

**12 BİTKİSEL ETKEN MADDELER**Kanber KARA<sup>1</sup>**GİRİŞ**

Bitkisel biyoaktif bileşikler (bitkisel etken maddeler ya da sekonder bileşikler), bitkilerde sentezlenen ve bitki organizmalarının normal büyümeye, gelişme veya üreme süreçlerinde doğrudan yer almayan kimyasal bileşiklerdir. Bu bileşiklerin bazları hastalıklara, herbivor hayvanlara, ultraviyole ve radyasyona, parazitlere ve oksidanlara karşı savunma maddesi olarak görev yaparlar. Üreme süreçlerini kolaylaştırır (çekici kokular ve renkendirici maddeler olarak işlev görürler) ve türler arası rekabete katkı sağlarlar. Bitki kökenli biyoaktif bileşikler, insan ve hayvan sağlığı üzerinde olumlu etkileri olan ikincil metabolitlerdir. Bitkiler; ışık, su, azot, fosfor ve kükürt gibi temel maddeleri kullanarak karbonhidratlar, proteinler ve yağlar gibi birincil ürünleri sentezler. Dünya genelinde yaklaşık 1.000.000 bitki türü bulunduğu, bunlardan 500.000'inin tanımlandığı tahmin edilmektedir. Türkiye, bitki çeşitliliği bakımından dünyanın en zengin ülkelerinden biridir. Ülkemizde yaklaşık 12.000 bitki türü bulunmakta olup bunların yaklaşık 4.000'i sadece Türkiye'de yetişen endemik

türlerdir. Sınırları belirli, dar bir alanda (birkaç metrekare ile bir ülke sınırları arasında değişebilir) yayılış gösteren türler, endemik (yerli) bitkiler olarak adlandırılır. Avrupa kıtasının tamamında da yaklaşık 12.000 bitki türü yetişmektedir.

Bitkilerde sentezlenen alkaloidler, fenoller, flavonoidler, glikozitler, saponinler, steroller, tanenler, terpenoidler ve uçucu yağlar gibi maddeler, ikincil bileşikler (sekonder metabolitler) olarak sınıflandırılır. Bitki hücrelerinde bulunup hayvan hücrelerinde yer almayan bir plastid olan kloroplastlar, fotosentez ve birçok sekonder bileşliğin üretiminden sorumludur. Bu plastidler, monoterpen, diterpen, karoten, fitol ve ubikinon gibi bileşiklerin sentezinde rol oynar. Bitkide pigment içeren bir diğer plastid türü olan kromoplastlar da sekonder bileşiklerle ilişkilidir. Bitkilerde 100.000'den fazla sekonder bileşliğin sentezlendiği düşünülmektedir. Sayıca en fazla bulunan bu bileşikler arasında ilk sıradı terpenoidler, ikinci sıradı ise alkaloidler yer almaktadır. Şekil 1'deki diyagramda bitkisel metabolitlerin karbonhidratlardan başlayarak çeşitli bileşiklere nasıl dönüştüğü görülmektedir.

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Tablo 11. Terpenlerin immun sistem üzerine etkileri

Bitki/Hayvan Türü	Terpen Türü	İmmün Sistem Üzerindeki Etkileri	İmmün Yanıt Ürünü	Kaynak
Lavanta ( <i>Lavandula angustifolia</i> ) - Holstein buzağı	Lavanta uçucu bileşenleri	Hücresel immün yanıtın desteklenmesi	TNF- $\alpha$ , IL-1 $\beta$ , IL-6, SAA	Kara ve Pirci, 2022
İzmir kekiği ( <i>Origanum onites L.</i> ) - Buzağı	İzmir kekiği uçucu bileşenleri	İmmünglobulin (IgA, IgG, IgM) seviyelerinin artırılması	IgA, IgG, IgM	Özkaya ve ark., 2018
Nane ( <i>Mentha piperita L.</i> )	Nane etanol ekstraktı	Antiviral aktivite, sitokin üretiminde azalma	NO, TNF- $\alpha$ , IL-6, PGE2	Li ve ark., 2017
Okaliptüs ( <i>Eucalyptus</i> ) - Broyler	Okaliptüs yaprağı uçucu bileşenleri	İmmün yanıtın artırılması	IL-6, IL-1 $\beta$ , TNF- $\alpha$	Farhadi ve ark., 2017
Adhatoda vasica, Curcuma longa, vb. - Buzağı	Bitkisel karışım (ögenol, piperin)	İmmün yanıtın olumlu etkilenmesi	Antikor titresini artırma	Sanchez ve ark., 2021
Sarımsak ( <i>Allium sativum</i> ) - Holstein buzağı	Sarımsak tozu	IgG seviyelerinin artışı, dışkı skorlarının iyileşmesi	IgG	Kekana ve ark., 2020
Deniz yosunu (KM) - Holstein buzağı	Kuru-öğütülmüş deniz yosunu	Fibrinojen ve SAA seviyelerinin artması	Fibrinojen, SAA	Samarasinghe ve ark., 2021
Ekinezya ( <i>Echinacea purpurea</i> ) - Holstein buzağı	Ekinezya tozu	Bağışıklık modülasyonu ve inflamasyonun azalması	Lenfosit sayıları, TNF- $\alpha$ , IL-6, IL-10	McNeil ve ark., 2023

artırarak patojenlere karşı daha etkili bir yanıt oluşmasını sağlarlar.

### Humoral bağışıklık üzerine etkileri

Vücutta antikor üretimini teşvik ederek humoral bağışıklık yanıtını desteklerler.

### Mukozal bağışıklık yanıtı

Uçucu bileşenler, bağırsak mukozasında yer alan immün hücreleri aktive ederek lokal bağışıklık yanıtlarını güçlendirir. İnce bağırsakta IgA üretiminin artışı, patojenlerin mukozal yüzeye tutunmasını engellerler.

### Anti-inflamatuar ve immün modülatör etkileri

Enflamasyona neden olan bazı sitokinlerin üretimi azaltırken; bağışıklık sistemini dengeleyen moleküllerin sentezini artırırlar. Bu sayede bağışıklık sisteminin aşırı tepkiler vermesi engellenir,

dokular korunur.

