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NOVEL EXTRACTS FROM *Boletus edulis* FOR FUNCTIONAL PRODUCT DEVELOPMENT

Emanuel VAMANU[1, 2]

[1]Anoom Laboratories SRL, Pipera-Tunari Road 1, 077190, Voluntari, Ilfov, Romania
[2]University of Agronomic Sciences and Veterinary Medicine of Bucharest,
59 Mărăşti Blvd, District 1, Bucharest, Romania

Corresponding author email: emanuel.vamanu@gmail.com

Abstract

This research presents advanced biotechnological techniques for extracting bioactive components from Boletus edulis, a well-known edible mushroom, sometimes referred to as porcini or king bolete, renowned for its gastronomic desirability and nutritional benefits. The study outlines the advancement of novel extraction methods for producing bioactive compounds that can improve health. These molecules are crucial in creating effective treatments to target different health issues. This research discusses advancements in functional product development that enhance the efficiency of obtaining these compounds from Boletus edulis. This contributes to the expanding domain of biofunctional ingredient research.

Key words*: microbiota, modulation, metabiotic, extraction, muchsroom.*

INTRODUCTION

New ways of using molecules from *Boletus edulis* have made it possible to get more β-glucans, ergosterol, antioxidants, and other bioactive substances. The patented methodologies include a range of extraction techniques, including solvent extraction, supercritical fluid extraction, and enzyme-assisted extraction (Avram et al., 2023; Vetter et al., 2023). These procedures have been specifically developed to enhance the preservation of the unique bioactive compounds of the mushroom. Furthermore, functional extracts derived from *Boletus edulis* extracts, such as dietary supplements, nutraceuticals, and medications, have been the subject of many patents (Niego et al., 2021). The research papers address several health issues, including immune system support, cardiovascular health, and anticancer capabilities. These uses highlight the flexibility and promise of *Boletus edulis* as a source of physiologically active chemical substances (Tan et al., 2022).

Patents enable the growth of these extraction processes and ensure the operating products' long-term stability and safety. Furthermore, an analysis was conducted on these patents to get valuable information about the competitive landscape and to identify potential trends for future research and commercialization in the biotechnology business (van Rijn et al., 2023). These papers investigate how important *Boletus edulis* is as a source of bioactive compounds, focusing on improving extraction methods and creating new valuable products. *Boletus edulis* has significant promise in biotechnology, offering opportunities for developing novel products that might enhance human welfare (Avram et al., 2023; Dimopoulou et al., 2022).

PATENT ANALYSIS AND FUTURE PROSPECTS

Examining patents related to the extraction of bioactive chemicals from *Boletus edulis* provides valuable insights into the competitive nature of the biotechnology sector and the potential popularity of research and commercial concepts (Anusiya et al., 2021). The findings demonstrate an increasing inclination towards innovative extraction methods to get functional goods that provide diverse health advantages. The patents also illustrate the versatility and potential of *Boletus edulis* as a rich source of biologically active compounds with potential

use in pharmaceuticals, nutritional supplements, and nutraceuticals (Heleno et al., 2015). The innovative extraction procedures guarantee these products' long-term stability and safety by preserving the mushroom's distinctive medicinal components (Łysakowska et al., 2023).

More study is required to fully understand the potential of *Boletus edulis* as a sustainable and natural source of bioactive compounds for functional product development. This involves researching novel extraction methods that optimize the output's quantity and quality while reducing the adverse environmental effects. Furthermore, it is necessary to discern novel uses for extracts derived from *Boletus edulis* based on growing health patterns and customer preferences (Avram et al., 2023; Witkowska et al., 2011). Recent research indicates that *Boletus edulis* may possess anti-inflammatory qualities that may be beneficial in treating chronic inflammatory conditions like arthritis or asthma (Wu et al., 2016). *Boletus edulis* extracts are increasingly being considered for use as natural preservatives or flavor enhancers in food items because of their antioxidant activity and appealing taste profile. In general, *Boletus edulis* shows excellent potential as a valuable source of bioactive chemicals, offering several possibilities for advancement and expansion in biotechnology (Djekic et al., 2020).

FROM FUNCTIONAL EXTRACTS TO METABIOTICS

Metabiotics have gained increasing attention as a promising category of supplements in recent years. Metabiotics, in contrast to conventional medications that target a limited number of particular objectives, are designed to impact the whole body's metabolic system by modulating the microbiota pattern (Shenderov, 2013).

