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ANALYSIS OF EXTRACTION METHODS AND THE PROSPECTS OF THEIR IMPLEMENTATION IN THE LIFE CYCLE OF HERBAL MEDICINAL PRODUCTS

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INFORMATION

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ABSTRACT

The aim of the work is to study and analyze available methods of extraction of herbal raw materials; to assess their advantages and disadvantages in terms of implementation in the development and production of herbal preparations as active pharmaceutical ingredients of medicinal products.

Materials and Methods. The bibliosemantic method was used during the research. The scientific publications in professional editions were used as materials.

Results and Discussion. Extraction methods can be divided into two groups: conventional and novel. Conventional extraction methods are based on classical methods of isolating certain groups of biologically active substances using solvents of different polarity as extractants. Novel methods are based on innovative approaches that ensure a high yield of extractive substances in a relatively short process time, combined with the absence or low need for organic solvents. An important criterion for choosing a method and its subsequent effectiveness are the physicochemical properties of phytochemical compounds.

Conclusions. The available methods of extraction of herbal raw materials have been analyzed from the point of view of their application at the development stages and the prospects of scaling up to production. It has been established that both conventional and novel extraction methods have advantages and disadvantages inherent to each method. It has been found that from scaling up point of view conventional methods look more acceptable based on their technological flexibility and economic feasibility. It has been noted that a promising direction is the implementation of combinations of novel and conventional extraction methods in the life cycle of products. The further stage of research should be the practical application of a combination of extraction methods in the development of active pharmaceutical ingredients and medicinal products based on them.

Introduction. Herbal medicinal products (HMP) are products that contain active pharmaceutical ingredients (API) of exclusively herbal origin and are multicomponent systems in terms of their chemical composition. The pharmacological action of HMP is quite diverse and is formed by the phytochemical composition of the API. It is the wide spectrum

of pharmacological action of HMP and their relative safety during prolonged use without medical supervision that give HMP a potential advantage in the treatment and prevention of diseases. An additional advantage of using HMP is the possibility of combining herbal APIs in composition of one product. This adds a certain therapeutic flexibility in terms of expanding the

therapeutic spectrum and/or enhancing the targeted action of the drug [1; 2; 3].

The formation of the composition of biologically active substances (BAS) in the API occurs at the stage of extraction of the starting material. That is why extraction can be considered a key stage in the development and production of APIs on the way to creating HMP. Isolation of BAS from herbal raw materials can be considered as a variation of solid-phase extraction where the prepared herbal raw materials act as a solid phase (matrix) and solvents of various nature act as an extractant. This method of isolation is based on the processes of dissolution and diffusion. Therefore, factors that can positively influence them potentially affect the efficiency of extraction in general. Such influencing factors include the degree of pre-extraction treatment of raw materials (degree of comminution), the type of extractant used and the process parameters that depend on the extraction method used. Accordingly, the choice of the extraction method in combination with the assessment of related technological factors is an important stage of the development design and life cycle. The correct choice of method will ensure the established quality profile of the product and achieve its predicted pharmacological action [4; 5; 6; 7].

The aim of the work is to study and analyze available methods of extraction of herbal raw materials; to assess their advantages and disadvantages in terms of

implementation in the development and production of herbal preparations as API of HMP.

Materials and Methods. The bibliosemantic method was used during the research. The scientific publications in professional editions were used as materials.

Results and Discussion. In general, extraction methods can be divided into two groups: conventional and novel (Fig. 1). The most common conventional methods for extracting medicinal plant raw materials include those based on traditional process management, namely: maceration, percolation, reflux extraction, Soxhlet extraction and hydrodistillation. The characteristics of modern methods are the use of innovative approaches to extraction. The novel methods include supercritical fluid extraction, pressurized liquid extraction, ultrasound-assisted extraction, enzyme-assisted extraction, microwave-assisted extraction, pulsed electric field extraction and mechanochemical-assisted extraction. Both groups of methods are characterized by several advantages and disadvantages, depending on the process conditions and their equipment. An important criterion for choosing a method and its further effectiveness is the physicochemical properties of phytochemical compounds. In addition, the extraction method can affect the bioavailability and efficacy of the product [8; 9; 10; 11].

Conventional extraction methods are based on classical methods of isolating certain groups of BAS using

