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Biological value of berry polyphenols and prospects for supercritical extraction application for their isolation: A review

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Abstract:
Plant polyphenols are known for their numerous health-promoting properties. This article reviews the current state of research in two related fields, namely beneficial effects of flavonoids for human health, e.g., gut microbiome, and supercritical fluid extraction applied to flavonoids of plant origin. The review covered research articles registered in eLIBRARY.RU, PubMed, and Science Direct in 2005–2025. Polyphenolic compounds obtained from various berries were reported to have a positive impact on gut microbiota, e.g., they stimulated the growth of lactobacilli, bifidobacteria, and other beneficial microorganisms, as well as improved the adhesion of probiotic and pathogenic microbes to intestinal epithelial cells.

The review revealed some promising application areas for berry extracts in the functional food industry. Polyphenols can be part of meat formulations due to their strong antioxidant activity. Their antimicrobial effect against a wide range of contaminants renders them good prospects in protecting food products from microbial spoilage. Supercritical extraction is a promising method that isolates biologically active substances from plant materials. The review summarizes its advantages and limitations, as well as the range of prospective co-solvents.

Ultrasonication, pulse electric field, and enzymic pretreatment make supercritical extraction more efficient. In general, this extraction method proved to be an excellent means of isolating flavonoids and related compounds from various plants and their parts.

Keyworlds: Plant materials, flavonoids, prebiotics, biological activity, intestinal microbiota, extraction, green technologies, supercritical fluid

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INTRODUCTION

Biologically active substances of plant origin, e.g., polyphenolic compounds and flavonoids, are known for a number of beneficial effects on human health. That is why the effect of flavonoids on gut microbiota has attracted much scientific attention in the last decade [1]. According to The International Scientific Association for Probiotics and Prebiotics (2017), prebiotics include not only carbohydrates, but also polyphenols, and all of them can be used as food components to improve gut microbiome [2]. Flavonoids are abundant in fruits. Russia boasts a wide diversity of wild and cultivated berries, which are part of many food products. Yet, their nutraceutical value seems to attract few domestic scientists [3, 4] although this area possesses an obvious research potential, especially in the sphere of public health.

The list of extractants that isolate biologically active compounds from plant materials includes alcohol, aqueous and alcoholic solutions, ethers, or carbon dioxide (CO_2). Each solvent has its advantages and disadvantages [5]. Currently, the food and pharmaceutical industries are trying to avoid organic and toxic solvents. The diffusion rate through the diffusive boundary layer between the plant material and the solvent is the most important extraction factor. The extraction yield depends on the efficiency of the extraction method. Inactive and inert solvents preserve the nutraceutical properties of the target plant components. They make it possible to skip some labor-intensive and energy-consuming production stages. Supercritical fluid extraction (SCFE) is a fast-developing method in Russia, China, and the USA. Supercritical fluids have been employed to isolate natural components since the late 1970s. Initially, their use was rare. Today, supercritical fluid technologies and equipment are a promising research direction [6].

This article reviews publications that describe the beneficial properties of flavonoids on gut microbiota and the method of supercritical fluid extraction applied to isolate flavonoids from plant materials.

STUDY OBJECTS AND METHODS

The review covered scientific publications registered in the Russian Research Citation Index (eLIBRARY.RU), PubMed, and Science Direct in 2005–2024. The articles under analysis featured flavonoids, their beneficial properties, and action mechanisms, as well as the method of supercritical extraction of polyphenols as biologically active compounds. The keyword list included *flavonoids*, *microbiota*, *supercritical fluid extraction*, and *plant materials*.

RESULTS AND DISCUSSION

Berry extracts in the food industry and medicine. Fruits and berries are a reliable source of bioactive extracts, and their biological properties are a popular research subject. Polyphenolic compounds of berry extracts are antioxidants with strong anti-inflammatory, anticancer, and neuroprotective effects. They are able to modulate gut microbiota, which has been confirmed both *in vitro* and *in vivo*. Berries owe their nutraceutical value to their phytochemical composition, represented by a wide variety of phenols, e.g., phenolic acids (derivatives of cinnamic and benzoic acids), flavonoids (anthocyanins, flavanols, and flavonols), tannins, stilbenes, etc. [7]. The growing scientific interest stimulates the market of functional foods and supplements, where berry extracts serve as biologically active ingredients [8]. This fact, in turn, encourages researchers to explore new applications of berry extracts that can improve the quality of human life. This section reviews relevant scientific data on the prospects of berry extracts in medicine and food.

Berry polyphenolic compounds in medicine. Polyphenolic compounds exert a positive effect on human health by interacting with gut microbiome. The colon microbiome is a complex ecosystem of diverse bacteria that controls the metabolism of chemical compounds that are consumed with food [9]. Unfortunately, most polyphenolic compounds, depending on their chemical composition and polymerization, demonstrate poor bioavailability in the digestive tract as a result of poor absorption and rapid excretion, which means they fail to reach the bloodstream in their natural form [10]. They need hydrolysis by either intestinal enzymes or intestinal microbiota to transform polyphenols into bioactive molecules that would be absorbed and transported to the target organ [11]. Many studies assess the prebiotic effect of polyphenolic compounds and how they affect probiotics.

Prebiotic effect of polyphenolic compounds in berry extracts on gut microbiota. Food polyphenols interact bidirectionally with the intestinal microbiota, stimulating beneficial bacteria or inhibiting potential pathogens. This phenomenon is called a selective prebiotic effect. Such representatives of beneficial microbiota as *Lactobacillus* spp. and *Bifidobacterium* spp. produce more short-chain fatty acids, e.g., butyric acid, when affected by polyphenols, especially catechins, anthocyanins, and proanthocyanidins [12].

Pan *et al.* [13] modeled healthy fecal culture fermentation *in vitro* to study the effect of flavonoids on structure and metabolism of the intestinal microbiota. They tested hesperidin, hesperetin 7-O-glucoside, naringin, prunin, rutin, isoquercitrin, and quercetin. Hesperetin 7-O-glucoside, prunin, and isoquercitrin had the greatest effect on the structure of the human intestinal microbiota at a concentration of 4 mg/mL, increasing the count of *Bifidobacterium*, *Lactobacillus*, and *Prevotella* after 24 h of simulated fermentation *in vitro*.

Perz *et al.* [14] studied the effect of flavonoids on the growth kinetics and count of pathogenic and probiotic microorganisms. Chalcones, flavans, and flavones substituted with -Br, -Cl, $-CH_3$, and $-NO_2$ inhibited or suppressed the growth of pathogenic bacteria without affecting health-beneficial probiotics. In the same research, 6-methyl-8-nitroflavone and 8-bromo-6-chloroflavone showed a positive modulation of gut microbiome in *in-vitro* digestion, raising the count of beneficial bacteria and reducing the count of potential pathogens.

Meng *et al.* [15] studied the metabolism of quercitrin in the colon and its effect on the colon microbiota in mice *in vivo*. Quercitrin changed the beta-diversity of gut microbiome, affecting such probiotics as *Akkermansia* and *Lactococcus*. In addition, it boosted the development of such short-chain fatty acids as propanoate, isovalerate, and hexanoate.

Multicomponent formulations of berry extracts had a positive effect on gut microbiome by increasing in the probiotic bacterial count. Attri *et al.* [16] studied *in vitro* the sustainability of sea-buckthorn polyphenols during digestion and their effect on colon microbiome. Fecal microbiota simulated digestion and fermentation by increasing the content of polyphenols and improving their antioxidant properties.

Sea-buckthorn juice increased the diversity of *Bacteroides*, *Prevotella*, *Lactobacteria*, and *Bifidobacteria*, which indicated a potential positive effect on colon microrobiota. Molan *et al.* [17] reported prebiotic beneficial effects of aqueous bilberry extracts with pure and mixed human fecal cultures *in vitro*. Blueberry extracts stimulated the growth of pure *Lactobacillus rhamnosus* and

Bifidobacterium breve. A mixed fecal culture batch fermentation system demonstrated similar results. When administered daily to rats *per os*, bilberry extracts increased the population of lactobacilli and bifidobacteria.

