Original Research Paper

Volume - 14 | Issue - 02 | February - 2024 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Pharmacy

PHARMACOLOGICAL ACTIVITY OF ALMONDS IN NEUROLOGICAL HEALTH: A REVIEW

Diksha*	CT College of Pharmacy, Shahpur, Jalandhar, India, Pincode-144020 *Corresponding Author
Harshpreet Kaur	CT College of Pharmacy, Shahpur, Jalandhar, India, Pincode-144020
Kamal Kumar	CT College of Pharmacy, Shahpur, Jalandhar, India, Pincode-144020
Shikha Sharma	CT College of Pharmacy, Shahpur, Jalandhar, India, Pincode-144020

ABSTRACT Almond is a wholesome natural food containing variety of nutrients essential for humans. Natural source of almond is the Prunus amygdalus L., belonging to family Rosaceae. The almond, also referred to as the "king of nuts," is a very nourishing food. Healthy fats, proteins, minerals, and vitamins are abundant in almonds. In addition to its nutritional benefits, it also contains some therapeutic qualities that could be useful in the treatment of several illnesses and health issues. The almond is a valuable food treatment for various common disorders and a powerful food that improves both physical and mental health. Almonds play major role in the regulation of some important neurotransmitters in the body and thus playing significant role in diseases related to the neurotransmitters. In this article, different components of almonds are discussed which are expected or assumed to play a role in regulation of different brain related diseases. Some of them are well defined and literature for the same is also available but some relations between different components and their uses are only assumed.

KEYWORDS : Almond, Alzheimer's disease, Neurological, Constituents

INTRODUCTION

Prunus amygdalus L., belonging to family Rosaceae, is the source of almonds. Almonds were once assigned to the Prunoideae (sub-family), but they are usually kept in their own family (Amygdalaceae or Prunaceae). It has recently been clear that almonds originated from the Spiraeoideae family [1].There are three different types of almonds; all of them yield nuts, but only some of them are edible. One almond variety yield the tasty, sweet nuts we consume, another yields bitter, toxic nuts, while a third variation yields a combination of bitter and sweet nuts. Commercial almond cultivation focuses on two main varieties: sweet almonds (*Prunus amygdalus* dulcis) and bitter almonds (*Prunus Amygdalus* amara) [2]. It is referred to as sweet almond in English, badamshireen in Persian, lauzulhulu in Arabic, almendro in Spanish, amendoeira in Portuguese, badanmu in Chinese, amendoeira in Greek, mandebaum in German, badamamu in Telgu, bilatibadam in Malayalam, and badam in Hindi and Urdu [3].

The Prunus amygdalus tree produces drupes containing edible kernels commonly referred to as almonds or badam (Prunus amygdalus L.) [4]. Almonds have been designated the "king of nuts" based on their rich composition of essential nutrients like proteins, minerals, fats and vitamins making them a noteworthy component of dietary regimes focused on health and well-being. Beyond established nutritional value, almonds possess therapeutic properties with potential applications in managing various medical conditions and mental health as well [5]. Prunus amygdalus kernels exhibit diverse pharmacological activities including anti-stress, antioxidant, immunostimulant, cholesterol-lowering, and laxative effects [6-7]. They are rich in copper, iron, and vitamin content suggests potential in treating anemia, while contributing to brain health, muscle building, and potentially longevity [8-9].

Almonds play major role in the regulation of some important neurotransmitters in the body and thus playing significant role in diseases related to the neurotransmitter. Neurotransmitters are endogenous chemical messengers that convey and amplify nerve-to-nerve signalling or signals between nerves and other cell types, play a crucial role in information transmission across the Brain and peripheral nervous system [10-11]. These substances are important regulators of neuronal development, differentiation, and survival, and they play crucial roles in the proper functioning of the brain. Because of the disruption of brain activities caused by elevated neurotransmitters levels, many physical, psychiatric, and neurodegenerative disorders can result [12-13]. In one study, almonds were discovered to increase the brain's Ach level and subsequently enhance rats' memory, as a result having a significant part in cognition-related disorders [14].