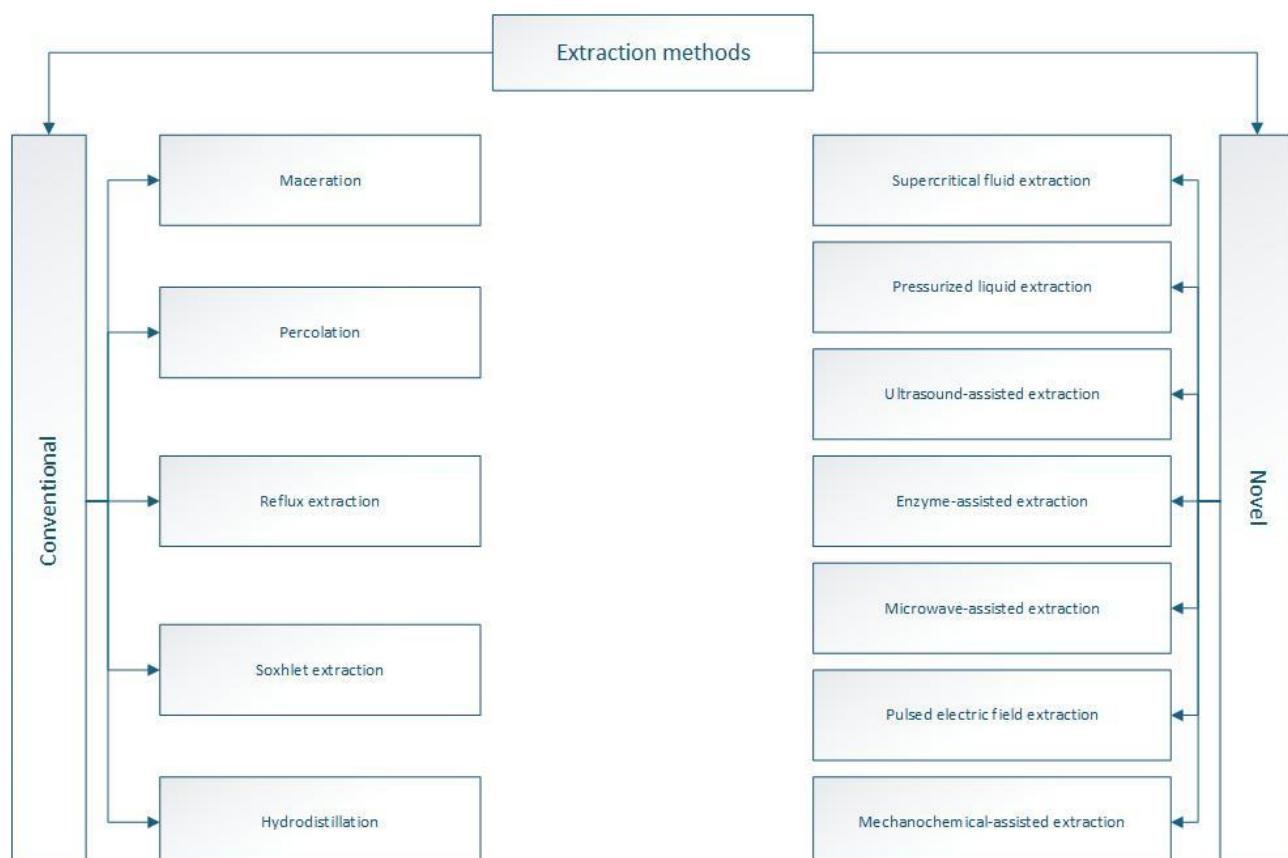


Fig. 1. Conventional and novel extraction methods of herbal raw material

solvents of different polarity as extractants. Despite the use of organic solvents, their quantity and relatively long process duration these methods have been effectively used in the industrial production of APIs of herbal origin for many years [12].

Maceration is one of the most widely used methods of extracting BAS in particular in the production of tinctures. In general, the method is distinguished by the simplicity of the equipment, static in relation to the movement of the extractant and relatively low efficiency due to the rapid achievement of the equilibrium of extractive substances in the extractant and the extracted raw material. In order to increase the efficiency of this conventional method it is possible to create certain dynamic conditions that are capable of increasing the diffusion or removal of extractable matters from the surface of the material: mixing, shaking, periodic circulation of the extractant, separation of the extractant into parts, etc. The advantages of using maceration can also include relatively low temperature conditions of the process, which characterizes this method as energy efficient [12; 13; 14].

Percolation is a widely used conventional extraction method which is based on the seeping of the extractant through a layer of plant raw materials at a certain speed. Unlike maceration, this method is characterized by the ability to constantly maintain the range in concentrations of extractable matters in the extractant and the extracted material which significantly increases the efficiency of diffusion and is the driving force of the process. In general, the percolation process can be divided into two main stages: infusing for the purpose of deaeration of the raw materials and maximum wetting of the raw material particles with the extractant and the percolation itself. The disadvantage of classical percolation can be considered large volumes of extractant and the duration of the process. However, such dynamic variations of percolation as filtration extraction, repercolation and others are able to ensure proper efficiency of the process. Due to the wide range of polarity of the extractants used this conventional method allows the extraction of polyphenolic compounds of various types, which gives the process significant technological volume. The main disadvantage of percolation is the relatively large volumes of the obtained extracts which require additional time and energy costs associated with the need to concentrate them [15; 16].

Reflux extraction is a process based on the evaporation of the extractant with its subsequent condensation in a reflux condenser the passing of the condensate through a layer of raw materials with saturation with extractive substances the return of the extract to the heating vessel for subsequent heating and distillation. The process is continuous, takes place in a closed system under atmospheric pressure according to the established time interval until the required concentration of extractable matters is achieved. This method is distinguished by its efficiency, simplicity of equipment and lower solvent consumption and speed compared to maceration and percolation. The main disadvantage of this conventional method can be considered

temperature conditions because due to constant heating of the reaction vessel thermolabile BAS can be destroyed. Therefore, before using reflux extraction, it is necessary to assess this risk and pre-analyze the properties of the target groups of substances that are planned to be extracted from the raw materials [5; 17].

Soxhlet extraction is a conventional extraction method that is traditionally used mostly in laboratory to study the conditions for extracting BAS from herbal materials. In principle, it is similar to reflux extraction. The difference is the use of a special element equipped with a siphon into which a cartridge with the extracted material is placed. The siphon promotes continuous circulation of the solvent through the layer of raw materials which ensures extraction efficiency. Similarly, to reflux extraction the extract is collected in a heating flask and the solvent undergoes the required number of evaporation and condensation cycles to ensure the required completeness of BAS extraction from the raw materials. This method can be effective for extracting substances with limited solubility in the extractant and allows its recycling, thereby operating with a small amount of it. The limitation of the application of this method is associated with heating the extraction medium which causes the risk of thermal degradation of BAS. In addition to the fact that the temperature of destruction of the extracted compounds must be lower than the boiling point of the extractant the target components must be soluble in it under heating conditions. In addition to the careful choice of solvent, temperature conditions and extraction duration an important factor determining the effectiveness of this conventional method is the proper preparation of the plant material sample [18; 19].

Hydrodistillation is one of the traditional conventional methods of extraction of plant raw materials based on boiling the extracted herbal raw materials in an aqueous extractant, subsequent evaporation of volatile components and their condensation and separation. This extraction method is limited by the polarity spectrum of the aqueous extractant used and the properties of the substances to be extracted. This method allows for the effective isolation of volatile components in contrast to heavier aromatic compounds, in particular polyphenols. The key disadvantage of the hydrodistillation extraction method is its high temperatures which can destructively affect labile compounds. Other factors affecting the effectiveness of this method are the "drug – solvent" ratio and the duration of the process [20].

Despite many years of practical experience in the use of conventional methods and their proven effectiveness in the isolation of BAS from herbal raw materials, their main disadvantages can be considered dependent on a significant amount of organic solvents which can significantly increase the cost of the technological process and affect the cost of the finished product. Another negative factor in choosing conventional methods is the use of high temperatures which poses a risk of degradation of thermolabile compounds and a potential decrease in the pharmacological activity of APIs and HMP based on them. The issue of the effectiveness of conventional methods in terms of the yield of extractable matters

and selectivity to certain groups of phytochemical compounds is also debatable. It should also be noted that some conventional methods cannot be scaled up due to the limited size of the main equipment and low productivity. Thus, the choice of a conventional extraction method should be justified at the early stages of API development and a detailed risk assessment should be carried out regarding the choice of organic extractant, its quantity and toxicity, process temperature conditions, possible extraction intensification tools, scaling of the method to full scale production, and potential productivity to ensure plans for industrial production of APIs and HMPs [9; 21; 22; 23].

