WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.453
Volume 14, Issue 1, 72-85. Review Article ISSN 2277–7105

PHARMACOLOGICAL MANAGEMENT OF NEURODEGENERATIVE DISEASE

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Article Received on
11 November 2024,

Revised on 02 Dec. 2024,
Accepted on 23 Dec. 2024

DOI: 10.20959/wjpr20251-34959

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ABSTRACT

The central nervous system (CNS), comprising the brain and spinal cord, serves as the body's essential control center. A key feature of this system is the blood-brain barrier, a semi-permeable membrane that shields the brain from harmful substances and toxins circulating in the blood. Neurological disorders, often marked by neuronal loss, include common neurodegenerative diseases such as Alzheimer's and Parkinson's. Current treatments for Alzheimer's disease involve drugs that exhibit anti-amyloid properties or mimic nerve growth factor activity. For Parkinson's disease, dyskinesia is frequently linked to L-dopa therapy. Huntington's disease treatments are exploring phase III drugs with anti-apoptotic effects, such as LAX 101. Therapies for rarer neurodegenerative disorders are being developed, often involving drugs with steroid-like activity.

KEYWORDS: Alzheimer's disease, Parkinson's disease, Neurodegenerative disease.

1] INTRODUCTION

Neurodegeneration is a hallmark of many brain disorders, significantly impacting patients and posing ongoing challenges for modern medicine.[1] Despite advancements, effective

treatments remain limited. Neurodegenerative diseases (ND) such as Alzheimer's, Parkinson's, multiple sclerosis (MS), amyotrophic lateral sclerosis (ALS), and Huntington's disease are increasingly prevalent, particularly as the global population ages.[2] These conditions often involve chronic neurodegeneration, heightened neuroinflammation, and central nervous system (CNS) dysfunction. The World Health Organization (WHO) predicts that neurological diseases will become the second leading cause of death globally within the next two decades. Treatment approaches depend heavily on understanding the underlying pathophysiology of these diseases. Pain, as defined by the International Association for the Study of Pain (IASP), is a subjective sensation often associated with tissue damage.[3] Pain syndromes are commonly neuropathic or nociceptive in origin. Neuropathic pain arises from dysfunction or damage to central or peripheral sensory nerves, while nociceptive pain results from actual or potential tissue damage and activation of nociceptors.[4]

1.1. Alzheimer's Disease

Alzheimer's sickness is a innovative and deadly neurodegenerative disease manifested through cognitive and memory deterioration, modern Impairment of activities of day by day dwelling, and a spread of neuropsychiatric signs and behavioral disturbances. occurrence research suggest that during 2000 the variety of individuals with alzheimer's disorder within the u.s. of america changed into four.5 million.[5] the percentage age of people with alzheimer's disease increases through the usage of a thing of with approximately every five years of age, that means that 1 percentage of 60-yr-olds and approximately 30 percentage of 85 yr olds have the disorder.[6]

1.1.1.causes of Alzheimer's disease 1.1.1.1.mind damage

Repeated thoughts trauma has been regarded to purpose the formation of neurofibrillary tangles in a few people, with many consequences on characteristic. due to the fact this circumstance is most often discovered in professional boxers, it is known as dementia pugilistica.[7]

1.1.1.2. Down syndrome

these days, the gene for the AB-precursor protein modified into observed to be located in part of chromosome 21. The presence of 3 copies, known as risomy, of chromosome 21 is present in each cell of humans with DS. due to the fact they have got a further reproduction of the AB-precursor protein gene, the danger for purchasing advert for the ones people with DS (trisomy 21) will boom extensively.

1.1.1.3. Apolipoprotein Epsilon

Apolipoprotein is a protein worried within the transport/transport of lipids and a aspect of advert plaques. the discovery that the apolipoprotein E four allele/gene on chromosome 19q13.2 is a prone gene or a top hazard difficulty for familial and sporadic advert with late-onset after age 60 has highlighted the position of genetic affects in this enormously common and disabling contamination.[8]

1.2. Parkinson's disease

Neurological illnesses are the leading cause of incapacity worldwide, and the superiority of Parkinson's disorder is growing quicker than other neurological illnesses. Parkinson's sickness is the maximum not unusual shape of Parkinson's disease; it's miles a time period that describes a group of neurological issues which can be much like Parkinson's sickness, which consist of pressure, slowness, and tremors.[9]

