ŁATA, Michał, CHYĆKO, Małgorzata, PRZYBOROWSKA, Kinga, KWIECIEŃ, Justyna, RUKAT, Mateusz, STROJNY, Agnieszka and SIEMIĄTKOWSKI, Robert. The efficacy of available supplements and medical drugs in longevity medicine - a review. Journal of Education, Health and Sport. 2025;77:56774. eISSN 2391-8306.
https://doi.org/10.12775/JEHS.2025.77.56774
https://apcz.umk.pl/JEHS/article/view/56774

The journal has had 40 points in Minister of Science and Higher Education of Poland parametric evaluation. Annex to the announcement of the Minister of Education and Science of 05.01.2024 No. 32318. Has a Journal's Unique Identifier: 201159. Scientific disciplines assigned: Physical culture sciences (Field of medical and health sciences); Health Sciences (Field of medical and health sciences).
Punkty Ministerialne 40 punktów. Załącznik do komunikatu Ministra Nauki i Szkolnictwa Wyższego z dnia 05.01.2024 Lp. 32318. Posiada Unikatowy Identyfikator Czasopisma: 201159. Przypisane dyscypliny naukowe: Nauki o kulturze fizycznej (Dziedzina nauk medycznych i nauk o zdrowiu); Nauki o zdrowiu (Dziedzina nauk medycznych i nauk o zdrowiu).
The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 08.12.2024. Revised: 09.01.2025. Accepted: 09.01.2025. Published: 09.01.2025.

The efficacy of available supplements and medical drugs in longevity medicine - a review

1. Michał Łata [MŁ]
District Medical Center in Grójec Piotra Skargi 10 street, 05-600 Grójec
https://orcid.org/0009-0001-0462-1141 michal.lataa@gmail.com

2. Małgorzata Chyćko [MC]
7th Navy Hospital in Gdańsk.
Polanki 117 street, 80-305 Gdańsk https://orcid.org/0000-0002-1515-6038
malgorzatachycko@gmail.com

3. Kinga Przyborowska [KP]
The National Institute of Medicine of the Ministry of Interior and Administration Wołoska 137 street, 02-507 Warszawa
https://orcid.org/0009-0009-8320-1580
kmprzyborowska@gmail.com

4. Justyna Kwiecień [JK]
District Medical Center in Grójec Piotra Skargi 10 street, 05-600 Grójec
https://orcid.org/0000-0002-1969-209X kwiecien.jstn@gmail.com

5. Mateusz Rukat [MR]
Mazovian Provincial Hospital in Siedlce Poniatowskiego 26 street, 08-110 Siedlce https://orcid.org/0009-0003-7742-6499
mateuszrukat97@gmail.com

6. Agnieszka Strojny [AS]
Warsaw Medical University,
Warsaw, Poland https://orcid.org/0000-0003-0893-1881
agnieszkastrojny@icloud.com

7. Robert Siemiątkowski [RS]
SPZOZ-ZZ Independent Health Care Center,
Maków Mazowiecki, Poland https://orcid.org/0009-0009-1499-9242
robert.siem98@gmail.com

Abstract

Ageing is a complex process occurring simultaneously on various levels - visual, physical, mental. Some among many factors responsible for maintenance of good physical and mental health are various nutrients, vitamins, antioxidants and medical drugs. Within this review, selected substances that show anti-ageing potential were examined. This paper reviews data on model organisms concerning the effects of widely used drugs and dietary supplements on the lifespan of model organisms.

key words: longevity, lifespan, supplements, metformin, rilmenidine, acarbose, mianserin, rapamycin, NMN, resveratrol, probiotics, vitamin D, coenzyme Q10, taurine

Introduction

Long life in good condition is one of the biggest desires of humankind. People found a solution for removing the visual effects of ageing in esthetic medicine, while methods for remaining in good health and mental condition are not always that obvious and simple. People are more and more conscious about healthy ageing, they seek for the most reliable and effective methods for extending their lives. Because of growing interest in ageing gracefully, more and more steps are being made towards meeting these expectations in the world of science. There is a great increase in supplements especially designed to promote healthy ageing, but also newest research is being performed on well-known drugs, that their contribution in extending lifespan was yet unknown. Within this research the wide variety of medical drugs and supplements was described, and their anti-ageing influence was analysed.