Considering a number of limitations and shortcomings typical of conventional methods, it is promising to use new extraction methods based on innovative approaches to the isolation of BAS from herbal raw materials. Among such methods, potentially interesting ones may be supercritical fluid extraction, enzyme-assisted extraction, ultrasound-assisted extraction, microwave-assisted extraction, pulsed electric field extraction, pressurized liquid extraction and mechanochemical-assisted extraction (Fig. 1) [9; 10; 24; 25; 26].

Supercritical Fluid Extraction is a representative of a group of novel extraction methods which is based on the use of an extractant compressed to supercritical conditions. The most common type of this method is supercritical carbon dioxide (CO_2) extraction where at certain pressure and temperature parameters CO_2 passes into a liquid state ($t>31^\circ\text{C}$; $P>73$ atm.) while possessing the diffusion properties of a gas. To perform the process the raw material is placed in an extractor where CO_2 pre-compressed to a supercritical state is fed and mass transfer of substances from the raw material to the extractant occurs. Subsequently, the extract is collected in a separator, and the pressure is balanced to atmospheric as a result of which the extractant is separated from the extract. The use of CO_2 as an extractant is a good alternative to organic solvents as it is safe, environmentally friendly and relatively cheap. According to its characteristics this extractant is non-polar, therefore it is the most effective in terms of isolating lipophilic compounds. To be able to separate substances of medium polarity it is possible to introduce a modifying agent, mostly ethanol in various concentrations, into the main extractant. Despite the efficiency, flexibility and environmental friendliness of supercritical fluid extraction this method is expensive due to the complexity and cost of the equipment. First of all, due to the operating pressure parameters at which the process is performed. Ensuring the effective and safe operation of the equipment requires the use of special materials, automation tools and high-precision instrumentations [27; 28; 29; 30].

Pressurized liquid extraction is a novel extraction method based on the use of conventional solvents at subcritical temperature and pressure parameters at which they remain in a liquid state. Under such conditions the viscosity and surface tension of the extractant decrease which allows it to better penetrate the extracted material and increase the rate of mass

transfer of extractable matters into the extract. The main extractants of this method are water and water-ethanol solutions. Compared to conventional methods, solvent consumption when using pressurized liquid extraction is lower. In addition, the advantages of this method include its speed, environmental friendliness, reproducibility and automation. The disadvantage of pressurized liquid extraction is its low efficiency when using hydrophobic organic solvents, so this method is optimal for extracting polar and medium-polar substances [19; 31; 32; 33].

Ultrasound-assisted extraction is one of the most widely used novel extraction methods in the production of APIs of herbal origin. The method is based on the use of acoustic vibrations or mechanical waves in the frequency range of 20-100 kHz. The method is predicated on cavitation, mechanical and thermal properties which together increase the efficiency of extraction of target compounds from the material by reducing the particle size, destroying cell walls and increasing mass exchange processes. The popularity of ultrasound-assisted extraction is associated with a relatively short process duration (10–30 min.), low energy consumption (0–100 W) and a less destructive effect on the BAS compared to conventional methods. An additional advantage is that cavitation is able to change the partial pressure of microbial cells and cause their death which in turn helps to reduce the microbiological load and extends the shelf life of extracts. Thus, ultrasound-assisted extraction can be successfully used to obtain BAS from herbal raw materials as well as combined with some conventional methods, optimizing them and increasing overall efficiency. The disadvantages include the limited productivity of cavitation equipment and therefore, the difficulties in organizing full-scale industrial production [34; 35; 36; 37; 38].

Enzyme-assisted extraction is a novel extraction method based on the addition of enzymes to increase the efficiency of extractable matters from the extracted raw material by softening its cell walls. Conventional extraction methods face difficulties in penetrating the extractant into the cell and require additional measures (commuting of the raw material, wetting, infusing, etc.). In the case of enzyme-assisted extraction the addition of enzymes can contribute to the breakdown of surrounding elements and help release the necessary substances into the extract. The most common enzymes used in enzyme-assisted extraction are lipases, α -amylases, pectinases, amyloglucosidase, laccases and proteases. The main process parameters of this extraction method are the particle size of the extracted raw material, the ratio of the amount of enzyme to the extracted raw material and the duration of the process. The enzyme is incubated at average ambient temperatures of 35–50°C and an acidic pH value. Water is most often used as a solvent. One of the advantages of the method is that enzymes can be added during hydrophilic and multi-stage lipophilic extractions, especially for the removal of ballast substances. However, when choosing this method, one should consider its duration, which can range from 3 to 48 hours and that is its main disadvantage [39; 40; 41; 42; 43].

Microwave-assisted extraction is a novel method that uses non-ionizing electromagnetic wave radiation with a frequency of 300 MHz to 300 GHz to induce molecular motion in polar or polarized materials or solvents by acting on dipoles. Heating the extracted material under the influence of molecular motion leads to evaporation of moisture which creates pressure and causes rupture of the cell wall with subsequent release of the necessary compounds. Microwave-assisted extraction involves the use of extractants. The choice of solvent should be justified and based on its dielectric properties, boiling point and dispersion. The method is selective for polar molecules and extractants with high dielectric permittivity. The advantage of this method over conventional methods is rapid heating, low thermal degradation and a higher yield of extractable matters. Similar to ultrasound-assisted extraction, the microwave-assisted method is characterized by low solvent requirements, high process speed, and low requirements for raw material preparation. Disadvantages include low extraction efficiency for molecules with a relatively large number of hydroxyl substituents (tannins) or thermolabile substances (anthocyanins) [5; 44; 45; 46].

Pulsed electric field extraction is a novel extraction method whose effectiveness is based on the destruction of cell membranes of the material under the action of a pulsed electric field. The electric potential flows through the cell membrane of the herbal material and, based on the dipole characteristics of the membrane molecules, is distributed in the membrane according to the charge. An excess of the transmembrane charge of more than 1V causes the repulsion of charged molecules and significantly increases permeability. The main advantage of this method is its intensity and energy efficiency. The absence of the need to heat the extraction medium allows it to be used for the isolation of thermolabile BAS. The disadvantages of extraction by pulsed electric action include the complexity of scaling, the risk of mechanical cracking of molecules and the higher cost of products compared to products obtained by conventional methods [47; 48; 49; 50].

