eISSN 2583-6986
IDEALISTIC JOURNAL OF ADVANCED RESEARCH IN PROGRESSIVE SPECTRUMS (IJARPS)
A MONTHLY, OPEN ACCESS, PEER REVIEWED (REFEREED) INTERNATIONAL JOURNAL
Volume 05, Issue 03, March 2026

Neurobiological aging and neuroprotection: Mechanisms, challenges and emerging therapeutic strategies

Dr. Akanksha Kushwaha[1]
[1]Assistant Professor Department of Zoology, K.N. Government P.G College, Gyanpur. Bhadohi UP

Received: 21 March 2026 Accepted & Reviewed: 25 March 2026, Published: 31 March 2026

Abstract

With continuous increase in human life expectancy, the number of old people has been growing throughout the world. Old age is a major risk factor for various neurodegenerative diseases that cause cognitive impairment. Cognitive decline is not only linked to the pathological brain aging, but it can also occur in aged people who are otherwise healthy. This can result from the age-related changes in the brain. Such changes lead to the loss of key brain functions and cause a variety of neurodegenerative and neuropsychiatric disorders including dementia and Alzheimer's disease, which can deteriorate the quality of life. Hence, a clear understanding of the mechanisms underlying age-related brain alterations and diseases will improve not only the quality of elderly life but also reduce the load on their families in terms of care giving and socioeconomic responsibilities. In this context, researchers have been endeavoring to comprehend the neurological changes causing cognitive impairment and explore the possibility to ameliorate it. However, this is challenging and complicated due to multiple biological dimensions spanning from genes to brain networks, behavior and individual variability. Recent advances in neuroscience research suggest a key role of lifestyle changes, herbal preparations and epigenetic modulators in the recovery of age-related cognitive decline. Also, factors like healthy diet, exercise and social interactions help in prevention of cognitive deterioration. This review briefly focuses on the changes that occur in the brain with advancing age, neural basis of cognitive impairment, and protective as well as preventive interventions.

Keywords:- Brain Aging, Cognition, Epigenetics, Neuroprotection

Introduction

Both increase in human life expectancy as well as reduction in birth rate cause a continuous change in the age structure of the population around the world. The growing proportion of elderly people is one of the major social transformations of the 21stcentury, having implications in practically every area of society. According to UN report on World Population Aging 2017, by 2030, older people aged 60 and above would outnumber children under the age of ten, with two-thirds of the elderly living in developing countries (United Nations, 2017). Such rising elderly population is a major concern for the health professionals, scientists, social workers and policy makers around the globe. Though aging is a natural part of life, old age is associated with several concerns because of which elderly have not only different emotional, physical and social demands, but they also require special care and support.

Almost 40% of the population over the age of 60 complain age-related cognitive decline, resulting partly from the underlying neurodegenerative diseases or a change in the lifestyle (VanGuilder and Freeman, 2011). Even healthy adults are at an increased risk of cognitive impairment and brain diseases as they get older. Of course, individuals can differ; for example, some people may have genetic or developmental flaws that cause them to age more quickly, whereas others may have a catastrophic injury or illness resulting in rapid but stable brain aging. Therefore, it is important to understand the impact of aging on brain and cognition, and explore the preventive and neuroprotective interventions.

Impact of aging on brain and cognition

Advancing age is associated with alterations in the structure and function of the brain. The hippocampus located in the temporal lobe of the brain is of particular importance in aging and cognition because it regulates learning and memory, which are intimately linked to cognitive decline (VanGuilder and Freeman 2011). Normal aging is accompanied with hippocampal atrophy caused by a decrease in spine density, neuron size and number of synapses (Fjell and Walhovd, 2010). Other pathways contributing to the aging process include reduced vascular density, increase in inflammation and oxidative stress, compromised neurotransmitter action (Rozycka and Liguz-Lecznar, 2017) and dysregulation of a number of key hippocampal proteins like glutamate receptors AMPA (alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid), NMDA (N-methyl-D-aspartate) and other pre- and post-synaptic proteins involved in learning and memory processes (VanGuilder and Freeman, 2011).

