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Pharmacology and Phytochemistry of Chia Seeds (Salvia hispanica L.)

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Abstract:

Due to their remarkable array of health advantages and therapeutic potential, chia seeds (*Salvia hispanica*) have become increasingly popular. Rich in fibre, protein, omega-3 fatty acids, and vital minerals, they are important for promoting general health. According to recent studies, they have potent anti-inflammatory and antioxidant qualities that aid the body in combating oxidative stress and inflammation, two primary causes of chronic illnesses. Additionally, chia seeds have the potential to improve glucose metabolism, which makes them advantageous for those with metabolic syndrome, diabetes, and cardiovascular problems. Beyond their nutritional significance, chia seeds include potent substances including quercetin, kaempferol, myricetin, caffeic acid, and chlorogenic acid. These antioxidants have anti-aging, anti-cancer, heart-protective, and liver-supporting properties. Because of their phenolic compounds and omega-3 content, chia seeds are now frequently utilised to help maintain healthy cholesterol and lipid levels. Even though current research shows encouraging results, more thorough clinical trials are required to completely comprehend their therapeutic mechanisms and efficacy. Nevertheless, chia seeds are a unique functional food that can be used in conjunction with conventional therapies for digestive, circulatory, and metabolic diseases.

Keywords: chia seeds, Omega-3 Fatty Acids, Health Benefits, Dietary Fiber

INTRODUCTION:

Once prized by ancient Central and South American societies, chia seeds (*Salvia hispanica L.) are today hailed as a superfood. They promote energy, nutrition, and general wellness since they are high in protein, fibre, vitamins, minerals, and omega-3 fatty acids.[1] Scientists are interested in chia seeds because of their high nutrient content, which may provide a number of health advantages. They have anti-inflammatory, antioxidant, blood sugar-lowering, and cholesterol-lowering properties, according to studies. While ALA promotes better heart health, their soluble fibre aids in blood sugar regulation and digestion. [2] It's becoming evident that chia seeds have a lot of potential as a natural supplement as scientists continue to investigate their pharmacological advantages. Their expanding list of healthpromoting qualities indicates that they may be useful in improving general wellbeing.[3]Chia seeds can be utilised to make a range of useful food products since they naturally gel when combined with liquid. They have a lot of potential as natural thickeners, emulsifiers, and stabilisers in the food sector because of their gelling ability.[4] Additionally, there is increasing interest in using chia seeds as animal feed. For example, the dairy industry has investigated including chia into livestock diets to organically increase the amount of omega-3 fatty acids in milk, so enhancing its total nutritional value.[5] The fat quality of milk can be enhanced by giving animals forages and oils high in omega-3 fatty acids. Chia has great potential for food security and is prized for its nutritional content and health advantages. This essay examines its origins, cultivation, characteristics, effects on health, and applications in the food sector. [6] Chlorogenic acid, caffeic acid, myricetin, quercetin, and kaempferol are among the phytochemicals found in chia seeds. These substances may have anti-aging and anti-cancer properties in addition to supporting liver and heart health.[7] Because chia seeds are high in fibre, they aid in digestion and aid in weight loss by prolonging feelings of fullness. Rich in antioxidants, they promote heart and brain health, may guard against Parkinson's and Alzheimer's disease, and function as a potent superfood against cancer. [8] Compared to many grains or oilseeds, chia seeds require less water, making them a potential crop. In Argentina and the USA, they are being investigated as a potential crop to diversify sustainable agriculture.[9]

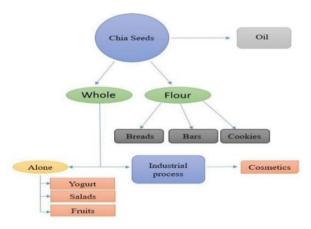


Fig.1: The various products produced from chia seeds

Nutritional composition

A very promising oilseed crop with amazing nutritional advantages is chia seeds. Omega-3 fatty acids, premium protein, vitamins, minerals, dietary fibre, and antioxidants like polyphenols are all abundant in them. Chia seeds' nutrient-rich makeup makes them a natural energy enhancer, and these antioxidants help shield the seeds from microbial and chemical harm.[10] Nutrients abound in chia seeds. They usually have 15–25% protein, 18–30% dietary fibre, 41% carbs, and 30–33% healthy fats. They are generally dry, with dry matter making up 90–95% of their weight, and include 4-5% minerals (ash).[11]

