

Role of bioactive substances in sheep's milk and its products in the prevention of neurodegenerative diseases

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Summary

Aging is a major risk factor for cognitive decline, such as Alzheimer's disease (AD). Sheep's milk may play a role in the prevention of neurodegenerative diseases because of its high content of functional peptides, such as lactoferrin. Lactoferrin can be used in AD both as an active therapeutic compound and as a drug nanocarrier. Compared to cow's and goat's milks, sheep's milk contains the highest content of isomers of conjugated linoleic acid (CLA). The c-9, t-11-CLA isomers reduce the pathological changes occurring in AD mainly by reducing the amount of amyloid- β aggregates in brain tissues. Sheep's milk also contains higher concentrations of vitamin D and B-group vitamins, which have neuroprotective effects. This review summarizes the current knowledge on sheep's milk and its products, with a special focus on its role in the prevention of neurodegenerative diseases.

Keywords: sheep's milk, bioactive substances, neurodegenerative diseases

Aging is a consequence of the dysfunction and impairment of many different mechanisms in the body (71). It is a complex process that involves a wide range of brain changes, beginning on the molecular level to ending on the functional level, with clear genetic and biophysical links (18, 72). Aging has a strong impact on a number of genes and biological pathways that are also linked with neurodegenerative diseases (70). Glorioso et al., 2011 reported a large overrepresentation of genes related to brain aging (27). Age-related genes include genes encoding neuropeptides (*SSZNPY*, *CCK*, *CRF*), trophic factors (*BDNF*, *IGF1*, *FGF*), receptors (*HTR2A*, *DRD1*, *CB1R*, *GABRAA5*, *FGF2R*), and numerous other disease-related genes, including those related to neurodegenerative diseases (*MAOB*, *PER3*, *CLU*, *SYN*, *HTT*, *NRG1*, *RLN*, *TAU*, *PARK*, *PINK1*, *NFKB*, *SOD2*, *RGS4*) (27). As we age, the brain undergoes significant changes in structure, function, and metabolic processes, often associated with cognitive decline and behavioral changes (18, 72). During aging, the brain shows characteristic signs of impaired bioenergetics at the cellular and molecular levels, including abnormal neural network activity,

impaired DNA repair mechanism, mitochondrial dysfunction, disturbed neuronal Ca²⁺ homeostasis, and accumulation of inflammatory and oxidatively modified organelles (9, 71). An excessive and abnormal accumulation of aging cells in body tissues can negatively affect the regenerative capacity and promote the onset and progression of various age-related diseases (69). The brain has a higher metabolic rate than the rest of the body and consumes a large proportion of the total oxygen intake, thereby increasing the potential for the production of reactive oxygen species and subsequent oxidative stress (66). Oxidative stress mediates specific neuronal damage, including modifications to lipids, proteins, and DNA, which leads to inflammation and altered neuronal function (70). A characteristic feature of the aging process is also a disturbed homeostasis of iron (45), manifested by excessive deposits of this element in the brain, which contributes to cognitive dysfunction (85). Aging is also associated with a significant decline in immunity and persistent inflammatory responses (67). Brain aging is characterized by degradation processes at the level of cells, tissues, and organs that lead to morphological changes, such as

loss of brain volume, thinning of the cerebral cortex, degradation of white matter, loss of gyrification and enlargement of ventricles (12). From the pathophysiological point of view, brain aging is associated with neural cell shrinkage, dendrite degeneration, demyelination, small vessel disease, metabolic slowdown, microglial activation, and white matter lesions (12). All of these changes significantly contribute to the decline of neurological abilities with age and make the aging brain vulnerable to neurodegenerative diseases (48, 70). Although cognitive decline is a natural aspect of aging, it can sometimes become pathological – for example, in Parkinson's disease (PD) or Alzheimer's disease (AD). Many other age-related factors influence brain changes, including exercise, high blood pressure, obesity, alcohol consumption, smoking, and diet. These factors may affect brain structure and function in multiple ways (72). However, aging is a major risk factor for cognitive decline, as well as many chronic and neurodegenerative diseases (18, 44). AD is the most common neurodegenerative disease in older adults (31). AD is a heterogeneous neurological disorder with a complex etiology (18). It is characterized by progressive memory loss that causes severe behavioural and cognitive problems. Worldwide, approximately 50 million patients suffer from dementia, and AD is responsible for 60-80% of these cases (1). Even in genetically predisposed people, AD does not always appear in middle age, which suggests that its development is due to an age-related process (13). Early cortical changes in AD include neuritis and elevated iron levels (79). However, the most characteristic factors responsible for the formation and progression of this disease are beta sheet protein aggregates, i.e. neuritic amyloid plaques (74), clusters of abnormal form of tau protein inside neurons (tau tangles), neurofibrillary tangles (NFT), oxidative stress, and cholinergic dysfunction (1, 9, 13). The main component of amyloid plaques is amyloid beta ($A\beta$) peptides, which cause damage to the plasma membrane of neurons, disturbances in calcium homeostasis, and changes in the levels of neurotrophic factors. Moreover, $A\beta$ triggers neurodegeneration by inducing *LVSCC AIC* expression and an increase in nerve growth factor (NGF) levels and by suppressing *VDR* expression (21). Due to their effects, $A\beta$ aggregates are considered to be one of the main factors causing AD (61). Additionally, tau tangles inside neurons block the transport of nutrients and other molecules necessary for the proper functioning and survival of neurons (1). In general, the aging process is also a risk factor for many chronic diseases, including cancer, atherosclerosis, arthritis, and other neurodegenerative diseases, which may prove their common origin with different consequences (13). Therefore, in older adults, it can be difficult to distinguish between the pathology of AD and the pathology of aging (56).