Thus, brain aging is a complex process marked by a steady reduction in cognitive abilities (Dearyetal., 2009) and increasing risk for neurodegenerative disorders such as Alzheimer's disease (AD), Huntington's disease, Parkinson's disease, amyotrophic lateral sclerosis, frontotemporal dementia and spinocerebellar ataxias. The etiology of these disorders varies; some induce memory and cognitive problems, while others impact mobility, speech and breathing (Abeliovich and Gitler, 2016; Canter et al., 2016; Taylor et al., 2016; Wyss-Coray, 2016). Even those who do not suffer from dementia or mild cognitive impairment (MCI) may have small cognitive changes as they age. Some cognitive talents such as language may increase with age, whereas other abilities such as reasoning, memory and processing speed may eventually diminish. Different domains of cognition such as attention, perception, execution, thinking, decision making, speech and language are all affected with age (Ballesteros et al., 2009; Baghel et al., 2019). A combination of symptoms that interfere with a person's ability to conduct daily activities such as thinking and remembering is referred to as dementia. The period between normal cognitive aging and dementia is known as MCI which does not affect routine activities. The most common form of dementia is AD characterized by the loss of intellectual functions, independence and identity.

Neural basis of cognitive decline– involvement of epigenetics and gut microbiota

Synaptic plasticity, which refers to the brain's ability to restructure, create and prune neuronal networks, is necessary for memory formation and maintenance. Its two components, long-term potentiation (LTP) and long-term depression (LTD), support the formation of learning and memory. Using normal aging and scopolamine-induced amnesic mice model, we have demonstrated changes in the expression, regulation and function of a wide range of molecules in the hippocampus (Srivas and Thakur, 2017; Singh and Thakur,2018). Other studies in the cerebral cortex and hippocampus have shown that the stress and inflammation-related genes are upregulated, while growth/trophic factors, energy metabolism, protein turnover, neuronal survival and synaptic plasticity genes are downregulated (Mattson and Arumugam, 2018). Reduced expression of synaptic plasticity genes is linked to an increase in oxidative stress, changes in neurotransmitter and hormone levels, and epigenetic modifications as people age (Singh and Thakur, 2014; Kushwaha and Thakur, 2020). Thus, a variety of factors contribute to cognitive impairment (Fig. 1).

Epigenetic modifications can occur at any stage of life, from childhood to adulthood and old age, and can be transmitted through multiple generations (Weyrich, 2018). They are caused by a variety of environmental factors including nutrition, pollution, pesticides, chemical species, medications, physical activity and stress (Fuso and Lucarelli, 2019). They can turn on/off relevant genes directly by interacting with DNA, RNA, or chromatin proteins, or indirectly through the use of different enzymes or epigenome-related pathways (Watson and Goodman, 2002; Martin and Fry, 2018). Alterations in DNA methylation, histone post-translational modifications, production of microRNA (miRNAs) and long non-coding RNAs (lncRNAs), and nucleosome positioning regulate gene expression patterns. DNA methylation is involved in a variety of diseases (Jin and Robertson; 2013) including AD (Condliffe et al., 2014), Parkinson's disease (Henderson-Smith et al., 2019), and amyotrophic lateral sclerosis (Dolinar et al., 2018; Maltby et al., 2018). In AD, genes involved in amyloid peptide production (CREB5, PSEN1, APP, S100A2, PP2A, BACE) are hypermethylated, while others (MTHFR, MAPT APOE, SORB3) are hypomethylated (Stoccoro and Coppede, 2018). Histone deacetylase inhibitors, which increase histone acetylation, improve learning and memory and have a neuroprotective effect.

