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Review Article

Bioactivity, Bioavailability and Bioaccessibility of Blackcurrant Anthocyanins: An Updated Comprehensive Review

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Abstract

Blackcurrant-based products are trending worldwide as potential functional foods consumed for diseases prevention. Blackcurrant is recognized as its abundant sources of bioactive compounds and dietary fiber. The phenolic compounds, especially proanthocyanins and anthocyanins existing in blackcurrant berry fruit, have been extensively studied by the scientific community for their various medicinal values. The benefits of the anthocyanins are associated with their free-radical scavenging capacity. Anthocyanins must be available or removed from the blackcurrant matrix and then bioaccessible in the gastrointestinal system and must pass through metabolism to the targeted tissue for this capability in humans or animals. This review was focused on the anthocyanin metabolism from the blackcurrant, including the bioavailability, bioaccessibility, and bioactivity, by summarizing factors affecting phytochemical profiles of blackcurrant-based products, including growing and processing and biokinetics of blackcurrant anthocyanins. Assessment of bioaccessibility and bioavailability of blackcurrant anthocyanin is important for understanding its limitations on absorption and functions of blackcurrant anthocyanin towards human nutrition.

Keywords: Anthocyanin; Bioavailability; Blackcurrant; Phenolic Compounds; Functional Foods

Introduction

Traditionally, blackcurrant is used as a natural food colorant and dye due to its high level of colored pigments content and is even used as medicine to treat various diseases [117]. Commercially, blackcurrant is grown mainly for juice production, and an increasing number of blackcurrant-containing products are available on the market [69]. The obtained blackcurrant juice or juice concentrate is abundant in polyphenols, especially proanthocyanins and anthocyanins [26]. The juice-producing byproduct (pomace) is known as an affluent source of bioactive compounds and dietary fiber [5,78,89,121,116]. The phenolic compounds, especially proanthocyanins and anthocyanins existing in blackcurrant berry fruit, have been extensively studied by the scientific community for their various medicinal values, such as antioxidant activity [55,72,73,114,129], anti-inflammatory activity [12,65,74,90,101,106,122], neuroprotective actions [38,115,123,127,146,147,148], anti-obesity properties [10,24,50,58,64,61,60,75,107,128,], anti-cancer properties [33,76,80,95,96,105], indicating that blackcurrant can be used as a potential pharmaceutical ingredient [100]. Blackcurrant-based products are trending worldwide as potential functional foods consumed to prevent diseases [26].

Anthocyanin is the main responsible compound in blackcurrant to have potential health benefits. The compound is biologically and pharmacologically capable of being antimicrobials, reducing oxidative stress, and counteracting the development of numerous non-communicable illnesses, according to *in vitro*, animal, and clinical studies [85]. The beneficial health of the anthocyanins is also associated with their free-radical scavenging capacity. Anthocyanins need to be available or extracted from the blackcurrant matrix and then become bioaccessible in the gastrointestinal system, extending into the target tissue to have this capacity in humans or animals [37]. These processes are called bioaccessibility and bioavailability of anthocyanins.

The assessment of bioaccessibility and bioavailability is important for understanding of the relationship between food and nutrition [85]. Therefore, this review focused on the anthocyanin metabolism from the blackcurrant, including bioavailability, bioaccessibility and bioactivity, by summarizing factors affecting phytochemical profiles of blackcurrant-based products, including growing and processing and biokinetic of blackcurrant anthocyanins. Development of blackcurrant-based ingredients and food products and their future potential applications were also be reviewed. Understanding this mechanism is important to enhance the efficacy of compounds from various processed products of blackcurrant.

Chemical profiles of blackcurrant

Bioactive profiles of blackcurrant berry, juice (concentrate) or extracts, and pomace

The product tree of the blackcurrant products and their processing has been shown in figure 1. Blackcurrants can be processed to be a variety of berry products, e.g., juice [53], extract [23,135], juice fortified [139], polyphenol-rich drink [19], polyphenol nectars [24].

The processed products with the content of anthocyanin, polyphenols and ascorbic acid are described to have potential health benefits, as overviewed in table 1. Products processed in juice, drink and nectars have polyphenols and ascorbic acid as the effective compounds on the health benefits, e.g., anti-atherosclerosis [53]and hypoglycemic response [138]. The intake of black currant juice with high ascorbic acid content and free radical-scavenging capacity in plasma enhances the state of postprandial antioxidant [53] in addition to postprandial glycemic control [138]. The polyphenol intake reduces the postprandial glycemic associated with intestinal glucose inhibition [19]. The inhibition of intestinal absorption of glucose is also found in the blackcurrant nectars containing high polyphenols [138]. Furthermore, in the blackcurrant extract, anthocyanins play role in the main benefits of blackcurrant consumption for cardiovascular protection, cognitive performance, repairment of endothelial dysfunction, and fat oxidation increase. Cook., *et al.* [24] reported that cardiovascular responses, muscle oxygen saturation, muscle activity were modified and enhanced fat oxidation with the anthocyanin during a cycle of 120 minutes at 65% CO_2 max in endurance-trained male cyclists, following ingestion of blackcurrant extracts for 7 days. Consumption of blackcurrant extracts improves cognitive performance and mood as the anthocyanin substantially alters the neuroendocrinological and cognitive benefits conveyed [146]. Besides the clinical report, few studies reported that the blackcurrant extracts have benefits on sport performance, as shown in table 2. The anthocyanin improves team sports performance with repeated maximal sprints [149], the sprint performance of football players [45], exercise performance [23], the overall performance of cycling [94] and climbing performance [113]. The consumption of blackcurrant extract influences physiological responses and does not have detrimental side effects [113].