Protein content

Proteins such as albumins, glutelins, globulins, and prolamins make up 16–26% of chia seeds. They are safe and readily digested for people with celiac disease because they are naturally gluten-free. [12] Chia seeds contain considerable levels of various important amino acids, but glutamic acid is the most prevalent of the 18. 11S and 7S proteins, which range in size from 15 to 50 kDa, make up around 52% of the protein in chia. [13]

Dietary fiber

A balanced diet should include 25–30 grammes of dietary fibre per day, which can be found in whole grains. Regular fibre consumption can help lower the risk of a number of health issues, including as kidney stones, metabolic disorders, heart disease, type 2 diabetes, haemorrhoids, and several types of cancer.[14] A3:1 ratio of insoluble to soluble fibre is advised by the American Dietetic Association. Chia has a total fibre content of 23–41%, of which 15% is soluble (5–10% as mucilage) and 85% is insoluble [15]

Lipids

Fat, which accounts for 25–40% of the seed, is the main bioactive component of chia seeds. Healthy polyunsaturated fatty acids, such as omega-3 (alphalinolenic acid) and omega-6 (linoleic acid), make up the majority of this fat.[16] Compared to other vegetable oils, chia seed oil has a higher concentration of polyunsaturated fatty acids. Chia seeds have an omega-6 to omega-3 fatty acid ratio of roughly 0.32 to 0.35.[17,18] Rich in nutrients, chia seeds include around 19% high-quality, physiologically useful protein and more than 30% dietary fibre.[19]

Vitamins and minerals

B vitamins are abundant in chia seeds. They have comparable levels of thiamine and riboflavin to other cereals, but they have higher niacin than rice and maize. [20] With six times more calcium, four times more magnesium, eleven times more phosphorus, and six times more iron than spinach, chia seeds are a great source of minerals. They also supply large amounts of manganese, zinc, sodium, calcium, and magnesium. [21] Important nutrients including potassium, phosphorus, magnesium, and calcium, which support a robust and healthy body, are abundant inchia seeds. Additionally, they include a number of vitamins, including as A, B, D, E, K, B1, B2, and niacin, which help bone health, energy production, and general wellbeing. [22,23]

CHIASEEDPHYTOCHEMICALS

Chia seeds are rich in healthy fats and other useful chemicals that promote general wellbeing. They include potent plant chemicals with anti-inflammatory and antioxidant qualities, including as myricetin, kaempferol, quercetin, and caffeic acid. Additionally, chia seeds are an excellent source of heart and brain-healthy fatty acids including Omega-3 and Omega-6.[24,25] Climate, soil, and growing circumstances can all affect the amounts of healthy chemicals in chia seeds. They are a nutritional powerhouse since they are high in fibre, carbs, protein, healthy fats, vitamins, minerals, and antioxidants.[26]

A. Flavonoids

Plants contain essential natural chemicals called flavonoids. These polyphenol- structured secondary metabolites are well-known for their antioxidant and health- promoting qualities.[27,28] Flavonoids are members of the polyphenol group, which is composed of two benzene rings and fifteen carbon atoms. These potent plant chemicals have antiviral, anti-inflammatory, liver-protective, antioxidant, and anticancer properties.[29,30] These healthy substances are found in chia seeds, and microbial diseases may even cause an increase in their production. Myricetin, Quercetin, and Kaempferol are the most prevalent flavonoids in chia seeds and are well-known for their beneficial effects on health.[24,31]

Molar mass: 302.236 g/mol

Formula: C15H10O7

B. Myricetin

Myricetin, a member of the flavonoid class of phenolic chemicals, is found in chia seeds and is well-known for its antioxidant qualities. Taxifolin is the primary component used in the production of myricetin. It first transforms into dihydromyricetin, after which it undergoes additional processing to produce laricitrin and ultimately syringetin, both of which are flavonoids. [32] Antioxidants are chemicals that help shield the body from illnesses like cancer and heart disease.