1.2.1.Reasons of Parkinson's disorder 1.2.1.1.Head trauma

Head trauma, sufficiently excessive to motive signs and symptoms and symptoms of concussion of the mind, is stated to stand up significantly extra regularly previous to illness onset in PD. it is even cautioned that number one involved gadget reorganization in response to peripheral nerve harm may additionally deliver upward push to Parkinsonism.[9]

1.2.1.2. Smoking

several studies have shown that the hazard of PD is inversely related to smoking. In maximum research, the threat of PD in non-people who smoke has typically been about two times that during those who smoke. numerous hypotheses were formulated asking why smoking might also need to guard against the development of PD.[10]

1.2.1.3. Nutritional elements

it's been counseled that in PD neural cellular loss outcomes from oxidative harm with the aid of the usage of unfastened radicals and peroxides. consequently, every the possibility of a shielding position of dietary antioxidants and the position of weight loss program as a likely deliver of toxic oxidative compounds have been studied. The locating that improved consumption of animal fat is associated with PD is constant with the speculation that oxidative reactions are worried.[11]

1.3. Correlation amongst Alzheimer's sickness and Parkinson's sickness

obesity is an excessive accumulation of fats stored in adipose and non-adipose tissue as triglycerides that may be damaged down into fatty acids, that may negatively have an impact on health through the improved expression of pro-inflammatory markers.[12] Globally, the superiority of obesity is growing.[13] definitely, it's miles a public health hassle, and in line with the arena health company, it's miles anticipated that greater than 1.9 billion adults, 18 years and older, have been obese in 2014.[14]

1.3.1. Obesity and Alzheimer's disease (AD)

Is the maximum common shape of dementia and a revolutionary neurodegenerative disorder that is specially recognized via its clinical functions.[15] Of the 5.4 million americans with advert, an expected 5.2 million human beings are 65 years of age and older and about two hundred,000 people are beneath 65 years of age. Age is an important hazard factor, with one in 9 people over 65 years old having advert.[16] It's miles important to highlight that greater girls than guys have ad and approximately two thirds of americans with the disorder are girls.[17]

1.3.2. Obesity and Parkinson's disease (PD)

PD is the second most regular neurodegenerative disorder after ad and is a chronic and modern ailment. PD is characterised by the demise of dopaminergic neurons inside the substantia nigra (SN), as well as intracellular accumulation of aggregates of α-synuclein in neurons of the brainstem, spinal twine, and cortex.[18] It's far anticipated that 10 million humans global and about 1 % of the population over 60 years of age are residing with PD.[19]

3] Pharmacological Management

3.1] Alzheimer's disease

Presently, there are two classes of medicines used within the treatment of Alzheimer's ailment: acetylcholinesterase inhibitors (AChEIs) and memantine, an N-methyl-D-aspartate (NMDA) receptor antagonist.

3.1.1. Cholinesterase Inhibitors

AChEIs lessen the breakdown of acetylcholine, thereby reducing the plain deficiency of cholinergic neurotransmitter activity. They're indicated for the remedy of slight to slight Alzheimer's ailment. To be eligible for Pharmaceutical Blessings Scheme (PBS) funding, the diagnosis ought to be showed or consulted by a expert together with a health practitioner,

psychiatrist or psychologist. Alzheimer's patients need to also bypass the Mini Mental State Exam (MMSE) or a trendy MSE rating of the selection of achei relies upon on ease of use, tolerability, value, and doctor and affected person desire.[20] A few folks that fail to reply to 1 achei may additionally display balance or minimal improvement after switching to some other achei.[21]

3.1.1.1.Mechanism of Action (Cholinesterase Inhibitors)