Almonds contain an abundant amount of magnesium and fulfil around 18% daily value of magnesium [15]. Magnesium plays a significant role as anti-depressant and it is expected to be associated with modulation of glutamatergic pathway. As glutamate is a crucial neurotransmitter playing role in memory and learning process [16]. Thus indicating role of almond in memory and learning process by regulating neurotransmitter glutamate indirectly.

Almonds are the rich source of different amino acids and one of them is tyrosine with 0.45g/100g value [17]. Tyrosine's hydroxylation into L-DOPA is catalysed by tyrosine hydroxylase enzyme. The pathway produces the catecholamines dopamine, epinephrine, and norepinephrine, which play crucial roles as neurotransmitters and hormones in both the central and peripheral nervous systems [18-19]. There is no evidence of direct effect of almonds on increase and decrease of neurotransmitters such as dopamine.

Geographical Description

The almond tree is indigenous to the warmer regions of western Asia and North Africa, but it has spread widely throughout the mild temperate portion of the world. It is grown in California as well as all the nations that border the Mediterranean Sea, including Spain, Italy, Portugal, and Morocco. The world's largest producer of almonds is the United States, particularly California. Its cultivation in India is primarily restricted to the Tibetan border regions of Kashmir and portions of Himachal Pradesh [20-21].

Chemical Constituents

Almonds are an excellent source of nutrients linked to heart health, including potassium, vitamin E, monounsaturated fatty acids, and polyunsaturated fatty acids [22].One of the best food sources of vitamin E is almonds, specifically RRR-tocopherol. Flavonols (isorhamnetin, kaempferol, quercetin, catechin, and epicatechin), flavanones (naringenin), anthocyanins (cyanidin and delphinidin), procyanidins, and phenolic acids (caffeic acid, ferulic acid, P-coumaric acid, and vanillic acid) are among the other phenolic compounds found in almonds that are localized in their skin [23]. Almonds contain globulins such as albumin and amandine along with amino acids including arginine, histidine, lysine, phenylalanine, leucine, valine, tryptophan, methionine, and cystine that are active components. Proteins and several minerals, including calcium and magnesium, are also found in almonds. Additionally, they are abundant in monounsaturated fat, dietary fiber, vitamin B, and essential minerals. Additionally, almonds contain phytosterols, which may have cholesterol-lowering effects as shown in Table I [24].

Table I: Composition of Natural Almond

NUTRIENTS	UNITS	AMOUNT PER 100g
PROXIMATES		

Water	G	4.70
Protein	G	21.22
Lipids (total)	G	49.42
Dietary fibre (total)	G	12.20
Sugars (total)	G	3.89
Ash	G	2.99
MINERALS		
Calcium (Ca)	Mg	264
Iron (Fe)	Mg	3.72
Magnesium (Mg)	Mg	268
Phosphorus (P)	Mg	484
Potassium (K)	Mg	705
Sodium (Na)	Mg	1
Zinc (Zn)	Mg	3.08
Copper (Cu)	Mg	1.00
Manganese (Mn)	Mg	2.29
VITAMINS		
Vitamin E (α-tocopherol)	Mg	26.22
Thiamin	Mg	0.21
Riboflavin	Mg	1.01
Niacin	Mg	3.39
Pantothenic acid	Mg	0.47
Vitamin B6	Mg	0.14
Folate, food	Mcg	50
FATTY ACIDS		
Saturated (total)	G	3.73
16:0 Palmitic	G	3.04
18:0 Stearic	G	0.66
Monounsaturated (total)	G	30.89
16:1 Palmitic	G	0.24
18:1 Oleic	G	30.61
Polyunsaturated (total)	G	12.07
18:2 Linoleic	G	12.06