Metformin

A drug, which is widely discussed and examined in terms of its ability to prolong patients' life is metformin, which is a synthetic derivative of French Lilac (Galega officials). It is an oral anti diabetic drug, most commonly prescribed for type II diabetes. In a study performed on male mice, 0,1% metformin concentration in diet, implemented at middle age, turned out to significantly extend lifespan and healthspan, while 1% concentration was toxic [1]. Metformin is believed to imitate the benefits of calories restriction, which result in enhanced physical performance, higher insulin sensitivity as well as reduced levels of low-

density lipoprotein and total cholesterol [2,3]. The intake of metformin came out to exhibit antioxidant properties and to reduce oxidative damage through the increase in the activity of AMP-activated protein kinase. Nevertheless, metformin cannot be called a miracle drug. Its main disadvantage is the fact that it can cause vitamin B12 deficiency and result in peripheral neuropathy or neuropsychiatric symptoms [4,5]. The preliminary findings of MILES (Metformin in Longevity Study) as well as TAME (Targeting Aging with Metformin) confirm the anti-aging properties of Metformin. However, it remains uncertain whether it can be effective for healthy participants [5]. Although metformin undeniably reduces early mortality linked with diseases, such as diabetes, cancer, cardiovascular disease and cognitive impairment, the evidence that it is capable of prolonging lifespan is highly controversial and the mechanism still unknown.

Rilmenidine

Rilmenidine is a medication used in the treatment of hypertension. It acts as an I1- imidazoline receptor agonist, which encourages scientists to consider the receptor as a target for longevity medicine scientists. In a study performed on Caenorhabditis elegans treated with rilmenidine at both young and old age, the medicine was proven to extend lifespan. Similar to metformin, it mimics the caloric restriction gene transcription observed in the tissue of mice kidneys and livers. The study of the mechanism of action showed that transcription factors, such as FOXO/ DAF-16 and NRF1,2,3/ SKN-1, were needed. Although the research showed the potential of rilmenidine to prolong lifespan, there is currently not enough studies to undeniably confirm its efficacy and mechanism of action [6].

Nicotinamide mononucleotide

NMN (Nicotinamide mononucleotide) has been a widely examined dietary supplement known for its anti-aging and neuroprotective properties. The nucleotide is transformed to NADH (nicotinamide adenine dinucleotide), which takes part in processes within mitochondria [7]. It has been noticed that the decline in NADH levels in tissues is associated with the progress of aging. Its levels can impact DNA repair, immune cell activity and metabolic pathways. The restoration of NADH levels act as a potential therapeutic target capable of reversing or delaying age-related diseases, such as cardiovascular disorder, diabetes or cognitive

impairment[8,9]. A 60-day clinical trial on 80 middle-aged healthy adult participants implemented oral doses of placebo, 300 mg, 600 mg, or 900 mg of NMN. No safety issues were mentioned after the study. Within the research, walking distance and blood biological age were evaluated. The walking distance during a 6-minute walking test was significantly higher in patients who received NMN supplementation in comparison to placebo group [10]. Nevertheless, the studies, which examine NMN effectiveness, are criticised not to be of high quality and not to properly prove its anti-aging action. It remains uncertain whether the benefits confirmed in animal studies can be referred to humans' physiology.

Resveratrol

Resveratrol is a polyphenol found in blueberries and grapes. It has been found to modulate the hallmarks of ageing by the reduction of oxidative damage, inflammation, cell senescence and attrition of telomeres. The mechanism of action includes several genes associated with longevity, which are PBEF, Sirt1, Sirt3, Sirt4, FoxO1 and Fofo3a [11]. Several studies suggested its effectiveness in the prevention of type II diabetes, hypertension, Alzheimer's disease, cancer and cardiovascular disease by reducing cholesterol levels and inflammatory response [12]. In a study performed on mice, the treatment with resveratrol enhanced their aerobic capacity by the increase in the running time and oxygen consumption in muscle fibres. Resveratrol intake contributed to decrease of PGC-1alpha acetylation and increase in PGC-1alpha activity. It resulted in the activation of genes associated with mitochondrial biogenesis and oxidative phosphorylation [13,14]. Nevertheless, research performed on mice has not been able to show an undeniable impact on survival or lifespan extension.