The importance of diet

Current treatments for AD focus mainly on the administration of symptomatic drugs that provide little relief to patients and may cause various side effects (38). That is why preventing or delaying the onset of the disease is so important in improving the health and quality of life of older people (73). Certain nutrients help prevent the onset and development of neurological diseases, such as AD. Thus, nutritional and neurological problems are linked with each other, which could lead to the development of new treatments (76). A promising strategy could be to use an appropriate diet (28), which can eliminate the problem of side effects of medication and reduce the number of patients requiring medical care. A diet rich in fatty acids, especially monounsaturated fatty acids (MUFA) and n-3 polyunsaturated fatty acids (PUFA), may play an important role in the prevention of cognitive decline associated with aging or dementia (73). The available literature reports that some diets may limit the risk of AD (20, 73). The most appropriate model to follow seems to be the Mediterranean diet including large quantities of MUFA-rich olive oil (60, 73). The latest research by Bagalagel et al., 2022 showed that the extract from *Olea europaea* L. cv. Picual (an olive variety from Saudi Arabia) had neuroprotective and anti-amnesic effects *in vivo* against cognitive decline and brain damage in a mouse AD model (9). In addition, the Mediterranean diet is also based on the consumption of large amounts of dairy products, mainly cheese. Cheese is a dairy product made by coagulating casein, mainly from the milk of cows, goats, and sheep (39). Mixed sheep's and goat's milk cheeses are common in many countries. In Greece, sheep's milk is used mainly to produce feta, which is made from sheep's milk or a mixture of sheep's and goat's milk and is the most important export product (62). Other traditional Greek cheeses made from sheep's milk include pecorino, manchego, and roquefort (62). The main sheep cheese produced in Italy is pecorino romano cheese, which is the leader in the international trade in sheep milk cheeses (62). Many biologically active substances have been found in fermented sheep's milk products, such as yogurt and cheese (34, 66, 68, 75). Sheep's milk and its products, which naturally contain bioactive substances, may be promising ingredients for the production of health-promoting functional food (25). Sheep's milk contains a favorable profile of fatty acids, especially essential fatty acids (EFAs), n-6, and n-3, and the highest content of conjugated linoleic acid (CLA) isomers (53). The pro-health qualities of sheep's milk are also evidenced by its high content of minerals, fat-soluble vitamins, and B-group vitamins (10). Sheep's milk proteins have antioxidant, antimicrobial, antihypertensive, and antithrombotic properties that affect many physiological processes (23). Moreover,

sheep's milk contains peptides that have a regenerating effect in neurodegenerative diseases and a number of multifunctional peptides with a comprehensive effect.

The importance of proteins

A major challenge in the treatment of AD is the very low efficacy of drugs due to the blood-brain barrier, which allows only a few types of molecules to penetrate from the circulation to the central nervous system. The solution seems to be the use of lactoferrin (LF), which penetrates the blood-brain barrier and can form micelles with other biologically active molecules and thus precisely deliver drugs to the brain. LF penetrates the brain parenchyma by absorption from the sublingual mucosa (30). LF is a multifunctional glycoprotein with high affinity for iron. LF plays a vital role in anti-inflammatory, antibacterial, and antiviral modulators of reactive oxygen species, anticancer immunity, and antiapoptotic processes (41). Because of its properties, LF can be used in AD both as an active therapeutic compound and as a drug nanocarrier (41). Research by Agwa et al., 2020 has shown that LF-CLA micelles show enhanced biodistribution *in vivo* in brain tissue because of the active targeting potential of LF (4). Moreover, CLA exhibited sustained release, good hemocompatibility, and no *in vivo* toxicity for the liver and kidneys. Additionally, LF-CLA micelles reduced oxidative stress, inflammation, and apoptosis, and increased cognitive performance in a mouse model of aluminum chloride-induced AD (4). Studies show that exogenous administration of LF reduces memory impairment and A β aggregation in a mouse model of AD (2) and improves cognitive performance in a model of naturally aging C57/BL6J mice (84). In addition, LF reduces the production of reactive oxygen species in the hippocampus, which is associated with the mitigation of oxidative stress and inflammatory reactions, as well as the reduction of iron deposits in brain tissues (84). Dietary LF administered to AD patients limits cognitive decline by modulating the p-Akt/PTEN pathway and thus reducing inflammation and oxidative stress that are involved in AD pathology (50). An important marker of early AD is an abnormal iron metabolism. Studies have shown that AD patients have elevated iron levels in the cerebral cortex, subcortex, and white matter of the brain (32). Sheep's milk is richer in LF (0.7-0.9 g/L) than cow's milk (0.02-0.5 g/L) (51). LF may be useful in treating brain pathologies related to iron accumulation because of its anti-inflammatory and antioxidant properties and its ability to bind and modulate iron (32). These protective effects of LF may represent promising targets for the prophylaxis and therapy of AD in the future (50). Milk protein comprises approximately 80% of caseins and 20% of whey proteins (8). Whey protein is a by-product of the production of cheese and other dairy products. Whey protein consists of, among others, β -lactoglobulin,

α -lactalbumin, immunoglobulins, serum, glycomacropptides, and smaller proteins, such as lactoperoxidase, lysozyme, and LF (8). Importantly, sheep's milk is the richest source of whey protein (1.02 g/100 g) (17). Recent studies have shown that a short-term administration of whey protein hydrolyzate to mice with scopolamine-induced amnesia resulted in a significant improvement in their memory and neuronal protection by reducing the aggregation of A β plaques (19). Whey proteins contain bioactive compounds that can reduce oxidative stress on the brain and restore normal cognitive function. Research by El-Beeh et al., 2022 showed that the administration of whey protein syrup to older Wistar albino rats (*Rattus norvegicus*) caused, among others, increased antioxidant activity while reducing A β deposits in brain tissue (22). Peptides in fermented milk products may also remedy memory disorders. Ano et al., 2019 identified the peptide KEMPFKYPVEP from β -Casein present in fermented milk products. Studies have shown that administration of that peptide prevents cognitive decline in a mouse model of scopolamine-induced amnesia (6). The level of KEMPFKYPVEP in Roquefort cheese made from sheep's milk (11.6 pmol/g) is higher than it is in cow cheddar cheese (1.52 pmol/g) (6).

PD is the second most common neurodegenerative disorder (80). It is characterized by, among others, increased oxidative stress and progressive loss of dopaminergic neurons derived from the substantia nigra pars compacta (35). Research by Ubaid et al., 2020 on a cellular model of PD induced by rotenone PC12 showed that a complex of camel α -lactalbumin and oleic acid (CLOA) may be a candidate for the development of future therapeutic drugs for PD (80). Moreover, treatment with the CLOA complex reduced oxidative stress and increased cell viability by increasing dopamine levels and the expression of *SIRT1*, *FOXO3a*, *HIF-1 α* , and *HSF-1* (80). Sheep's milk contains more α -lactalbumin (1.2-2.6 g/L) than cow's milk does (1-1.5 g/L) (51) and may therefore be another good alternative as a nutraceutical supplement for the neurological functions of older adults in the PD risk group.