Berry extracts proved effective as prebiotic supplements that restore the gut microbiota in various metabolic disorders. Lee *et al*. [18] studied the effect of blueberry extracts on microbiome, systemic inflammation, and insulin resistance in rats that received a high-fat diet. Blueberry increased the count of *Gammaproteobacteria*, decreased the villus length in the ileum, and improved the insulin sensitivity.

Li and Ming [19] described the effect of mulberry polyphenols on small and large intestinal microbiota during type 2 diabetes. Mulberry polyphenols improved the diversity of microbiota in both compartments. The small intestinal microbiota was found to affect the blood glucose balance. Mulberry polyphenols improved the pathophysiology of type 2 diabetes.

Polyphenolic compounds have a great potential as prebiotic supplements or synbiotic compositions that modulate or restore intestinal microbiota affected by chronic diseases or metabolic disorders.

Effect of polyphenolic compounds on probiotic activity: other mechanisms. Plant polyphenols promote probiotic adhesion. Yuan *et al*. [20] studied cell surface hydrophobicity and autoaggregation. Resveratrol enhanced the adhesion of *Lactobacillus acidophilus* NCFM to mucin (1.73 times), epicatechin (1.47 times), caffeic acid (1.30 times), and hesperidin (0.99 times). Quercetin demonstrated a certain degree of inhibition (0.84 times). According to a proteomic analysis, resveratrol altered proteins on the surface of *L. acidophilus* NCFM, as well as promoted the expression of mucin genes and glycosylation of mucins on the surface of HT-29 cells. Similar results were reported for resveratrol and ferulic acid [21].

Dietary flavan-3-ols altered the intestinal microecology by enhancing or inhibiting the adhesion of lactobacilli strains to intestinal cells. Flavan-3-ols inhibited the adhesion of *L. acidophilus* LA-5 and *Lactobacillus plantarum* IFPL379. Pigallocatechin gallate, on the contrary, enhanced the adhesion of *L. acidophilus* LA-5 to Caco-2. Procyanidins B1 and B2 improved the adhesion of *L. casei* LC115 to HT-29 cells, while epigallocatechin increased the adhesion of *L. casei* LC115 to Caco-2 [22].

Polyphenol-containing plant extracts and probiotics demonstrate a certain synergism. When combined with a probiotic, anthocyanin-rich blueberry extract reduced the count of adherent viable pathogenic cells on a mucin/BSA-treated surface more efficiently than in the sample where the probiotic was alone [23]. When combined with *Bifidobacterium animalis* Bo, blueberry extract was able to inhibit pathogen adhesion completely.

Polyphenolic compounds of berries in the food industry. ***Berry extracts as natural antioxidants in meat products.*** Berry extracts with polyphenolic compounds have good prospects as natural food preservatives because synthetic alternatives may be toxic. Berry extracts prevented the oxidation of lipids, proteins, and pigments in meat and meat products [24]. Grape seed and bearberry extracts reduced lipid oxidation during storage in pork chops while maintaining their sensory properties after cooking [25]. Blueberry extract increased the oxidative stability and antioxidant activity of a pork roll during storage at 8°C [26]. Blackcurrant extract (*Ribes nigrum* L.) in raw pork chops developed carbonyls and reduced the amount of substances that reacted with thiobarbituric acid during refrigerated storage. In addition, pork chops maintained the sulfhydryl level in a dose-dependent manner, indicating a significant inhibition of lipid and protein oxidation. [27]

Freeze-dried cranberries (*Vaccinium oxycoccus*) in nitrite-free fermented sausages with venison and pork fat reduced oxidative changes during storage [28]. Strawberry extracts (*Arbutus unedo* L.) proved more effective than rosehip (*Rosa canina* L.) in reducing lipid oxidation in sausages during refrigerated storage [29]. Chokeberry (*Aronia melanocarpa* L.) extract reduced oxidation processes in cooked ham or raw pork burgers [30].

Berry extracts demonstrated enough antioxidant activity for meat preservation as a prospective alternative to synthetic preservatives.

Berry extracts as antimicrobial agents against foodborne pathogens. Some berries have polyphenolic compounds that can disrupt the membrane of Gram-negative bacteria and reduce their viability [31]. Such berries are promising antimicrobial additives that protect foods from foodborne bacteria. Cranberry extracts demonstrated a dose-dependent antimicrobial activity against *Salmonella*, *Escherichia coli*, and *C. perfringens*, as well as *Staphylococcus*, *Listeria*, *Helicobacter*, *Bacillus*, and *Campylobacter* [31]. Cranberry extracts were more antimicrobial than those of blueberry, raspberry, and strawberry [32].

The antimicrobial profile of berry extracts may vary for one and the same species depending on where the berries grew. Georgescu *et al*. [33] studied antimicrobial activities of eight berry extracts (blueberry, blackcurrant, gooseberry, redcurrant, raspberry, sea buckthorn, strawberry, and cherry) collected simultaneously in Romania and Russia. The research featured seven pathogenic microorganisms, i.e., *Bacillus subtilis*, *Bacillus cereus*, *Staphylococcus aureus*, *E. coli*, *Salmonella typhi*, *Candida albicans*, and *Aspergillus niger*. Most of them showed resistance or intermediate activity against berry extracts from both countries. Raspberry and strawberry extracts had very low or no activity against Gram-positive pathogenic bacteria. Strawberry extract did not affect Gram-negative strains, while raspberry extract demonstrated zero or very low antifungal effect. *E. coli* proved to be the most berry-sensitive microorganism, especially to cherry extract, followed by sea buckthorn and blackcurrant. *S. typhi* proved to be the most berry-resistant microorganism. However, most Romanian berries showed higher antimicrobial efficacy against *B. subtilis*, *B. cereus*, *S. aureus*, *S. typhi*, and *C. albicans*, while Russian berries were more effective against *E. coli* and *A. niger*.

Polyphenolic compounds of berry origin as part of animal feed can affect the microbiological profile of products made from the meat of farm animals. For example, when pigs were fed an additive with cranberry pulp, lactic acid bacteria became the predominant microflora in meat stored under anaerobic conditions. It inhibited the growth of pathogenic bacteria [34]. A goji dietary supplement in the diet of rabbits improved the oxidative stability and increased the content of phenols in the meat [35]. Goji berries did not affect the hygienic profile of rabbit meat but boosted the growth of *Lactobacillus* spp., thus improving the sensory profile [36].

Berry extracts as antimicrobial additives are a good natural alternative to antibiotics. They satisfy the needs of consumers for high-quality and safe products, as well as allow producers to minimize the use of antibiotics in animal feed.

Berry extracts in functional foods. Fruit and berry juices are part of many fermented beverages, the most popular raw materials being pomegranate, mulberry, cherry, blueberry, blackberry, and goji. They act as a carrier matrix for probiotics [37]. Black goji juice (*Lycium ruthenicum* Murr.) developed more phenolic acids, gallic or chlorogenic, as well as flavonoids, amino acids, and dipeptides, when it was used to ferment *Lactobacillus rhamnosus* GG. Black goji juice also increased the production of lactic acid and the viability of probiotics during 24 h of fermentation [38].

When fermented with *L. plantarum*, sea-buckthorn (*Hippophae rhamnoides* L., subsp. *carpatica*) juice was used as a food matrix and caused a significant increase in phenols and flavonoids with a lactobacillus count of 8.5 log CFU/mL [39]. Markkinen *et al.* [40], who studied chokeberry, sea-buckthorn, and lingonberry juices fermented with *L. plantarum* and *Oenococcus oeni*, obtained different results. In their case, fermentation of chokeberry juice with DSM 10492 strain reduced the content of flavonols by 9–14% and hydroxycinnamic acids by 20–24%. The content of flavonol glycosides and sugar in sea buckthorn remained unchanged, as did the content of anthocyanins in chokeberry.

The phenolic profile of mulberry juice demonstrated an increase in the total concentration of anthocyanins, phenols, and flavonoids, when fermented with *L. plantarum*, *Lactobacillus acidophilus*, and *Lactobacillus paracasei*. The best result belonged to *L. plantarum* [41].