ROLE

Role RolRole Role of Almond in Brain

Almonds are incredibly nutrient-dense, packed with good fats, antioxidants, vitamins, and minerals that your body and brain both require to function well. High levels of antioxidants present in the almonds help shield your cells from oxidative stress and free radicals, which can speed up aging, increase the risk of cancer, and cause neurological illnesses like Alzheimer's disease (AD) and other types of dementia. One of the best sources of vitamin E in the world is almonds. Higher vitamin E levels have been linked by scientific research to a slower rate of cognitive aging, and a lower risk of cancer and AD. Almonds vitamin E contributes to the brain's defense against oxidative stress. When there is too much oxygen in circulation, oxidative stress happens. AD and other types of dementia are brought on by the damage this extra oxygen causes to the brain tissue.

Lean protein is moderately abundant in almonds and it aids in brain cell repair, enhancing mental abilities like memory. Almonds help prevent brain and memory issues by enhancing acetylcholine, a neurotransmitter that conveys impulses in the brain, according to many research that examined the advantages of routinely consuming almonds [25].

Acetylcholine is the important neurotransmitter playing role in many brain disorders specifically in AD.

Role of Acetylcholine in AD

The most prevalent form is a neurological condition that progresses over time and is frequently recognised [26]. It has a very high mortality rate and is strongly correlated with both genetic and ageing variables. The prevalent disease dementia, which begins with an irreversible deterioration in episodic memory and progresses to a more general decline in overall cognitive capacity in the aged, is largely caused by AD [27-28]. Disorientation and a slow decline in memory and intelligence are characteristics of AD. About 12% of elders are impacted. According to WHO estimates, the condition is present in more than 48.6 million persons worldwide[29-31].

The development of many senile plaques (SP) in the cerebral cortex and hippocampus, the loss of functional neurons and synapses in specific brain regions, and acetylcholine shortage are the key pathogenic characteristics of AD. Progressive memory loss and cognitive decline are the predominant clinical indications, which are accompanied by behavioural changes and signs of other neurological conditions. There are now a number of hypotheses for AD, including the cholinergic hypothesis, the au protein hypothesis, the αβ deposition hypothesis, and the neuroinflammation hypothesis, however, the precise etiology of AD is still unknown[32-33].

The cholinergic hypothesis, which has a considerable impact on AD pathogenesis, is one of the early theories regarding AD pathogenesis. A crucial excitatory neurotransmitter involved in memory, learning, and other cognitive actions is acetylcholine (ACh). The central cholinergic nerve system can influence the amount of acetylcholine by controlling the synthesis and release of ACh [34]. The function of the basic forebrain cholinergic neurons (BFCNs) is important for memory formation, learning, and cognitive processes. They dominate the cortical and hippocampus regions involved in memory and learning, and their survival and differentiation are dependent on nerve growth factor (NGF). The brain's hippocampus has a lot of nicotinic acetylcholine receptors (NACHR)[35-37].

Degeneration of deep and early BFCN is a constant symptom of AD patients. Memory loss is thought to be primarily caused by synapse loss between the basal forebrain and its target tissues, the hippocampus and cortex, which is correlated with the severity of dementia. Clinical evidence from recent years indicates that AD patients' brains have significant neurodegeneration, a loss in cholinergic neurons, and a severe ACh shortage [38-39]. As the treatment used in Alzheimer's disease is usually based on acetylcholine therapy thus the almonds play a significant role.

Role of Acetylcholine in Myasthenia Gravis

The most prevalent main disease of neuromuscular transmission is Myasthenia Gravis. More than 80–90% of patients with generalised myasthenia gravis, about 50% of patients with pure ocular myasthenia, and infrequently in healthy individuals have ACh receptor antibodies found in their serum [40]. It is the rare autoimmune disease in which immune system-produced antibodies target the neuromuscular junction, which connects muscles and neurons. Muscles weaken and fatigue quickly as a result of blocked nerve impulses. The severity of symptoms varies [41-42]. The main aim of treatment of myasthenia gravis is to increase the level of acetylcholine because acetylcholine binds to its receptors to activate the muscles and causes the muscle contraction. Hence the almonds with their acetylcholine increasing capacity can aid in Myasthenia Gravis disease treatment [43-44].