Probiotics

Probiotics are alive organisms which are administered in adequate amounts, continue to live in intestines and exhibit desirable effects on patients. This impact takes place through different pathways, that is gut-brain axis as well as gut skin axis [15]. While the benefits on gastrointestinal tract are generally well-recognized, new research suggests many various benefits for human body systems and homeostasis, for instance endocrine, immune, cardiovascular and CNS (central nervous system). Especially, their advantages for neurological and psychiatric symptoms are widely emphasised in disorders, such as depression, anxiety,

autism and Parkinson's disease. The possible mechanism of indirect impact on the central nervous system is through the calming effect of the vagus nerve. Cellular senescence has been recently stated to be an effect of microbiome imbalance. The senescent cells, which die because of stress and undergo growth arrest, tend to accumulate and be linked to chronic ang ageing pathologies. The mechanism is accompanied by inflammatory cytokines, growth factors and chemokines. Particularly, skin disease can be induced by senescence, because skin acts as a frequent site of senescent cells accumulation [16,17]. However, although probiotics can play a role in skin health and its ageing by inhibiting cell senescence, it remains questionable whether they are capable of prolonging lifespan and healthspan.

Acarbose

Acarbose is the α-glucosidase inhibitor, whose mechanism of action involves slowing down digestion of carbohydrates and inhibits postprandial increase of glucose levels in blood. It is basically used in treatment of patients with diabetes mellitus type 2 and patients with glucose intolerance. [18] Similarly to metformin, acarbose decreases mean weight value in patients, delays new onset of diabetes and positively influences cardiovascular health. [19] Looking closer into cardiovascular health, according to the STOP-NIDDM trial performed by Chiasson JL, et al. (2003) [20] it was shown that acarbose treatment increased the probability of remaining free of any cardiovascular event by 49%. This significant number brings hope for diabetic patients, being at particular risk of cardiovascular malfunctions. Research on acarbose gives important insight in increasing lifespan of patients, whose life is at higher risk due to diabetes and obesity.

Mianserin

Mianserin is an atypical antidepressant that is used primarily in the treatment of depression, at lower doses is used for patients suffering from insomnia. Its effect on extending the lifespan of humans was not yet determined, but promising research was performed in 2021 on nuisances. [21] To perform this research nuisances Caenorhabditis elegans (C. elegans) were investigated - a well-established model organism commonly used within ageing research. Treatment groups, besides control group, were given either mianserin alone, glucose alone, or combined doses of both mianserin and glucose. Lifespan was determined by monitoring the

worms until they died. Researchers observed that mianserin treatment resulted in a 12% increase in lifespan, but reduced lifespan by 6% of the glucose fed group. In the group fed with a combination of mianserin and glucose, the effect of increasing the lifespan was reduced. [21]. This research shows not only the potential of mianserin in increasing lifespan, but also underlines the importance of glucose level in diet. Observation form above research occurs, that there is additional advantage in improving longevity deriving from drugs lowering sugar blood levels. High glucose level not only reduced lifespan itself, but also abolished the lifespan-extension established by mianserin.