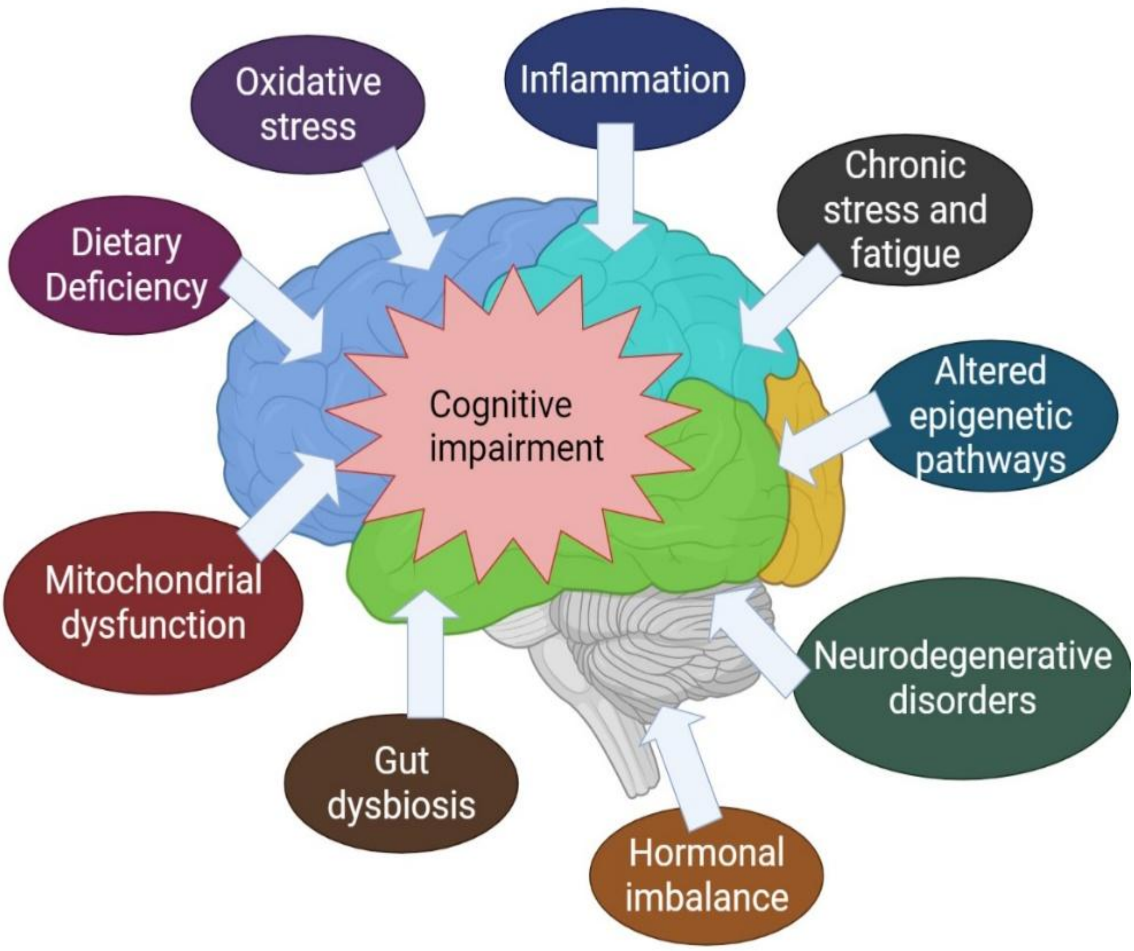

Figure 1: Factors leading to cognitive impairment

In addition to epigenetics, the recent research has revealed the impact of gut microbiota on the brain's physiological, behavioural and cognitive functioning. About 1014 microbial cells including bacteria, archaea, viruses, fungi, and protozoa populate the gastrointestinal system and maintain a symbiotic connection with the intestinal microbiota in the host (Wilkins et al., 2019). Diet- and obesity-related cognitive impairment has been linked to the gut microbiome's impacts on enteric and vagal signaling, immunological function and neuroactive metabolite synthesis.

Recovery of cognitive impairment: Neuroprotective interventions

Herbal preparations and epigenetic modulators exhibit neuroprotective properties and help in the recovery of cognitive impairment.

Herbal preparations are gaining popularity for use in cognitive disorders due to their perceived efficacy, safety and cost (Mehla et al., 2020; Kumar et al., 2021). Various neuroactive Indian herbs such as *Withania somnifera*, *Centella asiatica*, *Celastrus paniculatus* and *Bacopa monnieri* have shown cognitive improvement in animal models. Herbal crude extracts and their bioactive phytochemicals, such as alkaloids, saponins and flavonoids, play an important role in neuromodulation. These phytoconstituents have neuroprotective, immunomodulatory, anti-inflammatory and antioxidant properties, as well as the ability to increase the growth of good bacteria, which influence the gut-brain axis. Their direct influence on epigenetic modifications, gene expression profile, protein turnover and metabolism, eventually regulate redox signaling pathways, neurogenesis, neuritogenesis, synthesis and degradation of neurotransmitters, and synaptic transmission (Howes et al., 2020). Some of the popular herbs are mentioned in Table 1.