Metabiotics are obtained from natural sources, particularly fermented foods, and consist of diverse substances that may impact the body's metabolism (Shenderov, 2013; Pihurov et al., 2021). Metabiotics provide many advantages, such as greater gastrointestinal well-being, a strengthened immunological response, and decreased inflammation (Figure 1). An excellent example, first on the Romanian market, is represented by ColonX, the flagship product of the GreenBiom line produced by Anoom Laboratories SRL.

Metabiotics could be the metabolic by-products of probiotic microbes that have positively affected health. The by-products may include enzymes, peptides, and organic acids. Studies have shown that metabiotics provide several potential health advantages, such as strengthening gastrointestinal health, boosting immune system activity, diminishing inflammation, and lowering the likelihood of certain chronic illnesses (Pihurov et al., 2021; Sharma et al., 2016). Further investigation is required to fully comprehend the health implications of metabiotics and their potential to enhance general health and well-being. Metabiotics obtained from functional substrates, such as mushrooms, particularly wild edible and medicinal mushrooms, are a novel focus for metabiotic research. These products enhance the adaptability of the microbiota, resulting in specific health benefits and improved brain function (Sudo, 2019).

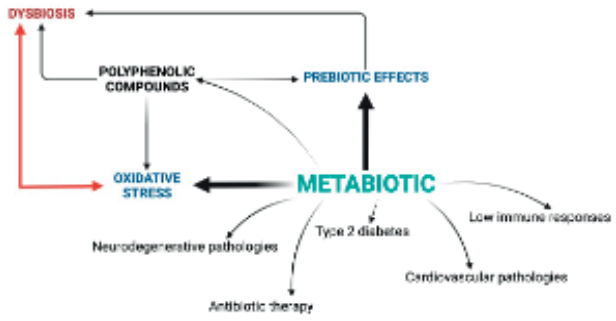

Figure 1. The mechanism of metabiotic actions in the human body. Figure realized with Biorender App.

The human body is a complex ecosystem, filled with many living organisms that are difficult to grasp fully. The microbiota, consisting of billions of bacteria, resides inside our bodies and is at the forefront of this concealed realm (Thursby & Juge, 2017). The microbiota, primarily located in our gastrointestinal system, is a constantly changing and developing population of bacteria, viruses, fungi, and other microbes (Jandhyala et al., 2015).

Microbiota plasticity refers to the remarkable ability of the microbial population to adapt and alter in response to variations in food, environment, and health. It represents a dynamic aspect of our biology (Ursell et al., 2012). This plasticity arises from the diversity

of microorganisms that make up the microbiota. It's been estimated that there are more bacterial cells in the human body than human cells. These microorganisms play essential roles in digestion, nutrient absorption, and immune system function and even influence our overall well-being. The microbiota's plasticity ensures it can quickly adapt to the changes we subject it to (Jandhyala et al., 2015; Appleton, 2018).

The adaptability of the microbiota also has a crucial impact on customized nutrition. Comprehending the distinct makeup of an individual's microbiota might assist in customizing dietary recommendations to achieve improved health results (Leeming et al., 2019). For example, some individuals may respond more favorably to a diet with high fiber. In contrast, others may benefit from a low-carbohydrate strategy based on the flexibility and preferences of their microbiota (Fu et al., 2022).

The lifestyle greatly influences the plasticity of the microbiota. Stress, antibiotic use, and exposure to contaminants may disturb the equilibrium of the microbial population (Liang et al., 2018). Antibiotics can eliminate both dangerous and good bacteria, temporarily reducing the variety of microbiota. Nevertheless, the adaptability of the microbiota enables it to restore and reestablish stability over some time (Langdon et al., 2016).

The adaptability of the microbiota extends beyond the confines of our stomachs. It also encompasses other body areas, like the skin and oral microbiota. The constitution and flexibility of these microbial communities are vital for preserving skin health and oral hygiene, respectively. Gaining insight into these microbial communities may facilitate the development of innovative approaches for maintaining well-being (Deo & Deshmukh, 2019; Xu et al., 2023).

The flexibility of the microbiota's involvement in the formation and operation of our immune system is a notable field of study. During the early stages of life, developing a robust and varied microbiota to educate the immune system to distinguish between hazardous pathogens and benign microbes is essential (Belkaid & Hand, 2014). Insufficient early exposure to various microbial species might cause an overactive immune system, increasing the risk of developing autoimmune disorders or allergies. The malleability of the microbiota may be used to foster an equilibrium in the immune response (Gensollen & Blumberg, 2017).

To summarize, microbiota plasticity reveals the impressive capacity of the microbial communities that live inside humans to adapt. Several elements, including nutrition, environment, and more, influence our microbiota, significantly impacting our health and overall well-being (Thriene et al., 2023). This area of study has great potential for personalized treatment and the creation of novel therapies that use the adaptability of the microbiota to enhance health results. As we further explore this ever-changing internal environment, our comprehension of the adaptability of the microbiota will indeed have a crucial impact on the future of healthcare and well-being (Hou et al., 2023).