Rapamycin

Rapamycin is a macrolide immunosuppressant used widely for the prevention of organ transplant rejection and for the treatment of lymphangioleiomyomatosis. Most important feature of rapamycin, while considering its anti-ageing effect, is its capacity of inhibiting the mammalian target of rapamycin (mTOR) by binding to the intracellular receptor FKBP12. [22] The mTOR pathway is a main regulator of tissue metabolism and cell physiology. It accounts for functioning of multiple tissues including liver, muscle, white and brown adipose tissue and the brain [23] and is dysregulated in human diseases, including diabetes and obesity [24]. Impairments in those pathways have such an impact on the human body, as the activity of the mTOR (precisely its subunit C1) is regulated by i.a insulin and growth factors, and oxidative stress. [25] Due to the observed correlation of rapamycin on mTOR, thus its direct influence on tissue metabolism, researchers decided to investigate the influence of this drug on the process of ageing. Study performed by Selvarani et al. (2021) showed clear influence of rapamycin on increase in lifespan in mice. Researchers found out that high doses of rapamycin increased the lifespan of male rats up to 61%. Moreover, there was no report stating any negative effect of rapamycin on the lifespan of laboratory mice. [26] This important observation gives us insight into cell metabolism and the possibility of its alteration.

Vitamin D

Vitamin D is the common name for a group of prohormones soluble in fats, that the main role is intestinal absorption of elements and compounds like calcium, magnesium, and phosphate [27]. In humans, the most important compounds in this group are vitamin D_3(cholecalciferol)

and vitamin D_2 (ergocalciferol) [28]. It was proven that vitamin D plays a significant role in prevention of neural degeneration [29]. In terms of high quality life, not only longevity is the most important, but a key aspect are years of life in full physical and mental health. Due to the observation of vitamin D's influence on the nervous system, researchers decided to measure its impact on ageing and age-related diseases. Caenorhabditis elegans was used as a model organism and its lifespan and healthspan were measured. Treatment with vitamin D3 significantly extended the lifespan of worms and rescued worms with a mutant vitamin D receptor gene (which typically have decreased life spans in comparison to the first group). What is interesting, treatment with vitamin D3 additionally, to a small extent, prolonged the lifespan of worms that were engineered to represent Alzheimer disease [32]. This observation brings insight into the possibilities of not only extending the lifespan, but also possible treatment of diseases substantially decreasing quality of life.

Not only the need of preventing neurodegenerative diseases speaks in favour of supplementation of vitamin D. Chowdhury et al. (2014) showed a direct relationship between low vitamin D levels and an increased risk of all-cause mortality [30]. The same conclusion derives from research performed by Autier et al. (2007), by showing the relationship between vitamin D supplementation and reduction of all-cause mortality by 7% [31].

Coenzyme Q10

This fat-soluble substance is present in every mitochondria of animals' and plants' cells. Main role of coenzyme Q10 is transporting electrons in the electron transport chain, which results in energy generation in the form of ATP. Presence of CoQ10 allows cells to create energy in the process of cellular respiration. Study performed by Mantle D. et al. (2019) show that supplementation of coenzyme Q10 has a positive effect on prevention or management of diseases that significantly shorten and decline in quality human life [33]. Researchers analysed the role of CoQ10 in terms of cardiovascular disease, diabetes, kidney disease and liver disease. Randomised controlled clinical trials have proven supplementation with CoQ10 or CoQ10 with selenium to be effective in reduction of mortality up to 50% in patients with cardiovascular disease [33]. These outstanding results prove the effectiveness of supplementation in terms of the deadliest diseases of the present times.

Taurine

Taurine is an amino sulfonic acid, it is the end product of the degradation of the sulphur amino acid, cysteine. Synthetic taurine is an ingredient in energy drinks, powdered modified milk for babies, cat food and sports nutrition products. Organically, it has been discovered that an exceptionally high concentration of taurine occurs in the developing brain and drops dramatically right after development is complete [34]. Taurine has also been shown to improve cognitive function by increasing glial metabolism, but in higher doses can cause encephalopathy [35]. As the effect of taurine on the developing brain was already proven, scientists started to investigate its effect on the ageing brain. Singh P. et al. (2023) focused on taurine supplementation in terms of healthspan and lifespan [36]. Firstly, they measured blood taurine concentrations at different ages in mice, monkeys, and humans. Results showed more than 80% decrease in taurine serum concentration in elderly humans, compared with the concentration in serum of younger individuals. Secondly, solution or taurine was administered to mice at different life stages. Results showed 10-12% increase in length of life in taurine-fed mice in comparison to control mice [36]. These results are very promising, yet more investigation on humans should be performed.