Table: List of herbs exhibiting effects on cognition, their bioactive components and pharmacological property

Herb	Bioactive components	Pharmacological property	References
Bacopa monnieri (Brahmi)	Triterpenoid saponins (bacosides)	anxiolytic, analgesic, anti-inflammatory, antioxidant	(Aguiar and Borowski, 2013; Konar et al., 2015)
Centella asiatica (Jalbrahmi / Gotu kola)	Asiaticosides, asiatic acid, madecassoside, and madasiatic	Anti-inflammatory, antioxidative stress, neuroprotective, antidepressant nootropic	(Kumar and Gupta, 2002)
Withania somnifera *(*Ashwagandha)	Isopellertierine, anferine, withanolides, withaferins, sitoindoside VII and VIII, andwithanoloides	Anti-inflammatory, antioxidant, neuroprotective,anxiolytic, antidepressant	(Kumar et al., 2015; Konar et al., 2011, 2019)
Curcuma longa (Turmeric)	Curcuminoids; mainly Curcumin (diferuloyl methane), demethoxycurcumin, andbisdemethoxycurcumin	neuroprotective, anti-inflammatory, antioxidant	(Sharifi-Rad et al., 2020)
Clitoria ternatea (Aparajita)	Taraxerol, teraxerone, ternatins, delphinidin-3	Nootropic, antidepressant, antianxiety, antistress,antioxidant, anti-inflammatory	(Mukherjee et al., 2008)

Celastrus paniculatus (Jyotismati)	Sesquiterpenoid polyalcohols and esters, alkaloids (paniculatine and celastrine), phenolic triterpenoids (celastrol and paniculatadiol	Neuroprotective,anti-inflammatory, antioxidant	(Ramaiah et al., 2018)
Convolvulus pluricaulis *(S*hankhpushpi)	Alkaloids (shankhpushpine and convolamine), volatile oils, favanoid-kampferol, phytosterol, amino acids, fattyacids, scopoletin, andbeta-sitosterol	Nootropic, antistress, antidepressant, anxyiolytic	(Agarwa et al., 2014)
Ginkgo biloba (Ginkgo)	Flavonoids, terpene trilactones, proanthocyanidines, ginkgolic acids, biflavone, polyflavones, and ginkgotoxins	Neuroprotective,cognitive improvement, and antioxidant	(Singh et al., 2017)
Tinospora cordifolia (Guduchi)	Alkaloids, diterpenoid, glycosides, steroids, lactones sesquiterpenoid, phenolics	Neuroprotection, antioxidant, anti-stress, learning and memory enhancement	(Sharma et al., 2019)
Coffea arabica (Arabian coffee)	Phenolic derivatives, alkaloids (caffeine), diterpenoid alcohols (cafestol and kahweol), carbohydrates, lipids,	Anti-oxidant and anti-inflammatory properties	(Islam et al., 2018)
Glycyrrhiza glabra (Yashtimadhu)	Glycyrrhizine, flavonones, isoflavones, glycyrrhetenic acid	Anti-oxidative, learning improvement	(Paudel et al., 2020)
Panax ginseng (Chinese ginseng)	Triterpenoid saponins (ginsenosides)	Neuroprotection, neuromodulation, antioxidant and anti-inflammation	(Shin et al., 2019)

Together with the phytochemicals, epigenetic modulators have a crucial role in the treatment of neurodegenerative diseases. HMT, HDM, HAT, HDAC, miRNAs, siRNAs and lncRNAs are small molecule modulators that affect a variety of epigenetic pathways. One of the advantages of epigenetic therapy is its specificity. L-Dopa, commonly used to treat Parkinson's disease, has been reported to enhance SNCA methylation in both *in vitro* and *in vivo* investigations. On the other hand, long-term use of L-dopa results in H4 deacetylation and dyskinesia. HDAC inhibitors have potential to improve cognition and can be used to treat Parkinson's disease. SIRT2 inhibitors reduce alpha-synuclein toxicity in a cellular model of parkinsonism, whereas siRNA inhibitors are useful in *in vivo* models of parkinsonism (Rathore et al., 2021)

Prevention of cognitive decline

Along with the methods employed for recovery of cognitive decline during aging, certain neurotransmitter modulatory drugs have been effective in treatment and they are often referred to as targeted therapeutics. In this regard, numerous compounds have been tested for their ability to improve cognition (Froestl et al., 2012, 2013a, b). They act mostly on discrete proteins or signaling cascades, which directly or indirectly influence cognition. A variety of pharmaceutical and behavioral methods have also been explored to improve cognitive functions as people age. Healthy diet, increased physical activity, social involvement, and participation in intellectual activities have been reported to have positive effect (Harada et al., 2013; Barman et al., 2021; Singh et al., 2021) (Fig. 2).

