymene (7-15%), dithymoquinone, thymohydroquinone, and 4 terpineol (2-7%) [77]. *N. sativa* seeds oil contains eicosadienoic, dihomo-linolenic, palmitic, oleic, linoleic acids, myristic, stearic, and arachidonic acids [78,79]. Their curative and remedial properties are due to compound such as TQ, dithymoquinone, thymol, and carvacrol.

Various toxicity studies reveal that the oral doses of TQ (10- 100 mg/kg) are non-toxic in rodent. Female rats tolerate 22.5 mg/kg and male rats up to 15 mg/kg when administered intraperitoneally. Lethality occurred at doses over 50 mg/kg intraperitoneally, with an LD_{50} of 90.3 mg/kg. TQ can be given IP, sub chronically, intravenously and orally in subacute doses. The half-life of TQ is approximately 217 min. [80].

TQ reduces Oxidative Stress (OS) and improves Ab1-42-instigated neurotoxicity and the potential of membrane of mitochondria shows depolarization. TQ mitigate the reduced recycling of synaptic vesicle in the hippocampal neurons and the primary cortical neurons. Studies suggests that TQ has therapeutic and protective benefits against Ab1-42 in the rat hippocampus by alleviating OS. AD pathologies are directly related with Beta-amyloid peptides. TQ as a natural antioxidant can check the pathways connected with Aβ-induced neurotoxicity may be potent in AD treatment [81]. TQ at a dose of 20 mg/kg showed anxiety reducing therapeutic effects by boosting brain GABA content and reducing plasma nitrite. [82]. The curative property in PD of TQ (7.5 and 15 mg/kg, po) in animal models exposed to rotenone shows that TQ with rotenone hindered PD symptoms. TQ-reduced oxidative stress indices. Findings indicates that TQ enhanced motor function in animal models of PD as a result of its antioxidant effects. α-lipoic acid and thymoquinone, in addition to these antioxidants, have displayed potential in preliminary research for their neuroprotective effects. Further research is needed to determine their efficacy, mechanisms of action, optimal dosage, duration, long-term safety, and combination of antioxidants to investigate their neuroprotective potential in neurodegenerative diseases.

CONCLUSION

Current review was an attempt to discuss that there are many therapies used in NDDs treatment but no one have potential to cure NDDs. With increasing severity, morbidity and mortality a safe and effective treatment is need of the hour. The development of neuroprotective strategies using phytochemicals such as α-lipoic acid and thymoquinone represents a promising approach for treating neurodegenerative diseases. While current pharmacotherapies

offer symptomatic relief, ongoing research aims to identify disease-modifying treatments that can halt or reverse neurodegeneration. Combination therapies targeting multiple pathways may provide synergistic effects and improve treatment outcomes. Current review focused on natural plants based active ingredients especially α-lipoic acid, thymoquinone etc. having neuroprotective properties, to be used for NDDs treatment as its part of our diet and show no side effects. Researchers could use these natural ingredients for their experimental findings to fill research gap for development of a potent therapy for NDDs. There is a possibility to develop a preventive health care product which could be used by healthy people and could be started from young age also so we can prevent neurodegeneration before its onset.

Abbreviations

Aβ: Amyloid β; AD: Alzheimer's Disease; α-LA: A-lipoic acid; APP: Amyloid Precursor Protein; ASL: Arterial Spin Labelling; BBB: blood brain barrier; CT: Computed Tomography; CSF: Cerebrospinal Fluid; CNS: Central nervous system; DHLA: Dihydro Lipoic Acid; DTI: Diffusion Tensor Imaging; FDG: Fluro deoxy-D-glucose; fMRI: functional Magnetic Resonance Imaging; GABA: Gamma Amino Butyric Acid; HD: Huntington Disease; IUPAC: International Union of pure and applied chemistry; MS: Multiple Sclerosis; NDDs: Neurodegenerative Diseases; NFT: Neurofibrillary Tangles; NMDAR: N-methyl-D-aspartate Receptor; OS: Oxidative Stress; PD: Parkinson's Disease; PrD: Prion disease; PSP: Progressive Supranuclear Palsy; PET: Positron Emission Tomography; ROI: Region of Interest; ROS: Reactive Oxygen Species; RNS: Reactive Nitrogen Species; SCA: Spinocerebellar Ataxias; SPECT: Single Photon Emission Computed Tomography; sMRI: structural Magnetic Resonance Imaging; TQ: Thymoquinone; TDP-43: Transactivation response DNA binding Protein 43; VBM: Voxel-based Morphology; WHO: World Health Organisation

Declaration by Authors

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