Importance of fatty acids

The fatty acids in milk have a number of biological effects and health benefits. A characteristic feature of ruminant milk fat is the presence of CLA, which is a mixture of positional and geometric isomers of octadecadienoic acid C18:2. CLA has a broad health-promoting effect on the body and can prevent the occurrence of type 2 diabetes, AD, and cancer (24). Research by Kawęcka and Pasternak in 2021 showed that bundz (traditional Polish fresh cheese) made from sheep's milk had a higher content of fat (24.92%) and protein (18.06%) than bundz made from goat's milk (21.33% fat; 16.74% protein) (33). Moreover, the content of CLA was also significantly higher (2.23%) in

traditional sheep cheese than in goat cheese (0.28%) (33). Szterk et al., 2022 also studied the amount and profile of fatty acids in various original sheep, cow, and goat cheeses (75). Studies showed that Polish seasonal sheep cheeses (oscypek) were characterized by the highest content of health-promoting fatty acids: CLA 2.1-3.1%, trans-MUFA 3.5-6%, branched chain fatty acids (BCFA) 2.7-2.9%, and short-chain fatty acids (SCSFA) 12-18% (75). CLA reduces pathological changes due to AD in a mouse model of this disease by Nrf2-mediated adaptive response and upregulation of the brain glucose transporter (15). Sheep's milk is rich in CLA (53), and particularly important isomers are t-10, c-12-CLA, and c-9, t-11-CLA. In sheep's milk yoghurts, the content of the c-9, t-11-CLA isomer is higher (0.47-0.76 g/100 g of fat) than it is in cow's milk yoghurts (0.24-0.45 g/100 g of fat) (68). Moreover, research by Serafeimidou et al., 2013 showed that during a 14-day storage of products at 5°C, the CLA content in sheep's milk yoghurts significantly increased, while in cow's milk yoghurts it significantly decreased (68). Recent studies show that c-9, t-11-CLA may also prevent neurodegenerative diseases in the elderly because of its role in protecting neurons from the damaging effects of A β (29). However, in the same mouse model study, treatment with t-10, c-12-CLA had no effect on A β production (29). The role of c-9, t-11-CLA was also confirmed by Fujita et al., 2021 whose research on a mouse model of AD showed that the presence of c-9, t-11-CLA in the diet reduced inflammation as well as the amount of A β aggregates in brain tissues (26).

Importance of vitamins and antioxidants

Sheep's milk is an excellent source of B vitamins, which ensure the proper functioning of the nervous system (25). Vitamins from this group, and in particular vitamins B1 (thiamine), B6 (pyridoxine) and B12 (cobalamin), increase the speed of nerve conduction because they are involved in the synthesis of myelin, and their deficiencies can lead to the development of many neurodegenerative diseases (16). Recent research shows that increasing the daily intake of B vitamins in regular meals can help minimize the risk of dementia (54). The content of B vitamins in sheep's milk, amounting to 650-800 μ g/l for vitamin B1 (thiamine), 600-800 μ g/l for vitamin B6 (pyridoxine), and 6-7.1 μ g/l for vitamin B12 (cobalamin), is much higher than it is in cow's milk (B1: 300-450 μ g/l, B6: 390-600 μ g/l, B12: 3.5-4.0 μ g/l) or human milk (B1: 140-200 μ g/l, B6: 100-110 μ g/l, B12: 0.1-0.5 μ g/l) (51). Decline in the levels of vitamin B1 is related to age and strongly correlates with the deterioration of cognitive functions, and its supplementation may have positive effects on the treatment of AD and other neurodegenerative diseases (64, 81). Research by Ramamoorthy et al., 2022 showed that expression levels of thiamine transporters (THTR-1 and THTR-2)

are significantly downregulated in the brain of AD patients and in an animal model of AD (65). Moreover, their findings implicate neuritis in the dysfunction of thiamine transporters and suggest a beneficial effect of optimizing thiamine levels in brain tissues of AD patients, which can be achieved by administering pharmacological doses of B1 (65). Dietary vitamin B6 restriction plays a functional role in neuronal degeneration by disturbing the gamma-aminobutyric acid (GABA) balance, increasing oxidative stress and endoplasmic reticulum stress, and inducing A β accumulation and tau protein deposition (36). Research by Xu et al., 2022 showed that an adequate dietary intake of vitamins B9 and B12 is significantly associated with better cognitive performance in older adults (83). The team of Rampazzo et al., 2022 analyzed the vitamin B12 content of different types of ripened cheeses made from cow's, sheep's, and goat's milks (66). This study showed that the concentration of vitamin B12 in sheep cheese (29.0 ng/g on average) was higher than it was in goat cheese (12.5 ng/g on average) or cow cheese (6.5 ng/g on average) (66).

An advantage of sheep's milk over cow's milk is its higher content of vitamin D (0.2 μ g/100 g vs. 0.15 μ g/100 g) (55). Vitamin D may reduce AD symptoms by modulating A β pathology. Research by Kang et al., 2022 showed that vitamin D deficiency caused memory impairment and an increase in the amount of A β aggregates in the brain of 5xFAD mice (33). In contrast, vitamin D supplementation improved memory function by alleviating amyloidopathies and gliopathy (33). In another study, long-term vitamin D3 supplementation alleviated cognitive impairment and cortical pathology in APP/PS1 transgenic mice (42). The neuroprotective properties of vitamin D3 have been associated with the inhibition of oxidative stress by activating the PI3K/AKT/Nrf2 pathway (42). Studies show that vitamin D3 supplementation can be proposed as a both preventive and therapeutic supplement in high-risk AD patients (11). A common comorbidity of AD is osteoporosis, in which patients show reduced bone mineralization and have a higher risk of bone fractures (46). Studies by Lines, et al., 2021 suggest that the dysfunction of the astrocyte network in mice with advanced AD may disturb the electrical activity of the cerebral cortex and contribute to cognitive decline (43). Moreover, according to Tsai et al., 2022, astrocyte dysfunction promotes calcium ion imbalance *in vivo*, leading to osteoporosis (78). Calcium ions released into the blood can cause ectopic calcifications in the pineal gland, which further promotes the development of AD. Studies on the effect of AD on bone quality have shown a lower volumetric bone mineral density in 5XFAD transgenic mice compared to control mice (46). Physical activity and proper nutrition, including an adequate intake of vitamin D and calcium, are highly recommended for osteoporosis prevention and early intervention (14). Sheep's milk