Mechanochemical-assisted extraction is a novel extraction method based on the application of high-energy mechanical force to the extracted material with the aim of physicochemical and chemical transformations of

the target components under its influence. The process takes place in an aqueous environment and at room temperature. Mechanical processing of plant material is carried out in combination with a solid reagent characterized by improved solubility. Na_2CO_3 , NaHCO_3 and NaOH are most often used as reagents. The advantages of this method over conventional methods can be considered its relative speed, selectivity and high yield of extractive substances, the absence of high process temperatures, the absence of organic solvents. The disadvantages include insufficient study of the influence of process parameters on its efficiency and the issue of scaling up to industrial conditions [5; 51; 52].

Thus, innovative approaches underlying the novel extraction methods have a positive impact on their extraction efficiency. In particular, they provide a high yield of extractable matters for a relatively short process duration combined with the absence or low consuming for organic solvents and the corresponding environmental friendliness. However, despite a number of significant advantages over conventional methods the novel extraction methods are characterized by a number of limitations that may hinder their implementation on a full scale production in the pharmaceutical industry: the need for specialized equipment and automation, the complexity of scaling and a narrow range of effective extraction capacity.

Conclusions. The available methods of extraction of herbal raw materials have been analyzed from the point of view of their application at the development stages and the prospects of scaling up to production. It has been established that both conventional and novel extraction methods have advantages and disadvantages inherent to each method. It has been found that from scaling up point of view conventional methods look more acceptable based on their technological flexibility and economic feasibility. It has been noted that a promising direction is the implementation of combinations of novel and conventional extraction methods in the life cycle of products. The further stage of research should be the practical application of a combination of extraction methods in the development of active pharmaceutical ingredients and medicinal products based on them.

Conflicts of interest: authors have no conflict of interest to declare.

АНАЛІЗ МЕТОДІВ ЕКСТРАКЦІЇ ТА ПЕРСПЕКТИВА ЇХ ІМПЛЕМЕНТАЦІЇ В ЖИТТЄВИЙ ЦИКЛ ЛІКАРСЬКИХ ЗАСОБІВ РОСЛИННОГО ПОХОДЖЕННЯ

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Мета роботи – вивчити та проаналізувати доступні методи екстракції рослинної сировини; оцінити їх переваги та недоліки з огляду імплементації в розробку та виробництво рослинних препаратів як активних фармацевтичних інгредієнтів лікарських засобів.

Матеріали і методи. Під час проведення дослідження було використано бібліосемантичний метод. Матеріалами дослідження були наукові публікації у фахових виданнях.

Результати й обговорення. Екстракційні методи можна розділити на дві групи: конвенційні та новітні. В основі конвенційних методів екстракції лежать класичні методи виділення певних груп біологічно активних речовин з використанням як екстрагентів розчинників різної полярності. В основу новітніх методів закладено інноваційні підходи, що забезпечують високий вихід екстрактивних речовин за відносну невелику тривалість процесу, в поєднанні з відсутністю або низькою потребою органічних розчинників. Важливим критерієм вибору методу та подальша його ефективність є фізико-хімічні властивості фітохімічних сполук.

Висновки. Проаналізовано доступні методи екстракції рослинної сировини, з точки зору застосування їх на етапах розробки та перспективи масштабування в промислове виробництво. Встановлено, що як конвенційні, так і новітні методи екстракції володіють властивими кожному методу перевагами та недоліками. З'ясовано, що з точки зору масштабування, конвенційні методи виглядають більш привабливими виходячи з їх технологічної гнучкості та економічної доцільності. Визначено, що перспективним напрямом є імплементація у життєвий цикл препарату комбінацій новітніх та конвенційних методів екстракції. Наступним етапом досліджень має стати практичне застосування комбінації екстракційних методів у розробку активних фармацевтичних інгредієнтів та лікарських засобів на їх основі.

Ключові слова: екстракція, рослинна сировина, препарат, технологія, технологічний процес, лікарський засіб.