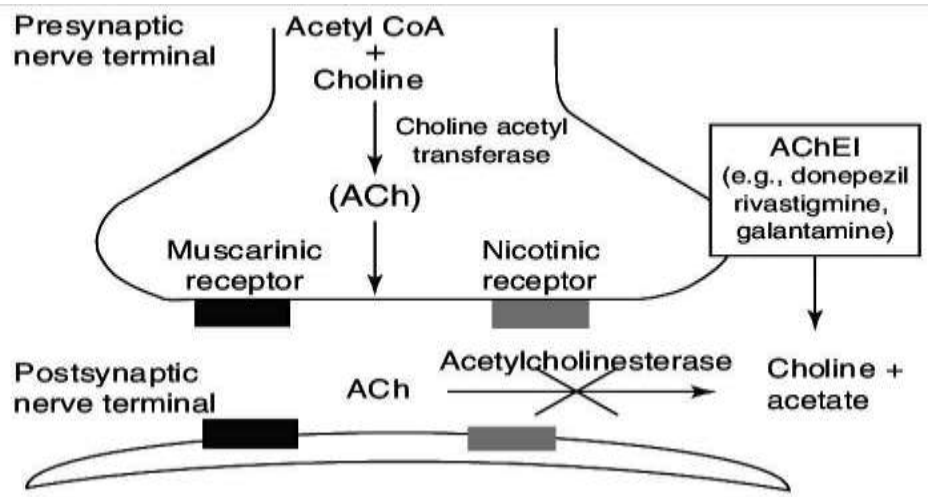

Fig. 1.1 Mechanism of Action (Cholinesterase Inhibitors).

3.1.1.2.Contraindications and precautions

AChEIs are contraindicated in human beings with gastrointestinal (GI) or ureteric obstruction, or active peptic ulcer. It's far endorsed that AChEIs be used with warning in people with a records of peptic ulcer disorder, seizures, heart block, bradyarrhythmias (which includes sick sinus syndrome), bronchial asthma and obstructive pulmonary sickness.[22]

3.1.1.3.Adverse outcomes

Destructive activities are specially GI-associated and encompass nausea, vomiting and diarrhoea. Toxicity is dose-associated and generally resolves with time or dose discount. Dizziness, drowsiness, bradycardia and syncope may get up, making older adults extra susceptible to falls and fractures.[22]

3.2.Parkinson's disease

Parkinson's sickness is the most common form of Parkinson's sickness; it's miles a time period that describes a group of neurological issues which are similar to Parkinson's sickness, consisting of pressure, slowness, and tremors.[23]

3.2.1.Dopaminergic agonists

Dopamine agonists thru binding without delay to the post-synaptic receptors, pass the nigrostriatal machine. Several studies have shown their effectiveness in improving feature in sufferers on levodopa.[24] until presently, the dopamine agonists to be had in canada had been ergot-derived compounds, bromocriptine and pergolide. Because of functionality thing consequences, in particular, nausea, it's miles recommended treatment have to be started at low doses (zero.05 mg OD of pergolide or 1.25 mg of bromocriptine) and multiplied very gradually, with the medication taken on a full belly.

3.2.2.Catechol-zero-methyltransferase (COMT) inhibitors

Catechol-O-methyltransferase (COMT) is an enzyme present every peripherally and inside the enormous involved gadget. Its important feature is to convert levodopa to a few-zero methyldopa (3-zero MD) peripherally and dopamine to homovanillic acid (HVA) centrally. Hence levodopa, administered as Sinemet or Prolopa, is broken down into inactive paperwork thru the interest of this enzyme. Inhibition of COMT might allow for prolonged bioavailability and longer length of movement, every of levodopa and dopamine.[24]

4] Common drugs used in the Alzheimer's disease and Parkinson's disease

4.1. Rivastigmine

Rivastigmine has been permitted for the symptomatic treatment of mild-to-mild ad. Rivastigmine selectively inhibits cortical acetylcholinesterase (ache) inside the primary nervous gadget. And also inhibits butyrylcholinesterase (BuChE) which is documented to be the essential cholinesterase in lots of key areas affected in each ad and PDD, which include the hippocampus, thalamic nuclei, and amygdala.[25]

Rivastigmine is the only FDA permitted medication for the treatment of mild-to-mild PDD. The efficacy of Rivastigmine in PDD turned into confirmed in one of the huge react on this populace, the specific have a look at.[26] In this study, 541 slight to moderate PDD participants were assigned to acquire both Rivastigmine (as much as 12mg/day) or placebo over 24 weeks.