Therefore, fermentation with lactic acid bacteria in non-dairy functional drinks increases the bioavailability of polyphenolic compounds. The synergistic action of probiotics and prebiotics have a beneficial potential for consumers' health.

Polyphenolic compounds from plant extracts: other applications. Flavonoids with two aromatic rings linked by C-C bonds and a 3-C-oxygenated heterocycle are the most diverse group of berry polyphenols [42]. Flavonoids (pure, in plant extracts, or combined with probiotics) can be used in agriculture.

In aquaculture, the freshwater dark sleeper (*Odontobutis potamophila*) improved its gut flora and increased the species range of probiotics *Bacillus* spp. and *Lactobacillus* spp. after exposure to 2.5 mg/L of quercetin. However, 5 and 10 mg/L of quercetin inhibited the growth of *Lactobacillus* spp. [43].

In cattle farming, natural plant extracts with flavonoids and probiotics proved to be a promising alternative to antibiotics. Weaned piglets that received flavonoids from Tartary buckwheat (*Fagopyrum tataricum*) supplements improved their average daily gain, immune capacity, and the antioxidant activity of *L. plantarum*. A combination of flavonoids from Tartary buckwheat and probiotics promoted nutrient digestibility [44].

In poultry farming, flavonoids from hawthorn-leaf in the diet of breeding hens affected the microbiota that the hens transmitted to chickens. The probiotic count in meconium increased, as did the average daily gain, while the feed conversion ratio of chickens went down [45].

Modern methods and trends in plant material extraction. *Types of extraction.* Plant materials are an important source of biologically active substances, e.g., polyphenolic compounds. When extracted, they are expected to maintain their initial integrity and biological activity. The content of valuable components in extracts varies greatly.

Polyphenolic compounds, such as flavonoids, are extracted with water vapor (lipid fraction), water, oil, glycerol, or organic solvents. Other methods include subcritical carbon dioxide extraction, supercritical extraction (desorption), and various combined techniques [46, 47].

Extraction is a popular method to obtain biologically active compounds. Table 1 summarizes the existing methods for extracting target components from plant materials with brief technological descriptions [48].

The extraction process should meet the following requirements: it is fast, simple, and cheap; the extract is rich in the target component; the target substance is yielded in a quantity sufficient enough to allow for final measurements to be conducted without additional concentration, and the waste is small and recyclable.

For many years, targeted extraction from oil have relied on hydrocarbon or chlorinated organic solvents in a Soxhlet extractor. Unfortunately, liquid extraction often fails to meet some important criteria. It takes several hours to obtain a satisfactory amount of the active component. Most organic solvents are expensive, and the resulting extracts are low in the target substance. As a result, the method needs additional concentration. However, some part of the target substance may decompose or get lost during this stage. Moreover, concentration often causes air-pollution [49].

Waters Corporation (USA) is a large manufacturer of supercritical extractors [50]. The Waters Prep Supercritical Fluid Extraction system (Fig. 1) makes it possible to substitute organic solvents with a supercritical CO_2 atmosphere. Waters Corporation systems extract and fractionate food fats and oils, allow obtaining biologically active substances from such plants as St. John's wort, ginger, garlic, or ginseng, as well as purify medicinal herbs and foods from pesticides and herbicides, etc.

Table 1 Extracting biologically active substances from plant materials: technical characteristics [48]

Extraction methods	Solvent	Temperature	Pressure	Time	Chances for organic solvent use	Polarity of target components
Maceration	Water and organic solvents	Room (295.2 K)	Atmospheric	Long	High	Depends on the extracting solvent
Soxhlet extractor	Organic solvents	Heating	Atmospheric	Long	Moderate	Depends on the extracting solvent
Hydrodistillation	Water	Heating	Atmospheric	Long	Moderate	Non-polar or moderately polar compounds
Pressurized liquid extraction	Aqueous and non-aqueous solvents	Heating	High	Short	Low	Depends on the extracting solvent
Subcritical water extraction	Water	Heating	High	Short	Low	Polar and moderately polar compounds
Supercritical fluid extraction	Supercritical fluid (CO_2), sometimes with organic co-solvents	Heating	High	Very short	No/low	Non-polar or moderately polar compounds
Ultrasonic extraction	Water and organic solvents	Room/heating	Atmospheric	Short or moderate	Low or moderate	Depends on the extracting solvent
Microwave extraction	Water and organic solvents	Room/heating	Atmospheric	Short	Low	Depends on the extracting solvent

Figure 1 Waters prep supercritical fluid extraction system (Waters Corporation, USA)

Figure 2 STS 316 supercritical fluid extraction system (Rexo Engineering, South Korea)

Rexo Engineering (South Korea) is a major supplier of supercritical extraction equipment [51]. Figure 2 shows its set for supercritical fluid extraction. The system consists of a cryostat circulator that cools CO_2, a pump that feeds it, an extractor with a tank for raw materials (0.5–20 L), a heated backpressure regulator, and a separator. The process is carried out at 40 MPa and 250°C, with an extractant flow rate of 100 mL/min. An STS 316 extractor is made of material that is inert to the solvent and the plant raw materials.

During supercritical fluid extraction, the solvent is in the supercritical state and is subjected to severe compression. The resulting supercritical fluid acquires the properties of both gas and liquid. It has the same diffusion rate, low viscosity, and compressibility as gas, and the same high density and dissolving capacity as liquid. The supercritical fluid can easily penetrate into small-diameter pores in the deep layers of the extracted material, where it dissolves and extracts the target components with the rapid mass transfer, which other solvents cannot provide. As the pressure increases, so does the supercritical fluid density, which makes the components more soluble. When the pressure is removed, the rapid expansion of supercritical solutions leads to the precipitation of finely dispersed solid particles. All flow reactors rely on this phenomenon. Unlike conventional solvents, supercritical fluids can dissolve gases, e.g., hydrogen and nitrogen, thus providing a rapid and pure hydrogenation.

A result, supercritical fluid extraction has become a popular method that targets specific components in various types of raw materials, including plants [52].

Supercritical solvents in obtaining biologically active components. To be used as an extractant for biologically active substances, a supercritical fluid is expected meet the following requirements [53]: the extract obtained has no unwanted smells or harmful components; the extractant is highly selective and possesses a good dissolving capacity; the extractant is chemically inert to the target components and the equipment; the extractant is safe, non-flammable, and inexplosive; the extractant is cheap, harmless, and available, and the extractant is colorless and non-hydrophobic.

The list of efficient solvents includes CO_2, water, ethane, methane, etc. In the supercritical state, all liquids mix with each other; beyond the critical point, the mix becomes a single phase.

Table 2 presents the critical values of density, temperature, and pressure, at which solvents enter the supercritical state [54].

CO_2 is the most popular supercritical fluid due to its non-flammability and low critical parameters (304.15 K, 7.4 MPa). Unfortunately, its polarity in a supercritical state is quite low. However, polar modifiers assed as co-solvents can change the polarity of the supercritical fluid and increase its solvating ability with respect to target components [55].

High-pressure extractors: modernization and intensification. A supercritical extractor that relies on CO_2 must contain the following units: a cylinder to store CO_2, a condenser to cool CO_2, a high-pressure pump, a tank for preheating CO_2, a high-pressure reactor, and a separator to collect the extract (Fig. 3) [56].

From cylinder (1), CO_2 goes to condenser (2), where it cools down and converts to liquid. Then, the liquid CO_2 is pumped by high-pressure pump (4) into thermostat (5), where it is heated to a temperature that exceeds the temperature of transition to the supercritical state. Then, the supercritical CO_2 enters high-pressure extractor (6) loaded with plant raw materials. Penetrating the raw materials, the supercritical CO_2 dissolves the extracted substances. The supercritical mix flows from the high-pressure extractor through fine adjustment valve (7) into extract collector (8), where the extracted substances are condensed while the CO_2 turns back to gas. It can be discharged into the atmosphere or liquified for another extraction.