References

- Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use. Retrieved from: <https://eur-lex.europa.eu/eli/dir/2001/83/oj/eng>
- Dobrovolnyi OO, Davtian LL, Solomennyi AM, Davydenko OO. Review of the pharmacological properties of herbal preparations as potential ingredients of combined medication for hepatobiliary disorders treatment among servicemen. Ukrainian journal of military medicine. 2025;6(1):186–93. DOI: 10.46847/ujmm.2025.1(6)-186
- Dobrovolnyi OO, Davtian LL, Solomennyi AM, Davydenko OO. Herbal medicines as a safe alternative to synthetic anxiolytics in the treatment of stress and anxiety among servicemen. Ukrainian journal of military medicine. 2024;5(4):152–8. DOI: 10.46847/ujmm.2024.4(5)-152
- Robards K, Ryan D. Chapter 10 – Sample handling in chromatography. Princ. Pract. Mod. Chromatogr. Methods. 2022;453–493. DOI: 10.1016/B978-0-12-822096-2.00007-4.
- Ilze L, Spalvins K. Methods for Extraction of Bioactive Compounds from Products: A Review. Environmental and Climate Technologies. 2023;27(1):422–437. DOI: 10.2478/rtect-2023-0031
- Drăghici-Popa AM, Boscornea AC, Brezoiu AM, Tomas ST, Pârvulescu OC, Stan R. Effects of Extraction Process Factors on the Composition and Antioxidant Activity of Blackthorn (*Prunus spinosa* L.) Fruit Extracts. Antioxidants. 2023;12(10):1897. DOI: 10.3390/antiox12101897
- Cañadas R, Gonzalez-Miquel M, González EJ, Díaz I, Rodriguez M. Overview of Neoteric Solvents as Extractants in Food Industry: A Focus on Phenolic Compounds Separation From Liquid Streams. Food Research International. 2020;136:109558. DOI: 10.1016/j.foodres.2020.109558
- Zaky AA, Witrowa-Rajchert D, Nowacka M. Revolution of Bioactive Compound Extraction: Impacts on Food Safety, Health, and Sustainability. Food safety and health. 2025;3(3):315–333. DOI: 10.1002/fsh3.70012
- Zaky AA, Akram MU, Rybak K, Witrowa-Rajchert D, Nowacka M. Bioactive Compounds From Plants and By-Products: Novel Extraction Methods, Applications, and Limitations. AIMS Molecular Science. 2024;11(2):150–188. DOI: 10.3934/molsci.2024010
- Putnik P, Lorenzo JM, Barba FJ, et al. Novel Food Processing and Extraction Technologies of High-Added Value Compounds From Plant Materials. Foods. 2018;7(7):106. DOI: 10.3390/foods 7070106
- Dalal D, Kunte S, Oblureddy VT, Anjali AK. Comparative Evaluation of Antimicrobial Efficacy of German Chamomile Extract, Tea Tree Oil, and Chlorhexidine as Root Canal Irrigants Against *E-Faecalis* and *Streptococcus Mutans* – An In Vitro Study. International Journal of Agriculture and Biosciences. 2023;12(4):252–256. DOI: 10.47278/journal.ijab/2023.072
- Ranjha MMAN, Amjad S, Ashraf S, et al. Extraction of Polyphenols From Apple and Pomegranate Peels Employing Different Extraction Techniques for the Development of Functional Date Bars. International Journal of Fruit Science. 2020;20(S3):S1201–S1221. DOI: 10.1080/15538362.2020.1782804
- Setford PC, Jeffery DW, Grbin PR, Muhlack RA. Factors Affecting Extraction and Evolution of Phenolic Compounds During Red Wine Maceration and the Role of Process Modelling. Trends in Food Science & Technology. 2017;69:106–117. DOI: 10.1016/j.tifs.2017.09.005
- Albuquerque BR, Prieto MA, Barreiro MF, et al. Catechin-Based Extract Optimization Obtained From *Arbutus unedo* L. Fruits Using Maceration/Microwave/Utrasound Extraction Techniques. Industrial Crops and Products. 2017;95:404–415. DOI: 10.1016/j.indcrop.2016.10.050
- Stéphane FFY, Jules BKJ, Batiha GES, Ali I, Bruno LN. Extraction of Bioactive Compounds from Medicinal Plants and Herbs. Nat. Med. Plants. 2021;1–39. DOI: 10.5772/intechopen.98602
- Wang WY, Bin QuH, Gong XC. Research progress on percolation extraction process of traditional Chinese medicines. Zhongguo Zhong Yao Za Zhi. 2020;45(5):1039–46. DOI: 10.19540/J.CNKI.CJCM.20191221.305
- Ma Y, et al. Reflux Extraction Optimization and Antioxidant Activity of Phenolic Compounds from *Pleioblastus amarus* (Keng) Shell. Molecules. 2022;27(2):362. DOI: 10.3390/molecules27020362
- Anton I, Húth B, Füller I, Rózsa L, Holló G, Zsolnai A. Effect of Single Nucleotide Polymorphisms on Intramuscular Fat Content in Hungarian Simmental Cattle. Asian-Australasian Journal of Animal Sciences. 2018;31(9):1415–19. DOI: 10.5713/ajas.17.0773
- Zhang QW, Lin LG, Ye WC. Techniques for Extraction and Isolation of Natural Products: A Comprehensive Review. Chinese medicine. 2018;13:1–26. DOI: 10.1186/s13020-018-0177-x
- Barros M, Redondo L, Rego D, Serra C, Miloudi K. Extraction of Essential Oils From Plants by Hydrodistillation With Pulsed Electric Fields (PEF) Pre-Treatment. Applied Sciences. 2022;12(16):8107. DOI: 10.3390/app12168107

21. Lee JE, Jayakody JTM, Kim JI, et al. The Influence of Solvent Choice on the Extraction of Bioactive Compounds From Asteraceae: A Comparative Review. *Foods*. 2024;13(19):3151. DOI: 10.3390/foods13193151

22. ElGamal R, Song C, Rayan AM, Liu C, Al-Rejaie S, ElMasry G. Thermal Degradation of Bioactive Compounds During Drying Process of Horticultural and Agro-nomic Products: A Comprehensive Overview. *Agronomy*. 2023;13(6):1580. DOI: 10.3390/agronomy13061580

23. Phong WN, Gibberd MR, Payne AD, Dykes GA, Coorey R. Methods Used for Extraction of Plant Volatiles Have Potential to Preserve Truffle Aroma: A Review. *Comprehensive Reviews in Food Science and Food Safety*. 2022;21(2):1677–1701. DOI: 10.1111/1541-4337.12927

24. Redondo D, Venturini ME, Luengo E, Raso J, Arias E. Pulsed Electric Fields as a Green Technology for the Extraction of Bioactive Compounds From Thinned Peach By-Products. *Innovative Food Science & Emerging Technologies*. 2018;45:335–343. DOI: 10.1016/j.ifset.2017.12.004

25. Zaky AA, Witrowa-Rajchert D, Nowacka M. Insights Into Plant-Origin Bioactive Peptides: Extraction, Bioactivities, In Silico Approaches, and Applications. *International Journal of Peptide Research and Therapeutics*. 2025;31(2):1–34. DOI: 10.1007/s10989-024-10684-w

26. Zaky AA, Gómez-Cortés P, Hernández-Ledesma B. Innovations in Biologically Active Nutrients Extraction and Delivery. *Frontiers in Nutrition*. 2024;11:1425911. DOI: 10.3389/fnut.2024.1425911

27. Abdulqahar FW, Mahdi ZI, Al-kubaisy SH, et al. Computational Study of Antiviral, Anti-Bacterial, and Anticancer Activity of Green-Extracted Sidr (*Ziziphus Spina-Christi*) Fruit Phenolics. *Bioactive Compounds in Health and Disease*. 2023;6(10):271–291. DOI: 10.31989/bchd.v6i10.1192

28. Abdulqahar FW, Morgab MA, Hussein FF, Apyantseva Y, El-Messery TM. In Silico Analyses of Bioactive Compounds Extracted From *Ziziphus Jujuba* Using Supercritical CO₂ Extraction: Potential Anti-Anxiety and Anti-Alzheimer's Disease. *Bioactive Compounds in Health and Disease*. 2023;6(10):215–234. DOI: 10.31989/bchd.v6i10.1180

29. Garg G, Gómez M, Masdeu-Bultó AM, González YM. Compressed Carbon Dioxide as a Medium in Catalytic Hydrogenations: Engineering and Chemistry. *Journal of CO₂ Utilization*. 2023;77:102605. DOI: 10.1016/j.jcou.2023.102605