Healthy diet - Several heart-healthy diets have been linked to lower incidence of cognitive decline and dementia (Scarmeas et al., 2006). They include antioxidant-rich foods and abundance of fruits and vegetables. Excess sodium, saturated fat, refined carbohydrates, red and processed meats, solid fat calories, and added sugar calories should be avoided. Nutraceuticals and supplements such as vitamins, proteins, and minerals are naturally present in foods. They have grown in popularity for targeting memory despite the lack of sufficient scientific data supporting their efficacy.

Exercise - There is robust evidence that participation in physical activity is associated with a decreased risk of cognitive decline and dementia. Epidemiological studies have demonstrated that high levels of exercise in mid- and late life are associated with increased cognitive performance, reduced rate of cognitive decline, and decreased risk of dementia (Casaletto et al., 2020). Exercise has beneficial effects against aging as an external environmental modulator by enhancing neuro-vascularization, neurogenesis, and neurotrophic factor synthesis (Morland et al., 2017; Horowitz et al., 2020).

Social interaction - Reduced social participation, less frequent social contact, and feelings of loneliness have been linked to cognitive impairment and dementia (Wang et al., 2002; Crooks et al., 2008; Evans et al, 2019). Maintenance of a large social network may aid in cognitive health as people age. Fewer years of education in early life are linked to lower cognitive reserve and a higher risk of dementia later in life (Livingston et al., 2020).

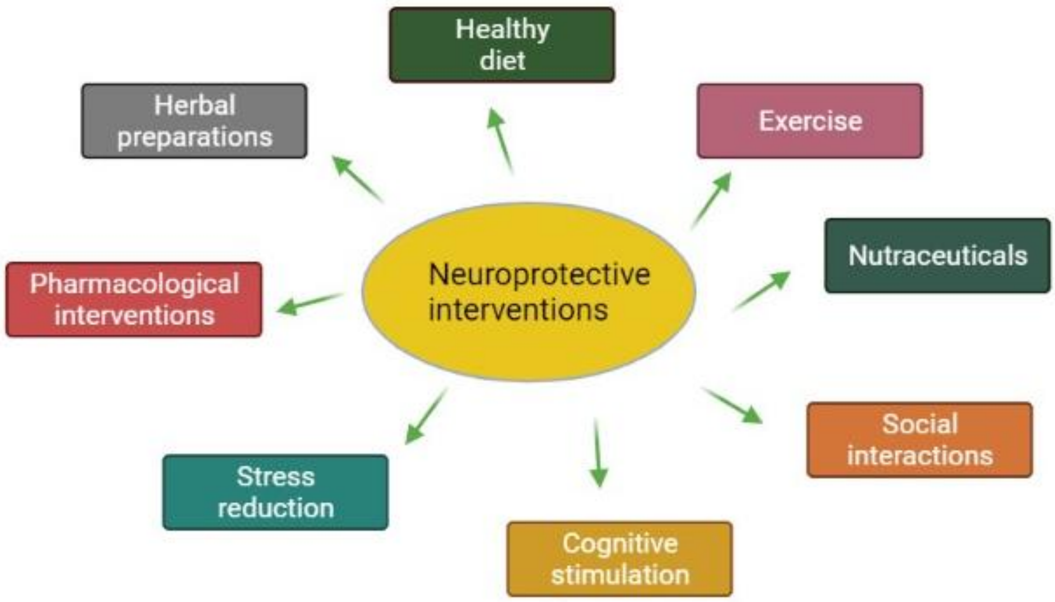

Figure 2: Prevention and recovery of cognitive impairment

Summary and Conclusion

Presently, there is no cure for age-related cognitive decline, partly due to poor knowledge of normal aging process and urgency in understanding the pathology of neurodegenerative diseases. Future research into the biological effects of aging will aid in determining which aberrant processes contribute to the cognitive decline in both normal and pathological aging. Although cholinergic system disruption is connected to the majority of memory problems, other factors also play a role in synaptic plasticity loss and cognitive decline. Physical activity, mental and social stimulation, and a balanced diet are essential to lower the risk of dementia and cognitive impairment. Several studies have shown that consuming a diet rich in antioxidants and anti-inflammatory components, such as those found in fruits and nuts, can help to reduce age-related cognitive decline and the onset of neurodegenerative diseases. Several herbal preparations that have been used in various parts of the world for centuries are combined in multi-herbal formulations that are regarded to have a synergistic effect and are more efficient than the individual herb. They should be made available to the elderly, allowing them to improve their quality of life with fewer side effects and less capital expenditure. Many traditional views about the use of herbal preparations to improve memory have been backed up by *in vitro* and *in vivo* experiments, as well as clinical studies.