Supercritical CO_2 extraction is one of the most attractive methods for extracting biologically active substances from plant materials. Its main advantage is that it can extract heat-labile substances that are important for pharmacy, including polyphenolic compounds [57, 58]. A lot of attempts have been made to modify the existing methods of supercritical CO_2 extraction in order to increase the yield of target components [58, 59].

Co-solvent. A polar co-solvent facilitates the process of CO_2 extraction of polyphenolic compounds from plant materials. A small amount of co-solvent improves the properties of non-polar supercritical CO_2, as well as increases the rate of mass transfer and the solubility of polar compounds [60]. Ethanol, methanol, water, or their mixes facilitate the extraction of highly polar phenolic phytocompounds [61]. The amount of quercetin was

Table 2 Critical parameters of solvents used as supercritical extractants [54]

Solvent	Chemical formula	Critical density, g/cm^3	Critical temperature, K	Critical pressure, MPa
Water	H_2O	0.32	647.30	22.10
CO_2	CO_2	0.47	304.15	7.39
Methane	CH_4	0.16	191.05	4.64
Ethane	C_2H_6	0.20	305.45	4.88
Propane	C_3H_8	0.22	369.95	4.26
Propylene	C_3H_6	0.23	364.90	4.60
Methanol	CH_3OH	0.27	512.60	8.09
Ethanol	C_2H_5OH	0.28	513.90	6.14

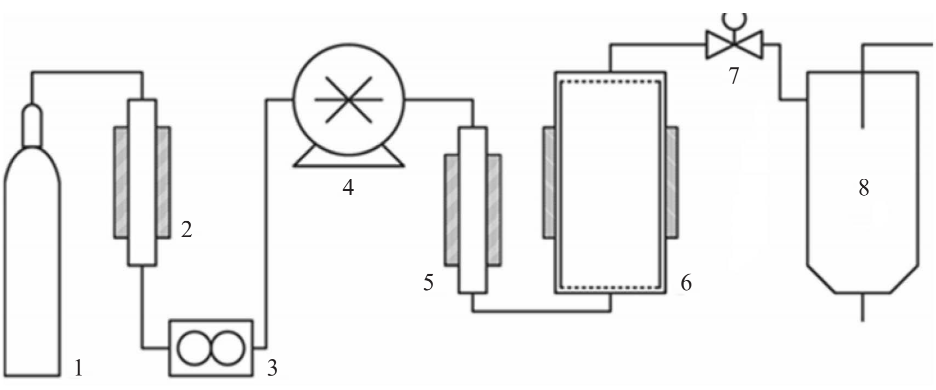

Figure 3 1 – CO_2 cylinder, 2 – refrigerator, 3 – flow meter, 4 – high-pressure pump, 5 – heater, 6 – extraction vessel in a heating jacket, 7 – automatic pressure regulator, 8 – polymer cyclone separator [49]

reported to increase together with the ethanol content in supercritical CO_2 [62]. When extracted with pure CO_2, the quercetin content in the extract was 64 µg/100 g; when extracted with 7.36 mass.% ethanol, it was 2402 µg/100 g. However, this intensification method requires an additional step to remove the co-solvent from the extract, which should be taken into account when calibrating the amount of the co-solvent.

Temperature and pressure. Temperature and pressure affect such properties of supercritical fluids as density, viscosity, diffusion coefficient, and, eventually, their solvation capacity [63]. As the pressure increases, so does the density of the extractant and the solubility of the extracted substances. However, after a certain point, an increase in pressure can reduce the diffusion capacity of the supercritical extractant, thereby reducing the amount of the extract dissolved. For instance, when the pressure exceeded 200 atm, the extract yield went down, following a decrease in the diffusion coefficient [64].

The correlation between the extract yield and the temperature is more complex. On the one hand, a temperature increase raises the diffusion coefficient and improves the extraction yield. On the other hand, as the temperature falls down, the vapor pressure of the dissolved substances decreases while the extractant gains more density, which, in turn, increases the dissolving capacity. This chain leads to the phenomenon called crossover pressure. Below the crossover pressure, higher temperatures reduce the extract yield. Above the crossover pressure, higher temperatures increase the extract yield. For instance, the amount of eugenol extracted from *Ocimum sanctum* Linn. went down as the temperature increased at lower pressures. When the pressure exceeded 200 bar, an increase in temperature led to an increase in the eugenol yield [65].

Extractant flow rate. Solvent flow rate also exerts a significant effect on supercritical extraction. An increase in the CO_2 flow rate increased the extract yield as the extractant flow in the high-pressure reactor became turbulent. The driving force grew because dissolved substances were carried away faster than before. This phenomenon reduced the resistance to external mass transfer and increased the extract yield [66]. However, upon reaching a certain flow rate, further growth of the solvent flow does not affect the extract yield. On the contrary, the yield may decrease because the plant material grows more compact in the extractor [67, 68].

Ultrasound radiation. A particular mechanical action on plant raw materials may also increase the extract yield. Ultrasound intensifies the process of supercritical extraction. This phenomenon can be explained by mechanical, cavitation, and thermal effects: they destroy cell membranes, reduce the particle size, and increase the mass transfer through membranes. The collapse of cavitation bubbles generates microturbulence and high-speed interparticle collisions, which accelerates diffusion of the extracted substance [69]. The cavitation on the surface of the source material causes a collision of microflows, thus eroding or destroying the particles [70]. Ultrasound processing made it possible to increase the yield of flavonoids by 19% [71].

Pulse electric field. Electric field affects cell membranes through the phenomenon known as electroporation [72]. Electrodes produce high-voltage electric pulses for several seconds, and the charge of the cytoplasmic membrane increases. Upon reaching the threshold of transmembrane potential, small pores appear: it is through them that the target component exits the cell. This intensification method is efficient both during raw material processing and during extraction. The electric field method was reported to increase the yield of polyphenolic compounds from grape skins [72] and almond husks [73].

Enzymes. Enzymes also increase the yield of target components during supercritical CO_2 extraction. They destroy cell membranes in plant materials, thus improving the access of supercritical CO_2 to bioactive substances and increasing their extraction [74]. Enzymes break the bonds between non-extractable polyphenols and macromolecules of lignin or cellulose, converting them into more extractable forms. This approach is suitable for a bigger range of compounds and improves the quality of the extract. For example, tea waste treated with enzymes allowed for a five-fold higher extract yield [75].

Extracting biologically active substances from plant raw materials using supercritical extraction. Supercritical extraction is a popular method of extracting biologically active substances. Tomatoes extracted after a preliminary enzymatic treatment demonstrated a better solubility in supercritical CO_2 [76]. Cranberry (*Viburnum opulus* L.) contains such beneficial substances as chlorogenic and quinic acids. Kraujalis *et al.* [77] effectively extracted cranberries in a 50-mL Helix extractor between two layers of cotton wool. The obtained extract contained oleic and linoleic acids, as well as a wide range of tocopherols.

Tangerine peel proved to be a promising secondary raw material for obtaining flavonoids by supercritical extraction [78]. Kueh *et al.* [79] obtained essential oils, sesquiterpenes, and phenols from the leaves of *Melaleuca pentavesica*. A good yield of terpenoids and tocopherols was registered in *Thymus munbyanus* extracts [80].

Additional co-solvents may increase the yield of target components. Bayrak *et al.* [81] used methanol as a co-solvent to obtain extracts from *Colchicum* species. The yield of colchicine increased, and the process became more selective. Ethanol is another popular co-solvent. Ethyl alcohol added to the CO_2 flow affected the yield of triterpene saponins (ginsenosides) [82].