EXTRACTION TECHNIQUES AND EMERGING APPLICATIONS FOR *Boletus edulis*

Recent advancements in biotechnology have led to the development of novel extraction techniques that enhance the quantity and quality of bioactive compounds found in *Boletus edulis*. These innovative methods include ultrasound (Chen et al., 2012), microwave (Özyürek et al., 2014), and pressurized liquid extraction (Kumar et al., 2021). These new techniques are designed to optimize yield and purity while minimizing environmental impact, making them ideal for sustainable, functional product development.

Emerging applications for *Boletus edulis* extracts include their potential use as natural preservatives or flavor enhancers in food products due to their antioxidant activity and pleasant taste profile (Tan et al., 2022). Additionally, studies have suggested that *Boletus edulis* may possess anti-inflammatory characteristics that might be beneficial in treating chronic inflammatory diseases through the modulation of microbiota dysbiosis (Avram et al., 2021). Other potential applications include developing skincare products that utilize the mushroom's unique bioactive

compounds to improve skin health and appearance (Magp et al., 2023).

The innovative techniques in obtaining bioactive compounds from *B. edulis* are designed to increase both the amount and the excellence of production while minimizing the negative environmental impacts. Consequently, they are well-suited for sustainable, functional product development (Nguyen et al., 2023).

The growing customer demand for organic and eco-friendly products and functional ingredients offers several opportunities for innovation and growth in the biotechnology sector. Boletus edulis, renowned for its exceptional flavor and nutritional properties, is a promising source of bioactive compounds that might provide various health benefits (Das et al., 2021).

The extraction method of *B. edulis* in the study involved several steps. Firstly, dried mushrooms were crushed into powder. This powder then underwent a water-based extraction at 95°C for 2 hours, followed by stirring for 24 hours without heating to extract polysaccharides and phenolics. The mixture was centrifuged to obtain the first extract. The remaining substrate was subjected to a second extraction using Viscozyme L and ethanol, followed by stirring and centrifugation. The two extracts were then combined and stored in sterile containers. This method efficiently extracted bioactive compounds from *B. edulis* (Avram et al., 2023).

METABIOTICS AND MICROBIOTA

The human microbiota, a primary defensive mechanism, has recently attracted significant attention to human health and well-being. Microbes, particularly bacteria, inhabit many body parts, such as the skin, mouth, stomach, and reproductive organs, which can have a crucial impact on overall well-being. The human microbiota is essential for the maturation of digestion, metabolism, and immune system. Furthermore, it hinders the growth of harmful bacteria and pathogens, protecting the body against infections and diseases (Ogunrinola et al., 2020).

Metabiotics are microbial metabolites or products that are generated by the human microbiota. These metabolites have been discovered to substantially influence human health, affecting several physiological systems such as metabolism, immunity, and brain function. Metabiotics are gaining recognition for their potential therapeutic advantages in treating many diseases, such as inflammatory illnesses, metabolic abnormalities, and autoimmune conditions (Pihurov et al., 2021).

Metabiotic studies have shown the possibility of using these microbial substances as therapeutic agents to regulate the human microbiota and enhance general health and well-being. Specific metabiotics have been discovered to possess anti-inflammatory characteristics and may aid in managing illnesses. Examples of conditions include inflammatory bowel disease, irritable bowel syndrome, and obesity (Shenderov, 2013).

The interaction between metabiotics and the human microbiota is complex and interdependent, and comprehending this relationship is essential for devising innovative therapy strategies for many health disorders. Given the increasing interest in the influence of the human microbiome on health and illness, investigating meta-biotics as possible therapeutic agents has great potential for the future of healthcare (Figure 2).

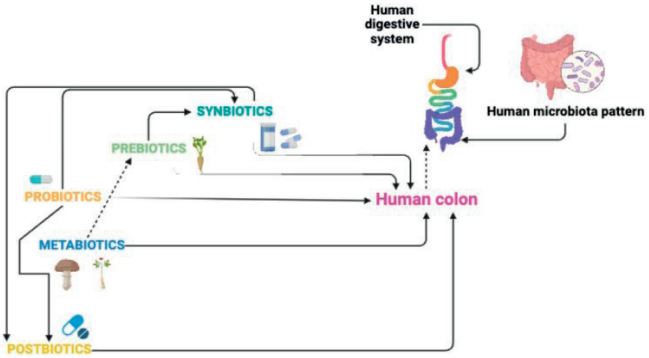

Figure 2. The relations between different types of functional products at the microbiota level (Figure realized with Biorender App.)