Discussion

There is no denying that there are both advantages and disadvantages of studies performed on the efficacy of available supplements and medical drugs in longevity medicine. Human beings have always been dreaming of immortality or even to extend lifetime and years in health and these days they see a possibility. First of all, the studies constitute a possibility to discover promising cellular targets and particular genes responsible for the length of life. They can act as a basis for further research of therapies for civilization diseases, such as cancers or cardiovascular incidents. Indirectly, the extension of people’s lives could lead to huge development of societies.

However, neither of the described substances can be considered as flawless. Researchers may be blinded by their eagerness for longer life as well as fame after their thesis for a particular substance is supported by a study. That is why the methodology of the studies is not always convincing. There is a question whether it is safe to use a medicine which extends life and is used for a particular disease in a healthy patient. For

instance, using rilmenidine for a patient without hypertension, metformin and acarbose without diabetes or mianserin with no depressive symptoms may seem unreasonable.

What is more, as with every substance, the mentioned medicines and dietary supplements are not free of side effects. For example, the usage of metformin can lead to life-threatening vitamin B12 deficiency. Moreover, polypharmacy is a common phenomenon nowadays and the recommendation to apply another drug or dietary supplement can result in deepening the condition. Also, it remains unobvious whether these substances actually prolong life or only extend it by preventing common diseases. Moreover, even if some of the substances undeniably confirmed its efficacy and was to be used globally, it could lead to ageing of the society as well as human overpopulation.

Conclusion

All things considered, it is uncertain whether the depicted medicines and dietary supplements inhibit ageing or they only exhibit an isolated impact on longevity by preventing common civilization diseases, such as cancer, diabetes and cardiovascular incidents. In spite of the fact that an outstanding amount of articles confirm the advantages of mentioned substances, the research is not always of high quality, is often performed on animals such as mice or Caenorhabditis elegans and a small number of human participants are involved. Therefore, their mechanism of action constitutes a promising target of research, but the existing evidence still does not undeniably confirm their effectiveness.

Disclosures

Funding statement: No external funding statement was received to perform this review

Conflict of interest: The authors declare no conflict of interest

Authors contribution:

Conceptualization: Michał Łata, Kinga Przyborowska, Małgorzata Chyćko;

methodology: Michał Łata, Agnieszka Strojny, Robert Siemiątkowski;

formal analysis: Justyna Kwiecień, Mateusz Rukat;

investigation: Michał Łata, Małgorzata Chyćko;

writing-rough preparation: Agnieszka Strojny, Mateusz Rukat, Robert Siemiątkowski;

writing-review and editing: Kinga Przyborowska, Agnieszka Strojny, Mateusz Rukat;

visualization: Justyna Kwiecień, Agnieszka Strojny, Michał Łata

All authors have read and agreed with the final of the manuscript.

Board statement: Not applicable - this review included analysis of the available literature.

Bibliography:

1. Martin-Montalvo A, Mercken EM, Mitchell SJ, Palacios HH, Mote PL, Scheibye-Knudsen M, Gomes AP, Ward TM, Minor RK, Blouin MJ, Schwab M, Pollak M, Zhang Y, Yu Y, Becker KG, Bohr VA, Ingram DK, Sinclair DA, Wolf NS, Spindler SR, Bernier M, de Cabo R. Metformin improves healthspan and lifespan in mice. Nat Commun. 2013;4:2192. doi: 10.1038/ncomms3192. PMID: 23900241; PMCID: PMC3736576.

2. Romero R, Erez O, Hüttemann M, Maymon E, Panaitescu B, Conde-Agudelo A, Pacora P, Yoon BH, Grossman LI. Metformin, the aspirin of the 21st century: its role in gestational diabetes mellitus, prevention of preeclampsia and cancer, and the promotion of longevity. Am

J Obstet Gynecol. 2017 Sep;217(3):282-302. doi: 10.1016/j.ajog.2017.06.003. Epub 2017 Jun 12. PMID: 28619690; PMCID: PMC6084482.