4.2. Donepezil

Donepezil is a reversible and pretty centrally selective inhibitor of ache that delays the breakdown of acetylcholine launched into synaptic clefts, thereby improving cholinergic transmission. Donepezil has additionally been determined to be efficacious in treating

cognitive impairment in patients with moderate to slight ad. Compared with placebo, research evaluating Donepezil have discovered sizeable blessings on each the ADAS-Cog and MMSE.[27]

Numerous small-scale react with Donepezil in PDD have additionally showed some diploma of improvement on at the least one of the assessed cognitive outcome measures . Further, inside the 2nd large RCT that assessed 550 PDD patients on Donepezil, some blessings had been located in comparison with the placebo arm.

5] Emerging therapies

5.1. Immunotherapies : (Aducanumab e.g. For AD)

Aducanumab is an igg1 monoclonal antibody, performing because the drug focused on Abeta. Its mechanism of motion is to selectively target low aggregates and insoluble fibrin fibril conformations that bind to soluble beta plaques aggregated within the brain by means of crossing the blood-brain barrier. This will extend its conformation to the n-terminal of Abeta, making it greater selective to Abeta that gathers. Consequently, Abeta plaques of the mind are decreased.[28] In previous research, the relationship of these proteins to the pathogenesis of ad has been elucidated. Some also are in brief described above. Furthermore, the first proteins are specifically up-regulated and the fourth proteins are mainly down regulated. This is a great indication that aducanumab ends in a useful proteomic analysis.[29]

5.2. Stem cell therapy

Stem cells are characterised via their unique capability to renew themselves with the aid of mobile division and differentiation into an extensive kind of specialised cells. They're observed inside the human frame from the primary periods of improvement until death, gambling a pivotal function inside the development, growth, and repair of all tissues and organs. Stem mobile approach is considered a ground breaking method in regenerative medicinal drug in organ problems, at the same time as every kind has its potencies and accompanying boundaries. In this regard, translating escs/ipscs into novel treatments in neurodegenerative illnesses wishes cautious interest due to the presence of tumor formation threat elicited by way of non-differentiated cells malignant transformation and genetic instability after pro-longed enlargement.[30]

6] herbal plants used in the Neurodegenerative disease

6.1. Piper nigrum (black pepper)

6.1.1.Therapeutic Potential

Black pepper, a widely used spice, has long been employed in traditional medicine. Its leaves and fruits are now being studied for their neuroprotective effects, particularly in AD and PD, which involve progressive neuronal damage and cognitive and motor dysfunctions.[31]

6.1.2.Key Components

Fig No. 1.2 Black pepper.

Black pepper contains various bioactive compounds such as alkaloids, flavonoids, and polyphenols, with piperine being the primary active compound. Piperine enhances the bioavailability of other drugs and demonstrates neuroprotective properties by reducing oxidative stress, preventing neuroinflammation, and modulating neurotransmitter levels.[31]

6.2.Withania somnifera

6.2.1 Plant Description: Withania somnifera, commonly known as Ashwagandha or Indian ginseng, is a small woody shrub from the Solanaceae family.

Fig No. 1.3: Withania somnifera.

6.2.2 Key Constituents: Major phytochemicals include withanolides, withaferins, sitoindosides, and isopelletierine. Other compounds include withanine, somniferine, tropine, and choline.

6.2.3 Pharmacological Activities: Ashwagandha exhibits a broad spectrum of pharmacological effects, including: Neuroprotective: Helps in managing neurodegenerative diseases. Antioxidant and anti-inflammatory: Reduces oxidative stress and inflammation. Anxiolytic and antidepressant: Enhances mental health. Cardioprotective, antidiabetic, and anticancer: Promotes overall health.[32]

6.3 Bacopa monnieri

6.3.1 Plant Description: Bacopa monnieri is a creeping herb from the Scrophulariaceae family, with small oblong leaves and light purple or white flowers.

6.3.2 Key Constituents: The plant contains triterpenoid saponins (bacosides), alkaloids such as brahmine and herpestine, and novel saponins known as bacopasides.

6.3.3 Pharmacological Activities: Bacopa monnieri offers diverse biological activities, iincluding Neuroprotective and anxiolytic: Supports cognitive health and reduces anxiety. Antioxidant and anti-inflammatory: Protects against oxidative stress and inflammation. Antidepressant and adaptogenic: Enhances resilience to stress.[33]

Fig No. 1.4 Bacopa Monnier.