### KAYNAKLAR

- Abdel-Latif MS, Elmeleigy KM, Aly TAA, Khattab MS, Mohamed SM. Pathological and biochemical evaluation of coumarin and chlorophyllin against aflatoxicosis in rat. *Exp Toxicol Pathol.* 2017;69(5):285-291.
- Abudayeh ZH, Al Azzam KM, Naddaf A, Karpiuk UV, Kislichenko VS. Determination of four major saponins in skin and endosperm of seeds of horse chestnut (*Aesculus hippocastanum L.*) using high performance liquid chromatography with positive confirmation by thin layer chromatography. *Adv Pharm Bull.* 2015 Nov;5(4):587-91.
- Afrose S, Hossain MS, Salma U, Miah AG, Tsujii H. Dietary Karaya saponin and Rhodobacter capsulatus exert hypocholesterolemic effects by suppression of hepatic cholesterol synthesis and promotion of bile acid synthesis in laying hens. *Cholesterol.* 2010;272731.
- Aguilar-Hernández JA, Urías-Estrada JD, López-Soto MA, Barreras A, Plascencia A, Montaño M, ve ark.. Evaluation of isoquinoline alkaloid supplementation levels on ruminal fermentation, characteristics of digestion, and microbial protein synthesis in steers fed a high-energy diet. *J Anim Sci.* 2016; 94(1):267-274.
- Aguilar-Hernández, R., Chaucheyras-Durand, F., Martín-Te-

- reso, J., & Bach, A. Effects of feeding isoquinoline alkaloids on rumen fermentation and nutrient utilization in beef cattle. *Journal of Animal Science*, 2016; 94(5): 134–135.
- Aja-Perez I., Krisa S., Hornedo-Ortega R., Begona Ruiz-Larrea M., Ruiz-Sanz J.I., Richard T., Courtois A. Stilbenes at low micromolar concentrations mitigate the NO, TNF- $\alpha$ , IL-1 $\beta$  and ROS production in LPS-stimulated Murine Macrophages. *J. Biol. Act. Prod. Nat.* 2021;11:3.
- Alamgir A.N.M. Secondary Metabolites: Secondary Metabolic Products Consisting of C and H.; C, H, and O.; N, S, and P Elements; and O/N Heterocycles. In: Alamgir A.N.M., editor. *Therapeutic Use of Medicinal Plants and Their Extracts: Volume 2: Phytochemistry and Bioactive Compounds*. Springer International Publishing; Cham, Switzerland: 2018. pp. 165–309.
- Al-Khayri JM, Mascarenhas R, Harish HM, Gowda Y, Lakshmaiah VV, Nagella P, Al-Mssallem MQ, Alessa FM, Almaghasla MI, Rezk AA. Stilbenes, a versatile class of natural metabolites for inflammation—an overview. *Molecules*. 2023 apr 28;28(9):3786.
- allowaimer a. ameliorative effects of antibiotic-, probiotic- and phytobiotic-supplemented diets on the performance, intestinal health, carcass traits, and meat quality of *Clostridium perfringens*-infected broilers. *Animals (Basel)*. 2020 Apr 12;10(4):669.
- Ansari N., Khodagholi F. Natural products as promising drug candidates for the treatment of alzheimer's disease: molecular mechanism aspect. *curr. Neuropharmacol.* 2013;11: 4.
- Aoki T, Akashi T & Ayabe S Flavonoids of leguminous plants: structure, biological activity, and biosynthesis. *J Plant Res* 2000;113: 475–488.
- Apekey, T.A.; Khokhar, S. Survey on the consumption of cinnamon-containing foods and drinks by the uk population; University of Leeds: Leeds, UK, 2015.
- Arévalo Sureda, E.; Zhao, X.; Artuso-Ponte, V.; Wall, S.-C.; Li, B.; Fang, W.; Uerlings, J.; Zhang, Y.; Schroyen, M.; Grelet, C.; et al. Isoquinoline alkaloids in sows' diet reduce body weight loss during lactation and increase igg in colostrum. *Animals* 2021, 11: 2195.
- Arslan Z, Bingül M. Kumarin ve izokumarin türevlerinin anti-enflamatuar aktivite profillerinin araştırılması. *Journal of Ata-Chem.*, 2021; 1: 38-51.
- Ashour, A.S.; El Aziz, M.M.A.; Gomha Melad, A.S. A review on saponins from medicinal plants: chemistry, isolation, and determination. *J. Nanomed. Res.* 2019; 7:282–288
- Ashour, A.S.; El Aziz, M.M.A.; Gomha Melad, A.S. A review on saponins from medicinal plants: chemistry, isolation, and determination. *J. Nanomed. Res.* 2019; 7: 282–288.
- Azzam MM, Jiang SQ, Chen JL, Lin XJ, Gou ZY, Fan QL, Wang YB, Li L, Jiang ZY. Effect of soybean isoflavones on growth performance, immune function, and viral protein 5 mRNA expression in broiler chickens challenged with infectious bursal disease virus. *Animals (Basel)*. 2019; 9 (5):247.
- Balcells J., Aris A., Serrano A., Seradj A. R., Crespo J., and Devant M., Effects of an extract of plant flavonoids (Bioflavex) on rumen fermentation and performance in heifers fed high-concentrate diets, *Journal of Animal Science*. 2012; 90(13): 4975–4984.
- Bao L, Zhang Z, Dai X, Ding Y, Jiang Y, Li Y and Li Y: Effects of grape seed proanthocyanidin extract on renal injury in type 2 diabetic rats. *Mol Med Rep* 2015; 11: 645–652.
- Barceloux, D. G. Potatoes, tomatoes, and solanine toxicity (*Solanum tuberosum* L., *Solanum lycopersicum* L.). *Dis. Mon.* 2009; 55: 391–402.
- Berhow MA, Kong SB, Vermillion KE, Duval SM. Complete quantification of group A and group B soyasaponins in soybeans. *J Agric Food Chem.* 2006 Mar 22;54(6):2035–2044.
- Blahová, J.; Svobodov, Z. Assessment of coumarin levels in ground cinnamon available in the Czech retail market. *Sci. World J.* 2012; 1–4.
- Brito EF, Pereira MLA, Silva HGDO, Soares ACM, Soares Correia G, Sousa LB, et al.. Effects of enriched mesquite piperidine alkaloid extract in diets with reduced crude protein concentration on the rumen microbial efficiency and performance in lambs. *Czech J. Anim. Sci.* 2020; 65(7):268–280.
- Catalgal B., Batirel S., Taga Y., Ozer N.K. Resveratrol: French Paradox Revisited. *Front. Pharmacol.* 2012;3:141.
- Chaturvedi, M.M.; Kumar, A.; Darnay, B.G.; Chainy, G.B.N.; Agarwal, S.; Aggarwal, B.B. Sanguinarine (Pseudochelerythrine) is a potent inhibitor of NF- $\kappa$ B activation, I $\kappa$ B phosphorylation, and degradation. *J. Biol. Chem.* 1997; 272: 30129–30134.
- Cheeke PR (2000) Actual and potential applications of *Yucca schidigera* and *Quillaja saponaria* saponins in human and animal nutrition. *Proceedings of the Phytochemical Society of Europe* 45: 241–254.
- Chen K, Liu Y, Cheng Y, Yan Q, Zhou C, He Z, Zeng J, He J, Tan Z. Supplementation of *Lactobacillus plantarum* or *Macleaya cordata* extract alleviates oxidative damage induced by weaning in the lower gut of young goats. *Animals (Basel)*. 2020 Mar 25;10(4):548.
- Chen, S., Liu, H., Zhang, J., Zhou, B., Zhuang, S., He, X., Wang, C. Effects of different levels of rutin on growth performance, immunity, intestinal barrier and antioxidant capacity of broilers. *Italian Journal of Animal Science*, 2022; 21(1):1390–1401.
- Chepete HJ, Xin H, Mendes LB, Li H & Bailey TB. 2012. Ammonia emission and performance of laying hens as affected by different dosages of *Yucca schidigera* in the diet. *Journal of Applied Poultry Research*, 21: 522-530.
- Chin C.-K. (2008). "Plant cell culture as a source of valuable chemicals," in *Biotechnology in flavor production* (Hoboken, United States: John Wiley & Sons; ), 104–117.
- Cho KS, Lim YR, Lee K, Lee JI, Lee IS. Terpenes from forests and human health. *Toxicol Res.* 2017 Apr; 33(2): 97-106.
- Colomer R, Sarrats A, Lupu R, Puig T. Natural polyphenols and their synthetic analogs as emerging anticancer agents. *Curr Drug Targets*. 2017; 18(2): 147-159.
- Dabbou S, Gasco L, Rotolo L, Pozzo L, Tong JM, Dong XF, Rubiolo P, Schiavone A, Gai F. Effects of dietary alfalfa flavonoids on the performance, meat quality and lipid oxidation of growing rabbits. *Asian-Australas J Anim Sci.* 2018 Feb; 31(2): 270-277.
- Datte JY, Ziegler A (2001) Pharmacological investigation on nigrescigenin cardenolide from *Paquetina nigrescens* (Afzel.) Bullock: comparative studies on cardiotonic effects of *Paquetina nigrescens*, g-strophanthin and noradrenaline in guinea-pig isolated atria. *J Pharm Pharmacol* 53:859–866.