METABIOTICS AS PREBIOTIC

Recent research (2023) has yielded valuable information on metabiotics and their prebiotic effects. The study emphasizes explicitly their impact on modifying the gut microbiota and their possible use in therapy (Avram et al., 2023; Zanfirescu et al., 2023). The effects of an in vivo investigation conducted on healthy

newborns were to examine the impact of a synbiotic intervention formula on the composition of bacteria in their feces (Fabiano et al., 2021). The synbiotic formula resulted in notable alterations in microbial profiles, defined by a higher prevalence of *Bifidobacterium* spp. and *Lactobacillaceae* and decreased abundance of *Blautia* spp. and *Ruminoccocus gnavus*. The alterations were most evident around four months of age. The research emphasized that colonizing the stomach after birth has long-lasting effects on the immune system. Baby formulae containing synbiotics might improve health by replicating the microbial alterations seen in breastfed newborns (Simeoni et al., 2016).

A double-blind, randomized, placebo-controlled experiment investigated the benefits of a dietary formula enriched with prebiotic fiber on the health-related quality of life in individuals with Type 2 Diabetes (Brownawell et al., 2012). It assessed the impact of metabolic management regarding the health-related quality of life (HRQoL) in persons with type 2 diabetes. The research observed significant enhancements in Health-Related Quality of Life (HRQoL) and reductions in glycated hemoglobin (HbA1c) among the participants who were administered the prebiotic fiber. The active group exhibited a noteworthy rise in the prevalence of butyrate-producing bacterial species, such as *Roseburia feces and Anaerostipes phaedrus*, within their gut microbiome, in contrast to the placebo group (Jain et al., 2014). A comprehensive analysis of randomized controlled trials examined the influence of prebiotics on the gut microbiota in persons with different inflammatory diseases. A thorough evaluation, which included thirty research studies, discovered significant alterations in the gut microbiome makeup after prebiotics administration. The most prevalent change seen was an augmentation in the presence of *Bifidobacterium* (Ji et al., 2023; Ribeiro et al., 2023). These findings indicate that prebiotics may benefit the gut microbiota in people with inflammatory disorders, possibly impacting the inflammatory process (Oniszczuk et al., 2021). The potential of metabiotics: Metabiotics, which consist of the active compounds or signaling molecules produced by probiotics, have shown encouraging potential in preventing, relieving, and treating certain illnesses or disorders (Singh et al., 2022). This is in addition to the positive effects seen with pharmabiotics and postbiotics. These biotics have a role in modulating immunological function, controlling metabolic dysbiosis, and regulating signaling pathways. These substances have been acknowledged for their potential as novel medicinal agents (Figure 3). They serve a vital function in the communication between GMB and host cells, therefore helping the overall balance and integrity of the host microbiome (Sadeghi et al., 2023).

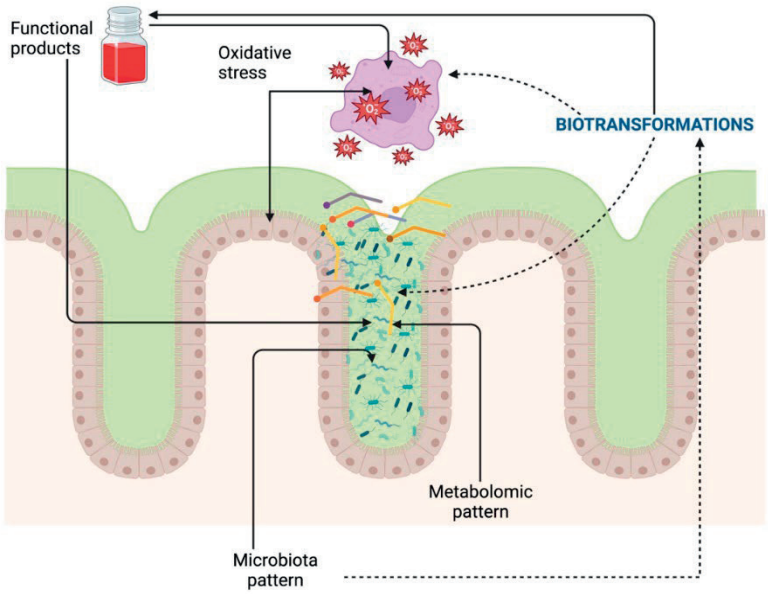

Figure 3. The biological effects of metabiotics at the microbiota level (Figure realized with Biorender App.)