Tab. 1. The amount of selected nutrients in sheep's milk and in other products of animal and non-animal origin (3, 37, 40, 47, 51, 55, 63, 82)

Bioactive substance	Sheep's milk (51, 55)	Cow's milk (51, 55)	Pork (81)	Chicken (81)	Salmon (47, 40)	Red tomato (63)	Spinach (63)	Sweet potato (37)	Apple juice (3, 40)
Lactoferrin	0.7-0.9 g/L	0.02-0.5 g/L	–	–	–	–	–	–	–
α -lactalbumin	1.2-2.6 g/L	1-1.5 g/L	–	–	–	–	–	–	–
Vitamin B1 (thiamine)	650-800 μ g/L	300-450 μ g/L	0.98 mg/100 g	0.14 mg/100 g	–	0.037 mg/100 g	0.078 mg/100 g	0.156 mg	0.0172 mg/100 g
Vitamin B6 (pyridoxine)	600-800 μ g/L	390-600 μ g/L	0.54 mg/100 g	0.38 mg/100 g	0.046 mg/100 g	0.08 mg	0.195 mg	0.190 mg	0.013 mg/100 g
Vitamin B12 (cobalamin)	6-7.1 μ g/L	3.5-4.0 μ g/L	1 μ g/100 g	Trace amounts	0.0028 mg/100 g	–	–	–	–
Vitamin D	0.2 μ g/100 g	0.15 μ g/100 g	0.5 μ g/100 g	0.1 μ g/100 g	2.58 μ g/100 g	–	–	–	–
Calcium	197.5 mg/100 g	112 mg/100 g	7 mg/100 g	6 mg/100 g	–	10 mg	99 mg	37 mg	2.95 mg/L

contains more calcium (197.5 mg/100 g of milk) than goat's milk (130 mg/100 g of milk) or cow's milk does (112 mg/100 g of milk) (55). Moreover, pecorino cheese also contains a large amount of calcium (almost 1%) in a highly bioavailable organic form (49). As little as 30 grams of pecorino can meet nearly 30% of the daily requirement of an adult woman for calcium (49).

Conclusions

There is ample evidence that the consumption of fermented milk products can prevent neurodegenerative diseases, especially AD in the elderly (5, 7, 57, 58). Studies (58, 59) conducted in a group of over 1,000 Japanese people aged 60-79 showed that the introduction of milk or fermented milk products, such as yogurt, kefir, or buttermilk, into the diet reduces the risk of dementia in the general Japanese population. Another clinical study showed that AD patients with cognitive deficits who consumed kefir for 90 days showed marked improvements in memory, executive/language function, and visuospatial/abstract abilities (77). Moreover, kefir consumption had a reparative effect on systemic inflammation (by reducing pro-inflammatory cytokines) and systemic oxidative stress (77). However, the bioactive substances and mechanisms responsible for this effect are still not fully understood. Fermented dairy products, such as yoghurts and cheeses, are easy to consume as a daily meal, which may be a key strategy for the prevention and treatment of neurodegenerative disorders in elderly patients. Among the types of milk suitable for yogurt production, sheep's milk is becoming increasingly attractive to consumers. Sheep's milk products show many physiological effects due to the content of lactic acid bacteria, fatty acids, and peptides formed during fermentation. Compared to goat's and cow's milks, sheep's milk has a higher content of proteins, lipids, minerals, vitamins, CLA, and fatty acids (10, 24). Moreover, sheep's milk products can be a suitable alternative for people allergic to cow's milk protein. Compared to other products of

animal and non-animal origin, sheep's milk is rich in many bioactive substances (Tab. 1). Therefore, in the era of functional foods, sheep's milk and its products may play an important role as a promising therapy, providing benefits to human health (52). Previous studies on the health-promoting properties of dairy products and their effect on neurodegenerative diseases and the aging process focused mainly on cow's milk. The evidence presented here suggests that sheep's milk and its products may also be valuable in the study of AD and the related aging process. Nevertheless, further research is warranted to use the available information for future clinical trial design.

References

- 2021 Alzheimer's Disease facts and figures. *Alzheimers Dement.* 2021, 17 (3), 327-406, doi: 10.1002/alz.12328.
- Abdelhamid M., Jung C. G., Zhou C., Abdullah M., Nakano M., Wakabayashi H., Abe F., Michikawa M.: Dietary lactoferrin supplementation prevents memory impairment and reduces amyloid- β generation in J20 mice. *J. Alzheimers Dis.* 2020, 74 (1), 245-259, doi: 10.3233/JAD-191181.
- Abid M., Jabbar S., Wu T., Hashim M. M., Hu B., Lei S., Zeng X.: Sonication enhances polyphenolic compounds, sugars, carotenoids and mineral elements of apple juice. *Ultrasonics Sonochemistry* 2014, 21 (1), 93-97, doi: 10.1016/j.ultrasonch.2013.06.002.
- Agwa M. M., Abdelmonsif D. A., Khattab S. N., Sabra S.: Self-assembled lactoferrin-conjugated linoleic acid micelles as an orally active targeted nanoplateform for Alzheimer's Disease. *Int. J. Biol. Macromol.* 2020, 162, 246-261, doi: 10.1016/j.ijbiomac.2020.06.058.
- Ano Y., Ayabe T., Kutsukake T., Ohya R., Takaichi Y., Uchida S., Yamada K., Uchida K., Takashima A., Nakayama H.: Novel lactopeptides in fermented dairy products improve memory function and cognitive decline. *Neurobiol. Aging* 2018, 72, 23-31, doi: 10.1016/j.neurobiolaging.2018.07.016.
- Ano Y., Kutsukake T., Sasaki T., Uchida S., Yamada K., Kondo K.: Identification of a novel peptide from β -casein that enhances spatial and object recognition memory in mice. *J. Agric. Food Chem.* 2019, 67 (29), 8160-8167, doi: 10.1021/acs.jafc.9b02495.
- Ano Y., Ozawa M., Kutsukake T., Sugiyama S., Uchida K., Yoshida A., Nakayama H.: Preventive effects of a fermented dairy product against Alzheimer's Disease and identification of a novel oleamide with enhanced microglial phagocytosis and anti-inflammatory activity. *PLOS ONE* 2015, 10 (3), e0118512, doi: 10.1371/journal.pone.0118512.
- Atanasova J., Ivanova I.: Antibacterial peptides from goat and sheep milk proteins. *Biotechnol. Biotechnol. Equip.* 2010, 24 (2), 1799-1803, doi: 10.2478/v10133-010-0049-8.
- Bagalagel A. A., El-hawary S. S., Alaaeldin R., Elmaidomy A. H., Altemani F. H., Waggas D. S., Algehainy N. A., Saeedi N. H., Alsenani F., Mokhtar F. A., Elrehany M. A., Al-Sanea M. M., Abdelmohsen U. R.: The protective