- de Jesus Pereira, T.C., Pereira, M.L.A., Moreira, J.V. et al. Effects of alkaloid extracts of mesquite pod on the products of in vitro rumen fermentation. *Environ Sci Pollut Res* 2017; 24: 4301–4311.
- Devienne K.F., Redd M.S.G., Coelho R.G., Vilegas W. Structure-anti microbial activity some natural isocoumarins and their analogs. *Phytomedicine*, 2005; 12 (5): 78-381.
- Dewick, P. M. (2002). Medicinal natural products: a biosynthetic approach. John Wiley & Sons.
- Dixon R & Ferreira D (2002) Molecules of interest: genistein. *Phytochemistry* 60, 205–211.
- Dugrand, A.; Olry, A.; Duval, T.; Hehn, A.; Froelicher, Y.; Bourgaud, F. Coumarin and furanocoumarin quantitation in Citrus peel via ultraperformance liquid chromatography coupled with mass spectrometry (UPLC-MS). *J. Agric. Food Chem.* 2013; 61: 10677–10684.
- Durán, A.G.; Calle, J.M.; Butrón, D.; Pérez, A.J.; Macías, F.A.; Simonet, A.M. Steroidal saponins with plant growth stimulation effects; *Yucca schidigera* as a commercial source. *Plants* 2022; 11: 3378.
- Duta-Bratu, C.-G.; Nitulescu, G.M.; Mihai, D.P.; Olaru, O.T. Resveratrol and other natural oligomeric stilbenoid compounds and their therapeutic applications. *Plants* 2023; 12: 2935.
- Elmusa F, Elmusa M. Mini-Review on Coumarins: Sources, biosynthesis, bioactivity, extraction and toxicology. *JOT-CSA*. 2024; 11(3): 933-944
- EURL-FA., European Union Reference Laboratory for Feed Additives, *Macleaya cordata* extract (FAD-2010-0071; CRL/100111). Evaluation Report on the Analytical Methods submitted in connection with the Application for Authorisation of a Feed Additive according to Regulation (EC) No 1831/2003, 2018 Belgium
- Faehnrich, B., Pastor, A., Heide, C., Kröger, S., & Zentek, J. (2019). Effects of isoquinoline alkaloids from *Macleaya cordata* on physiological, immunological and inflammatory parameters in healthy beagles. *Journal of Animal Physiology and Animal Nutrition*, 103: 661–667.
- Fenwick, G.R. Saponins. In *Toxic Substance in Crop Plants*; Felix D'Mello, J.P., Duffus, C.M., Duffus, J.H., Eds.; The Royal Society of Chemistry: London, UK, 1991; pp. 285–327.
- Frenț, O.-D.; Stefan, L.; Morgovan, C.M.; Duteanu, N.; Dejeu, I.L.; Marian, E.; Vicaș, L.; Manole, F. A Systematic Review: Quercetin—Secondary metabolite of the flavonol class, with multiple health benefits and low bioavailability. *Int. J. Mol. Sci.* 2024; 25:12091.
- Friedman M. Potato glycoalkaloids and metabolites: roles in the plant and in the diet. *J Agric Food Chem.* 2006;54(23): 8655-8681.
- Friedman, M. Potato glycoalkaloids and metabolites: roles in the plant and in the diet. *J. Agric. Food Chem.* 2006; 54: 8655–8681.
- Friedman, M., Lee K. R., Kim H. J., Lee I. S., and Kozukue N. Anticarcinogenic effects of glycoalkaloids from potatoes against human cervical, liver, lymphoma, and stomach cancer cells. *J. Agric. Food Chem.* 2005; 53: 6162–6169.
- Ghosh D. Tannins from foods to Combat diseases. *International Journal of Pharma Research & Review*, May 2015; 4(5):40-44
- Gohlke A., Ingemann C. J., Nurnberg G., Starke A., Wolffram S., and Metges C. C., Bioavailability of quercetin from its glycone and its glucorhamnoside rutin in lactating dairy cows after intraduodenal administration, *Journal of Dairy Science*. (2013); 96(4): 2303–2313
- Goliomytis M, Kartsonas N, Charismiadou MA, Symeon GK, Simitzis PE, Deligeorgis SG. The Influence of Naringin or Hesperidin dietary supplementation on broiler meat quality and oxidative stability. *PLoS One*. 2015; 28; (10):e0141652.
- Góral I, Wojciechowski K. Surface activity and foaming properties of saponin-rich plants extracts. *Adv Colloid Interface Sci.* 2020; 279:102145.
- Grgic D, Varga E, Novak B, Müller A, Marko D. Isoflavones in Animals: Metabolism and effects in livestock and occurrence in feed. *Toxins (Basel)*. 2021; 24;13(12):836.
- Gunun, P.; Cherdthong, A.; Khejornsart, P.; Wanapat, M.; Pol-yorach, S.; Kang, S.; Kaewwongsu, W.; Gunun, N. The Effect of phytonutrients in *Terminalia chebula* retz. on rumen fermentation efficiency, nitrogen utilization, and protozoal population in goats. *Animals*. 2022;12(16), <https://doi.org/10.3390/ani12162022>
- Hager-Theodorides AL, Massouras T, Simitzis PE, Moschou K, Zoidis E, Sfakianaki E, Politis K, Charismiadou M, Goliomytis M, Deligeorgis S. Hesperidin and Naringin improve broiler meat fatty acid profile and modulate the expression of genes involved in fatty acid β-oxidation and antioxidant defense in a dose dependent manner. *Foods*. 2021; 10(4):739.
- Harborne, J. B. *Phytochemical Methods: A Guide to Modern Techniques of Plant Analysis*. (1998). Springer.
- Hartmann T. From waste products to ecochemicals: fifty years research of plant secondary metabolism. *Phytochemistry*. 2007; 68: 2831–2846.
- Hassan AA, Abu Hafsa SH, Elghandour MMMY, Kanth Reddy PR, Monroy JC, Salem AZM. Dietary supplementation with sodium bentonite and coumarin alleviates the toxicity of aflatoxin B<sub>1</sub> in rabbits. *Toxicon*. 2019;171: 35-42. doi:10.1016/j.toxicon.2019.09.014
- Hayashi H, Sudo H. Economic importance of licorice. *Plant Biotechnology* 2009; 26: 101-104
- Hollman A. Plants and cardiac glycosides. *Br Heart J.* 1985; 54: 258-61
- Hoult JR, Paya M. The pharmacological and biochemical action of simple coumarins: natural products with therapeutic potential. *Gen. Pharmacol. Vasc. Syst.*, 1996; 27 (4): 713-722.
- Hristov, A.N.; Ivan, M.; Neill, L.; McAllister, T.A. Evaluation of several potential bioactive agents for reducing protozoal activity in vitro. *Anim Feed Sci Technol* 2003; 105:163–184.
- Hua, D.; Hendriks, W.H.; Xiong, B.; Pellikaan, W.F. Starch and cellulose degradation in the rumen and applications of metagenomics on ruminal microorganisms. *Animals* 2022; 12:3020.
- Huang Y, Oikonomou G., Hu J., Li Y., Du X., Du Y., Liu Y., Zhang P., Wang P., Yu H., Tu J., Kakatsidis N., Colina A.H., He B. Effect of feeding grape seed Proanthocyanidin extract on production performance, metabolic and anti-oxidative status of dairy cattle. *Arq. Bras. Med. Vet. Zootec.* 2019; 71(4):1207-1216.
- Hussein EOS, Ahmed SH, Abudabos AM, Suliman GM, Abd El-Hack ME, Swelum AA, N
- Hussein, E.O.S., Ahmed, S.H., Al-Sagan, A.A., et al. Use of