THE ROLE OF EXTRACTS IN METABIOTIC DEVELOPMENT

Extracts play a crucial role in the advancement of metabiotics. By extracting precise molecules from natural sources, scientists may generate metabiotics that are more focused and powerful. For instance, research has shown that some probiotic strains possess extracts that exhibit anti-inflammatory properties. This suggests that these extracts successfully treat conditions like inflammatory bowel disease (Шендеров et al., 2019).

The research paper "*Boletus edulis* Extract-A New Modulator of Dysbiotic Microbiota" presents a comprehensive study of the effects of *B. edulis* extract (BEE) on human gut microbiota, particularly under conditions of antibiotic-induced dysbiosis. The study's methodology encompasses various analyses, including cytotoxicity assessment, immune response evaluation, polyphenolic content analysis, in vitro simulations of BEE's effects on dysbiotic microbiota post-antibiotic consumption, and quantification of resultant short-chain fatty acids (SCFAs). The research findings highlight BEE's potential in modulating microbial patterns, alleviating inflammation, and demonstrating antioxidant properties. By mitigating antibiotic-induced dysbiosis without using probiotic products, BEE emerges as a promising natural alternative for gut health maintenance. This study contributes significantly to understanding the relationship between natural extracts and gut microbiota, particularly in the context of antibiotic use and its subsequent impact on gut health (Avram et al., 2023).

The therapeutic potential of extracts in metabiotic development has attracted considerable attention. Phytochemicals obtained from plants, sea creatures, and fungi, traditionally used in medicine, are now being studied using modern scientific methods. These compounds include anti-neurodegenerative, cytotoxic, anti-proliferative, anti-tumor, and anti-diabetic actions (Figure 4). The research centers on identifying precise molecules accountable for these effects, essential for the accurate and efficient therapy of illnesses, including neurodegenerative disorders, cancer, and diabetes (Avram et al., 2023; Zanfirescu et al., 2023).

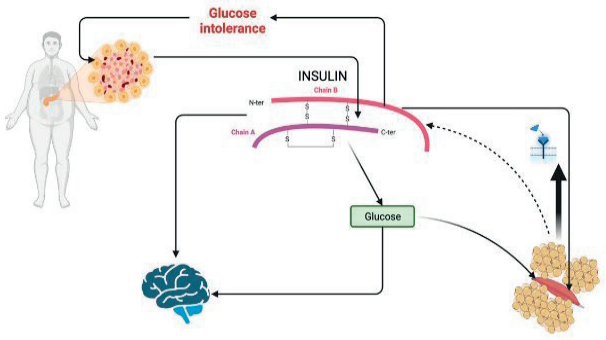

Figure 4. The effects of metabiotics for the type 2 diabetes target groups of populations (Figure realized with Biorender App.)

Employing these molecules in metabiotic development is an innovative strategy that has the potential to result in new and unique therapies. Isolating and characterizing bioactive substances allows for accurate treatment approaches targeting particular biological factors associated with illnesses. Implementing this precision medicine strategy may enhance effectiveness and reduce adverse effects. Research on *Ligusticum chuanxiong* Hort extract, which can decrease β-amyloid peptide levels, can potentially lead to advancements in therapeutic approaches for Alzheimer's illness (Chen et al., 2021). Moreover, the precise identification of the specific antiglycation chemicals present in *L. ovalifolia* has the potential to enhance the field of diabetes therapy significantly (Sahu et al., 2003).

The progress in biotechnology and synthetic biology enables the regulated manufacturing of these organic substances, improving the discovery and development of drugs. By explicitly targeting disease pathways and biological targets, these phytochemicals can trigger apoptosis or hinder inhibiting the proliferation of malignant cells while reducing detrimental effects on healthy cells. This results in a reduction of the typical side effects that accompany chemotherapy (Yan et al., 2023).

CONCLUSIONS

Metabiotics, due to their capacity to impact the body's metabolic system, are a promising field of study that may result in novel and groundbreaking treatments. Furthermore, extracts will persist in playing a pivotal job in their advancement. These extracts possess a

distinct bioactive chemical profile that could improve health and mitigate illness. By incorporating them into functional meals and supplements, these substances might provide a plant-derived, organic remedy to enhance certain facets of human well-being. Subsequent investigations must prioritize the refinement of extraction techniques, the preservation of these substances in product compositions, and thorough clinical studies to assess their physiological advantages in human subjects. It is essential to consider the sustainable procurement and capacity to expand the production of *B. edulis* extracts to satisfy anticipated market needs while conserving natural resources.