3. Glossmann HH, Lutz OMD. Metformin and Aging: A Review. Gerontology. 2019;65(6):581-590. doi: 10.1159/000502257. Epub 2019 Sep 13. PMID: 31522175.

4. Soukas AA, Hao H, Wu L. Metformin as Anti-Aging Therapy: Is It for Everyone? Trends Endocrinol Metab. 2019 Oct;30(10):745-755. doi: 10.1016/j.tem.2019.07.015. Epub 2019 Aug 9. PMID: 31405774; PMCID: PMC6779524.

5. Mohammed I, Hollenberg MD, Ding H, Triggle CR. A Critical Review of the Evidence That Metformin Is a Putative Anti-Aging Drug That Enhances Healthspan and Extends Lifespan. Front Endocrinol (Lausanne). 2021 Aug 5;12:718942. doi: 10.3389/fendo.2021.718942. PMID: 34421827; PMCID: PMC8374068.

6. Bennett DF, Goyala A, Statzer C, Beckett CW, Tyshkovskiy A, Gladyshev VN, Ewald CY, de Magalhães JP. Rilmenidine extends lifespan and healthspan in Caenorhabditis elegans via a nischarin I1-imidazoline receptor. Aging Cell. 2023 Feb;22(2):e13774. doi: 10.1111/acel.13774. Epub 2023 Jan 20. PMID: 36670049; PMCID: PMC9924948.

7. Soma M, Lalam SK. The role of nicotinamide mononucleotide (NMN) in anti-aging, longevity, and its potential for treating chronic conditions. Mol Biol Rep. 2022 Oct;49(10):9737-9748. doi: 10.1007/ s11033-022-07459-1. Epub 2022 Apr 20. PMID: 35441939.

8. Nadeeshani H, Li J, Ying T, Zhang B, Lu J. Nicotinamide mononucleotide (NMN) as an anti-aging health product - Promises and safety concerns. J Adv Res. 2021 Aug 11;37:267-278. doi: 10.1016/ j.jare.2021.08.003. PMID: 35499054; PMCID: PMC9039735.

9. Yoshino J, Baur JA, Imai SI. NAD+ Intermediates: The Biology and Therapeutic Potential of NMN and NR. Cell Metab. 2018 Mar 6;27(3):513-528. doi: 10.1016/j.cmet.2017.11.002. Epub 2017 Dec 14. PMID: 29249689; PMCID: PMC5842119.

10. Yi L, Maier AB, Tao R, Lin Z, Vaidya A, Pendse S, Thasma S, Andhalkar N, Avhad G, Kumbhar V. The efficacy and safety of β-nicotinamide mononucleotide (NMN) supplementation in healthy middle-aged adults: a randomized, multicenter, double-blind, placebo-controlled, parallel- group, dose-dependent clinical trial. Geroscience. 2023 Feb;45(1):29-43. doi: 10.1007/ s11357-022-00705-1. Epub 2022 Dec 8. PMID: 36482258; PMCID: PMC9735188.

11. Li YR, Li S, Lin CC. Effect of resveratrol and pterostilbene on aging and longevity. Biofactors. 2018 Jan;44(1):69-82. doi: 10.1002/biof.1400. Epub 2017 Dec 6. PMID: 29210129.

12. Li Z, Zhang Z, Ren Y, Wang Y, Fang J, Yue H, Ma S, Guan F. Aging and age-related diseases: from mechanisms to therapeutic strategies. Biogerontology. 2021 Apr;22(2):165-187. doi: 10.1007/

s10522-021-09910-5. Epub 2021 Jan 27. PMID: 33502634; PMCID: PMC7838467.

13. Das DK, Mukherjee S, Ray D. Resveratrol and red wine, healthy heart and longevity. Heart Fail Rev. 2010 Sep;15(5):467-77. doi: 10.1007/s10741-010-9163-9. Corrected and republished in: Heart Fail Rev. 2011 Jul;16(4):425-35. PMID: 20238161.