Myricetin increases the activity of glutathione S-transferase, an enzyme that protects cells from oxidative stress by blocking the damage caused by free radicals. [33]

Molar mass: 318.2351

Formula: C15H10O8 Pharmacological activity of chia seeds A.Antioxidant and antimicrobial activity

Phenolic chemicals and antioxidants promote general health and shield the body from long-term conditions like cancer, diabetes, and heart disease.[34,35] Chia seeds include bioactive compounds such as myricetin, quercetin, kaempferol, caffeic acids, and chlorogenic acids.[36] Important components including DNA, proteins, and lipids can be harmed by oxidative stress brought on by reactive oxygen species (ROS). This damage can accumulate over time and lead to conditions like diabetes, cancer, blood clots, and chronic inflammation.[37] Consuming foods high in antioxidants, like chia seeds, can help reduce the risk of diseases like cancer, heart disease, and memory or brain deterioration that are brought on by free radicals.[38]

B.Anti-carcinogenic activity;:

Omega-3 good fats, fibre, B vitamins, protein, calcium, magnesium, zinc, and numerous other minerals are all abundant in chia seeds. When combined, these nutrients fortify the body and promote general Healthy[39] In some cervical and breast cancer cells, alpha-linolenic acid (ALA) has been demonstrated to induce apoptosis, or programmed cell death, while sparing healthy cells. The body normally employs apoptosis to eliminate damaged or superfluous cells, but cancer cells frequently lose this capacity, allowing them to proliferate uncontrollably.[40,41] Myricetin, a substance found in chia seeds, may help reduce the incidence of skin cancer brought on by dangerous substances like the extremely hazardous benzo(a)pyrene.[42,43]

C. Anti-inflammatory and Anticholesterolemic

The body's normal reaction to damage or disease is inflammation. Although it can aid in the defence against dangerous bacteria, prolonged exposure can occasionally result in tissue damage. Cancer and heart disease have been connected to this persistent inflammation.[44] Although chronic inflammation typically doesn't show any symptoms, some blood markers, such as hs-CRP, can identify it. While bad behaviours like smoking, eating poorly, and not exercising all raise the risk of chronic inflammation, eating healthy foods like chia seeds can help lower these signs.[45] Because of their anti-inflammatory properties, chia seeds can lessen swelling brought on by chemicals like croton oil and carrageenan. They include two flavonoids, quercetin and myricetin, which have also been demonstrated to reduce inflammation.[46] Flavonoids help reduce inflammation by lowering cytokine production (like interleukin-12 and interleukin-1β) and by blocking key inflammatory pathways, including tumor necrosis factor-alpha and kinases.[47,48]

D.Anti hypertensive

High blood pressure is prevalent and is increasingly regarded as a risk factor. [45] Studies have indicated that chia seeds can lower blood pressure. [49] Eating chia seeds has been found to lower triglycerides, insulin resistance, inflammation, and belly fat while raising "good" HDL cholesterol in rats. [50,51] By altering specific bodily enzymes, chia seeds may help reduce hypertension. Proteins in chia seeds can affect the function of the angiotensin-converting enzyme (ACE), much like synthetic ACE inhibitors, which block the enzyme to lower blood pressure. [52,53]

CONCLUSION

Because of its diverse pharmacological characteristics and extensive phytochemical profile, chia seeds (Salvia hispanica L.) are becoming a desirable functional food. They have the potential to promote health since they are a powerful source of omega-3 fatty acids, high-quality proteins, dietary fibre, antioxidants, vitamins, and minerals. Preclinical and limited clinical research has shown that the bioactive substances found in chia seeds, such as phenolic acids, flavonoids, and phytosterols, have important antioxidant, anti-inflammatory, cardioprotective, antidiabetic, neuroprotective, and anticancer properties.

Reference:

- 1) Nieman, D. C., et al., "Nutritional and functional properties of chiaseed." Journal of Nutritional Biochemistry, 2012; 23(1), 100-106
- 2) Mäkelä, J., et al.. "Chia seed supplementation and its effects on glycemic control: A systematic review and meta-analysis." Food C Function, 2020; 11(2), 1125-1137
- 3) It's becoming evident that chia seeds have a lot of potential as a natural supplement as scientists continue to investigate their pharmacological advantages. Their expanding list of health-promoting qualities indicates that they may be useful in improving general wellbeing.
- 4) Coorey, R., Tjoe, A., C Jayasena, V., "Gelling Properties of Chia Seed and Flour." Journal of Food Science, 2014;79(5), 859-866
- Dewhurst, R., Shingfield, K., Lee, M., C Scollan, N., "Increasing the concentrations of beneficial polyunsaturated fatty acids in milk produced by dairy cows in high-forage systems." Journal of Animal Feed Science. 2006: 131. 168-206
- 6) Chilliard, Y., Ferlay, A., C Doreau, M., "Effect of different types of forages, animal fat or marine oils in cow's diet on milk fat secretion and composition, especially conjugated linoleic acid (CLA) and polyunsaturated fatty acids." Journal of Livestock Production Science, 2001;70, 31-48.
- 7) Melo D, Machado TB, Oliveira MBPP. Chia seeds: an ancient grain trending in modern human diets. Food Funct. 2019;10(6):3068–89. https://doi.org/10.1039/c9fo00239a.
- 8) Grancieri M, Martino HSD, Gonzalez de Mejia E. Chia seed (Sal- via hispanica L.) as a source of proteins and bioactive peptides with health benefits: a review. Compr Rev Food Sci Food Saf. 2019;18(2):480–99. https://doi.org/10.1111/1541-4337.12423.
- 9) Şengül AY. Possibilities of using chia oil as an omega-3 source in laying quail diets chia oil supplementation on quails. Braz J Poult Sci. 2022;24 https://doi.org/10.1590/1806-9061-2021-1444.
- 10) Muñoz LA, Cobos A, Diaz O, Aguilera JM. Chia seed (Salvia his-panica): an ancient grain and a new functional food. Food Rev Intl. 2013;29(4):394–408. https://doi.org/10.1080/87559129.2013.818014
- Ullah R, Nadeem M, Khalique A, Imran M, Mehmood S, Javid A, Hussain J. Nutritional and therapeutic perspectives of chia (Salvia hispanica L.): a review. J Food Sci Technol. 2016;53(4):1750–8. https://doi.org/10.1007/s13197-015-1967-0.
- Kulczyński B, Kobus-Cisowska J, Taczanowski M, Kmiecik D, Gramza-Michałowska A. The chemical composition and nutritional value of chia seedscurrent state of knowledge. Nutrients. 2019;11(6):1242. https://doi.org/10.3390/nu11061242.
- 13) Molina-Tizo N, Victoria MT, Soriano-García M. Isolation, biochemical characterization, oxido-reductive and proteolytic activities of globulin protein isolates from seeds of chia. J Anal PharmRes. 2017;5(1):00132. https://doi.org/10.15406/japlr. 2017.05.00132.
- 14) Segura-Campos MR, Ciau-Solís N, Rosado-Rubio G, Chel- Guerrero L, Betancur-Ancona D. Chemical and functional properties of chia seed (Salvia hispanica L.) gum. Int J Food Sci. 2014;2014:241053. https://doi.org/10.1155/2014/241053.
- 15) Valdivia-López M, Ángeles Tecante A. Chia (Salvia hispanica): a review of native Mexican seed and its nutritional and functional properties. Adv Food Nutr Res. 2015;75:53–75. https://doi.org/10.1016/bs.afnr.2015.06.002.