Mora *et al.* [83] considered the extraction of flavonoids and coumarins from industrial fruit peel waste. Atwi-Ghaddar *et al.* [84] extracted dihydrorobinetin and robinetin from *Robinia pseudoacacia* L. for their antimicrobial and antioxidant properties. Quercetin, kaempferol, and catechin were extracted from the flowers of medicinal *Dendrobium* plants [85]. The extracts demonstrated antitumor, hypoglycemic, anti-inflammatory, and

Table 3 Obtaining plant extracts using various extraction methods [76–89]

Plant raw material	Bioactive substances	Extractant	Temperature, K (Pressure, MPa)	Reference
Tomatoes	Lycopene	CO_2	359.2 (50)	[76]
Cranberries	Oleic acid, linoleic acid, tocopherols	CO_2	323.2 (57)	[77]
Tangerine peels	Flavonoids	CO_2	303.2 (3)	[78]
Melaleuca pentavecchia	Sesquiterpenes and phenols	CO_2	316.2 (25)	[79]
Thymus munbyanus	Phenolic compounds	CO_2	343.2 (450)	[80]
Colchicum	Colchicine	CO_2 + 3% methanol	308.2 (24.7)	[81]
Ginseng	Triterpene saponins	CO_2 + 6% ethanol	343.2 (20)	[82]
Citrus peels	Flavonoids, coumarins	80% CO_2, 20% ethanol	333 (30)	[83]
Robinia pseudoacacia	Flavonoids, phenolic compounds	80% CO_2, 20% ethanol	353 (10)	[84]
Dendrobium	Flavonoids	40% CO_2, 60% ethanol	323 (20)	[85]
Pueraria lobata	Flavonoids	CO_2, ethanol	323.54 (20.04)	[86]
Odentema	Flavonoids	85% CO_2, 15% ethanol	238.2 (20)	[87]
Ziziphus jujuba	Flavonoids	85% CO_2, 15% ethanol	324.7 (27.12)	[88]
Costus spicatus	Linoleic acid, flavonoids, phenols	90% CO_2, 10% ethanol	323.2 (14)	[89]

antibacterial potentials. The total yield of flavonoids was three times as high as in the extract obtained by ultrasonic circulating extraction.

Pueraria lobata is a source of five flavonoids, i.e., puerarin, daidzin, genistin, daidzein, and genistein. Its extracts are known for their anticancer, antigiardiasic, and antidiabetic properties. The supercritical extraction involved a Spe-ed SFE Basic laboratory extractor (250 mL, USA) [86].

Odentema leaves were reported to contain a complex of flavonoids, alkaloids, carbohydrates, glycosides, saponins, phytosterols, and tannins. The main target component was quercetin: its extracts help against hypertension and possess excellent antioxidant properties. The supercritical extraction involved an SFE 2 X 100 F extractor (USA) [87].

Ziziphus jujuba leaves were extracted in a high-pressure ASI Spe-ed SFE-2 extractor (USA). The extracts contained glycosides of kaempferol and quercetin, which are popular in the food industry due to their antioxidant, anti-inflammatory, antigenotoxic, and antiprotozoal activities [88].

Costus spicatus extracts were reported to possess analgesic, antioxidant, antimicrobial, antifungal, and nephroprotective properties. Its leaves and stems contained triterpenes, sterols, flavonoids, saponins, alkaloids, and tannins. A supercritical extraction with ultrasound pretreatment made it possible to rationalize the optimal technological variables with the maximal flavonoid extraction [89].

Table 3 provides data on supercritical extraction from various plant raw materials, including the most efficient extractants and the main technological variables, i.e., temperature and pressure.

Carefully selected parameters make it possible to control the flavonoid extraction from various types of plant raw materials. The method of supercritical extraction provides their complete extraction at low temperatures and requires small amounts of expensive co-solvents, such as ethanol. As a result, the method of supercritical extraction remains energetically and environmentally efficient.

CONCLUSION

Berries are rich in polyphenolic compounds and flavonoids. They boost the growth and metabolism of beneficial intestinal microorganisms while suppressing potential pathogens, which classifies them as prebiotics. In addition, they can stimulate the adhesion of probiotic microorganisms to intestinal epithelial cells. Polyphenols give berry extracts their strong antioxidant properties, which makes it possible to use them as natural ingredients in meat products. The ability to inhibit microbial contaminants in food makes them efficient biopreservatives.

New technologies yield more valuable bioactive substances than traditional extraction methods. Supercritical fluids are a promising alternative to such expensive solvents as hexane or dichloromethane. Carbon dioxide used as an extractant in supercritical extraction requires no additional stages and is environmentally neutral. In addition, the method of supercritical fluid extraction was approved by the Soil Association for organic foods.

Supercritical extraction is popular in Russia, China, the USA, and Brazil. Many research articles feature novel laboratory installations or extraction models with subsequent scaling to industrial volumes.

Process control makes it possible to vary the dissolving capacity of the extractant. The extraction efficiency depends on the selectivity: a highly-selective extractant makes it possible to obtain pure substances while maintaining their structural integrity. Flavonoids are diverse in structure. As a result, the extraction of target components from plant materials requires different conditions. The optimal parameters provide the maximal yield.

By varying the pressure, temperature, and quantity of the co-solvent in the extractant flow, producers optimize the extraction process, which is impossible in traditional methods.

CONTRIBUTION

N.Yu. Khromova, J.M. Puzankova, and I.V. Shakir wrote the first section about berry extracts in the food industry and medicine; E.V. Guseva, A.I. Artemiev, and K.M. Demkin wrote the second section about the method of supercritical extraction; B.A. Karetkin, and V.I. Panfilov reviewed and edited the original draft. All the authors proofread the final version.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

1. Fraga CG, Croft KD. Kennedy DO, Tomás-Barberán FA. The effects of polyphenols and other bioactives on human health. Food and Function. 2019;10:514–528. https://doi.org/10.1039/C8FO01997E
2. Gibson GR, Hutkins R, Sanders ME, Prescott SL, Reimer RA, Salminen SJ, *et al.* Expert consensus document: The International Scientific Association for Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of prebiotics. Nature Reviews Gastroenterology and Hepatology. 2017;14:491–502. https://doi.org/10.1038/nrgastro.2017.75
3. Averyanova EV, Shkolnikova MN, Rozhnov ED, Batashov ES. Bioconversion of sea buckthorn meal into physiologically active ingredients. Khimija Rastitelnogo Syrja. 2023;(1):297–305. (In Russ.). https://doi.org/10.14258/jcprm.20230111884; https://elibrary.ru/YKDNFH
4. Razgonova MP, Senotrusova TA, Li NG, Timoschenko EE, Murzina OG, Rusakova EA, *et al.* Aspects of complex processing of far eastern berry crops. Siberian Herald of Agricultural Science. 2023;53(8):15–26. (In Russ.). https://doi.org/10.26898/0370-8799-2023-8-2; https://elibrary.ru/AYWAUO
5. Frolova AS, Fokina AD, Milentyeva IS, Asyakina LK, Proskuryakova LA, Prosekov AYu. The biological active Substances of *Taraxacum officinale* and *Arctium lappa* from the Siberian Federal District. International Journal of Molecular Sciences. 2024;25(6):3263. https://doi.org/10.3390/ijms25063263.
6. Zilfikarov IN, Chelombitko VA, Aliev AM. Medicinal plant materials processed with liquefied gases and supercritical fluids. Pyatigorsk. 2007. 244 p. (In Russ.).
7. Dumitrașcu L, Banu I, Patrașcu L, Vasilean I, Aprodu I. The Influence of Processing on the Bioactive Compounds of Small Berries. Applied Sciences. 2024;14(19):8713. https://doi.org/10.3390/app14198713
8. Nile SH, Park SW. Edible berries: bioactive components and their effect on human health. Nutrition. 2014;30(2):134–144. https://doi.org/10.1016/j.nut.2013.04.007
9. Duda-Chodak A, Tarko T, Satora P, Sroka P. Interaction of dietary compounds, especially polyphenols, with the intestinal microbiota: a review. European Journal of Nutrition. 2015;54:325–341. https://doi.org/10.1007/s00394-015-0852-y
10. Zhu B, Wang X, Li L. Human gut microbiome: the second genome of human body. Protein and Cell. 2010;1(8):718–725. https://doi.org/10.1007/s13238-010-0093-z
11. Lavefve L, Howard LR, Carbonero F. Berry polyphenols metabolism and impact on human gut microbiota and health. Food and Function. 2020;11:45–65. https://doi.org/10.1039/C9FO01634A
12. Plamada D, Vodnar DC. Polyphenols–Gut microbiota interrelationship: A transition to a new generation of prebiotics. Nutrients. 2021;14(1):137. https://doi.org/10.3390/nu14010137
13. Pan L, Ye H, Pi X, Liu W, Wang Z, Zhang Y, *et al.* Effects of several flavonoids on human gut microbiota and its metabolism by *in vitro* simulated fermentation. Frontiers in Microbiology. 2023;14:1092729. https://doi.org/10.3389/fmicb.2023.1092729
14. Perz M, Szymanowska D, Kostrzewa-Susłow E. The Influence of Flavonoids with -Br, -Cl Atoms and -NO_2, -CH_3 Groups on the Growth Kinetics and the Number of Pathogenic and Probiotic Microorganisms. International Journal of Molecular Sciences. 2024;25(17):9269. https://doi.org/10.3390/ijms25179269
15. Meng X, Xia C, Wu H, Gu Q, Li P. Metabolism of quercitrin in the colon and its beneficial regulatory effects on gut microbiota. Journal of the Science of Food and Agriculture. 2024;104(15):9255–9264. https://doi.org/10.1002/jsfa.13747
16. Attri S, Sharma K, Raigond P, Goel G. Colonic fermentation of polyphenolics from Sea buckthorn (*Hippophae rhamnoides*) berries: Assessment of effects on microbial diversity by Principal Component Analysis. Food Research International. 2018;105:324–332. https://doi.org/10.1016/j.foodres.2017.11.032
17. Molan AL, Lila MA, Mawson J, De S. In vitro and in vivo evaluation of the prebiotic activity of water-soluble blueberry extracts. World Journal of Microbiology and Biotechnology. 2009;25:1243–1249. https://doi.org/10.1007/s11274-009-0011-9