30. Ahmad T, Masoodi FA, Rather SA, Wani SM, Gull A. Supercritical Fluid Extraction: A Review. *Journal of Biological and Chemical Chronicles*. 2019;5(1):114–122. DOI: 10.33980/jbcc.2019.v05i01.019

31. Hossain MB, Rawson A, Aguiló-Aguayo I, Brunton NP, Rai DK. Recovery of Steroidal Alkaloids From Potato Peels Using Pressurized Liquid Extraction. *Molecules*. 2015;20(5):8560–73. DOI: 10.3390/molecules20058560

32. Pasrija D, Anandharamakrishnan C. Techniques for Extraction of Green Tea Polyphenols: A Review. *Food and Bioprocess Technology*. 2015;8(5):935–950. DOI: 10.1007/s119470151479-y

33. Xynos N, Papaefstathiou G, Gikas E, Argyropoulou A, Aligiannis N, Skaltsounis AL. Design Optimization Study of the Extraction of Olive Leaves Performed With Pressurized Liquid Extraction Using Response Surface Methodology. *Separation and Purification Technology*. 2014;122:323–330. DOI: 10.1016/j.seppur.2013.10.040

34. Kumar K, Srivastav S, Sharangapat VS. Ultrasound assisted extraction (UAE) of bioactive compounds from fruit and vegetable processing by-products: A review. *Ultrason. Sonochem.* 2021;70:105325. DOI: 10.1016/j.ultrasonch.2020.105325

35. González M, Barrios S, Budelli E, Pérez N, Lema P, Heinzen H. Ultrasound Assisted Extraction of Bioactive Compounds in Fresh and Freeze-Dried *Vitis Vinifera* cv Tannat Grape Pomace. *Food and Bioproducts Processing*. 2020;124:378–386. DOI: 10.1016/j.fbp.2020.09.012

36. Chaudhary N, et al. A review on instant controlled pressure drop technology – a strategic tool for extraction of bioactive compounds. *Int. J. Food Sci. Technol.* 2022;57(11):e1–e11. DOI: 10.1111/ijfs.15408

37. Azmir J, Zaidul ISM, Rahman MM, et al. Techniques for Extraction of Bioactive Compounds From Plant Materials: A Review. *Journal of Food Engineering*. 2013;117(4):426–436. DOI: 10.1016/j.jfoodeng.2013.01.014

38. Cravotto G, Mariatti F, Gunjovic V, et al. Pilot Scale Cavitation Reactors and Other Enabling Technologies to Design the Industrial Recovery of Polyphenols From Agro-Food By-Products, a Technical and Economical Overview. *Foods*. 2018;7(9):130. DOI: 10.3390/foods7090130

39. Zaky AA, Shim JH, Abd El-Aty AM. A Review on Extraction, Characterization, and Applications of Bioactive Peptides From Pressed Black Cumin Seed Cake. *Frontiers in Nutrition*. 2021;8:743909. DOI: 10.3389/fnut.2021.743909

40. Gligor O, Mocan A, Moldovan C, Locatelli M, Crișan G, Ferreira IC. Enzyme-assisted Extractions of Polyphenols – A Comprehensive Review. *Trends in Food Science & Technology*. 2019;88:302–315. DOI: 10.1016/j.tifs.2019.03.029

41. Malik J, Mandal SC. Extraction of Herbal Biomolecules. *Herbal Biomolecules in Healthcare Applications*, edited by C. Subhash, AKN. Mandal, AK. Dhara. Academic Press. 2022:21–46. DOI: 10.1016/B978-0-323-85852-6.00015-9

42. Zhang M, et al. Optimization of Enzyme-Assisted Extraction and Purification of Flavonoids from *Pinus koraiensis* Nut-Coated Film and Antioxidant Activity Evaluation. *Molecules*. 2021;26(7):1950. DOI: 10.3390/molecules26071950

43. Streimikyte P, Viskelis P, Viskelis J. Enzymes-Assisted Extraction of Plants for Sustainable and Functional Applications. *Int. J. Mol. Sci.* 2022;23(4):2359. DOI: 10.3390/ijms23042359

44. Zaky AA, Witrowa-Rajchert D, Nowacka M. Turning Apple Pomace Into Value: Sustainable Recycling in Food Production A Narrative Review. *Sustainability*. 2024;16(16):7001. DOI: 10.3390/su16167001

45. Rostagno MA, Villares A, Guillamón E, García-Lafuente A, Martínez JA. Sample preparation for the analysis of isoflavones from soybeans and soy foods. *J. Chromatogr. A*. 2009;1216(1):2–29. DOI: 10.1016/j.chroma.2008.11.035

46. Sonar MP, Rathod VK. Optimization Study of Marmelosin (Imperatorin) Extraction From *Aegle Marmelos* Using Three Phase Partitioning. *Journal of Biologically Active Products from Nature*. 2020;10(5):418–428. DOI: 10.1080/22311866.2020.1816215

47. Gorte O, Nazarova N, Papachristou I, et al. Pulsed Electric Field Treatment Promotes Lipid Extraction on Fresh Oleaginous Yeast *Saitozyma Podzolica* DSM 27192. *Frontiers in Bioengineering and Biotechnology*. 2020;8:575379. DOI: 10.3389/fbioe.2020.575379

48. Bozinou E, Karageorgou I, Batra GG, Dourtoglou V, Lalas SI. Pulsed Electric Field Extraction and Antioxidant Activity Determination of *Moringa Oleifera* Dry Leaves: A Comparative Study With Other Extraction Techniques. *Beverages*. 2019;5(1):8. DOI: 10.3390/beverages5010008

49. Kokkali M, Martí-Quijal FJ, Taroncher M, Ruiz MJ, Kousoulaki K, Barba FJ. Improved Extraction Efficiency of Antioxidant Bioactive Compounds From *Tetraselmis Chuii* and *Phaeodactylum Tricornutum* Using Pulsed Electric Fields. *Molecules*. 2020;25(17):3921. DOI: 10.3390/molecules25173921

50. Carullo D, Pataro G, Donsì F, Ferrari G. Pulsed Electric Fields-Assisted Extraction of Valuable Compounds From *Arthrosira Platensis*: Effect of Pulse Polarity and Mild Heating. *Frontiers in Bioengineering and Biotechnology*. 2020;8:551272. DOI: 10.3389/fbioe.2020.551272