6.4. Curcuma longa

6.4.1. Plant description: Curcuma longa, a perennial herb from the Zingiberaceae family, is primarily grown in South and Southeast Asia. The rhizome of the plant, commonly known as

turmeric, has been extensively used in Ayurvedic medicine as a food additive and therapeutic agent.

Fig No. 1.5 Curcuma longa.

6.4.2 Key Constituents: The main components are curcuminoids, including curcumin, demethoxycurcumin, and bisdemethoxycurcumin. Other compounds include turmerone, zingiberene, and curcumol.

6.4.3 Pharmacological Activities: Turmeric is renowned for its wide range of therapeutic properties, such as: Neuroprotective: Enhances brain health and reduces neuroinflammation. Anti- inflammatory and antioxidant: Alleviates inflammation and oxidative damage. Anticancer, antidiabetic, and antimicrobial: Provides systemic health benefits.

7] Futures Outcome

7.1.Biomarker improvement: (e. g for AD)

Driven in component with the aid of ad drug discovery research, ad is at the vanguard of biomarker improvement for neuro-degenerative sicknesses, and many cutting-edge ideas about ideal biomarkers for those issues have come from advert research. With appreciate to the goal populace for ad biomarkers, this consists of sufferers tormented by either familial or sporadic ad; there's also developing hobby in identifying markers of prodromal ad (this is, MCI), in addition to assays which might be predictive of ad years earlier than its onset. These concepts have emerged from genetic studies that allow the identification of asymptomatic individuals with pathogenic mutations within the Aβ Precursors Protein (APP), Presenilin 1 (PSEN1) and 2 (PSEN2) genes that purpose autosomal dominantly inherited familial ad (FAD), and the recognition that individuals with MCI have an multiplied risk for developing advert inside three–five years, such that ~forty five% of people with MCI will convert to ad within 5 years.

7.2.Novel goals

It's far well known that maximum neurodegenerative sicknesses have a multifactorial nature. From this perspective the development of unique multitarget pills that engage concurrently with the complete organization of biotargets and method concerned in pathogenesis of neurodegenerative sicknesses looks particularly promising. The overview of appeal to attention of the readers to polypharmacological methods within the development of medication for complicated neurodegenerative issues along with alzheimer's sickness.[38] Numerous pharmacological opportunities, from drug mixtures to multitarget-directed ligands (both codrugs and hybrids) and the improvement of successful alzheimer's ailment's multitarget drug-discovery are discussed with examples taken from the current literature.

CONCLUSION

Neurodegenerative illnesses are the most devastating mission all over the global, and inside the future extended range of ND sufferers are anticipated due to worsening of the lifestyles style and burden. even though advanced techniques efficaciously provide transport of medication into the mind of those patients. however none of those approaches offer best effects inside the cases of CNS diseases disorder. This remains a mission because of the specific body structure of the mind, along with tight regulation and limited distribution of materials alongside ECF waft routes. for that reason, immediate development of novel approaches for ND illnesses are relatively demanded that may hinder the ailment development.

It surprises that, notwithstanding the wealth of knowledge that exists concerning advert, best a handful of options are to be had currently for its management. The disorder system is likewise complicated in its own methods. current evidences indicate the disease editing capability of the previously thought symptomatic capsules (achr ligands and memantine) of medication that their right utilization will enhance the medical final results in ad. Immunotherapy to stimulate endogenous removal of Ab and tau is any other attractive option.

Rivastigmine, in particular transdermal administration because of extra tolerability, has the satisfactory proof for remedy of cognitive impairment in PDD. evidence for other acetylcholinesterase inhibitors and memantine is mostly supportive however much less conclusive. Psychotic signs of PDD are great controlled with pimavanserin, which became recently investigated and accredited in the america. caution is needed in prescribing practices, together with remedy of motor symptoms, to keep away from iatrogenic worsening of

nonmotor symptoms. Palliative care ought to be included into the control of PDD.