- and therapeutic anti-Alzheimer potential of *Olea Europaea* L. Cv. Picual: An in silico and in vivo study. *Metabolites* 2022, 12 (12), 1178, doi: 10.3390/metabo12121178.
10. Balthazar C. F., Pimentel T. C., Ferrão L. L., Almada C. N., Santillo A., Albenzio M., Mollakhalili N., Mortazavian A. M., Nascimento J. S., Silva M. C., Freitas M. Q., Sant'Ana A. S., Granato D., Cruz A. G.: Sheep milk: physicochemical characteristics and relevance for functional food development. *Compr. Rev. Food Sci. Food Saf.* 2017, 16 (2), 247-262, doi: 10.1111/1541-4337.12250.
 11. Bashraheel J. K., Alrefaie Z. A., Hammad H. E. A. A., Ali S. S.: The Possible Effects of vitamin D3 on AIC1 3-Induced Histological and Morphometric Alterations of Adult Male Albino Rat Hippocampus 2022.
 12. Blinkouskaya Y., Caçoilo A., Gollamudi T., Jalalian S., Weickenmeier J.: Brain aging mechanisms with mechanical manifestations. *Mech. Ageing Dev.* 2021, Dec, 200, 111575, doi: 10.1016/j.mad.2021.111575.
 13. Castellani R. J., Rolston R. K., Smith M. A.: Alzheimer Disease. *Dis.-Mon.* 2010, 56 (9), 484-546, doi: 10.1016/j.disamonth.2010.06.001.
 14. Ciancia S., Högl W., Sackers R. J. B., Appelman-Dijkstra N. M., Boot A. M., Sas T. C. J., Renes J. S.: Osteoporosis in children and adolescents: how to treat and monitor? *Eur. J. Pediatr.* 2022, doi: 10.1007/s00431-022-04743-x.
 15. Cuciniello R., Luongo D., Ferramosca A., Lunetti P., Rotondi-Aufiero V., Crispi S., Zara V., Maurano F., Filosa S., Bergamo P.: Conjugated Linoleic Acid downregulates Alzheimer's hallmarks in aluminum mouse model through an Nrf2-mediated adaptive response and increases brain glucose transporter levels. *Free Radic. Biol. Med.* 2022, 191, 48-58, doi: 10.1016/j.freeradbiomed.2022.08.027.
 16. Dantas A. S. F. M., Brito J. S., Carvalho Serquiz F. M. C.: A importância das vitaminas do Complexo B para prevenção e tratamento do Alzheimer: uma revisão integrativa. B Complex vitamins for prevention and treatment of Alzheimer's: an integrative review. *Repositório Universitário da Ânima (RUNA)* 2022, 1-20.
 17. Dario C., Carnicella D., Dario M., Bufano G.: Genetic polymorphism of β -lactoglobulin gene and effect on milk composition in Leccese sheep. *Small Rumin. Res.* 2008, 74 (1-3), 270-273.
 18. Deery H. A., Di Paolo R., Moran C., Egan G. F., Jamadar S. D.: The older adult brain is less modular, more integrated, and less efficient at rest: a systematic review of large-scale resting-state functional brain networks in aging. *Psychophysiology* 2023, 60 (1), e14159, doi: 10.1111/psyp.14159.
 19. Ding N., Meng H., Wu Ch., Yokoyama W., Hong H., Luo Y., Tan Y.: Whey protein hydrolysate renovates age-related and scopolamine-induced cognitive impairment. *Nutrients* 2023, 15 (5), 1228, doi: 10.3390/nu15051228.
 20. Dobrev I., Marston L., Mukadam N.: Which components of the Mediterranean diet are associated with dementia? A UK Biobank Cohort Study. *GeroScience* 2022, 44 (5), 2541-2554, doi: 10.1007/s11357-022-00615-2.
 21. Dursun E., Gezen-Ak D., Yilmazer S.: A novel perspective for Alzheimer's Disease: vitamin D receptor suppression by amyloid- β and preventing the amyloid- β induced alterations by vitamin D in cortical neurons. *J. Alzheimers Dis.* 2011, 23 (2), 207-219, doi: 10.3233/JAD-2010-101377.
 22. El-Beeh M. E., El-Badawi A. A., Amin A. H., Qaril S. H., Ramadan M. F., Filfan W. M., El-Sayyad H. I. H.: Anti-aging trait of whey protein against brain damage of senile rats. *J. Umm Al-Qura Univ. Appl. Sci.* 2022, 8, 8-20, doi: 10.1007/s43994-022-00001-w.
 23. El-Salam M. H. A., El-Shibiny S.: Bioactive peptides of buffalo, camel, goat, sheep, mare, and yak milks and milk products. *Food Rev. Int.* 2013, 29 (1), 1-23, doi: 10.1080/87559129.2012.692137.
 24. Flis Z., Molik E.: Importance of bioactive substances in sheep's milk in human health. *Int. J. Mol. Sci.* 2021, 22 (9), 4364, doi: 10.3390/ijms22094364.
 25. Flis Z., Szczecina J., Molik E.: The role of sheep's milk bioactive substances in the prevention of metabolic and viral diseases. *J. Anim. Feed Sci.* 2022, 31 (3), 211-216, doi: 10.22358/jafs/151020/2022.
 26. Fujita Y., Kano K., Kishino S., Nagao T., Shen X., Sato C., Hatakeyama H., Ota Y., Niibori S., Nomura A., Kikuchi K., Yasuno W., Takatori S., Kikuchi K., Sano Y., Tomita T., Suzuki T., Aoki J., Zou K., Natori S., Komano H.: Dietary cis-9, trans-11-conjugated linoleic acid reduces amyloid β -protein accumulation and upregulates anti-inflammatory cytokines in an Alzheimer's Disease mouse model. *Sci. Rep.* 2021, 11 (1), 9749, doi: 10.1038/s41598-021-88870-9.
 27. Glorioso C., Oh S., Douillard G. G., Sibille E.: Brain molecular aging, promotion of neurological disease and modulation by Sirtuin 5 longevity gene polymorphism. *Neurobiol. Dis.* 2011, 41 (2), 279-290, doi: 10.1016/j.nbd.2010.09.016.
 28. Grant W. B.: Using multicountry ecological and observational studies to determine dietary risk factors for Alzheimer's Disease. *J. Am. Coll. Nutr.* 2016, 35 (5), 476-489, doi: 10.1080/07315724.2016.1161566.
 29. Hata S., Kano K., Kikuchi K., Kinoshita S., Sobu Y., Saito H., Saito T., Saido T. C., Sano Y., Taru H., Aoki J., Komano H., Tomita T., Natori S., Suzuki T.: Suppression of amyloid- β secretion from neurons by cis-9, trans-11-octadecadienoic acid, an isomer of conjugated linoleic acid. *J. Neurochem.* 2021, 159 (3), 603-617, doi: 10.1111/jnc.15490.