Memory Enhancing Effect of Almonds That Can Aid In Brain Health

The effectiveness of *Prunus Amygdalus* L. nuts in improving memory in rats with scopolamine-induced amnesia was investigated in a study. Three different dose levels of Prunus Amygdalus L. nuts were orally administered to rats for seven to fourteen days utilizing the elevated plus maze, motor activity, and passive avoidance models. Piracetam was employed as a reference medication at a dose level of 0.2g/kg. After therapy, it was found that rats' brain ChE activity was decreased [45]. Another study used the Radial Arm Maze and Elevated plus maze assays to measure the effect of almond paste on memory. Rats given almond paste orally for 28 days showed a considerable improvement in their learning and memory abilities [46].

Antidepressant Activity of Almond

A prolonged sense of sadness and a lack of interest in routine activities are two characteristics of the mental illness known as depression. The World Health Organisation estimates that depression affects about 21% of people worldwide. Forced swim and passive avoidance tests were used in a study to examine the antidepressant efficacy of almond and lavender oils. Model animals were male Wister mice with body weights one heavy and another lightweight. An oral dose of almond oil (3.2g/kg) was given. Model animals were exposed to lavender oil inhalation for 30 to 60 minutes. After receiving combination therapy, significant anti-depressant benefits were seen in rats [47].

Role of Magnesium in Brain

Almond is rich source of magnesium. Magnesium is necessary for the synthesis of DNA, RNA, and proteins as well as for the regulation of blood pressure, insulin metabolism, and muscle contraction, particularly that of the cardiovascular system. Magnesium helps the

nervous system function properly in terms of nerve conduction, neuromuscular coordination, and protection against excitotoxicity [48-49].

The quantity and quality of information on the relationship between magnesium and the many neurological illnesses studied vary substantially. Strong evidence supports magnesium's significance in migraine and depression. Magnesium has a strong chance of helping with diseases including chronic pain as well as frequently coexisting psychological problems like anxiety and depression. The effects of magnesium in epilepsy require a much more extensive investigation, including clinical trials examining the utilization of magnesium as an additional therapy.

Additional studies that take CSF and MRS measurements of CNS magnesium levels to better understand neurological illnesses like Parkinson's and Alzheimer's would be very helpful. Finally, some research points to magnesium as a valuable nutritional strategy for potentially preventing stroke and for improving after-stroke outcomes, while more prospective trials are required in this area [50].

Role of Riboflavin in Brain

Almonds contain a moderate amount of riboflavin (Vitamin B2). Riboflavin exerts neuroprotective mechanisms. Significant pathogenesis-related pathways include but are not limited to, those that are shared by migraine headaches and Parkinson's disease (PD). The neuroprotective mechanisms proposed for riboflavin can address such pathogenesis-related pathways. It has been discovered that riboflavin reduces the pathogenesis of PD, migraine headaches, and other neurological illnesses by reducing oxidative stress, mitochondrial dysfunction, neuroinflammation, and glutamate excitotoxicity. Additionally, pyridoxine activation, the tryptophan-kynurenine pathway, and homocysteine metabolism all depend on riboflavin-dependent enzymes. In fact, it has been discovered that the active form of pyridoxine, pyridoxal phosphate, has independent neuroprotective potential. Additionally, the kynurenines generated have an impact on glutamate receptors and the ensuing excitotoxicity. In conclusion, riboflavin has the potential to be a neuroprotective agent for a variety of neurological conditions, such as PD, a neurodegenerative disorder, and migraine headache, a pain disorder. In a recent study, it was discovered that long-term riboflavin insufficiency could contribute to the development of multiple neurological disorders, especially in vulnerable populations, given that only 10-15% of the world's population has adequate riboflavin absorption and utilisation [51]. Thus to maintain adequate concentration of riboflavin in body or specifically absorption of riboflavin in body almonds can be of great help.