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REFERENCES

Adams, R. S., & Ishler, V. A. (2009). Trouble-shooting problems with low milk production. *Dairy and Animal Science*, *4*(1), 98–16. Retrieved June 3, 2018, from www.das.psu.edu/teamdairy. TNR 10, indentation hanging 0.5 cm, alignment justified. The references must be written in alphabetical order by authors' names, in APA style (https://courses.lumenlearning.com/boundless-writing/chapter/apa-citations-and-references/).

Anusiya, G., Gowthama Prabu, U., Yamini, N. V., Sivarajasekar, N., Rambabu, K., Bharath, G., Banat, F. (2021). A review of edible and wild mushrooms' therapeutic and biological effects. *Bioengineered*., *12*, 11239-11268.

Appleton, J. (2018). The Gut-Brain Axis: Influence of Microbiota on Mood and Mental Health. *Integr. Med*., *17*, 28-32.

Avram, I., Pelinescu, D., Gatea, F., Ionescu, R., Barcan, A., Rosca, R., Zanfirescu, A., Vamanu, E. (2023). *Boletus edulis* Extract-A New Modulator of Dysbiotic Microbiota. *Life, 13*, 1481.

Belkaid, Y., Hand, T. W. (2014). Role of the microbiota in immunity and inflammation. *Cell*., *157*, 121-41.

Brownawell, A. M., Caers, W., Gibson, G. R., Kendall, C. W. C., Lewis, K. D., Ringel, Y., Slavin, J. L. (2012). Prebiotics and the Health Benefits of Fiber: Current Regulatory Status, Future Research, and Goals. *J. Nutr*., *142*, 962-974.

Chen, W., Wang, W. P., Zhang, H. S., Huang, Q. (2012). Optimization of ultrasonic-assisted extraction of water-soluble polysaccharides from *Boletus edulis* mycelia using response surface methodology. *Carbohydr. Pol*., *87*, 614-619.

Chen, X., Drew, J., Berney, W., Lei, W. (2021). Neuroprotective Natural Products for Alzheimer's Disease. *Cells*, *10*, 1309.

Das, A. K., Nanda, P. K., Dandapat, P., Bandyopadhyay, S., Gullón, P., Sivaraman, G. K., McClements, D. J., Gullón, B., Lorenzo, J. M. (2021). Edible Mushrooms as Functional Ingredients for Development of Healthier and More Sustainable Muscle Foods: A Flexitarian Approach. *Molecules*, *26*, 2463.

Deo, P. N., Deshmukh, R. (2019). Oral microbiome: Unveiling the fundamentals. J Oral *Maxillofac Pathol*., *23*, 122-128.

Dimopoulou, M., Kolonas, A., Mourtakos, S., Androutsos, O., Gortzi, O. (2022). Nutritional Composition and Biological Properties of Sixteen Edible Mushroom Species. *Appl. Sci.*, *12*, 8074.

Djekic, I., Klaus, A., Vunduk, J., Đorđević, V., Tomovic, V., Koćić-Tanackov, S., Lorenzo, J. M., Barba, F. M., Tomasevi, I. (2020). Application of porcini mushroom (*Boletus edulis*) to improve the quality of frankfurters. *Food Proc. Preserv*., *44*, e14556.

Fabiano, V., Indrio, F., Verduci, E., Calcaterra, V., Pop, T. L., Mari, A., Zuccotti, G. V., Cullu Cokugras, F., Pettoello-Mantovani, M., Goulet, O. (2021). Term Infant Formulas Influencing Gut Microbiota: An Overview. *Nutrients*, *13*, 4200.

Fu, J., Zheng, Y., Gao, Y., Xu, W. (2022). Dietary Fiber Intake and Gut Microbiota in Human Health. *Microorganisms*, *10*, 2507.

Gavrilescu, D. (2000). Dairy farming in small subsistence households. *Tribuna Economica*, *1*(5), 5–7.

Gensollen, T., Blumberg, R. S. (2017). Correlation between early-life regulation of the immune system by microbiota and allergy development. J *Allergy Clin Immunol., 139*(4), 1084-1091.

Grodea, M. (2009). Milk chain in Romania-post adhesion effects. *Scientific Papers Agricultural Management*, *XI*(2), 53–57.

Heleno, S. A., Barros, L., Martins, A., Morales, P., Fernández-Ruiz, V., Glamoclija, J., Sokovic, M., Ferreira, I. C. F. R. (2015). Nutritional value, bioactive compounds, antimicrobial activity and bioaccessibility studies with wild edible mushrooms. *LWT - Food Sci. Technol*., *63*, 799-806.

Hou, K., Wu, Z. X., Chen, X. Y., Wang, J. Q., Zhang, D., Xiao, C., Zhu, D., Koya, J. B., Wei, L., Li, J., Chen, Z. S. (2022). Microbiota in health and diseases. *Signal Transduct Target Ther*., *7*, 135.