 30. Hayashi T., To M., Saruta J., Sato C., Yamamoto Y., Kondo Y., Shimizu T., Kamata Y., Tsukinoki K.: Salivary lactoferrin is transferred into the brain via the sublingual Route. *Biosci. Biotechnol. Biochem.* 2017, 81 (7), 1300-1304, doi: 10.1080/09168451.2017.1308241.
 31. Honda K., Saito Y., Saito H., Toyoda M., Abe R., Saito T., Saido T. C., Michikawa M., Taru H., Sobu Y., Hata S., Nakaya T., Suzuki T.: Accumulation of amyloid- β in the brain of mouse models of Alzheimer's Disease is modified by altered gene expression in the presence of human ApoE isoforms during aging. *Neurobiol. Aging* 2023, 123, 63-74, doi: 10.1016/j.neurobiolaging.2022.12.003.
 32. Ianiro G., Rosa L., Bonaccorsi di Patti M. C., Valenti P., Musci G., Cutone A.: Lactoferrin: from the structure to the functional orchestration of iron homeostasis. *BioMetals* 2022, doi: 10.1007/s10534-022-00453-x.
 33. Kang J., Park M., Lee E., Jung J., Kim T.: The role of vitamin D in Alzheimer's Disease: a transcriptional regulator of amyloidopathy and gliopathy. *Biomedicines* 2022, 10, 1824, doi: 10.3390/biomedicines10081824.
 34. Kawęcka A., Pasternak M.: Nutritional and dietetic quality of milk and traditional cheese made from the milk of native breeds of sheep and goats. *J. Appl. Anim. Res.* 2022, 50 (1), 39-46, doi: 10.1080/09712119.2021.2020125.
 35. Kistner A., Krack P.: Parkinson's Disease: no milk today? *Front. Neurol.* 2014, 5.
 36. Ko J. W., Jeon S., Kwon Y. H.: Dietary vitamin B6 restriction aggravates neurodegeneration in mice fed a high-fat diet. *Life Sci.* 2022, 309, 121041, doi: 10.1016/j.lfs.2022.121041.
 37. Krochmal-Marczak B., Sawicka B.: Możliwości wykorzystania batata (*Ipomoea batatas* L. [Lam]) w produkcji żywności funkcjonalnej, [w:] Słupski J., Tarko T., Drodz I. (red.): Składniki bioaktywne surowców i produktów roślinnych. Wyd. Oddział Małopolski Polskiego Towarzystwa Technologii Żywności 2018, 5-14.
 38. Kumar M. R., Azizi N. F., Yeap S. K., Abdullah J. O., Khalid M., Omar A. R., Osman M. A., Leow A. T. C., Mortadza S. A. S., Alitheen N. B.: Clinical and preclinical studies of fermented foods and their effects on Alzheimer's Disease. *Antioxidants* 2022, 11 (5), 883, doi: 10.3390/antiox11050883.
 39. Laranjo M., Potes M. E.: Chapter 6 – Traditional Mediterranean cheeses: lactic acid bacteria populations and functional traits, [in:] Ray R. C., Paramithiotis S., de Carvalho Azevedo V. A., Montet D.: Lactic Acid Bacteria in Food Biotechnology. *Applied Biotechnology Reviews*, 2022, 97-124, doi: 10000.1016/B978-0-323-89875-1.00011-0.
 40. Lebedzińska A., Marszał M. L., Kuta J., Szefer P.: Reversed-phase high-performance liquid chromatography method with coulometric electrochemical and ultraviolet detection for the quantification of vitamins B1 (thiamine), B6 (pyridoxamine, pyridoxal and pyridoxine) and B12 in animal and plant foods. *J. Chromatogr.* 2007, 1173 (1-2), 71-80, doi: 10.1016/j.chroma.2007.09.072.
 41. Li Y. Q., Guo C.: A review on lactoferrin and central nervous system diseases. *Cells* 2021, 10 (7), 1810, doi: 10.3390/cells10071810.
 42. Lin J., Niu Z., Xue Y., Gao J., Zhang M., Li M., Peng Y., Zhang S., Li W., Zhang Q., Li X.: Chronic vitamin D3 supplementation alleviates cognition impairment via inhibition of oxidative stress regulated by PI3K/AKT/Nrf2 in APP/PS1 transgenic mice. *Neurosci. Lett.* 2022, 783, 136725, doi: 10.1016/j.neulet.2022.136725.
 43. Lines J., Baraibar A. M., Fang C., Martin E. D., Aguilar J., Lee M. K., Araque A., Kofuji P.: Astrocyte-neuronal network interplay is disrupted in Alzheimer's Disease mice. *Glia* 2022, 70 (2), 368-378, doi: 10.1002/glia.24112.
 44. Liu R. M.: Aging, cellular senescence, and Alzheimer's Disease. *Int. J. Mol. Sci.* 2022, 23 (4), 1989, doi: 10.3390/ijms23041989.
 45. Liu Y., Nguyen M., Robert A., Meunier B.: Metal ions in Alzheimer's Disease: A key role or not? *Acc. Chem. Res.* 2019, doi: 10.1021/acs.accounts.9b00248.
 46. LLabre J. E., Gil C., Amatya N., Lagalwar S., Possidente B., Vashishth D.: Degradation of bone quality in a transgenic mouse model of Alzheimer's Disease. *J. Bone Miner. Res.* 2022, 37 (12), 2548-2565, doi: 10.1002/jbmr.4723.
 47. Lozano-Muñoz I., Muñoz S., Díaz N. F., Medina A., Bazaes J., Riquelme C.: Nutritional enhancement of farmed salmon meat via non-GMO nannochloropsis gaditana: eicosapentaenoic acid (EPA, 20:5 n-3), docosapentaenoic acid (DPA, 22:5 n-3) and vitamin D3 for human health. *Molecules* 2020, 25 (20), 4615, doi: 10.3390/molecules25204615.
 48. Mattson M. P., Arumugam T. V.: Hallmarks of brain aging: adaptive and pathological modification by metabolic states. *Cell Metab.* 2018, 27 (6), 1176-1199, doi: 10.1016/j.cmet.2018.05.011.
 49. Mele M., Bulleri E.: Nutritional properties of Pecorino Toscano PDO cheese, as affected by the rearing system. *Georgofili* 2015, vol. 12, No. Supplemento 1, 65.
 50. Mohamed W. A., Salama R. M., Schaalman M. F.: A pilot study on the effect of lactoferrin on Alzheimer's Disease pathological sequelae: impact of the p-Akt/PTEN pathway. *Biomed. Pharmacother.* 2019, 111, 714-723, doi: 10.1016/j.biopha.2018.12.118.