There is no significant evidence of almonds use in brain disorders directly but with the indirect way of modulating neurotransmitter, increasing magnesium amount and for providing enough number of antioxidants and vitamins (like riboflavin) it can be expected that almonds are beneficial in brain disorders and is an important portion of human diet.

CONCLUSION

Almond is the promising natural food with various uses and also significant role in disease regulation. It plays a significant role in brain health. There are number of studies which have revealed about the clinical significance of daily use of almond or the use of almond as a part of daily diet. Still the mechanism of action of almond in regulation of this variety of disease is unclear and also which component is responsible for the same is also not clear in many cases. In future, further studies should be conducted to clarify the mechanism of action and role of different components of almonds in disease regulation by using number of observational, case control studies.

REFERENCES

1. Potter D, Eriksson T, Evans RC, Oh S, Smedmark S, Morgan DR, Kerr M, Robertson KR, Arsenault M, Dickinson TA. Phylogeny and classification of Rosaceae. Plant systematics and evolution, 2007, 266(1-2): 5-43.
2. Rao H. Therapeutic applications of almonds (Prunus amygdalus L.): a review. J. Clin. Diagn. Res. 2012, 6: 130-135.
3. Abdullah MK, Hussain MK. Badam (Prunus amygdalus Bail.): A Fruit with Medicinal Properties. International Journal of Herbal Medicine. 2017, 5(5): 114-117.
4. Agunbiade SO, Olankolun JO. Evaluation of some nutritional characteristics of the Indian almond (Prunus amygdalus) nut. Pak J Nutr 2006, 5:316-18.
5. Bansal P, Sannd R, Srikanth N, Lavekar GS. Effect of a traditionally designed nutraceutical on the stress induced immunoglobulin changes at Antarctica. Afr J Biochem Res. 2009, 3:1084-88.
6. Pinelo M, Rubilar M, Sineiro J, Nunez MJ. Extraction of anti-oxidant phenolics from almond hulls (Prunus amygdalus) and pine sawdust (Pinus pinaster). Food Chem. 2004, 85:267-73.
7. Puri A, Sahai R, Singh KL, Saxena RP, Tan don JS, Saxena KC, Immunostimulant activity of dry fruits and plant materials which are used in the Indian traditional medical system for mothers after child birth and invalids. J Ethanopharmacol. 2000, 71:89-92.
8. Spiller GA, Jenikins DA, Bosello O, Gates JE, Cragen LN. Bruce nuts and plasma lipids: An almond –based diet lowers the LDL-C while it preserves the HDL-C. J Am Coll Nutr. 1998, 17:285-90.
9. Sharma RP, Saamhita C. Agnivesha Treatise. Sutrashana. Varanasi: Chokambha Sanskrit Sansthan. 1981.
10. Banerjee S, McCracken S, Hossain F, Slaughter, G. Electrochemical Detection of Neurotransmitters. Biosensors. 2020, 10: 101.
11. Moini J, Koenitzer J, LoGalbo A. Chapter 2—Brain neurotransmitters. In Global Emergency of Mental Disorders Eds.; Academic Press: Cambridge, MA, USA. 2021, 31–40.
12. Bhat S, El-Kasaby A, Freissmuth M, Sucic S. Functional and Biochemical Consequences of Disease Variants in Neurotransmitter Transporters: A Special Emphasis on Folding and Trafficking Deficits. Pharmacol. Ther. 2021, 222:107785.