References

1. Abeliovich A and Gitler AD (2016) Defects in trafficking bridge Parkinson's disease pathology and genetics. Nature 10;539(7628):207-216
2. Agarwa P, Sharma B, Fatima A and Jain SK (2014) An update on ayurvedic herb *Convolvulus pluricaulis* Choisy. Asian Pac J Trop Biomed 4(3):245-52
3. Aguiar S and Borowski T (2013) Neuropharmacological review of the nootropic herb *Bacopa monnieri*. Rejuvenation Res 16, 313–326
4. Baghel MS and Thakur MK (2017) Differential proteome profiling in the hippocampus of amnesic mice. Hippocampus 27(8):845-859

5. Baghel MS, Singh P, Srivas S and Thakur MK (2019) Cognitive changes with aging. Proc. Natl. Acad. Sci., India, Sect. B Biol. Sci. 89(3):765
6. Ballesteros S, Nilsson L-G and Lemaire P (2009) Ageing, cognition, and neuroscience: an introduction. Eur J Cogn Psychol 21:161–17
7. Barman B, Kushwaha A and Thakur MK (2021) Vitamin B_{12}-folic acid supplementation regulates neuronal immediate early gene expression and improves hippocampal dendritic arborization and memory in old male mice. Neurochem Int 9; 150:105181
8. Canter RG, Penney J and Tsai LH (2016) The road to restoring neural circuits for the treatment of Alzheimer's disease. Nature 10;539(7628):187-196
9. Casaletto KB, Staffaroni AM, Wolf A, Appleby B, Brushaber D, Coppola G et al. (2020) Active lifestyles moderate clinical outcomes in autosomal dominant frontotemporal degeneration. Alzheimers Dement 16, 91-105.
10. Condliffe D, Wong A, Troakes C, Proitsi P, Patel Y, Chouliaras L, et al. (2014) Cross-region reduction in 5-hydroxymethylcytosine in Alzheimer’s disease brain. Neurobiol Aging 35:1850– 4
11. Crooks VC, Lubben J, Petitti DB, Little D and Chiu V (2008) Social network, cognitive function, and dementia incidence among elderly women. Am J Public Health 98, 1221-1227
12. Deary IJ, Corley J, Gow AJ, Harris SE, Houlihan LM et al (2009) Age-associated cognitive decline. Br Med Bull 92:135–152
13. Dolinar A, Ravnik-Glavac M and Glavac D (2018) Epigenetic mechanisms in amyotrophic lateral sclerosis: a short review. Mech Ageing Dev 174:103–10
14. Evans IEM, Martyr A, Collins R, Brayne C and Clare L (2019) Social isolation and cognitive function in later life: A systematic review and meta-analysis. J Alzheimer’s Dis 70, S119-S144
15. Fjell AM and Walhovd KB (2010) Structural brain changes in aging: courses, causes and cognitive consequences. Rev Neurosci 21:187–222
16. Froestl W, Muhs A and Pfeifer A (2012) Cognitive enhancers (nootropics). Part 1: drugs interacting with receptors. J Alzheimer’s Dis 32:793–887
17. Froestl W, Muhs A and Pfeifer A (2013a) Cognitive enhancers (nootropics). Part 2: Drugs interacting with enzymes. J Alzheimer’s Dis 33:547–658
18. Froestl W, Pfeifer A and Muhs A (2013b) Cognitive enhancers (nootropics). Part 3: drugs interacting with targets other than receptors or enzymes. disease-modifying drugs. J Alzheimer’s Dis 34:1–114
19. Fuso A and Lucarelli M (2019) CpG and Non-CpG Methylation in the dietepigenetics-neurodegeneration connection. Curr Nutr Rep. 8:74– 82
20. Harada CN, Love MCN and Triebel KL (2013) Normal cognitive aging. Clin Geriatr Med 29:737–752
21. Henderson-Smith A, Fisch KM, Hua J, Liu G, Ricciardelli E, Jepsen K, et al. (2019) DNA methylation changes associated with Parkinson’s disease progression: outcomes from the first longitudinal genome-wide methylation analysis in blood. Epigenetics 14:365–82
22. Horowitz AM, Fan X, Bieri G, Smith LK, Sanchez-Diaz CI, Schroer AB et al. (2020) Blood factors transfer beneficial effects of exercise on neurogenesis and cognition to the aged brain. Science 369(6500):167-173
23. Howes MR, Perry NSL, Vásquez-Londoño C and Perry EK (2020) Role of phytochemicals as nutraceuticals for cognitive functions affected in ageing. Br J Pharmacol. 177(6):1294-1315
24. Islam MT, Tabrez S, Jabir NR, Ali M, Kamal MA, da Silva Araujo L et al. (2018) An insight into the therapeutic potential of major coffee components. Curr Drug Metab 19(6):544-556