51. Moatsou G., Sakkas L.: Sheep milk components: focus on nutritional advantages and biofunctional potential. *Small Rumin. Res.* 2019, 180, 86-99, doi: 10.1016/j.smallrumres.2019.07.009.
52. Mohapatra A., Shinde A. K., Singh R.: Sheep milk: a pertinent functional food. *Small Rumin. Res.* 2019, 181, 6-11, doi: 10.1016/j.smallrumres.2019.10.002.
53. Molik E., Blasiak M., Pustkowiak H.: Impact of photoperiod length and treatment with exogenous melatonin during pregnancy on chemical composition of sheep's milk. *Animals* 2020, 10 (10), 1721, doi: 10.3390/ani10101721.
54. Nguyen H. D., Kim M. S.: The role of mixed B vitamin intakes on cognitive performance: modeling, genes and MiRNAs involved. *J. Psychiatr. Res.* 2022, 152, 38-56, doi: 10.1016/j.jpsychires.2022.06.006.
55. Nguyen V. Q.: Nutritional value and factors affecting milk production and milk composition from dairy sheep: a review. *Can Tho Univ. J. Sci.* 2022, 14 (3), 53-64, doi: 10.22144/ctu.jen.2022.047.
56. Nelson P. T., Braak H., Markesbery W. R.: Neuropathology and cognitive impairment in Alzheimer Disease: a complex but coherent relationship. *J. Neuropathol. Exp. Neurol.* 2009, 68 (1), 1-14, doi: 10.1097/NEN.0b013e3181919a48.
57. Ohsawa K., Uchida N., Ohki K., Nakamura Y., Yokogoshi H.: Lactobacillus Helveticus – fermented milk improves learning and memory in mice. *Nutr. Neurosci.* 2015, 18 (5), 232-240, doi: 10.1179/1476830514Y.0000000122.
58. Ozawa M., Ninomiya T., Ohara T., Doi Y., Uchida K., Shirota T., Yonemoto K., Kitazono T., Kiyohara Y.: Dietary patterns and risk of dementia in an elderly Japanese population: the Hisayama Study. *Am. J. Clin. Nutr.* 2013, 97, 1076-1082.
59. Ozawa M., Ohara T., Ninomiya T., Hata J., Yoshida D., Mukai N., Nagata M., Uchida K., Shirota T., Kitazono T., Kiyohara Y.: Milk and dairy consumption and risk of dementia in an elderly Japanese population: The Hisayama Study. *J. Am. Geriatr. Soc.* 2014, 62 (7), 1224-1230, doi: 10.1111/jgs.12887.
60. Panza F., Solfrizzi V., Colacicco A. M., D'Introno A., Capurso C., Torres F., Del Parigi A., Capurso S., Capurso A.: Mediterranean diet and cognitive decline. *Public Health Nutr.* 2004, 7 (7), 959-963, doi: 10.1079/phn2004561.
61. Patel P., Shah J.: Role of vitamin D in amyloid clearance via LRP-1 upregulation in Alzheimer's Disease: a potential therapeutic target? *J. Chem. Neuroanat.* 2017, 85, 36-42, doi: 10.1016/j.jchemneu.2017.06.007.
62. Pulina G., Milán M. J., Lavín M. P., Theodoridis A., Morin E., Capote J., Thomas D. L., Francesconi A. H. D., Caja G.: Invited review: Current production trends, farm structures, and economics of the dairy sheep and goat sectors. *J. Dairy Sci.* 2018, 101 (8), 6715-6729, doi: 10.3168/jds.2017-14015.
63. Płocharski W., Markowski J., Pytasz U., Rutkowski K.: Owoce, warzywa, soki – ich kaloryczność i wartość odżywcza na tle zapotrzebowania na energię i składniki odżywcze Cz. 2. Wartość odżywcza i zdrowotna w świetle dozwolonych oświadczeń zdrowotnych. *Przemysł Fermentacyjny i Owocowo-Warzywny* 2013, 1, 4-8.
64. Qian T., Zhao L., Pan X., Sang S., Xu Y., Wang C., Zhong C., Fei G., Cheng X.: Association between blood biochemical factors contributing to cognitive decline and B vitamins in patients with Alzheimer's Disease. *Front. Nutr.* 2022, 9, 823573, doi: 10.3389/fnut.2022.823573.
65. Ramamoorthy K., Yoshimura R., Al-Juburi S., Anandam K. Y., Kapadia R., Alachkar A., Abbott G. W., Said H. M.: Alzheimer's Disease is associated with disruption in thiamin transport physiology: a potential role for neuroinflammation. *Neurobiol. Dis.* 2022, 171, 105799, doi: 10.1016/j.nbd.2022.105799.
66. Rampazzo G., Zironi E., Pagliuca G., Gazzotti T.: Analysis of cobalamin (vit B12) in ripened cheese by ultra-high-performance liquid chromatography coupled with mass spectrometry. *Foods* 2022, 11 (18), 2745, doi: 10.3390/foods11182745.
67. Reseco L., Atienza M., Fernandez-Alvarez M., Carro E., Cantero J. L.: Salivary lactoferrin is associated with cortical amyloid-beta load, cortical integrity, and memory in aging. *Alzheimers Res. Ther.* 2021, 13 (1), 150, doi: 10.1186/s13195-021-00891-8.
68. Serafeimidou A., Zlatanov S., Kritikos G., Tourianis A.: Change of fatty acid profile, including conjugated linoleic acid (CLA) content, during refrigerated storage of yogurt made of cow and sheep milk. *J. Food Compos. Anal.* 2013, 31 (1), 24-30, doi: 10.1016/j.jfca.2013.02.011.