51. Wu K, Ju T, Deng Y, Xi J. Mechanochemical assisted extraction: A novel, efficient, eco-friendly technology.

List of literature

- Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use. URL: <https://eur-lex.europa.eu/eli/dir/2001/83/oj/eng>.
- Review of the pharmacological properties of herbal preparations as potential ingredients of combined medication for hepatobiliary disorders treatment among servicemen / O. O. Dobrovolnyi et al. *Ukrainian journal of military medicine*. 2025. Vol. 6. No. 1. P. 186–193.
- Herbal medicines as a safe alternative to synthetic anxiolytics in the treatment of stress and anxiety among servicemen / O. O. Dobrovolnyi et al. *Ukrainian journal of military medicine*. 2024 Vol. 5. No. 4. P. 152–8.
- Robards K., Ryan D. Chapter 10 – Sample handling in chromatography. *Princ. Pract. Mod. Chromatogr. Methods*. 2022. P. 453–493.
- Ilze L., Spalvins K. Methods for Extraction of Bioactive Compounds from Products: A Review. *Environmental and Climate Technologies*. 2023. Vol. 27. No. 1. P. 422–437.
- Effects of Extraction Process Factors on the Composition and Antioxidant Activity of Blackthorn (*Prunus spinosa* L.) Fruit Extracts / A. M. Drăghici-Popa et al. *Antioxidants*. 2023. Vol. 12. No. 10. P. 1897.
- Overview of Neoteric Solvents as Extractants in Food Industry: A Focus on Phenolic Compounds Separation From Liquid Streams / R. Cañadas et al. *Food Research International*. 2020. Vol. 136. 109558.
- Zaky A. A., Witrowa-Rajchert D., Nowacka M. Revolution of Bioactive Compound Extraction: Impacts on Food Safety, Health, and Sustainability. *Food safety and health*. 2025. Vol. 3. No. 3. P. 315–333.
- Bioactive Compounds From Plants and By-Products: Novel Extraction Methods, Applications, and Limitations / A. A. Zaky et al. *AIMS Molecular Science*. 2024. Vol. 11. No. 2. P. 150–188.
- Novel Food Processing and Extraction Technologies of High-Added Value Compounds From Plant Materials / P. Putnik et al. *Foods*. 2018. Vol. 7. No. 7. 106.
- Comparative Evaluation of Antimicrobial Efficacy of German Chamomile Extract, Tea Tree Oil, and Chlorhexidine as Root Canal Irrigants Against *E-Faecalis* and *Streptococcus Mutans* – An In Vitro Study / D. Dalal et al. *International Journal of Agriculture and Biosciences*. 2023. Vol. 12. No. 4. P. 252–256.
- Extraction of Polyphenols From Apple and Pomegranate Peels Employing Different Extraction Techniques for the Development of Functional Date Bars / M. M. A. N. Ranjha et al. *International Journal of Fruit Science*. 2020. Vol. 20. S3. P. S1201–S1221.
- Factors Affecting Extraction and Evolution of Phenolic Compounds During Red Wine Maceration and the Role of Process Modelling / P. C. Setford et al. *Trends in Food Science & Technology*. 2017. Vol. 69, Part A. P. 106–117.
- Catechin-Based Extract Optimization Obtained From *Arbutus unedo* L. Fruits Using Maceration/Microwave/
- Trends Food Sci. Technol. 2017;66:166–175. DOI: 10.1016/j.tifs.2017.06.011
- Dobroslavić E, Repajić M, Dragović-Uzelac V, Garofulić IE. Isolation of *Laurus nobilis* Leaf Polyphenols: A Review on Current Techniques and Future Perspectives. *Foods*. 2022;11(2):235. DOI: 10.3390/foods11020235
- Ultrasound Extraction Techniques / B. R. Albuquerque et al. *Industrial Crops and Products*. 2017. Vol. 95. P. 404–415.
- Extraction of Bioactive Compounds from Medicinal Plants and Herbs / F. F. Y. Stéphane et al. *Nat. Med. Plants*. 2021. P. 1–39. DOI: 10.5772/intechopen.98602.
- Wang W. Y., Bin Qu H., Gong X. C. Research progress on percolation extraction process of traditional Chinese medicines. *Zhongguo Zhong Yao Za Zhi*. 2020. Vol. 45. No. 5. P. 1039–46.
- Reflux Extraction Optimization and Antioxidant Activity of Phenolic Compounds from *Pleioblastus amarus* (Keng) Shell / Y. Ma et al. *Molecules*. 2022. Vol. 27. No. 2. 362.
- Effect of Single Nucleotide Polymorphisms on Intramuscular Fat Content in Hungarian Simmental Cattle / I. Anton et al. *Asian-Australasian Journal of Animal Sciences*. 2018. Vol. 31. No. 9. P. 1415–19.
- Zhang Q.W., Lin L.G., Ye W.C. Techniques for Extraction and Isolation of Natural Products: A Comprehensive Review. *Chinese medicine*. 2018. Vol. 13:20. P. 1–26.
- Extraction of Essential Oils From Plants by Hydrodistillation With Pulsed Electric Fields (PEF) Pre-Treatment / M. Barros et al. *Applied Sciences*. 2022. Vol. 12. No. 16. 8107.
- The Influence of Solvent Choice on the Extraction of Bioactive Compounds From Asteraceae: A Comparative Review / J. E. Lee et al. *Foods*. 2024. Vol. 13. No. 19. 3151.
- Thermal Degradation of Bioactive Compounds During Drying Process of Horticultural and Agronomic Products: A Comprehensive Overview / R. ElGamal et al. *Agronomy*. 2023. Vol. 13. No. 6. 1580.
- Methods Used for Extraction of Plant Volatiles Have Potential to Preserve Truffle Aroma: A Review / W. N. Phong et al. *Comprehensive Reviews in Food Science and Food Safety*. 2022. Vol. 21. No. 2. P. 1677–1701.
- Pulsed Electric Fields as a Green Technology for the Extraction of Bioactive Compounds From Thinned Peach By-Products / D. Redondo et al. *Innovative Food Science & Emerging Technologies*. 2018. Vol. 45. P. 335–343.
- Zaky A.A., Witrowa-Rajchert D., Nowacka M. Insights Into Plant-Origin Bioactive Peptides: Extraction, Bioactivities, In Silico Approaches, and Applications. *International Journal of Peptide Research and Therapeutics*. 2025. Vol. 31. No. 2. P. 1–34.
- Zaky A. A., Gómez-Cortés P., Hernández-Ledesma B. Innovations in Biologically Active Nutrients Extraction and Delivery. *Frontiers in Nutrition*. 2024. Vol. 11. 1425911.
- Computational Study of Antiviral, Anti-Bacterial, and Anti-cancer Activity of Green-Extracted Sidr (*Ziziphus Spina-Christi*) Fruit Phenolics / F. W. Abdulqahar et al. *Bioactive Compounds in Health and Disease*. 2023. Vol. 6. No. 10. P. 271–291.
- In Silico Analyses of Bioactive Compounds Extracted From *Ziziphus Jujuba* Using Supercritical CO₂ Extraction: Potential Anti-Anxiety and Anti-Alzheimer's Disease / F. W. Abdulqahar et al. *Bioactive Compounds in Health and Disease*. 2023. Vol. 6. No. 10. P. 215–234.