REFERENCE

1. Merelli A., Czornyj L., Lazarowski A. Erythropoietin: A neuroprotective agent in cerebral hypoxia, neurodegeneration, and epilepsy. *Curr. Pharm. Des*, 2013; 19: 6791–6801. Doi:10.2174/1381612811319380011. [pubmed] [crossref] [Google Scholar]
2. Choonara Y.E., Pillay V., Du Toit L.C., Modi G., Naidoo D., Ndesendo V.M., Sibambo S.R. Trends in the molecular pathogenesis and clinical therapeutics of common neurodegenerative disorders. *Int. J. Mol. Sci*, 2009; 10: 2510–2557. Doi: 10.3390/ijms10062510.
3. Faden AI, Barrett JP, Stoica BA, Henry RJ. Bidirectional brain-systemic interactions and outcomes after TBI. *Trends Neurosci*, 2021; 44: 406–18. [PMC free article] [pubmed] [Google Scholar]
4. Gupta, S.; mccoll, M.A.; Guilcher, S.J.T.; Smith, K. Managing Medication Cost Burden: A Qualitative Study Exploring Experiences of People with Disabilities in Canada. *Int. J. Environ. Res. Public Health*, **2019;** *16:* 3066. [**Google Scholar**] [**crossref**] [**pubmed**]
5. Hebert LE, Scherr PA, Bienias JL, Bennett DA, Evans DA. Alzheimer disease in the US population: prevalence estimates using the 2000 Census. Arch Neurol, 2003; 60: 1119-22.
6. Jorm AF. Cross-national comparisonsof the occurrence of Alzheimer's and vascular dementias. Eur Arch Psychiatry clinclin Neurosci, 1991; 240: 218-22.
7. Roberts, G. W., Gentleman, S. M., Lynch, A. And Graham, D. 1. 1991. BA4 amyloid protein deposition in brain after head trauma. The Lancet, 338: 1422-1423.
8. Roses, A. D., Saunders, A. M., Corder, E. H. Risch, N. J., Haines, J. L., Pericak-Vance, M. A., Han, S-H., Einstein, G., Hulette, C., Schmechel, D. E., Goedert, M., Jakes, R., Dong, L-M., Weisgraber, K. H., Holsti, M., Huang, D. And Strittmatter, W. L. 1994. Apoli- poprotein E and Alzheimer's.
9. Cardoso F, Jankovic J. Peripherally induced tremor and Parkinsonism. Arch Neurol, 1995; 52: 263–70.
10. De Michele G, Filla A, Volpe G, et al. Environmental and genetic risk factors in Parkinson's disease: a case-control study in southern Italy. Mov Disord, 1996; 11: 17–23.
11. Logroscino G, Marder K, Cote L, Tang MX, Shea S, Mayeux R. Dietary lipids and antioxidants in Parkinson's disease: a population-based, case-control study. Ann Neurol, 1996; 39: 89–94.
12. Chen WW, Zhang X, Huang WJ (2016) Role of neuronflammation in neurodegenerative