69. Sharpless N. E., Sherr C. J.: Forging a signature of in vivo senescence. *Nat. Rev. Cancer* 2015, 15 (7), 397-408, doi: 10.1038/nrc3960.
70. Sibille E.: Molecular aging of the brain, neuroplasticity, and vulnerability to depression and other brain-related disorders. *Dialogues Clin. Neurosci.* 2013, 15 (1), 53-65, doi: 10.31887/DCNS.2013.15.1/sibille.
71. Smirnov D., Eremenko E., Stein D., Kaluski S., Jasinska W., Cosentino C., Martinez-Pastor B., Brotman Y., Mostoslavsky R., Khrameeva E., Toiber D.: SIRT6 is a key regulator of mitochondrial function in the brain. *Cell Death Dis.* 2023, 14 (1), 1-12, doi: 10.1038/s41419-022-05542-w.
72. Smith S. M., Elliott L. T., Alfaro-Almagro F., McCarthy P., Nichols T. E., Douaud G., Miller K. L.: Brain aging comprises many modes of structural and functional change with distinct genetic and biophysical associations. *eLife* 2020, 9, e52677, doi: 10.7554/eLife.52677.
73. Solfrizzi V., Panza F., Frisardi V., Seripa D., Logroscino G., Imbimbo B. P., Pilotto A.: Diet and Alzheimer's Disease risk factors or prevention: the current evidence. *Expert Rev. Neurother.* 2011, 11 (5), 677-708, doi: 10.1586/ern.11.56.
74. Swerdlow R. H.: Is aging part of Alzheimer's Disease, or is Alzheimer's Disease part of aging? *Neurobiol. Aging* 2007, 28 (10), 1465-1480, doi: 10.1016/j.neurobiolaging.2006.06.021.
75. Szterk A., Ofiara K., Strus B., Abdullaev I., Ferenc K., Sady M., Flis S., Gajewski Z.: Content of health-promoting fatty acids in commercial sheep, cow and goat cheeses. *Foods* 2022, 11 (8), 1116, doi: 10.3390/foods11081116.
76. Thabitha A., Vignesh N., Saravanan R.: Nutrients' role in the treatment of Parkinson's and Alzheimer's Diseases, [in:] Rajagopal S., Ramachandran S., Sundararaman G., Gadde Venkata S. (eds.): *Role of Nutrients in Neurological Disorders. Nutritional Neurosciences*; Springer, Singapore 2022, 237-246, doi: 10.1007/978-981-16-8158-5_12.
77. Ton A. M. M., Campagnaro B. P., Alves G. A., Aires R., Côco L. Z., Arpini C. M., Guerra e Oliveira T., Campos-Toimil M., Meyrelles S. S., Pereira T. M. C., Vasquez E. C.: Oxidative stress and dementia in Alzheimer's patients: effects of synbiotic supplementation. *Oxidative Med. Cell. Longev.* 2020 Jan 13, 2020, 2638703, doi: 10.1155/2020/2638703.
78. Tsai Y. L., Yen C. T., Wang Y. F.: Astrocyte dysregulation and calcium ion imbalance may link the development of osteoporosis and Alzheimer's Disease. *J. Alzheimers Dis.* 2022, 88 (2), 439-445, doi: 10.3233/JAD-220218.
79. Tsatsanis A., McCorkindale A. N., Wong B. X., Patrick E., Ryan T. M., Evans R. W., Bush A. I., Sutherland G. T., Sivaprasadarao A., Guenewig B., Duce J. A.: The acute phase protein lactoferrin is a key feature of Alzheimer's Disease and predictor of Aβ Burden through induction of APP amyloidogenic processing. *Mol. Psychiatry* 2021, 26 (10), 5516-5531, doi: 10.1038/s41380-021-01248-1.
80. Ubaid S., Rumman M., Singh B., Akhtar M. S., Mahdi A. A., Pandey S.: Elucidating the neuroprotective role of formulated camel α-lactalbumin-oleic acid complex by curating the SIRT1 pathway in Parkinson's Disease model. *ACS Chem. Neurosci.* 2020, 11 (24), 4416-4425, doi: 10.1021/acscchemneuro.0c00639.
81. Valle M. L., Zastre J.: Thiamine insufficiency induced hypoxia-inducible factor 1-α (HIF-1α) regulates Alzheimer's Disease-like neuropathology. *FASEB J.* 2020, 34 (S1), 1-1, doi: 10.1096/fasebj.2020.34.s1.09455.
82. Wood J. D.: Meat composition and nutritional value. *Lawrie's Meat Science* 2017, 635-659, doi: 10.1016/b978-0-08-100694-8.00020-0.
83. Xu H., Wang S., Gao F., Li C.: Vitamin B6, B9, and B12 intakes and cognitive performance in elders: National Health and Nutrition Examination Survey, 2011-2014. *Neuropsychiatr. Dis. Treat.* 2022, 18, 537-553, doi: 10.2147/NDT.S337617.
84. Zheng J., Xie Y., Li F., Zhou Y., Qi L., Liu L., Chen Z.: Lactoferrin improves cognitive function and attenuates brain senescence in aged mice. *J. Funct. Foods* 2020, 65, 103736, doi: 10.1016/j.jff.2019.103736.
85. Zucca F. A., Segura-Aguilar J., Ferrari E., Muñoz P., Paris I., Sulzer D., Sarna T., Casella L., Zecca L.: Interactions of iron, dopamine and neuromelanin pathways in brain aging and Parkinson's Disease. *Prog. Neurobiol.* 2017, 155, 96-119, doi: 10.1016/j.pneurobio.2015.09.012.

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