25. Jin B and Robertson KD (2013) DNA methyltransferases, DNA damage repair, and cancer. Adv Exp Med Biol 754:3– 29

26. Konar A, Gautam A and Thakur MK (2015) *Bacopa monniera* (CDRI-08) upregulates the expression of neuronal and glial plasticity markers in the brain of scopolamine-induced amnesic mice. Evid Based Complement Alternat Med2015:837012

27. Konar A, Gupta R, Shukla RK, Maloney B, Khanna VK, Wadhwa R, Lahiri DK and Thakur MK (2019) M1 muscarinic receptor is a key target of neuroprotection, neuroregeneration and memory recovery by i-Extract from *Withania somnifera*. Sci Rep 30;9(1):13990

28. Konar A, Shah N, Singh R, Saxena N, Kaul SC, Wadhwa R and Thakur MK (2011) Protective role of ashwagandha leaf extract and its component withanone on scopolamine- induced changes in the brain and brain-derived cells. PLoS One 6(11): e27265

29. Kumar A, Konar A, Garg S, Kaul SC and Wadhwa R (2021) Experimental evidence and mechanism of action of some popular neuro-nutraceutical herbs. Neurochem Int. 149:105124

30. Kumar MV and Gupta Y (2002) Effect of different extracts of *Centella asiatica* on cognition and markers of oxidative stress in rats. J. Ethnopharmacol 79, 253–260

31. Kumar V, Dey A, Hadimani MB, Marcovic T and Emerald M (2015) Chemistry and pharmacology of *Withania somnifera*: An update. Tang (Humanit. Med.), 5, e1

32. Kushwaha A and Thakur MK (2020) Increase in hippocampal histone H3K9me3 is negatively correlated with memory in old male mice. Biogerontology 21(2):175-189

33. Livingston G, Huntley J, Sommerlad A, Ames D, Ballard C, Banerjee S, Brayne C et al. (2020) Dementia prevention, intervention, and care: 2020 report of the Lancet Commission. Lancet 396, 413-446

34. Maltby VE, Lea RA, Graves MC, Sanders KA, Benton MC, Tajouri L, et al. (2018) Genome-wide DNA methylation changes in CD19+ B cells from relapsing-remitting multiple sclerosis patients. Sci Rep 8:17418

35. Martin EM and Fry RC (2018) Environmental influences on the epigenome: exposure -associated DNA methylation in human populations. Annu Rev Public Health 39:309–33

36. Mattson MP and Arumugam TV (2018) Hallmarks of Brain Aging: Adaptive and Pathological Modification by Metabolic States. Cell Metab. 27(6):1176-1199

37. Mehla J, Gupta P, Pahuja M, Diwan D and Diksha D (2020) Indian medicinal herbs and formulations for Alzheimer's disease, from traditional knowledge to scientific assessment. Brain Sci 10;10(12):964

38. Morland C, Andersson KA, Haugen OP, Hadzic A, Kleppa L, Gille A, et al (2017) Exercise induces cerebral VEGF and angiogenesis via the lactate receptor HCAR1. Nat Commun 8:15557

39. Mukherjee PK, Kumar V, Kumar NS, Heinrich M (2008) The ayurvedic medicine *Clitoria ternatea* - From traditional use to scientific assessment. J. Ethnopharmacol., 120, 291–301

40. Paudel YN, Angelopoulou E, Semple B, Piperi C, Othman I and Shaikh MF (2020) Potential neuroprotective effect of the HMGB1 inhibitor glycyrrhizin in neurological disorders. ACS Chem Neurosci. 19;11(4):485-500