29. Compressed Carbon Dioxide as a Medium in Catalytic Hydrogenations: Engineering and Chemistry / G. Garg et al. *Journal of CO₂ Utilization*. 2023. Vol. 77. 102605.

30. Supercritical Fluid Extraction: A Review / T. Ahmad et al. *Journal of Biological and chemical Chronicles*. 2019. Vol. 5. No. 1. P. 114–122.

31. Recovery of Steroidal Alkaloids From Potato Peels Using Pressurized Liquid Extraction / M. B. Hossain et al. *Molecules*. 2015. Vol. 20. No. 5. P. 8560–73.

32. Pasrija D., Anandharamakrishnan C. Techniques for Extraction of Green Tea Polyphenols: A Review. *Food and Bioprocess Technology*. 2015. Vol. 8. No. 5. P. 935–950.

33. Design Optimization Study of the Extraction of Olive Leaves Performed With Pressurized Liquid Extraction Using Response Surface Methodology / N. Xynos et al. *Separation and Purification Technology*. 2014. Vol. 122. P. 323–330.

34. Kumar K., Srivastav S., Sharanagat V. S. Ultrasound assisted extraction (UAE) of bioactive compounds from fruit and vegetable processing by-products: A review. *Ultrason. Sonochem.* 2021. Vol. 70. 105325.

35. Ultrasound Assisted Extraction of Bioactive Compounds in Fresh and Freeze-Dried Vitis Vinifera cv Tannat Grape Pomace / M. González et al. *Food and Bioproducts Processing*. 2020. Vol. 124. P. 378–386.

36. A review on instant controlled pressure drop technology – a strategic tool for extraction of bioactive compounds / N. Chaudhary et al. *Int. J. Food Sci. Technol.* 2022. Vol. 57. No. 11. P. e1–e11.

37. Techniques for Extraction of Bioactive Compounds From Plant Materials: A Review / J. Azmir et al. *Journal of Food Engineering*. 2013. Vol. 117. No. 4. P. 426–436.

38. Pilot Scale Cavitational Reactors and Other Enabling Technologies to Design the Industrial Recovery of Polyphenols From Agro-Food By-Products, a Technical and Economical Overview / G. Cravotto et al. *Foods*. 2018. Vol. 7. No. 9. 130.

39. Zaky A. A., Shim J. H., Abd El-Aty A. M. A Review on Extraction, Characterization, and Applications of Bioactive Peptides From Pressed Black Cumin Seed Cake. *Frontiers in Nutrition*. 2021. Vol. 8. 743909.

40. Enzyme-assisted Extractions of Polyphenols – A Comprehensive Review / O. Gligor et al. *Trends in Food Science & Technology*. 2019. Vol. 88. P. 302–315.

41. Malik J., and Mandal S. C. Extraction of Herbal Biomolecules. *Herbal Biomolecules in Healthcare Applications*, / edited by C. Subhash, A. K. N. Mandal, and A. K. Dhara. Academic Press. 2022. P. 21–46.

42. Optimization of Enzyme-Assisted Extraction and Purification of Flavonoids from Pinus koraiensis Nut-Coated Film and Antioxidant Activity Evaluation / M. Zhang et al. *Molecules*. 2021. Vol. 26. No. 7. 1950.

43. Streimikyte P., Viskelis P., Viskelis J. Enzymes-Assisted Extraction of Plants for Sustainable and Functional Applications. *Int. J. Mol. Sci.* 2022. Vol. 23. No. 4. 2359.

44. Zaky A. A., Witrowa-Rajchert D., Nowacka M. Turning Apple Pomace Into Value: Sustainable Recycling in Food Production A Narrative Review. *Sustainability*. 2024. Vol. 16. No. 16. 7001.

45. Sample preparation for the analysis of isoflavones from soybeans and soy foods / M. A. Rostagno et al. *J. Chromatogr. A*. 2009. Vol. 1216. No. 1. P. 2–29.

46. Sonar M. P., Rathod V. K. Optimization Study of Marmelosin (Imperatorin) Extraction From Aegle Marmelos Using Three Phase Partitioning. *Journal of Biologically Active Products from Nature*. 2020. Vol. 10. No. 5. P. 418–428.

47. Pulsed Electric Field Treatment Promotes Lipid Extraction on Fresh Oleaginous Yeast Saitozyma Podzolica Dsm 27192 / O. Gorte et al. *Frontiers in Bioengineering and Biotechnology*. 2020. Vol. 8. 575379.

48. Pulsed Electric Field Extraction and Antioxidant Activity Determination of Moringa Oleifera Dry Leaves: A Comparative Study With Other Extraction Techniques / E. Bozinou et al. *Beverages*. 2019. Vol. 5. No. 1. 8.

49. Improved Extraction Efficiency of Antioxidant Bioactive Compounds From Tetraselmis Chuii and Phaeodactylum Tricornutum Using Pulsed Electric Fields / M. Kokkali et al. *Molecules*. 2020. Vol. 25. No. 17. 3921.

50. Pulsed Electric Fields-Assisted Extraction of Valuable Compounds From Arthrospira Platensis: Effect of Pulse Polarity and Mild Heating / D. Carullo et al. *Frontiers in Bioengineering and Biotechnology*. 2020. Vol. 8. 551272.

51. Mechanochemical assisted extraction: A novel, efficient, eco-friendly technology / K. Wu et al. *Trends Food Sci. Technol.* 2017. Vol. 66. P. 166–175.

52. Isolation of Laurus nobilis Leaf Polyphenols: A Review on Current Techniques and Future Perspectives / E. Dobroslavić et al. *Foods*. 2022. Vol. 11. No. 2. 235.

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