14. Lagouge M, Argmann C, Gerhart-Hines Z, Meziane H, Lerin C, Daussin F, Messadeq N, Milne J, Lambert P, Elliott P, Geny B, Laakso M, Puigserver P, Auwerx J. Resveratrol improves mitochondrial function and protects against metabolic disease by activating SIRT1 and PGC-1alpha. Cell. 2006 Dec 15;127(6):1109-22. doi: 10.1016/j.cell.2006.11.013. Epub 2006 Nov 16. PMID: 17112576.

15. Boyajian JL, Ghebretatios M, Schaly S, Islam P, Prakash S. Microbiome and Human Aging: Probiotic and Prebiotic Potentials in Longevity, Skin Health and Cellular Senescence. Nutrients. 2021 Dec 18;13(12):4550. doi: 10.3390/nu13124550. PMID: 34960102; PMCID: PMC8705837.

16. Coman V, Vodnar DC. Gut microbiota and old age: Modulating factors and interventions for healthy longevity. Exp Gerontol. 2020 Nov;141:111095. doi: 10.1016/j.exger.2020.111095. Epub 2020 Sep 23. PMID: 32979504; PMCID: PMC7510636.

17. Moskalev A, Guvatova Z, Lopes IA, Beckett CW, Kennedy BK, De Magalhaes JP, Makarov AA. Targeting aging mechanisms: pharmacological perspectives. Trends Endocrinol Metab. 2022 Apr;33(4):266-280. doi: 10.1016/j.tem.2022.01.007. Epub 2022 Feb 17. PMID: 35183431.

18. Hanefeld M, Schaper F. Acarbose: oral anti-diabetes drug with additional cardiovascular benefits. Expert Rev Cardiovasc Ther. 2008 Feb;6(2):153-63. doi: 10.1586/14779072.6.2.153. Erratum in: Expert Rev Cardiovasc Ther. 2009 Mar;7(3):330. PMID: 18248270.

19. McCarty MF, DiNicolantonio JJ. Acarbose, lente carbohydrate, and prebiotics promote metabolic health and longevity by stimulating intestinal production of GLP-1. Open Heart. 2015 Jan 29;2(1):e000205. doi: 10.1136/openhrt-2014-000205. PMID: 25685364; PMCID: PMC4316590.

20. Chiasson JL, Josse RG, Gomis R, Hanefeld M, Karasik A, Laakso M; STOP-NIDDM Trial Research Group. Acarbose treatment and the risk of cardiovascular disease and hypertension in patients with impaired glucose tolerance: the STOP-NIDDM trial. JAMA. 2003 Jul 23;290(4):486-94. doi: 10.1001/jama.290.4.486. PMID: 12876091.

21. Almotayri A, Thomas J, Munasinghe M, Jois M. The Effect of Mianserin on Lifespan of Caenorhabditis elegan is Abolished by Glucose. Curr Aging Sci. 2021;14(2):118-123. doi: 10.2174/1874609813999210104203614. PMID: 33397278.

22. Crino PB. Mechanistic target of rapamycin (mTOR) signaling in status epilepticus. Epilepsy Behav. 2019 Dec;101(Pt B):106550. doi: 10.1016/j.yebeh.2019.106550. Epub 2019 Nov 13. PMID: 31732331.

23. Beevers CS, Li F, Liu L, Huang S. Curcumin inhibits the mammalian target of rapamycin-mediated signaling pathways in cancer cells. Int J Cancer. 2006 Aug 15;119(4):757-64. doi: 10.1002/ijc.21932. PMID: 16550606.

24. Kennedy BK, Lamming DW. The Mechanistic Target of Rapamycin: The Grand ConducTOR of Metabolism and Aging. Cell Metab. 2016 Jun 14;23(6):990-1003. doi: 10.1016/j.cmet.2016.05.009. PMID: 27304501; PMCID: PMC4910876.

25. Kim DH, Sarbassov DD, Ali SM, King JE, Latek RR, Erdjument-Bromage H, Tempst P, Sabatini DM. mTOR interacts with raptor to form a nutrient-sensitive complex that signals to the cell growth machinery. Cell. 2002 Jul 26;110(2):163-75. doi: 10.1016/s0092-8674(02)00808-5. PMID: 12150925.