18. Lee S, Keirsey KI, Kirkland R, Grunewald ZI, Fischer JG, de La Serre C. B. Blueberry supplementation influences the gut microbiota, inflammation, and insulin resistance in high-fat-diet–fed rats. The Journal of Nutrition. 2018;148(2): 209–219. https://doi.org/10.1093/jn/nxx027

19. Li F, Ming J. Mulberry polyphenols restored both small and large intestinal microflora in *db/db* mice, potentially alleviating type 2 diabetes. Food and Function. 2024;15:8521–8543. https://doi.org/10.1039/D4FO01291G

20. Yuan Y, Zhang X, Pan S, Xu X, Wu T. Effects and Mechanisms of Resveratrol on the Adhesion of *Lactobacillus acidophilus* NCFM. Probiotics and Antimicrobial Proteins. 2023;15:1529–1538. https://doi.org/10.1007/s12602-022-10007-9

21. Celebioglu HU, Delsoglio M, Brix S, Pessione E, Svensson B. Plant Polyphenols Stimulate Adhesion to Intestinal Mucosa and Induce Proteome Changes in the Probiotic *Lactobacillus acidophilus* NCFM. Molecular Nutrition Food Research. 2018;62(4):1700638. https://doi.org/10.1002/mnfr.201700638

22. Bustos I, García-Cayuela T, Hernández-Ledesma B, Peláez C, Requena T, Martínez-Cuesta MC. Effect of flavan-3-ols on the adhesion of potential probiotic lactobacilli to intestinal cells. Journal of Agricultural and Food Chimistry. 2012;60(36):9082–9088. https://doi.org/10.1021/jf301133g

23. Silva S, Costa EM, Oliveira H, Freitas V, Morais RM, Calhau C, *et al*. Impact of a Purified Blueberry Extract on In Vitro Probiotic Mucin-Adhesion and Its Effect on Probiotic/Intestinal Pathogen Systems. Molecules. 2022;27(20):6991. https://doi.org/10.3390/molecules27206991

24. Lorenzo JM, Pateiro M, Domínguez R, Barba FJ, Putnik P, Kovačević DB, *et al.* Berries extracts as natural antioxidants in meat products: A review. Food Research International. 2018;106:1095–1104. https://doi.org/10.1016/j.foodres.2017.12.005

25. Carpenter R, O'Grady MN, O'Callaghan YC, O'Brien NM, Kerry JP. Evaluation of the antioxidant potential of grape seed and bearberry extracts in raw and cooked pork. Meat Science. 2007;76(4):604–610. https://doi.org/10.1016/j.meatsci.2007.01.021

26. Muzolf-Panek M, Waśkiewicz A, Kowalski R, Konieczny P. The effect of blueberries on the oxidative stability of pork meatloaf during chilled storage. Journal of Food Processing and Preservation. 2016;40(5):899–909. https://doi.org/10.1111/jfpp.12668

27. Jia N, Kong B, Liu Q, Diao X, Xia X. Antioxidant activity of black currant (*Ribes nigrum* L.) extract and its inhibitory effect on lipid and protein oxidation of pork patties during chilled storage. Meat Science. 2012;91(4):533–539. https://doi.org/10.1016/j.meatsci.2012.03.010

28. Karwowska M, Dolatowski ZJ. Effect of acid whey and freeze-dried cranberries on lipid oxidation and fatty acid composition of nitrite-/nitrate-free fermented sausage made from deer meat. Asian-Australasian Journal of Animal Sciences. 2017;30(1):85–93. https://doi.org/10.5713/ajas.16.0023

29. Armenteros M, Morcuende D, Ventanas S, Estévez M. Application of natural antioxidants from strawberry tree (*Arbutus unedo* L.) and dog rose (*Rosa canina* L.) to frankfurters subjected to refrigerated storage. Journal of integrative agriculture. 2013;12(11):1972–1981. https://doi.org/10.1016/S2095-3119(13)60635-8

30. Tamkutė L, Vaicekauskaitė R, Melero B, Jaime I, Rovira J, Venskutonis PR. Effects of chokeberry extract isolated with pressurized ethanol from defatted pomace on oxidative stability, quality and sensory characteristics of pork meat products. LWT. 2021;150:111943. https://doi.org/10.1016/j.lwt.2021.111943

31. Das Q, Islam R, Marcone MF, Warriner K, Diarra MS. Potential of berry extracts to control foodborne pathogens. Food Control. 2017;73:650–662. https://doi.org/10.1016/j.foodcont.2016.09.019

32. Khalifa HO, Kamimoto M, Shimamoto T, Shimamoto T. Antimicrobial effects of blueberry, raspberry, and strawberry aqueous extracts and their effects on virulence gene expression in *Vibrio cholerae.* Phytotherapy Research. 2015;29(11):1791–1797. https://doi.org/10.1002/ptr.5436

33. Georgescu C, Frum A, Virchea L-I, Sumacheva A, Shamtsyan M, Cligor F-G, *et al.* Geographic variability of berry phytochemicals with antioxidant and antimicrobial properties. Molecules. 2022;27(15):4986. https://doi.org/10.3390/molecules27154986

34. Fortier MP, Saucier L, Guay F. Effects on microbial quality of fresh pork loin during storage from oregano oil and cranberry pulp diet supplementation in pigs. Canadian Journal of Animal Science. 2012;92(4):465–471. https://doi.org/10.4141/cjas2012-078

35. Menchetti L, Brecchia G, Branciari R, Barbato O, Fioretti B, Codini M, *et al.* The effect of Goji berries (*Lycium barbarum*) dietary supplementation on rabbit meat quality. Meat Science. 2020;161:108018. https://doi.org/10.1016/j.meatsci.2019.108018

36. Castrica M, Menchetti L, Balzaretti CM, Branciari R, Ranucci D, Cotozzolo E, *et al.* Impact of dietary supplementation with goji berries (*Lycium barbarum*) on microbiological quality, physico-chemical, and sensory characteristics of rabbit meat. Foods. 2020;9(10):1480. https://doi.org/10.3390/foods9101480