- plant-derived alkaloids as an alternative to antibiotic growth promoters in broilers. *Animals*. 2020;10(11):2066.
- Ihenetu K, Espinosa R, de Leon R, Planas G, Perez-Pinero A, Waldbeser L. Digoxin and digoxin-like immunoreactive factors (DLIF) modulate the release of pro-inflammatory cytokines. *Inflamm Res*. 2008; 57: 519–523.
- Iwashina T Flavonoid properties of five families newly incorporated into the order caryophyllales (Review). *Bull Natl Mus Nat Sci*. 2013; 39: 25–51.
- Jain P. K., and Joshi, H., "Coumarin: Chemical and pharmacological profile," *Journal of Applied Pharmaceutical Science*, 2012; 2(6): 236–240, doi: 10.7324/JAPS.2012.2643.
- Jankowski J., Zduńczyk Z., Juśkiewicz J., Kozłowski K., Lecewicz A., Jeroch H. Gastrointestinal tract and metabolic response of broilers to diets with the Macleaya cordata alkaloid extract. *Arch. Geflugelkd.*, 2009;73: 95-101
- Ji, Y. B., Gao S. Y., Ji C. F., and Zou X. Induction of apoptosis in HepG2 cells by solanine and Bcl2 protein. *J. Ethnopharmacol.* 2008;115:194–202.
- Jiang ZY, Jiang SQ, Lin YC, Xi PB, Yu DQ, Wu TX. Effects of soybean isoflavone on growth performance, meat quality, and antioxidation in male broilers. *Poult Sci*. 2007; 86(7):1356-1362.
- Kamboh A.A., Zhu W.Y. Individual and combined effects of genistein and hesperidin on immunity and intestinal morphometry in lipopolysaccharide-challenged broiler chickens. *Poult. Sci.* 2014; 93: 2175–2183.
- Kamboh AA, Zhu WY. Individual and combined effects of genistein and hesperidin supplementation on meat quality in meat-type broiler chickens. *J Sci Food Agric.* 2013; 93(13):3362-3367.
- Kammoun HL, Kraakman MJ, Febbraio MA. Adipose tissue inflammation in glucose metabolism. *Rev Endocr Metab Disord*. 2014;15(1):31–44.
- Kamtcha DW, Tene M, Bedane KG, Knauer L, Strohmann C, Tane P, Kusari S, Spiteller M Cardenolides from the stem bark of Salacia staudtiana. *Fitoterapia*. 2018; 127:402–409.
- Kantas, D., Papatsiros, V.G., Tassis, P.D., Athanasiou, L.V., Tsika, E.D. Effects of a natural feed additive containing Macleaya cordata on the health status and performance of weaned piglets. *Research in Veterinary Science*. 2015; 100: 275–282.
- Kara, K., Guclu, B. K., Senturk, M., Eren, M., Baytok, E. Effects of catechin and copper or their combination in diet on productive performance, egg quality, egg shelf-life, plasma 8-OHdG concentrations and oxidative status in laying quail (*Coturnix coturnix japonica*). *Journal of Applied Animal Research*. 2021; 49(1):97–103.
- Kara, K., Kocaoglu Güçlü, B., Şentürk, M., & Konca, Y. Influence of catechin (flavan-3-ol) addition to breeder quail (*Coturnix coturnix japonica*) diets on productivity, reproductive performance, egg quality and yolk oxidative stability. *Journal of Applied Animal Research*. 2015; 44(1): 436–441.
- Kara, K., Özkaya, S., Baytok, E., Güçlü, B. K., Aktug, E., Erbas, S. "Effect of phenological stage on nutrient composition, in vitro fermentation and gas production kinetics of *Plantago lanceolata* herbage". *Veterinarni Medicina*. 2018; 63: 251-260.
- Kara, K., Pirci, G., Yilmaz Öztaş, S. et al. Effect of milk thistle (*Silybum marianum* L.) oil on pro-inflammatory cyto-kines, acute phase proteins, rumen metagenomic profile, rumen fluid variables and performance in calves. *Vet Res Commun*. 2025; 49: 48
- Kara, K., Şentürk, M., Guclu, B. K., Sariözkan, S., Eren, M. Effect of catechins on fattening performance, meat quality, some antioxidant and blood parameters and fattening costs in Japanese quail (*Coturnix coturnix japonica*). *British Poultry Science*. 2016; 57(4):522–530.
- Karaca M, Erbaş O. Solanine Poisoning: Effects, risks, and management strategies. *JEB Med Sci* 2024;5(2):189-193.
- Kaur S, Das M Functional foods: an overview. *Food Sci Biotechnol*. 2011; 20(4):861–875.
- Kaur, R., Das, M. "Functional foods: An overview". *Food Science and Technology International*. 2011; 17(2): 87–103.
- Kezwon A., Wojciechowski K. Interaction of Quillaja bark saponins with food-relevant proteins. *Adv. Colloid Interfa-ce Sci*. 2014; 209:185–195.
- Khiaosa-Ard R, Mahmood M, Lerch F, Traintinger FP, Petri RM, Münnich M, Zebeli Q. Physicochemical stressors and mixed alkaloid supplementation modulate ruminal microbiota and fermentation in vitro. *Anaerobe*. 2020; 65:102263.
- Kholif, A.E. A Review of effect of saponins on ruminal fermentation, health and performance of ruminants. *Vet. Sci.* 2023; 10(7): 450.
- Kim, H.; Kim, B.-W.; Yoo, D.; Moon, J.; Kwon, I.; Lee, Y.; Seo, J. In vitro evaluation of *Aloe saponaria* as a potential feed additive to modulate ruminal fermentation and microbial diversity. *J. Appl. Anim. Res.* 2023; 51: 115–122.
- Kolling, G. J.; Stivanin, S. C. B.; Gabbi, A. M.; Machado, F. S.; Ferreira, A. L.; Campos, M. M.; Tomich, T. R.; Cunha, C. S.; Klein, C. P.; August, P. M.; Matté, C.; Dill, S. W.; Pereira, L. G. R. and Fischer, V. Milk production and hematological and antioxidant profiles of dairy cows supple-mented with oregano and green tea extracts as feed additives. *Revista Brasileira de Zootecnia*. 2022; 51:e20210150.
- Koronowski K.B., Dave K.R., Saul I., Camarena V., Thompson J.W., Neumann J.T., Young J.I., Perez-Pinzon M.A. Resveratrol preconditioning induces a novel extended window of ischemic tolerance in the mouse brain. *Stroke*. 2015; 46:2293–2298.
- Kozłowska, M., Cieślak, A., Józwik, A., El-Sherbiny, M., Sto-chmal, A., Oleszek, W., Kowalczyk, M., Filipiak, W. and Szumacher-Strabel, M. (2020), The effect of total and individual alfalfa saponins on rumen methane production. *J Sci Food Agric.* 100: 1922–1930.
- Kozłowski K., Lecewicz A., Jeroch H., Zdunczyk Z., Jankowski J.: Effect of a phytogenic feed additive from Macleaya cordata on performance and carcass parameters of broilers. *Arch. Geflugelkd.* 2008; 72: 140-142.
- Kriegel D., Berlowska J., Witonska I., Antolak H., Proestos C., Babic M., Babic L., Zhang B. Saponin-based, biological-active surfactants from plants. In: Najjar R., editor. Application and characterization of surfactants. Volume 6. Intech Open; Rijeka, Croatia: 2017; 184–205. DOI: 10.5772/68062
- Krishna AB, Manikyam HM, Sharma VK, Sharma N. Plant cardenolides in therapeutics. *Int J Indig Med Plants*. 2015; 48(2):1871–1896
- Krüger, S., Winheim, L., Morlock, G.E. Planar chromatographic screening and quantification of coumarin in food, confirmed by mass spectrometry. *Food Chem*. 2018; 239:

- 1182–1191.
- Kulkarni, S.S.; Cantó, C. The molecular targets of resveratrol. *Biochim. Biophys. Acta Mol. Basis Dis.* 2015; 1852:1114–1123.
- Lacy, A. Studies on Coumarins and Coumarin-Related Compounds to Determine their Therapeutic Role in the Treatment of Cancer. *Curr. Pharm. Des.* 2005; 10, 3797–3811.
- Lacy, A. Studies on coumarins and coumarin-related compounds to determine their therapeutic role in the treatment of cancer. *Curr. Pharm. Des.* 2005; 10: 3797–3811.
- Lake, B.G. Coumarin metabolism, toxicity and carcinogenicity: Relevance for human risk assessment. *Food Chem. Toxicol.* 1999; 37: 423–453.
- Lee, K. R. , Kozukue N., Han J. S., Park J. H., Chang E. Y., Baek E. J., et al. Glycoalkaloids and metabolites inhibit the growth of human colon (HT29) and liver (HepG2) cancer cells. *J. Agric. Food Chem.* 2004; 52:2832–2839.
- Lewis SE . Recent advances in the chemistry of macroline, sargagine and ajmaline-related indole alkaloids. *Tetrahedron.* 2006; 62(37):8655–8681.
- Li P, Liu Y, Gao M, Fu J, Guo Y. Dietary soy saponin improves antioxidant and immune function of layer hens. *J Poult Sci.* 2022; 25;59(3):197–205. doi: 10.2141/jpsa.0210073.
- Li, P., Zhao, Y., Yan, S. et al. Soya saponin improves egg-laying performance and immune function of laying hens. *J Animal Sci Biotechnol.* 2021; 12: 126.
- Li, Y.; Mei, H.; Liu, Y.; Li, Z.; Qamar, H.; Yu, M.; Ma, X. Dietary supplementation with rutin alters meat quality, fatty acid profile, antioxidant capacity, and expression levels of genes associated with lipid metabolism in breast muscle of Qingyuan partridge chickens. *Foods.* 2023; 12: 2302.
- Lingrel, J. B.; Argüello, J. M.; Van Huysse, J.; Kuntzweiler, T. A. Cation and cardiac glycoside binding sites of the Na,K-ATPase. *Ann. N. Y. Acad. Sci.* 1997; 834(1): 194– 206
- Liu ZY, Wang XL, Ou SQ, Hou DX, He JH. Sanguinarine modulates gut microbiome and intestinal morphology to enhance growth performance in broilers. *PLoS One.* 2020; 19; 15(6):e0234920.
- Lončar M, Jakovljević M, Šubarić D, Pavlić M, Buzjak Služek V, Cindrić I, Molnar M. Coumarins in Food and Methods of Their Determination. *Foods.* 2020; 18;9(5):645. doi: 10.3390/foods9050645.
- Lv Z, Fan H, Zhang B, Xing K, Guo Y. Dietary genistein supplementation for breeders and their offspring improves the growth performance and immune function of broilers. *Sci Rep.* 2018; 26;8(1):5161.
- Maia, H.; Haddad, C.; Pinheiro, N.; Casoy, J. Advantages of the association of resveratrol with oral contraceptives for management of endometriosis-related pain. *Int. J. Women's Health.* 2012; 4: 543–549.
- Maistro, E.L.; De Souza, M.E.; Fedato, R.P.; Tolentino, F.; Da Silva, C.A.; Tsuboy, M.S.; Resende, F.A.; Varanda, E.A. In Vitro Assessment of Mutagenic And Genotoxic Effects of Coumarin Derivatives 6,7-Dihydroxycoumarin and 4-Methylesculetin. *J. Toxicol. Environ. Heal.* 2015; 78: 109–118.
- Manaa EA, Abdel-Latif MA, Ibraheim SE, Sakr A, Dawood M, Albadrani GM, El-Kott AF, Abdel-Daim MM, Shafik BM. Impacts of Macleaya cordata on Productive Performance, Expression of Growth-Related Genes, Hematological, and Biochemical Parameters in Turkey. *Front Vet Sci.* 2022; 11;9:873951.
- Marella, A.; Tanwar, O.P.; Saha, R.; Ali, M.R.; Srivastava, S.; Akhter, M.; Shaquiquzzaman, M.; Alam, M.M. Quinoline: A versatile heterocyclic. *Saudi Pharm. J.* 2013; 21: 1–12.
- Matsuura, H.N., Fett-Neto, A.G. Plant Alkaloids: Main Features, Toxicity, and Mechanisms of Action. In: Gopalakrishnakone, P., Carlini, C., Ligabue-Braun, R. (eds) *Plant Toxins. Toxinology.* Springer, Dordrecht. 2015.
- Matthies A, Clavel T, Gütschow M, et al. (2008) Conversion of daidzein and genistein by an anaerobic bacterium newly isolated from the mouse intestine. *Appl Environ Microbiol* 74: 4847–4852.
- Meneses-Sagrero SE, Rascón-Valenzuela LA, Sotelo-Mundo R, Vilegas W, Velazquez C, García-Ramos JC, Robles-Zepeda RE. Antiproliferative activity of cardenolides on cell line A549: structure-activity relationship analysis. *Mol Divers.* 2021; 25(4):2289–2305.
- Michels A, Neumann M, Mattos Leão GF, Reck AM, Bertagnon HG, Lopes LS, et al. Isoquinoline alkaloids supplementation on performance and carcass traits of feedlot bulls. *Asian-Australas J Anim Sci.* 2018; 31(9):1474–1480.
- Mickdam E, Khiaoasa-Ard R, Metzler-Zebeli BU, Klevenhusen F, Chizzola R, Zebeli Q. Rumen microbial abundance and fermentation profile during severe subacute ruminal acidosis and its modulation by plant derived alkaloids in vitro. *Anaerobe.* 2016; 39: 4–13.
- Mohsenikia, M. , Alizadeh A. M., Khodayari S., Khodayari H., Kouhpayeh S. A., Karimi A., et al. The protective and therapeutic effects of alpha solanine on mice breast cancer. *Eur. J. Pharmacol.* 2013;718:1–9.
- Moser M., Messikomer R., Pfirter H. P., Wenk C.: Influence of the phytogenic feed additive Sangrovit® on zootechnical effects in broiler field trials. 14th Europ. Symp. Nutr. 2003; 205–206.
- Moses T, Papadopoulou KK, Osbourn A. Metabolic and functional diversity of saponins, biosynthetic intermediates and semi-synthetic derivatives. *Crit Rev Biochem Mol Biol.* 2014; 49(6): 439–462.
- Murias, M.; Handler, N.; Erker, T.; Pleban, K.; Ecker, G.; Saiko, P.; Szekeres, T.; Jäger, W. Resveratrol analogues as selective cyclooxygenase-2 inhibitors: Synthesis and structure–activity relationship. *Bioorg. Med. Chem.* 2004; 12: 5571–5578.
- Nagumo M., Ninomiya M., Oshima N., Itoh T., Tanaka K., Nishina A., Koketsu M. Comparative analysis of stilbene and benzofuran neolignan derivatives as acetylcholinesterase inhibitors with neuroprotective and anti-inflammatory activities. *Bioorg. Med. Chem. Lett.* 2019; 29:17.
- Nakahigashi J, Kurikami M, Iwai S, Iwamoto S, Kobayashi S, Kobayashi E. Exploring the pharmacokinetics and gut microbiota modulation of hesperidin and nobiletin from mandarin orange peel in experimental dogs: A Pilot Study. *Metabolites.* 2024; 25;15(1):3.
- Nakayasu, M.; Yamazaki, S.; Aoki, Y.; Yazaki, K.; Sugiyama, A. Triterpenoid and Steroidal Saponins Differentially Influence Soil Bacterial Genera. *Plants* 2021; 10: 2189.
- Ni, H., Martínez, Y., Guan, G., Rodríguez, R., Más, D., Peng, H., Navarro, M. V., & Liu, G. Analysis of the impact of isoquinoline alkaloids derived from Macleaya cordata on the development and innate immune response in swine and poultry. *BioMed Research International*, 2016, Article-