Jain, V., Shivkumar, S., Gupta, O. (2014). Health-related quality of life (hr-qol) in patients with type 2 diabetes mellitus. *N Am J Med Sci*., *6*, 96-101.

Jandhyala, S. M., Talukdar, R., Subramanyam, C., Vuyyuru, H., Sasikala, M., Nageshwar Reddy, D. (2015). Role of the normal gut microbiota. *World J Gastroenterol*., *21*, 8787-803.

Ji, J., Jin, W., Liu, S. J., Jiao, Z., Li, X. (2023). Probiotics, prebiotics, and postbiotics in health and disease. *MedComm*, *4*, e420.

Kumar, K., Mehra, R., Guiné, R. P. F., Lima, M. J., Kumar, N., Kaushik, R., Ahmed, N., Yadav, A. N., Kumar, H. (2021). Edible Mushrooms: A

Comprehensive Review on Bioactive Compounds with Health Benefits and Processing Aspects. *Foods*, *10*, 2996.

Langdon, A., Crook, N., Dantas, G. (2016). The effects of antibiotics on the microbiome throughout development and alternative approaches for therapeutic modulation. *Genome Med*., *8*, 39.

Leeming, E. R., Johnson, A. J., Spector, T. D., Le Roy, C. I. (2019). Effect of Diet on the Gut Microbiota: Rethinking Intervention Duration. *Nutrients*, *11*, 2862.

Liang, S., Wu, X., Jin, F. (2018). Gut-Brain Psychology: Rethinking Psychology from the Microbiota–Gut–Brain Axis. *Front. Integr. Neurosci.*, *12*, 33.

Łysakowska, P., Sobota, A., Wirkijowska, A. (2023). Medicinal Mushrooms: Their Bioactive Components, Nutritional Value and Application in Functional Food Production-A Review. *Molecules*, *28*, 5393.

Mago, P., Sharma, R., Hafeez, I., Nawaz, I., Joshi, M., Mehrotra, R. (2023). Mushroom based Cosmeceuticals: An Upcoming Biotechnology Sector. *Biosci Biotech Res Asia*, *20*.

Millogo, V., Ouedraogo, G. A., Agenas, S., & Svennersten-Sjaunja, K. (2008). Survey on dairy cattle milk production and milk quality problems in peri-urban areas in Burkina Faso. *African Journal of Agricultural Research*, *3*(3), 215–224.

Nguyen, T. L., Ora, A., Häkkinen, S. T., Ritala, A., Raisanen, R., Manttari, M. K. Melin, K. (2023). Innovative extraction technologies of bioactive compounds from plant by-products for textile colorants and antimicrobial agents. *Biomass Conv. Bioref.,* 2023.

Niego, A. G., Rapior, S., Thongklang, N., Raspé, O., Jaidee, W., Lumyong, S., Hyde, K. D. (2021). Macrofungi as a Nutraceutical Source: Promising Bioactive Compounds and Market Value. *J. Fungi 7*, 397.

Oancea, M. (2003). *Modern management of agricultural holdings*. Bucharest, RO: Ceres Publishing House.

Ogunrinola, G. A., Oyewale, J. O., Oshamika, O. O., Olasehinde, G. I. (2020). The Human Microbiome and Its Impacts on Health. *Int J Microbiol*., 8045646.

Oniszczuk, A., Oniszczuk, T., Gancarz, M., Szymańska, J. (2021). Role of Gut Microbiota, Probiotics and Prebiotics in the Cardiovascular Diseases. *Molecules*, *26*, 1172.

Özyürek, M., Bener, M., Güçlü, K., Apak, R. (2014). Antioxidant/antiradical properties of microwave-assisted extracts of three wild edible mushrooms. *Food Chem*., *157*, 323-331.

Pihurov, M., Păcularu-Burada, B., Cotârleț, M., Vasile, M. A., Bahrim, G. E. (2021). Novel Insights for Metabiotics Production by Using Artisanal Probiotic Cultures. *Microorganisms*, *9*, 2184.

Ribeiro, M. C., Levi, Y., Moraschini, V., Messora, M. R., Furlaneto, F. A. C. (2023). Effects of Prebiotic Therapy on Gastrointestinal Microbiome of Individuals with Different Inflammatory Conditions: A Systematic Review of Randomized Controlled Trials. *Probiotics & Antimicro. Prot.,* 2023.

Sadeghi, A., Ebrahimi, M., Kharazmi, M. S., Jafari, S. M. (2023). Effects of microbial-derived biotics (meta/pharma/post-biotics) on the modulation of gut microbiome and metabolome; general aspects and emerging trends. *Food Chem*., *411*, 135478.