diseases (review). Mol Med Rep, 13(4): 3391–3396. Doi:10.3892/mmr.2016.4948

13. Ashrafian H, Harling L, Darzi A, Athanasiou T (2013) Neurodegenerative disease and obesity: what is the role of weight loss and bariatric interventions? Metab Brain Dis. Doi:10.1007/s11011- 013-9412-4
14. World Health Organization (WHO) (2011) World health statistics 2011. WHO Press, Geneva, p. 162.
15. Naderali EK, Ratcliffe SH, Dale MC (2009) Obesity and Alzheimer's disease: a link between body weight and cognitive function in old age. Am J Alzheimer's Dis Other Demen, 24(6): 445–449. Doi:10.1177/1533317509348208
16. A. S. Association: In Alzheimer´s Association (2016) http://www.alz.org/
17. Hebert L, Weuve J, Scherr P, Evans D (2013) Alzheimer disease in the United States (2010– 2050) estimated using the 2010 census. Neurology, 80(19): 1778–1783. Doi:10.1212/WNL.0 b013e31828726f5
18. Lees AJ, Hardy J, Revesz T (2009) Parkinson's disease. Lancet. Doi:10.1016/S0140-6736(09)60492-X
19. Maragakis NJ, Rothstein JD (2006) Mechanisms of disease: astrocytes in neurodegenerative disease. Nat Clin Pract Neurol, 2(12): 679–689. Doi:10.1038/ncpneuro0355
20. Statistics on Parkinson's (2016) Parkinson's Disease Foundation, Inc. Http://www.pdf.org/en/parkinson_statistics
21. Australian Medicines Handbook. Adelaide: AMH Pty Ltd, 2018.
22. Sink KM, Thomas J, Xu H, Craig B, Kritchevsky S, Sands LP. Dual use of bladder anticholinergics and cholinesterase inhibitors: Long-term functional and cognitive outcomes. J Am Geriatr Soc, 2008; 56(5): 847–53. Doi:10.1111/j.1532-5415.2008.01681.x.
23. Kim DH, Brown RT, Ding EL, Kiel DP, Berry SD. Dementia medications and risk of falls, syncope, and related adverse events: Meta-analysis of randomized controlled trials. J Am Geriatr Soc, 2011; 59(6): 1019–31. Doi:10.1111/j.1532-5415.2011.03450.x.
24. Pezzoli G. Martignoni E, Pacchetti C, et al, A crossover, controlled study comparing pergolide with bromocriptine as an adjunct to levodopa for the treatment of Parkinson's disease. Neurology, 1995; 43: S22-S27.
25. Anand, P.; Singh, B. A review on cholinesterase inhibitors for Alzheimer's disease. Arch. Pharm. Res., 2013; 36: 375-399. Http://dx.doi.org/10.1007/s12272-013-0036-3
26. Emre, M.; Aarsland, D.; Albanese, A.; Byrne, E.J.; Deuschl, G.; De Deyn, P.P.; Durif, F.;

Kulisevsky, J.; van Laar, T.; Lees, A.; Poewee, W.; Robillard, A.; Rosa, M.M.; Wolters, E.; Quarg, P.; Tekin, S.; Lane, R. Rivastigmine for dementia associated with Parkinson's disease. N. Engl. J. Med., 2004; 351: 2509-2518. http://dx.doi.org/10.1056/nejmoa041470

27. Birks, J. Cholinesterase inhibitors for Alzheimer's disease (Review).Cochrane Libr., 2009. Doi: 10.1002/14651858.CD001191.pub2.
28. A. Zainab, (2022) The mechanism of action of the controversial drug; aducanumab and the story behind its speedy approval. J Pak Med Assoc., 72 (5): 1019.
29. J. Bastrup et al, (2021) Anti-Aβ antibody aducanumab regulates the proteome of senile plaques and closely surrounding tissue in a transgenic mouse model of Alzheimer's disease. J. Alzheimer's Dis., 79(1): 249 - 265.
30. Ross, C. A., & Akimov, S. S. (2014). Human-induced pluripotent stem cells: Potential for neurodegenerative diseases. Human Molecular Genetics, 23(R1): R17–R26.
31. Bone, K. Clinical Applications of Ayurvedic and Chinese Herbs. Monographs for the Western Herbal Practitioner; Phytotherapy Press: Queensland, Australia, 1996; 137 141.
32. Kumar, V.; Dey, A.; Hadimani, M.B.; Marcovi´c, T.; Emerald, M. Chemistry and pharmacology of Withania somnifera: An update. Tang (Humanit. Med.), 2015; 5: e1. [crossref]
33. Aguiar, S.; Borowski, T. Neuropharmacological Review of the Nootropic Herb Bacopa monnieri. Rejuvenation Res, 2013; 16: 313–326. [crossref]
34. Majeed, M.; Badmaev, V.; Murrray, F. Turmeric and the Healing Curcuminoids; Keats Publishing, Inc.: New Canaan, CT, USA, 1996.
35. Sharifi-Rad, J.; El Rayess, Y.; Rizk, A.A.; Sadaka, C.; Zgheib, R.; Zam, W.; Sestito, S.; Rapposelli, S.; Neffe-Skoci ´nska, K.; Zieli ´nska, D.; et al. Turmeric and Its Major Compound Curcumin on Health: Bioactive Effects and Safety Profiles for Food, Pharmaceutical, Biotechnological and Medicinal Applications. Front. Pharm, 2020; 11. [crossref].
36. Kumar GP, Khanum F. Neuroprotective potential of phytochemicals. Pharmacogn Rev, 2012; 6(12): 81–90. Https://doi.org/10.4103/0973-7847.99898.