- le ID 1352146.
- Oleszek, M.; Oleszek, W. Saponins in Food. In *Handbook of Dietary Phytochemicals*; Xiao, J., Sarker, S.D., Asakawa, Y., Eds.; Springer: Singapore, 2020; pp. 1–40.
- Oskoueian E, Abdullah N, Oskoueian A. Effects of flavonoids on rumen fermentation activity, methane production, and microbial population. *Biomed Res Int.* 2013;2013:349129.
- Önder, A. Anticancer activity of natural coumarins for biological targets. *Stud. Nat. Prod. Chem.* 2020; 85–109.
- Panche AN, Diwan AD, Chandra SR. Flavonoids: an overview. *J Nutr Sci.* 2016; 29(5):e47.
- Patil A, Paikrao HM, Patil S. The Chemistry and biology of the plant poisons and their forensic significance. *Studies in Natural Products Chemistry.* 2023;78: 255-321.
- Patra, A.K.; Saxena, J. The Effect and Mode of Action of Saponins on the Microbial Populations and Fermentation in the Rumen and Ruminant Production. *Nutr. Res. Rev.* 2009; 22: 204–219.
- Patra, A.K.; Saxena, J. The Effect and Mode of Action of Saponins on the Microbial Populations and Fermentation in the Rumen and Ruminant Production. *Nutr. Res. Rev.* 2009; 22: 204–219.
- Payne RL, Bidner TD, Southern LL, Mcmillin KW. Dietary effects of soy isoflavones on growth and carcass traits of commercial broilers. *Poult Sci.* 200; 80(8):1201-1207
- Pessoa MTC, Barbosa LA, Villar JAFP Chapter 3. Synthesis of cardiac steroids and their role in heart failure and cancer. In: Atta-ur-Rahman (ed) *Studies in natural products chemistry*, 2018; 57: 79–113
- Pessôa MTC, Barbosa LA, Villar FPJA. 2018. Synthesis of Cardiac Steroids and Their Role on Heart Failure and Cancer. *Studies in Natural Products Chemistry.* 2018; 57:79-113
- Piacente, S., Pizza, C. & Oleszek, W. Saponins and phenolics of *Yucca schidigera roezl*: chemistry and bioactivity. *Phytochem Rev* 2005; 4:177–190
- Poulsen, M.M.; Vestergaard, P.F.; Clasen, B.F.; Radko, Y.; Christensen, L.P.; Stødkilde-Jørgensen, H.; Møller, N.; Jessen, N.; Pedersen, S.B.; Jørgensen, J.O.L. High-dose resveratrol supplementation in obese men: An investigator-initiated, randomized, placebo-controlled clinical trial of substrate metabolism, insulin sensitivity, and body composition. *Diabetes.* 2013; 62: 1186–1195.
- Prassas I, Diamandis EP. Novel therapeutic applications of cardiac glycosides. *Nat Rev Drug Discov.* 2008;7(11):926-935.
- Price, K.R.; Johnson, I.T.; Fenwick, G.R. The chemistry and biological significance of saponins in foods and feeding stuffs. *CRC Crit. Rev. Food Sci. Nutr.* 1987; 26: 27–135
- Ranjbar Z, Shariatmadari F & Torshizi MA. Effect of different levels of yucca extract and antibiotic on growth performance, immune response and blood factors of broiler chickens. *Iranian Journal of Medicinal and Aromatic Plants Research.* 2014; 30: 675–680.
- Rivière, C.; Pawlus, A.D.; Mérillon, J.M. Natural stilbenoids: Distribution in the plant kingdom and chemotaxonomic interest in Vitaceae. *Nat. Prod. Rep.* 2012;29:1317–1333.
- Rundle CM, Artuso-Ponte V, Stein HH. Effects of isoquinoline alkaloids on apparent ileal digestibility of amino acids, acid hydrolyzed ether extract, and starch by young growing pigs fed corn-soybean meal diets. *Transl Anim Sci.* 2020; 9;4(2):txaa054.
- Saeed M, Arain MA, Naveed M, Alagawany M, ElHack MEA,
- Bhutto ZA & Chao S. 2018. *Yucca schidigera* can mitigate ammonia emissions from manure and promote poultry health and production. *Environmental Science and Pollution Research.* 25: 35027-35033.
- San Martin, R.; Briones, R. Industrial Uses and Sustainable Supply of Quillaja saponaria (Rosaceae) Saponins. *Econ. Bot.* 1999;53: 302–311.
- Senchina DS, Hallam JE, Kohut ML, Nguyen NA, Perera MAN. Alkaloids and athlete immune function: caffeine, theophylline, gingerol, ephedrine, and their congeners. *Exerc Immunol Rev.* 2014; 20:68–93.
- Setten DC, Werken G. Molecular Structures of Saponins from Quillaja saponaria Molina. In: Waller GR and Yamasaki K. (eds) *Saponins used in traditional and modern medicine*; Plenum Press; 1996. 185-193.
- Shao, Y.; Xu, J.; Wang, M.; Ren, Y.; Wei, M.; Tian, B.; Luo, J.; Loor, J.J.; Shi, H. Preliminary Results on the Effects of Soybean Isoflavones on Growth Performance and Ruminal Microbiota in Fattening Goats. *Animals* 2024; 14:1188.
- Shi, Y., Zhong, L., Liu, Y., Xu, S., Dai, J., Zhang, Y., & Hu, Y. Dietary sanguinarine supplementation recovers the decrease in muscle quality and nutrient composition induced by high-fat diets of grass carp (*Ctenopharyngodon idella*). *Animal Nutrition.* (2024); 17: 208–219.
- Simitzis P, Massouras T, Goliomytis M, Charismiadou M, Moschou K, Economou C, Papadedes V, Lepesiotti S, Deligeorgis S. The effects of hesperidin or naringin dietary supplementation on the milk properties of dairy ewes. *J Sci Food Agric.* 2019; 99(14): 6515-6521.
- Simitzis PE, Charismiadou MA, Goliomytis M, Charalambous A, Ntetska I, Giamouri E, Deligeorgis SG. Antioxidant status, meat oxidative stability and quality characteristics of lambs fed with hesperidin, naringin or α-tocopherol acetate supplemented diets. *J Sci Food Agric.* 2019; 15;99(1):343-349.
- Simitzis PE, Ilias-Dimopoulos V, Charismiadou MA, Biniari EE, Deligeorgis SG. Effects of dietary hesperidin supplementation on lamb performance and meat characteristics. *Anim Sci J.* 2013; 84(2):136-143.
- Song B, He J, Pan X, Kong L, Xiao C, Keerqin C, Song Z. Dietary Macleaya cordata extract supplementation improves the growth performance and gut health of broiler chickens with necrotic enteritis. *J Anim Sci Biotechnol.* 2023; 7;14(1):113.
- Song Z, Cheng K, Zhang L, Wang T. Dietary supplementation of enzymatically treated *Artemisia annua* could alleviate the intestinal inflammatory response in heat-stressed broilers. *J Therm Biol.* 2017; 69:184–190.
- Song, Z., Zhang, Q., Zhang, X., et al. Effects of Macleaya cordata extract on growth performance and intestinal morphology in broilers with necrotic enteritis. *Poultry Science.* (2023); 102(1):102431.
- Sreij R., Dargel C., Hannappel Y., Jestin J., Prévost S., Dattani R., Wrede O., Hellweg T. Temperature dependent self-organization of DMPC membranes promoted by intermediate amounts of the saponin aescin. *Biochimica et Biophysica acta. Biomembranes.* 1997;1861(5): 897–906.
- Stefanachi, A., Leonetti, F., Pisani, L., Catto M., and Carotti, A. “Coumarin: A natural privileged and versatile scaffold for bioactive compounds”, *Molecules.* 2018; 23(2): 250, 1–34, DOI: 10.3390/molecules23020250
- Su JL, Shi BL, Zhang PF, Sun DS, Li TY & Yan SM. Effects of