Sahu, N., Singh, N., Arya, K. R., Reddy, S. S., Rai, A. K., Shukla, V., Pandey, J., Narender, T., Tamrakar, A. K., Kumar, B., Rajak, B. K., Malik, S., Rustagi, S. (2023). Assessment of the dual role of *Lyonia ovalifolia* (Wall.) Drude in inhibiting AGEs and enhancing GLUT4 translocation through LC-ESI-QTOF-MS/MS determination and *in silico* studies. *Front. Pharmacol.*, *14*, 1073327.

Sharma, M., Shukla, G. (2016). Metabiotics: One Step ahead of Probiotics; an Insight into Mechanisms Involved in Anticancerous Effect in Colorectal Cancer. *Front. Microbiol.*, *7*, 1940.

Shenderov, B. A. (2013). Metabiotics: novel idea or natural development of probiotic conception. *Microb Ecol Health Dis*., *24*.

Simeoni, U., Berger, B., Junick, J., Blaut, M., Pecquet, S., Rezzonico, E., Grathwohl, D., Sprenger, N., Brüssow, H., Study, Team., Szajewska, H., Bartoli, J. M., Brevaut-Malaty, V., Borszewska-Kornacka, M., Feleszko, W., François, P., Gire, C., Leclaire, M., Maurin, J. M., Schmidt, S., Skórka, A., Squizzaro, C., Verdot, J. J. (2016). Gut microbiota analysis reveals a marked shift to bifidobacteria by a starter infant formula containing a synbiotic of bovine milk-derived oligosaccharides and *Bifidobacterium animalis* subsp. *lactis* CNCM I-3446. *Environ Microbiol*., *18*, 2185-95.

Singh, R. P., Shadan, A., Ma, Y. (2022). Biotechnological Applications of Probiotics: A Multifarious Weapon to Disease and Metabolic Abnormality. *Probiotics Antimicrob Proteins*., *14*, 1184-1210.

Sudo, N. (2019). Role of gut microbiota in brain function and stress-related pathology. *Biosci. Microbiota Food Health*., *38*, 75-80.

Tan, Y., Zeng, N. K., Xu, B. (2022). Chemical profiles and health-promoting effects of porcini mushroom (*Boletus edulis*): A narrative review. *Food Chem*., *390*, 133199.

Thriene, K., Michels, K. B. (2023). Human Gut Microbiota Plasticity throughout the Life Course. *Int. J. Environ. Res. Public Health*, *20.*

Thursby, E., Juge, N. (2017). Introduction to the human gut microbiota. *Biochem J*., *474*, 1823-1836.

Ursell, L. K., Metcalf, J. L., Parfrey, L. W., Knight, R. (2012). Defining the human microbiome. *Nutr. Rev*., *70*, S38-44.

van Rijn, T., Timmis, J. K. (2023). Patent landscape analysis-Contributing to the identification of technology trends and informing research and innovation funding policy. *Microb Biotechnol*., *16*, 683-696.

Vetter, J. (2023). The Mushroom Glucans: Molecules of High Biological and Medicinal Importance. *Foods*, *12*, 1009.

Witkowska, A. M., Zujko, M. E., Mironczuk-Chodakowska, I. (2011). Comparative Study of Wild Edible Mushrooms as Sources of Antioxidants. *13*, 335-341.

Wu, S., Wang, G., Yang, R., Cui, Y. (2016). Anti-inflammatory effects of *Boletus edulis* polysaccharide on asthma pathology. *Am. J. Transl. Res*., *8*, 4478-4489.

Xu, T., Chen, N., He, X., Chen, F. (2023). Editorial: The relationship of oral and other body sites microbiome in human diseases. *Front. Cell Infect. Microbiol*., *13*, 1276473.

Zahiu, L., Toma, E. (2010). *Agriculture in Romania's economy-between expectations and realities*. Bucharest, RO: Ceres Publishing House.

Zanfirescu, A., Avram, I., Gatea, F., Roșca, R., Vamanu, E. (2024). In Vitro and In Vivo Antihyperglycemic Effects of New Metabiotics from *Boletus edulis*. *Life*, *14*, 68.

Yan, X., Liu, X., Zhao, C., Chen, G. Q. (2023). Applications of synthetic biology in medical and pharmaceutical fields. *Sig Transduct Target Ther*, *8*, 199.

Шендеров, Б. А., Ткаченко, Е. И., Захарченко, М. М., Синица, А. В. (2019). Метабиотики: перспективы, вызовы и возможности. *Медицинский алфавит*., *2*, 43-48.