13. Yadav D, Kumar P. Restoration and targeting of aberrant neurotransmitters in Parkinson's disease therapeutics. Neurochem. Int. 2022, 156: 105327.
14. Kulkarni KS, Kastura SB, Mengi SA. Efficacy of the Prunus amygdalus (almonds) nuts in scopolamine induced amnesia in rats. Indian J Pharmacol. 2010, 42:168-73.
15. https://www.fda.gov/food/new-nutrition-facts-label/daily-value-new-nutrition-and-supplement-facts-labels.
16. Song C, Leonard BE. The olfactory bulbectomised rat as a model of depression. Neurosci Biobehav Rev. 2005, 29:627–647.
17. U.S. Department of Agriculture, A.R.S U.S. Department of Agriculture, Agricultural Research Service. Food Data Central. [accessed on 1 March 2020]
18. Molinoff PB, Axelrod J. Biochemistry of catecholamines. Annual Review of Biochemistry. 1971, 40:465–500.
19. Weiner N. Tyrosine-3-monooxygenase (tyrosine hydroxylase) In: Youdim MBH, editor. Aromatic amino acid hydroxylases and mental disease. John Wiley & Sons, Ltd; New York. 1979, 141–190.
20. Parle M, bohria M. Almond: A health diamond' Annals of Pharmacy and Pharmaceutical Sciences, 2010, 1: 147-151.
21. Verma MK. Almond Production Technology. 2014, 274-280.
22. Nuts, almonds [online]. USDA National Nutrient Database for Standard Reference, Release 17 (2004). Agricultural Research Service, U.S. Department of Agriculture. Http://www.nal.usda.gov/fnic/foodcomp/ search/index.html.
23. Frison-Norrie S, Sporns P. Identification and quantification of flavonol glycosides in almond seed coats by using MALDI-TOF.MS. J. Agric. Food chem. 2002, 50:2782-2787.
24. Phillips KM, Ruggio DM, Ashraf-khorassani M. The phytosterol composition of the nuts and seeds which are commonly consumed in the United States. J Agric Food Chem. 2005, 53:9436-45.
25. U.S. Department of Agriculture, A.R.S U.S. Department of Agriculture, Agricultural Research Service. FoodData Central. [accessed on 1 March 2020]
26. Ozdemir B. Health properties of almond. Journal of Hygienic Engineering and Design. 2016, 17: 28-33.
27. Park HJ, Kwon H, Lee JH, Cho E, Lee YC, Moon M, Jun. β-Amyrin Ameliorates Alzheimer's Disease-Like Aberrant Synaptic Plasticity in the Mouse Hippocampus. Biomol. Ther. 2020, 28: 74–82.
28. Hafez HS, Ghareeb DA, Saleh SR, Abady MM. Neuro-protective effect of ipriflavone against scopolamine-induced memory impairment in rats. Psychopharmacology. 2017, 234: 3037–3053.
29. Osborn LM, Kamphuis W, Wadman WJ, Hol EM. Astrogliosis: An integral player in the pathogenesis of Alzheimer's disease. Prog. Neurobiol. 2016, 121–141.
30. Garabadu D, Verma J. Exendin-4 attenuates brain mitochondrial toxicity through PI3K/Akt-dependent pathway in amyloid β (1–42)-induced cognitive deficit rats. Neurochem. Int. 2019, 128: 39–49.
31. Semwal BC, Garabadu D. 5-N-ethyl Carboxamidoadenosine Stimulates Adenosine-2b Receptor-Mediated Mito-gen-Activated Protein Kinase Pathway to Improve Brain Mitochondrial Function in Amyloid B-Induced Cognitive Deficit Mice. Neuromolecular Med. 2020, 22: 542–556.
32. Morales I, Cerda-Troncoso C, Andrade V, Maccion RB. The Natural Product Curcumin as a Potential Coadjuvant in Alzheimer's Treatment. J. Alzheimer's Dis. 2017, 60: 451–460.