- 16) Kulczyński B, Kobus-Cisowska J, Taczanowski M, Kmiecik D, Gramza-Michałowska A. The chemical composition and nutritional value of chia seeds-current state of knowledge. Nutrients. 2019;11(6):1242. https://doi.org/10.3390/nu110 61242.
- 17) Reyes-Caudillo E, Tecante A, Valdivia-López MA. Dietary fibre content and antioxidant activity of phenolic compounds present in Mexican chia (Salvia hispanica L.) seeds. Food Chem. 2008;107(2):656–63. https://doi.org/10.1016/j.foodchem.2007.08.062
- 18) Ciftci ON, Przybylski R, Rudzińska M. Lipid components of flax, perilla, and chia seeds. Eur J Lipid Sci Technol. 2012;114(7):794–800. https://doi.org/10.1002/ejlt.201100207. 19)Capitani MI, Spotorno V, Nolasco SM, Tomás MC. Physico- chemical and functional characterization of byproducts from chia (Salvia hispanica L.) seeds of Argentina. LWT- Food Sci Technol.2012;45(1):94–102. https://doi.org/10.1016/j.lwt.2011.07.012. 20)Reyes-Caudillo E, Tecante A, Valdivia-López MA. Dietary fibre content and antioxidant activity of phenolic compounds present in Mexican chia (Salvia hispanica L.) seeds. Food Chem. 2008;107(2):656–63. https://doi.org/10.1016/j.foodchem.2007.08.062.
- 21) Muñoz LA, Cobos A, Diaz O, Aguilera JM. Chia seed (Salvia his-panica): an ancient grain and a new functional food. Food Rev Intl. 2013;29(4):394–408. https://doi.org/10.1080/87559129.2013.818014
- 22) Muñoz LA, Cobos A, Diaz O C Aguilera JM. "Chia Seed (Salvia hispanica): An AncientGrain and a New Functional Food." Food Reviews International, 2013; 29, 394–408. 38. Suri S, Passi SJ C Goyat J. "Chia seed (Salvia hispanica L.)—A new age functional food." International Journal of Advanced Technology in Engineering and Science, 2016;4(3): 286-299.
- 23) Suri S, Passi SJ C Goyat J. "Chia seed (Salvia hispanica L.)—A new age functional food." International Journal of Advanced Technology in Engineering and Science, 2016;4(3): 286-299.
- 24) Capitani MI, Spotorno V, Nolasco SM C Tomás MC. Physicochemical and functional characterization of by-products from chia (Salvia hispanica L.) seeds of Argentina. LWT-Food Science and Technology 2012; 45, 94–102.
- 25) Melo D, Machado TB C Oliveira MBPP. Chia seeds: an ancient grain trending in modern human diets. Food Funct, 2019; 10, 3068–3089.
- da Silva BP, Toledo RCL, Grancieri M, Moreira ME de C, Medina NR, Silva RR, Costa NMB C Martino HSD. Effects of chia (Salvia hispanica L.) on calcium bioavailability and inflammation in Wistar rats. Food Res. Int, 2019; 116, 592–599.
- 27) Panche AN, Diwan ADC Chandra SR. Flavonoids: an overview. J. Nutr. Sci., 2016; 5, e47.
- 28) Crozier A, Yokota T, Jaganath IB, Marks S, Saltmarsh M C Clifford MN. Secondary Metabolites in Fruits, Vegetables, Beverages and Other Plant-based Dietary Components. In Plant Secondary Metabolites (Crozier A, Clifford MN, C Ashihara H, eds), 2006; pp. 208–302. Blackwell Publishing Ltd, Oxford, UK.
- 29) Das A. Advances in chia seed research. AIBM 5, 2017.
- 30) Lee YK, Yuk DY, Lee JW, Lee SY, Ha TY, Oh KW, Yun YP C Hong JT. (-)-Epigallocatechin-3-gallate prevents lipopolysaccharide-induced elevation of beta-amyloid generation and memory deficiency. Brain Res., 2009; 1250, 164–174.