- yucca extract on feed efficiency, immune and antioxidantive functions in broilers. *Brazilian Archives of Biology and Technology* 2016;59.
- Su, Y., Chang, G., Liu, J., Huang, P., & Zeng, J. Dietary sanguinarine supplementation improves the growth performance and intestinal immunity of broilers. *Animal Nutrition*. 2024; 19:76–89.
- Sun A, Xu X, Lin J, Cui X, Xu R. Neuroprotection by saponins. *Phytother Res*. 2015; 29(2):187-200.
- Sun, H., Zhao, F., Hou, F., Jin, Y., Zhang, X., Ma, Y., Wang, H. Influences of naringin supplementation on ruminal fermentation, inflammatory response, antioxidant capacity and bacterial community in high-concentrate diet of fattening goats. *Italian Journal of Animal Science*. 2022; 21(1): 1498–1507.
- Szumacher-Strabel, M., Stochmal, A., Cieslak, A., Kozłowska, M., Kuznicki, D., Kowalczyk, M. and Oleszek, W. Structural and quantitative changes of saponins in fresh alfalfa compared to alfalfa silage. *J. Sci. Food Agric.* 2019; 99: 2243-2250.
- Tamura M, Utsunomiya H, Nakamura M, Landon EJ. Effect of dietary cardiac glycosides on blood pressure regulation in rats. *Can J Physiol Pharmacol*. 2000;78 (7):548-556.
- Tamura Y, Miyakoshi M, Yamamoto M. Application of Saponin-Containing Plants in Foods and Cosmetics [Internet]. Alternative Medicine. InTech; 2012. Available from: DOI: 10.5772/53333
- Tedesco D., Tava A., Galletti S., Tameni M., Varisco G., Costa A., and Steidler S., Effects of silymarin, a natural hepatoprotector, in periparturient dairy cows, *Journal of Dairy Science*. 2004; 87(7): 2239–2247
- Thawabteh, A.; Juma, S.; Bader, M.; Karaman, D.; Scrano, L.; Bufo, S.A.; Karaman, R. The Biological Activity of Natural Alkaloids against Herbivores, Cancerous Cells and Pathogens. *Toxins* 2019; 11: 656.
- Timilsena YP, Phosanam A, Stockmann R. Perspectives on saponins: Food functionality and applications. *Int J Mol Sci.* 2023; 31;24(17):13538.
- Tomé-Carneiro, J.; Larrosa, M.; González-Sarriás, A.; Tomás-Barberán, F.; García-Conesa, M.; Espín, J. Resveratrol and clinical trials: The crossroad from in vitro studies to human evidence. *Curr. Pharm. Des.* 2013; 19: 6064–6093.
- Tomé-Carneiro, J.; Larrosa, M.; Yáñez-Gascón, M.J.; Dávalos, A.; Gil-Zamorano, J.; Gonzálvez, M.; García-Almagro, F.J.; Ruiz Ros, J.A.; Tomás-Barberán, F.A.; Espín, J.C.; et al. One-year supplementation with a grape extract containing resveratrol modulates inflammatory-related microRNAs and cytokines expression in peripheral blood mononuclear cells of type 2 diabetes and hypertensive patients with coronary artery disease. *Pharmacol. Res.* 2013; 72: 69–82.
- Toprak NN. Effects of Macleaya cordata extract supplementation in milk on growth performance, some biochemical parameters and a number of selected bacterial groups of the recto-anal microbiota of calves. *Med. Weter.* 2020;76 (8): 435-440.
- Tufarelli, V., Lacalandra, G.M., Laudadio, V. Dietary supplementation with plant-derived sanguinarine on productive traits and expression of pro-inflammatory cytokines in pigs. *Animal Feed Science and Technology*. 2014; 192: 95–102.
- Tulayakul P, Dong KS, Li JY, Manabe N, Kumagai S. The effect of feeding piglets with the diet containing green tea extracts or coumarin on in vitro metabolism of aflatoxin B1 by their tissues. *Toxicon*. 2007;50(3): 339–348.
- Ungurianu, A.; Zanfirescu, A.; Margină, D. Sirtuins, resveratrol and the intertwining cellular pathways connecting them. *Ageing Res. Rev.* 2023; 88: 101936.
- Upton R Goldenseal root (*Hydrastis canadensis*): standards of analysis, quality control, and therapeutics. *American Herbal Phramacopoeia*, Santa Cruz, 2001 pp 1–37.
- Vezikov LV, Simpson M. Plant Alkaloids Toxicity. 2023 Apr 29. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024
- Vieira S.L., Oyarzabal O.A. , Freitas D.M., Berres J. , Pena J.E.M. , Torres C.A. , Coneglian J.L.B. 2008. Performance of broilers fed diets supplemented with sanguinarine-like alkaloids and organic acid. *J. Appl. Poult. Res.* 2008; 17: 128-133
- Vyas K.B. , Nimavat K.S. , Jani G.R., Hathi M.V. Synthesis and antimicrobial activity of coumarin derivatives metal complex: an invitro evaluation. *Orbital*, 2009; 1(2): 183-192.
- Wallace RJ, Arthaud L & Newbold CJ Influence of *Yucca schidigera* extract on ruminal ammonia concentrations and ruminal microorganisms. *Appl. Environ. Microbiol.* 1994; 60: 1762–1767.
- Wang JKT, Portbury S, Thomas MB, Barney S, Ricca DJ, Morris DL, Warner DS, Lo DC Cardiac glycosides provide neuroprotection against ischemic stroke: discovery by a brain slice-based compound screening platform. *PNAS*. 2006; 103(27):10461–10466.
- Wang W., Dolan L. C., von Alvensleben S., Morlacchini M., Fusconi G. Safety of standardized *macleaya cordata* extract in an eighty-four-day dietary study in dairy cows. *J. Anim. Physiol. Anim. Nutr.* 2018; 102: 61–68.
- Wang, Y.; McAllister, T.A.; Yanke, L.J.; Cheeke, P.R. Effect of steroidal saponin from *Yucca schidigera* extract on ruminal microbes. *J. Appl. Microbiol.* 2000; 88:887–896.
- Wang, Y.H.; Avula, B.; Nanayakkara, N.P.D.; Zhao, J.; Khan, I.A. Cassia cinnamon as a source of coumarin in cinnamon-flavored food and food supplements in the United States. *J. Agric. Food Chem.* 2013; 61: 4470–4476.
- Weimer, P.J. Degradation of Cellulose and Hemicellulose by ruminal microorganisms. *Microorganisms*. 2022; 10: 2345
- Wen S, Chen Y, Lu Y, Wang Y, Diang L, Jiang M (2016) Cardenolides from Apocynaceae and their anticancer activity. *Fitoterapia*. 112: 74–84.
- Widyarini, S.; Nagari, F.S.; Hanim, C.; Bachruddin, Z.; Muhibin, M.; Mira Yusiat, L. Effect of *Nigella sativa* L. as saponin sources on in vitro rumen fermentation, enzyme activity and nutrients digestibility. *Adv. Anim. Vet. Sci.* 2021; 9: 2247–2257
- Wiles, D., Pearson, J.S. & Beddoe, T. Harnessing plant-derived terpenoids for novel approaches in combating bacterial and parasite infections in veterinary and agricultural settings. *Curr Microbiol.* 2025; 82: 134.
- Williams, CA. Specialized dietary supplements, Editor(s): Geor RJ, Harris PA, Coenen M, Equine Applied and Clinical Nutrition, W.B. Saunders, 2013: 351-366,
- Wink, M. “Introduction: Biochemistry, physiology and ecological functions of secondary metabolites”. In Annual