37. Doriya K, Kumar DS, Thorat BN. A systematic review on fruit-based fermented foods as an approach to improve dietary diversity. Journal of Food Processing and Preservation. 2022;46(11):e16994. https://doi.org/10.1111/jfpp.16994
38. Kamonsuwan K, Balmori V, Marnpae M, Chusak C, Thilavech T, Charoensiddhi S, *et al.* Black Goji Berry (*Lycium ruthenicum*) Juice Fermented with *Lactobacillus rhamnosus* GG Enhances Inhibitory Activity against Dipeptidyl Peptidase-IV and Key Steps of Lipid Digestion and Absorption. Antioxidants. 2024;13(6):740. https://doi.org/10.3390/antiox13060740
39. El-Sohaimy SA, Shehata MG, Mathur A, Darwish AG, Abd El-Aziz NM, Gauba P, *et al.* Nutritional Evaluation of Sea Buckthorn "*Hippophae rhamnoides*" Berries and the Pharmaceutical Potential of the Fermented Juice. Fermentation. 2022;8(8):391. https://doi.org/10.3390/fermentation8080391
40. Markkinen N, Laaksonen O, Nahku R, Kuldjärv R, Yang B. Impact of lactic acid fermentation on acids, sugars, and phenolic compounds in black chokeberry and sea buckthorn juices. Food Chemistry. 2019;286:204–215. https://doi.org/10.1016/j.foodchem.2019.01.189
41. Kwaw E, Ma Y, Tchabo W, Apaliya MT, Wu M, Sackey AS, *et al.* Effect of lactobacillus strains on phenolic profile, color attributes and antioxidant activities of lactic-acid-fermented mulberry juice. Food Chemistry. 2018;250:148–154. https://doi.org/10.1016/j.foodchem.2018.01.009
42. Manganaris GA, Goulas V, Vicente AR, Terry LA. Berry antioxidants: Small fruits providing large benefits. Journal of the Science of Food and Agriculture. 2014;94(5):825–833. https://doi.org/10.1002/jsfa.6432
43. Zhu C, Liu G, Gu X, Zhang T, Xia A, Zheng Y, *et al.* Effects of Quercetin on the Intestinal Microflora of Freshwater Dark Sleeper *Odontobutis potamophila.* Antioxidants. 2022;11(10):2015. https://doi.org/10.3390/antiox11102015
44. Cui K, Wang Q, Wang S, Diao Q, Zhang N. The Facilitating Effect of Tartary Buckwheat Flavonoids and *Lactobacillus plantarum* on the Growth Performance, Nutrient Digestibility, Antioxidant Capacity, and Fecal Microbiota of Weaned Piglets. Animals. 2019;9(11):986. https://doi.org/10.3390/ani9110986
45. Dai H, Huang Z, Shi F, Li S, Zhang Y, Wu H, *et al.* Effects of maternal hawthorn-leaf flavonoid supplementation on the intestinal development of offspring chicks. Poultry Science. 2024;103(9):103969. https://doi.org/10.1016/j.psj.2024.103969
46. Kafarov VV, Dorokhov IN. Systems analysis of chemical engineering processes: Fundamental strategy. Moscow: Yurayt. 2018. 499 p. (In Russ.). https://elibrary.ru/ZCYHSC
47. Gumerov FM, Yarullin LY, Hung TN, Gabitov FR, Kayumova VA. Sub- and supercritical fluid media in food, perfume, and pharmacy. Herald of Technological University. 2017;20(8):30–35. (In Russ.). https://elibrary.ru/YLFXJH
48. Mazzutti S, Pedrosa RC, Ferreira SRS. Green processes in foodomics. Supercritical fluid extraction of bioactives. In: Cifuentes A, editor. Comprehensive Foodomics. Elsevier; 2021. pp. 725–743. https://doi.org/10.1016/B978-0-08-100596-5.22816-3
49. Gallego R, Bueno M, Herrero M. Sub-and supercritical fluid extraction of bioactive compounds from plants, food-by-products, seaweeds and microalgae – An update. TrAC Trends in Analytical Chemistry. 2019;116:198–213. https://doi.org/10.1016/j.trac.2019.04.030
50. Waters: official website [Internet]. [cited 2024 Jul 14]. Available from: https://waters.com/
51. Rexo Engineering: official website [Internet]. [cited 2024 Jul 14]. Available from: https://rexo.co.kr/en/product
52. Sapkale GN, Patil SM, Surwase US, Bhatbhage PK. Supercritical fluid extraction. International Journal of Chemical Sciences. 2010;8(2):729–743.
53. Arumugham T, Rambabu K, Hasan SW, Show PL, Rinklebe J, Banat F. Supercritical carbon dioxide extraction of plant phytochemicals for biological and environmental applications – A review. Chemosphere. 2021;271:129525. https://doi.org/10.1016/j.chemosphere.2020.129525
54. Zaharil HA. An investigation on the usage of different supercritical fluids in parabolic trough solar collector. Renewable Energy. 2021;168:676–691. https://doi.org/10.1016/j.renene.2020.12.090
55. Menshutina NV, Kazeev IV, Artemiev AI, Bocharova OA, Khudeev II. Application of supercritical extraction for isolation of chemical compounds. ChemChemTech. 2021;64(6):4–19. (In Russ.). https://doi.org/10.6060/ivkkt.20216406.6405
56. Griffiths MW, Walkling-Ribeiro M. Pulsed electric field processing of liquid foods and beverages. In: Sun D-W, editor. Emerging technologies for food processing. Academic Press; 2014. pp. 115–145. https://doi.org/10.1016/B978-0-12-411479-1.00007-3
57. Rombaut N, Savoire R, Thomasset B, Bélliard T, Castello J, Van Hecke É, *et al*. Grape seed oil extraction: Interest of supercritical fluid extraction and gas-assisted mechanical extraction for enhancing polyphenol co-extraction in oil. Comptes Rendus Chimie. 2014;17(3):284–292. https://doi.org/10.1016/j.crci.2013.11.014