33. Thangnipon W, Puangmalai N, Soi-Ampornkul R, Suwanna N, Tuchinda P, Nobsathian S. Neuroprotection of Nbenzylcinnamide on scopolamine-induced cholinergic dysfunction in human SH-SY5Y neuroblastoma cells. Neural Regen. Res. 2017, 12: 1492–1498.
34. Thompson KJ, Tobin AB. Crosstalk between the M1 muscarinic acetylcholine receptor and the endocannabinoid system: A relevance for Alzheimer's disease Cell Signal. 2020, 70: 109545.
35. Bekdash R. The Cholinergic System, the Adrenergic System and the Neuropathology of Alzheimer's Disease. Int. J. Mol. Sci. 2021, 22: 1273.
36. Hu Y, Qu ZY, Cao SY, Li Q, Ma L, Krencik R, Xu M, Liu Y. Directed differentiation of basal forebrain cholinergic neurons from human pluripotent stem cells. J. Neurosci. Methods 2016, 266: 42–49.
37. Latina V, Caioli S, Zona C, Ciotti MT, Borreca A, Calissano P, Amadoro G. NGF-Dependent Changes in Ubiquitin Homeostasis Trigger Early Cholinergic Degeneration in Cellular and Animal AD-Model. Front. Cell Neurosci. 2018, 12: 487.
38. Cafe-Mendes CC, Garay-Malpartida HM, Malta MB, Marcourakis T. Chronic nicotine treatment decreases LPS signalling through NF-kappaB and TLR-4 modulation in the hippocampus. Neurosci. Lett. 2017, 636: 218–224.
39. Fahnestock M, Shekari A. ProNGF and Neurodegeneration in Alzheimer's Disease. Front. Neurosci. 2019, 13: 129.
40. Bowen DM, Smith CB, White P, Davison AN. Neurotransmitter-related enzymes and indices of hypoxia in senile dementia and other abiotrophies. Brain. 1976, 99: 459–496.
41. Lindstrom JM, Seybold ME, Lennon VA, Whittingham S, Duane DD. Antibody to acetylcholine receptor in myasthenia gravis: prevalence, clinical correlates, and diagnostic value. Neurology. 1976, 26:1054-9.
42. Vincent A, Palace J, Hilton.Jones D. Myasthenia gravis. Lancet. 2001, 357(9274): 2122.8.
43. Hart IK, Sathasivam S, Sharshar T. Immunosuppressive agents for myasthenia gravis. Cochrane Database of Systematic Reviews 2007, 4.
44. Gajdos P, Chevret S, Toyka K. Intravenous immunoglobulin for myasthenia gravis. Cochrane Database of Systematic Reviews 2009, 1.
45. Schneider.Gold C, Gajdos P, Toyka KV, Hohlfeld RR. Corticosteroids for myasthenia gravis. Cochrane Database of Systematic Reviews 2005, 2.
46. Kulkarni KS, Kasture S, Mengi S. Efficacy study of Prunus amygdalus (almond) nuts in scopolamine-induced amnesia in rats. Indian journal of pharmacology. 2010, 42(3): 168.
47. Haider S, Batool Z, Haleem D. Nootropic and hypophagic effects following long term intake of almonds (Prunus amygdalus) in rats. Nutricion hospitalaria. 2012, 27(6): 2109-2115.
48. Al-Sayari A, Ghazwani M, Alhamhoom Y, Almaghaslah D, Louis JV, Gurusamy N. The

antidepressant-like effect of almond oil: An additive effect with lavender oil. Biomedical Research. 2018, 29(18).
49. Grober, U.; Schmidt, J.; Kisters, K. Magnesium in prevention and therapy. Nutrients 2015, 7: 8199–8226.
50. Vink R, Nechifor M. Magnesium in the Central Nervous System; University of Adelaide Press: Adelaide, 2011, 342.
51. Kirkland AE, Sarlo GL, Holton KF. The Role of Magnesium in Neurological Disorders. Nutrients. 2018, 10(6): 730.