- Plant Reviews: Biochemistry of Plant Secondary Metabolism Wiley-Blackwell. 2010; 1–19.
- Yang CW, Chang HY, Hsu HY, Lee YZ, Chang HS, Chen IS, Lee SJ Identification of anti-viral activity of the cardenolides, Na/K-ATPase inhibitors, against porcine transmissible gastroenteritis virus. *Toxicol Appl Pharmacol.* 2017; 332:129–137.
- Yang L, Stöckigt J. Trends for diverse production strategies of plant medicinal alkaloids. *Nat Prod Rep.* 2010; 27: 1469–1479.
- Yang, Z.; Kinoshita, T.; Tanida, A.; Sayama, H.; Morita, A.; Watanabe, N. Analysis of coumarin and its glycosidically bound precursor in Japanese green tea having sweet-herbaceous odour. *Food Chem.* 2009; 114:289–294.
- Yu, A.; Tang, C.; Wang, S.; Wang, Y.; Chen, L.; Li, Z.; Luo, G.; Zhong, J.; Fang, Z.; Wang, Z.; et al. Effects of dietary supplementation with mulberry leaf powder on the growth performance, lipid metabolism parameters, immunity indicators, and gut microbiota of dogs. *Metabolites* 2023; 13: 918.
- Zdunczyk Z., Gruzauskas R., Juskiewicz J., Semaskaite A., Jankowski J., Godycka I., Klos J., Jarule V., Miezeliene A., Alencikiene G.: Growth performance, gastrointestinal tract responses, and meat characteristics of broiler chick-
- kens fed a diet containing the natural alkaloid sanguinarine from Macleaya cordata. *The J. Appl. Poult. Res.* 2010; 19: 393–400.
- Zhao L., Alvensleben S., Fusconi G., Morlacchini M.: Safety evaluation of a standardized Macleaya cordata extract in a ninety day feeding study in weaned piglets. *Open J. Anim. Sci.* 2017; 7: 213–231.
- Zhao Y, Wu Y, Wang M. Bioactive Substances of Plant Origin. Eds: Cheung P.C.K., Mehta B.M., *Handbook of Food Chemistry.* 2015: 967–1008.
- Zhao, J., Davis, L. C., & Verpoorte, R. “Elicitor signal transduction leading to production of plant secondary metabolites”. *Biotechnology Advances.* 2015; 23(4): 283–333.
- Zhao, L., et al. Effects of Macleaya cordata extract on growth performance and intestinal health of weaned piglets. *Livestock Science.* 2017; 197: 73–77.
- Zhao, Y., Wu, Y., Wang, M. Bioactive Substances of Plant Origin. In: Cheung, P. (eds) *Handbook of Food Chemistry.* Springer, Berlin, Heidelberg. 2014.