58. Avilés-Betanzos KA, Scampicchio M, Ferrentino G, Ramírez-Sucre MO, Rodríguez-Buenfil IM. *Capsicum chinense* Polyphenols Extraction by Supercritical Fluids Using Response Surface Methodology (RSM). Processes. 2023;11(7):2055. https://doi.org/10.3390/pr11072055
59. Vinitha UG, Sathasivam R, Muthuraman MS, Park SU. Intensification of supercritical fluid in the extraction of flavonoids: A comprehensive review. Physiological and Molecular Plant Pathology. 2022;118:101815. https://doi.org/10.1016/j.pmpp.2022.101815
60. Panja P. Green extraction methods of food polyphenols from vegetable materials. Current Opinion in Food Science. 2918;*23*:173–182. https://doi.org/10.1016/j.cofs.2017.11.012
61. Lee YH, Charles AL, Kung HF, Ho CT, Huang TC. Extraction of nobiletin and tangeretin from *Citrus depressa* Hayata by supercritical carbon dioxide with ethanol as modifier. Industrial Crops and Products. 2010;31(1):59–64. https://doi.org/10.1016/j.indcrop.2009.09.003
62. Mohamed M, Mahmood, Daud WRW, Markom M. Cosolvent selection for supercritical fluid extraction (SFE) of bioactive compounds from *Orthosiphon stamineus*. Sains Malaysiana. 2018;47(8):1741–1747. https://doi.org/10.17576/jsm-2018-4708-13
63. Ekinci MS. Supercritical fluid extraction of quercetin from sumac (*Rhus coriaria* L.): effects of supercritical extraction parameters. Separation Science and Technology. 2022;57(2):256–262. https://doi.org/10.1080/01496395.2021.1893333
64. Bimakr M, Rahman RA, Ganjloo A, Taip FS, Salleh LM, Sarker MZI. Optimization of supercritical carbon dioxide extraction of bioactive flavonoid compounds from spearmint (*Mentha spicata* L.) leaves by using response surface methodology. Food and Bioprocess Technology. 2012;*5*:912–920. https://doi.org/10.1007/s11947-010-0504-4
65. Ghosh S, Chatterjee D, Das S, Bhattacharjee P. Supercritical carbon dioxide extraction of eugenol-rich fraction from *Ocimum sanctum* Linn and a comparative evaluation with other extraction techniques: process optimization and phytochemical characterization. Industrial Crops and Products. 2013;47:78–85. https://doi.org/10.1016/j.indcrop.2013.02.030
66. Da Porto C, Natolino A. Supercritical fluid extraction of polyphenols from grape seed (*Vitis vinifera*): Study on process variables and kinetics. The Journal of Supercritical Fluids. 2017;130:239–245. https://doi.org/10.1016/j.supflu.2017.02.013
67. Fachri BA, Sari P, Yuwanti S, Subroto E. Experimental study and modeling on supercritical CO_2 extraction of Indonesian raw propolis using response surface method: Influence of pressure, temperature and CO_2 mass flowrate on extraction yield. Chemical Engineering Research and Design. 2020;153:452–462. https://doi.org/10.1016/j.cherd.2019.11.014
68. Moges A, Barik CR, Sahoo L, Goud VV. Optimization of polyphenol extraction from *Hippophae salicifolia* D. Don leaf using supercritical CO_2 by response surface methodology. 3 Biotech. 2020;12:292. https://doi.org/10.1007/s13205-022-03358-1
69. Shirsath SR, Sonawane SH, Gogate PR. Intensification of extraction of natural products using ultrasonic irradiations–A review of current status. Chemical Engineering and Processing: Process Intensification. 2012;53:10–23. https://doi.org/10.1016/j.cep.2012.01.003
70. Balachandran S, Kentish SE, Mawson R, Ashokkumar M. Ultrasonic enhancement of the supercritical extraction from ginger. Ultrasonics Sonochemistry. 2006;13(6):471–479. https://doi.org/10.1016/j.ultsonch.2005.11.006
71. Yang Y-C, Wang C-S, Wei M-C. Kinetics and mass transfer considerations for an ultrasound-assisted supercritical CO_2 procedure to produce extracts enriched in flavonoids from *Scutellaria barbata*. Journal of CO_2 Utilization. 2019;32:219–231. https://doi.org/10.1016/j.jcou.2019.04.008
72. Ćurko N, Lukić K, Tušek AJ, Balbino S, Pavičić TV, Tomašević M, *et al.* Effect of cold pressing and supercritical CO_2 extraction assisted with pulsed electric fields pretreatment on grape seed oil yield, composition and antioxidant characteristics. LWT. 2023;184:114974. https://doi.org/10.1016/j.lwt.2023.114974
73. Salgado-Ramos M, Martí-Quijal FJ, Huertas-Alonso AJ, Sánchez-Verdú MP, Cravotto G, Moreno A, *et al.* Sequential extraction of almond hull biomass with pulsed electric fields (PEF) and supercritical CO_2 for the recovery of lipids, carbohydrates and antioxidants. Food and Bioproducts Processing. 2023;139:216–226. https://doi.org/10.1016/j.fbp.2023.04.003
74. Bogolitsin KG, Druzhinina AS, Ovchinnikov DV, Parshina AE, Shulgina EV, Turova PN. Polyphenols of brown algae. Khimija Rastitelnogo Syrja. 2018;(3):5–21. (In Russ.). https://doi.org/10.14258/jcprm.2018031898; https://elibrary.ru/YABURN
75. Mushtaq M, Sultana B, Akram S, Anwar F, Adnan A, Rizvi SS. Enzyme-assisted supercritical fluid extraction: An alternative and green technology for non-extractable polyphenols. Analytical and Bioanalytical Chemistry. 2017;409:3645–3655. https://doi.org/10.1007/s00216-017-0309-7

76. Lenucci MS, De Caroli M, Marrese PP, Iurlaro A, Rescio L, Böhm V, *et al*. Enzyme-aided extraction of lycopene from high-pigment tomato cultivars by supercritical carbon dioxide. Food Chemistry. 2015;170:193–202. https://doi.org/10.1016/j.foodchem.2014.08.081
77. Kraujalis P, Kraujalienė V, Kazernavičiūtė R, Venskutonis PR. Supercritical carbon dioxide and pressurized liquid extraction of valuable ingredients from *Viburnum opulus* pomace and berries and evaluation of product characteristics. The Journal of Supercritical Fluids. 2017;122:99–108. https://doi.org/10.1016/j.supflu.2016.12.008
78. Ko M-J, Kwon H-L, Chung M-S. Pilot-scale subcritical water extraction of flavonoids from satsuma mandarin (*Citrus unshiu* Markovich) peel. Innovative Food Science and Emerging Technologies. 2016;38:175–181. https://doi.org/10.1016/j.ifset.2016.10.008
79. Kueh BWB, Yusup S, Osman N. Supercritical carbon dioxide extraction of *Melaleuca cajuputi* leaves for herbicides allelopathy: Optimization and kinetics modelling. Journal of CO2 Utilization. 2018;24:220–227. https://doi.org/10.1016/j.jcou.2018.01.005
80. Bendif H, Adouni K, Miara MD, Baranauskienė R, Kraujalis P, Venskutonis PR, *et al.* Essential oils (EOs), pressurized liquid extracts (PLE) and carbon dioxide supercritical fluid extracts (SFE-CO_2) from Algerian *Thymus munbyanus* as valuable sources of antioxidants to be used on an industrial level. Food Chemistry. 2018;260:289–298. https://doi.org/10.1016/j.foodchem.2018.03.108
81. Bayrak S, Sökmen M, Aytac E, Sökmen A. Conventional and supercritical fluid extraction (SFE) of colchicine from *Colchicum speciosum.* Industrial Crops and Products. 2019;128:80–84. https://doi.org/10.1016/j.indcrop.2018.10.060
82. Wang H-C, Chen C-R, Chang CJ. Carbon dioxide extraction of ginseng root hair oil and ginsenosides. Food Chemistry. 2001;72(4):505–509. https://doi.org/10.1016/S0308-8146(00)00259-4
83. Mora JJ, Tavares HM, Curbelo R, Dellacassa E, Cassel E, Apel MA, *et al.* Supercritical fluid extraction of coumarins and flavonoids from citrus peel. The Journal of Supercritical Fluids. 2025;215:106396. https://doi.org/10.1016/j.supflu.2024.106396
84. Atwi-Ghaddar S, Destandau E, Lesellier E. Optimization of supercritical fluid extraction of polar flavonoids from *Robinia pseudoacacia* L. heartwood. Journal of CO2 Utilization. 2023;70:102440. https://doi.org/10.1016/j.jcou.2023.102440
85. Hu Y, Yang L, Liang Z, Chen J, Zhao M, Tang Q. Comparative analysis of flavonoids extracted from *Dendrobium chrysotoxum* flowers by supercritical fluid extraction and ultrasonic cold extraction. Sustainable Chemistry and Pharmacy. 2023;36:101267. https://doi.org/10.1016/j.scp.2023.101267
86. Wang L, Yang B, Du X, Yi C. Optimisation of supercritical fluid extraction of flavonoids from *Pueraria lobata*. Food chemistry. 2008;108(2):737–741. https://doi.org/10.1016/j.foodchem.2007.11.031
87. Ouédraogo JCW, Dicko C, Kini FB, Bonzi-Coulibaly YL, Dey ES. Enhanced extraction of flavonoids from *Odontonema strictum* leaves with antioxidant activity using supercritical carbon dioxide fluid combined with ethanol. The Journal of Supercritical Fluids. 2018;131:66–71. https://doi.org/10.1016/j.supflu.2017.08.017
88. Song L, Liu P, Yan Y, Huang Y, Bai B, Hou X, *et al.* Supercritical CO_2 fluid extraction of flavonoid compounds from Xinjiang jujube (*Ziziphus jujuba Mill*.) leaves and associated biological activities and flavonoid compositions. Industrial Crops and Products. 2019;139:111508. https://doi.org/10.1016/j.indcrop.2019.111508
89. Laurintino TKS, Laurintino TNS, Tramontin DP, Cruz AB, Paiva DW, Bolzan A, *et al.* Ultrasound pretreatment combined with supercritical CO_2 extraction of *Costus spicatus* leaf extract. The Journal of Supercritical Fluids. 2024;213:106372. https://doi.org/10.1016/j.supflu.2024.106372

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