- 31) Reyes-Caudillo E, Tecante A C Valdivia-López MA. Dietary fibre content and antioxidant activity of phenolic compounds present in Mexican chia (Salvia hispanica L.) seeds. Food Chem. 2008; 107,656–663.
- 32) Liu I-M, Liou S-S, Lan T-W, Hsu F-L C Cheng J-T. Myricetin as the active principle of Abelmoschus moschatus to lower plasma glucose in streptozotocin-induced diabetic rats. Planta Med., 2005; 71, 617–621. 33)Alcântara MA, de Lima Brito Polari I, de Albuquerque Meireles BRL, de Lima AEA, da Silva Junior JC, de Andrade Vieira É, Dos Santos NA C de Magalhães Cordeiro AMT. Effect of the solvent composition on the profile of phenolic compounds extracted from chia seeds. Food Chem., 2019; 275, 489–496.
- 34) Aggarwal BB C Shishodia S. "Molecular targets of dietary agents for prevention and therapy of cancer." Biochemistry Pharmacology. 2006; 71, 1397–1421.
- 35) Ellulu MS. "Obesity, cardiovascular disease, and role of vitamin C on inflammation: a review of facts and underlying mechanisms." Inflammopharmacology, 2017; 25.313–328.
- 36) Suri S, Passi SJ C Goyat J. "Chia seed (Salvia hispanica L.)—A new age functional food." International Journal of Advanced Technology in Engineering and Science. 2016;4(3): 286-299.
- 37) Brglez Mojzer E, Knez Hmčič M, Škerget M, Knez Ž C Bren U. "Polyphenols: extraction methods, antioxidative action, bioavailability and anticarcinogenic effects." Molecules, 2006; 11:21(7):90
- 38) Rittmaster M. "Antioxidants: The Unbiased Scientific Truth, EvidenceBased Health Benefits, and Important Facts". Healthinsiders, 2024;11:123-134.
- 39) Haque, E., R. Chand, and S. "Kapila, Biofunctional properties of bioactive peptides of milk origin." Food Reviews International, 2008. 25 (1): p. 28-43.
- 40) INE, I., "Estatísticas da Cultura." Lisboa: INE, 2012; 63, 1049–1055.
- 41) Tong, W.-G., X.-Z. Ding, and T. E. "Adrian, The mechanisms of lipoxygenase inhibitor- induced apoptosis in human breast cancer cells." Biochemical and biophysical research communications, 2002. 296(4): p. 942-948.
- 42) Imran M, Salehi B, Sharifi-Rad J, Aslam Gondal T, Saeed F, Imran A, Shahbaz M, Tsouh Fokou PV, Umair Arshad M, Khan H, Guerreiro SG, Martins N C Estevinho LM. "Kaempferol: A key emphasis to its anticancer potential." Molecules, 2019, 24(12), 2277.
- 43) Alfredo V-O, Gabriel R-R, Luis C-G C David B-A. "Physicochemical properties of a fibrous fraction from chia (Salvia hispanica L.)." LWT Food Science and Technology, 2009; 42, 168–173.
- 44) Khansari N, Shakiba Y C Mahmoudi M. "Chronic inflammation and oxidative stress as a major cause of age-related diseases and cancer." Recent Pathophysiology of Inflammational ,Allergy Drug Discovery, 2009; 3, 73–80.
- 45) Vuksan V, Whitham D, Sievenpiper JL, Jenkins AL, Rogovik AL, Bazinet RP, Vidgen E C Hanna A. "Supplementation of conventional therapy with the novel grain Salba (Salvia hispanica L.) improves major and emerging cardiovascular risk factors in type 2 diabetes: results of a randomized controlled trial." Diabetes Care, 2007; 30, 2804–2810.
- 46) Hämäläinen M, Nieminen R C Vuorela P. "Anti-inflammatory effects of flavonoids: genistein, kaempferol, quercetin, and daidzein inhibit STAT-1 and NF-kappaB activations, whereas flavone, isorhamnetin, naringenin, and pelargonidin inhibit only NF-kappaB activation along with their inhibitory effect on iNOS expression and NO production in activated macrophages." Mediators Inflammation, 2007:45673.
- 47) Spencer JPE. "Flavonoids and brain health: multiple effects underpinned by common mechanisms." Genes Nutrients, 2009; 4, 243–250.
- 48) Liu C-M, Sun Y-Z, Sun J-M, Ma J-Q C Cheng C. "Protective role of quercetin against lead- induced inflammatory response in rat kidney through the ROS-mediated MAPKs and NF-κB pathway." Biochemistry Biophysiology Acta, 2012; 1820, 1693–1703.
- 49) Fowokan AO, Sakakibara BM, Onsel N, Punthakee Z, Waddell C, Rosin M C Lear SA. "Correlates of elevated blood pressure in healthy children: a systematic review." Clinical Obesity, 2018; 8, 366–381
- 50) Ayerza R C Coates W. "Effect of dietary alpha-linolenic fatty acid derived from chia when fed as ground seed, whole seed and oil on lipid content and fatty acid composition of rat plasma." Annal Nutrients Metabolism, 2007; 51, 27–34.
- 51) Chicco AG, D'Alessandro ME, Hein GJ, Oliva ME C Lombardo YB. "Dietary chia seed (Salvia hispanica L.) rich in alpha-linolenic acid improves adiposity and normalizes hypertriacylglycerolaemia and insulin resistance in dyslipaemic rats." British Journal of Nutrition., 2009; 101, 41–50.
- 52) Costantini L, Molinari R C Merendino N. "Effects of chia seed supplementation on biochemical markers of cardiometabolic diseases in spontaneously hypertensive rats." Acta Alimentaria, 2019; 48, 538–545.
- 53) Suzuki A, Kagawa D, Fujii A, Ochiai R, Tokimitsu I C Saito I. "Shortand long-term effects of ferulic acid on blood pressure in spontaneously hypertensive rats. Am." J. Hypertension, 2002; 15, 351–357