41. Ramaiah CV, Kumar GS and Rajendra W (2018) Traditional, ethnomedical, and pharmacological uses of *Celastrus paniculatus*. Asian J. Pharm 12, S1119–S1126

42. Rathore AS, Birla H, Singh SS, Zahra W, Dilnashin H, Singh R, Keshri PK and Singh SP (2021). Epigenetic modulation in Parkinson's disease and potential treatment therapies. Neurochem Res 46(7):1618-1626

43. Rozycka A and Liguz-Lecznar M (2017) The space where aging acts: focus on the GABAergic synapse. Aging Cell 16(4):634–643

44. Scarmeas N, Stern Y, Tang M-X, Mayeux R and Luchsinger JA (2006) Mediterranean diet and risk for Alzheimer's disease. Ann Neurol 59, 912-921
45. Sharifi-Rad J, El Rayess Y, Rizk AA, Sadaka C, Zgheib R, Zam, et al. (2020) Turmeric and its major compound curcumin on health: Bioactive effects and safety profiles for food, pharmaceutical, biotechnological and medicinal applications. Front Pharmacol. 11:01021
46. Sharma P, Dwivedee BP, Bisht D, Dash AK and Kumar D (2019) The chemical constituents and diverse pharmacological importance of *Tinospora cordifolia*. Heliyon. 12;5(9): e02437
47. Shin SJ, Jeon SG, Kim JI, Jeong YO, Kim S, Park YH, Lee SK, Park HH et al. (2019) Red ginseng attenuates Aβ-induced mitochondrial dysfunction and Aβ-mediated pathology in an animal model of Alzheimer's disease. Int J Mol Sci. 21;20(12):3030
48. Singh P and Thakur MK (2014) Reduced recognition memory is correlated with decrease in DNA methyltransferase1 and increase in histone deacetylase2 protein expression in old male mice. Biogerontology 15:339–346
49. Singh P and Thakur MK (2018) Histone Deacetylase 2 Inhibition Attenuates Downregulation of Hippocampal Plasticity Gene Expression during Aging. Mol Neurobiol. 55(3):2432-2442
50. Singh P, Sivanandam TM, Konar A and Thakur MK (2021) Role of nutraceuticals in cognition during aging and related disorders. Neurochem Int 143:104928
51. Singh SK, Barreto GE, Aliev G and Echeverria V (2017) *Ginkgo biloba* as an alternative medicine in the treatment of anxiety in dementia and other psychiatric disorders. Curr Drug Metab 18(2):112-119
52. Srivas S and Thakur MK (2017) Epigenetic regulation of neuronal immediate early genes is associated with decline in their expression and memory consolidation in scopolamine-induced amnesic mice. Mol Neurobiol 54(7):5107-5119
53. Stoccoro A and Coppedè F (2018) Role of epigenetics in Alzheimer's disease pathogenesis. Neurodegener Dis Manag. 8:181– 93
54. Taylor JP, Brown RH Jr and Cleveland DW (2016) Decoding ALS: from genes to mechanism. 10;539(7628):197-206
55. United Nations, Department of Economic and Social Affairs, Population Division (2017) World population prospects: the 2017 revision, key findings and advance tables. Working Paper No. ESA/P/WP/248
56. VanGuilder H and Freeman W (2011) The hippocampal neuroproteome with aging and cognitive decline: past progress and future directions. Front Aging Neurosci 3:8
57. Wang H-X, Karp A, Winblad B and Fratiglioni L (2002) Late-life engagement in social and leisure activities is associated with a decreased risk of dementia: A longitudinal study from the Kungsholmen Project. Am J Epidemiol 155, 1081-1087
58. Watson RE and Goodman JI (2002) Epigenetics and DNA methylation come of age in toxicology. Toxicol Sci. 67:11–6
59. Weyrich A, Jeschek M, Schrapers KT, Lenz D, Chung TH, Rübensam K, et al (2018) Diet changes alter paternally inherited epigenetic pattern in male Wild guinea pigs. Environ Epigen. 4: dvy011
60. Wilkins LJ, Monga M, Miller AW (2019) Defining dysbiosis for a cluster of chronic diseases. Sci Rep 9:12918
61. Wyss-Coray T (2016) Ageing, neurodegeneration and brain rejuvenation. Nature. 10;539(7628):180-186