26. Selvarani R, Mohammed S, Richardson A. Effect of rapamycin on aging and age-related diseases-past and future. Geroscience. 2021 Jun;43(3):1135-1158. doi: 10.1007/s11357-020-00274-1. Epub 2020 Oct 10. PMID: 33037985; PMCID: PMC8190242.

27. Bikle DD. Vitamin D metabolism, mechanism of action, and clinical applications. Chem Biol. 2014 Mar 20;21(3):319-29. doi: 10.1016/j.chembiol.2013.12.016. Epub 2014 Feb 13. PMID: 24529992; PMCID: PMC3968073.

28. Norman AW. From vitamin D to hormone D: fundamentals of the vitamin D endocrine system essential for good health. Am J Clin Nutr.

2008 Aug;88(2):491S-499S. doi: 10.1093/ajcn/88.2.491S. PMID: 18689389.

29. Wang W, Li Y, Meng X. Vitamin D and neurodegenerative diseases. Heliyon. 2023 Jan 12;9(1):e12877. doi: 10.1016/j.heliyon.2023.e12877. PMID: 36820164; PMCID: PMC9938420.

30. Chowdhury R, Kunutsor S, Vitezova A, Oliver-Williams C, Chowdhury S, Kiefte-de-Jong JC, Khan H, Baena CP, Prabhakaran D, Hoshen MB, Feldman BS, Pan A, Johnson L, Crowe F, Hu FB, Franco OH. Vitamin D and risk of cause specific death: systematic review and meta-analysis of observational cohort and randomised intervention studies. BMJ. 2014 Apr 1;348:g1903. doi: 10.1136/bmj.g1903. PMID: 24690623; PMCID: PMC3972416.

31. Autier P, Gandini S. Vitamin D supplementation and total mortality: a meta-analysis of randomized controlled trials. Arch Intern Med. 2007 Sep 10;167(16):1730-7. doi: 10.1001/archinte.167.16.1730. PMID: 17846391.

32. Huggins B, Farris M. Vitamin D3 promotes longevity in Caenorhabditis elegans. Geroscience. 2023 Feb;45(1):345-358. doi:10.1007/s11357-022-00637-w. Epub 2022 Aug 24. PMID: 36001277; PMCID: PMC9886739.

33. Mantle D, Hargreaves I. Coenzyme Q10 and Degenerative Disorders Affecting Longevity: An Overview. Antioxidants (Basel). 2019 Feb 16;8(2):44. doi: 10.3390/antiox8020044. PMID: 30781472; PMCID: PMC6406788.

34. Cichocki, M.(2012). Napoje energetyzujące – współczesne zagrożenie zdrowotne dzieci i młodzieży. *Przegląd lekarski*, vol. 69, no. 10**,** p.856-860.

35. Bigard, A.X.(2011). Risks of energy drinks in youths. *Pediatria* ,25,1,p.947-948.

36. Singh P, Gollapalli K, Mangiola S, Schranner D, Yusuf MA, Chamoli M, Shi SL, Lopes Bastos B, Nair T, Riermeier A, Vayndorf EM, Wu JZ, Nilakhe A, Nguyen CQ, Muir M, Kiflezghi MG, Foulger A, Junker A, Devine J, Sharan K, Chinta SJ, Rajput S, Rane A, Baumert P, Schönfelder M, Iavarone F, di Lorenzo G, Kumari S, Gupta A, Sarkar R, Khyriem C, Chawla AS, Sharma A, Sarper N, Chattopadhyay N, Biswal BK, Settembre C, Nagarajan P, Targoff KL, Picard M, Gupta S, Velagapudi V, Papenfuss

AT, Kaya A, Ferreira MG, Kennedy BK, Andersen JK, Lithgow GJ, Ali AM, Mukhopadhyay A, Palotie A, Kastenmüller G, Kaeberlein M, Wackerhage H, Pal B, Yadav VK. Taurine deficiency as a driver of aging. Science. 2023 Jun 9;380(6649):eabn9257. doi: 10.1126/science.abn9257. Epub 2023 Jun 9. PMID: 37289866; PMCID: PMC10630957.