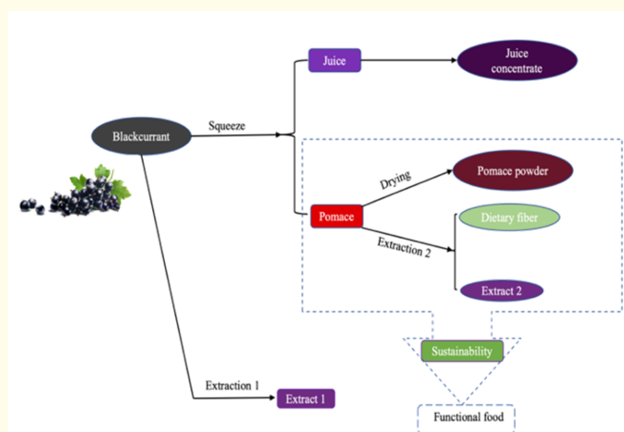

Figure 1: The diagram of blackcurrant processing.

Main benefits	Materials	Effective factors	Main methodologies	Conclusions	Reference
Anti-atherosclerosis	blackcurrant (BC) juice	Polyphenols and ascorbic acid	In human subjects with an atherosclerosis-prone phenotype (after consumption of a high-energy meal).	Blackcurrant juice consumption may improve postprandial antioxidant status as indicated by higher ascorbic acid levels and free radical-scavenging capacity in plasma.	Huebbe., *et al.* [53]
Cardiovascular protection	blackcurrant extract	Anthocyanins	Cardiovascular function (i.e., blood pressure, heart rate, ejection time, cardiac output, stroke volume, and total peripheral resistance) during supine rest was examined	7-days intake of New Zealand blackcurrant extract demonstrated dose-dependent changes on some cardiovascular parameters during supine rest in endurance-trained male cyclists.	Cook., *et al.* [22]
	blackcurrant extract	Anthocyanins	The effect of 7-day intake of New Zealand blackcurrant extract on arterial functions, e.g., arterial stiffness, and serum lipids.	Short-term New Zealand blackcurrant intake reduces central arterial stiffness and central blood pressure in older adults. Anthocyanin-rich blackcurrants might be beneficial for maintaining or improving cardiovascular health as an alternative to pharmaceutical medications.	Okamoto., *et al.* [102]
Cognitive performance	blackcurrant extract	Anthocyanins	The effects of two blackcurrant extracts on cognitive outcomes, mood, autonomic measures, peripheral and central monoamine tone, and anthocyanin bioavailability to plasma.	A cognitive benefit of acute blackcurrant supplementation in healthy young humans and the first description of a clinically significant inhibition of monoamine oxidase-B and monoamine oxidase-A using a commonly consumed fruit. Compounds other than anthocyanins may be responsible for the observed *in vivo* monoamine oxidase inhibition and that the degree of processing and the cultivar of blackcurrant fruit used substantially alter the neuroendocrinological and cognitive benefits conveyed.	Watson., *et al.* [146]
	blackcurrant anthocyanins	Anthocyanins	The changes of IGF-1 before and after the supplementation	The blackcurrant anthocyanin has the potential to be developed to treat neurological conditions with IGF-1 deficiency.	Fan., *et al.* [38]
	blackcurrant extract	Anthocyanins	The influence of the acute administration of anthocyanin-rich blackcurrant juice, standardized at 500 mg of polyphenols, on mood and attention	Highlighting an anxiolytic effect of the consumption of a single serve blackcurrant juice, and an indication of greater alertness and lower fatigue in healthy young adults. These changes did not improve cognitive performance and slowed responses in the choice reaction time task	Watson., *et al.* [147]

Main benefits	Materials	Effective factors	Main methodologies	Conclusions	Reference
Hypoglycemic response	A basic blackcurrant juice and a blackcurrant juice fortified with crowberry powder	Bioactive polyphenols	Evaluate postprandial glycemic responses to a basic blackcurrant juice and a blackcurrant juice fortified with crowberry powder (respective polyphenol contents 159 and 293 mg/100 mL), both sweetened with sucrose.	Fortification of blackcurrant juice with crowberry doubled the polyphenol content and improved postprandial glycemic control in healthy subjects.	Torronen., *et al.* [140]
	Blackcurrant	Anthocyanins	Determine the dose dependent effects of blackcurrant extract on postprandial glycemia.	Consumption of blackcurrant extract in amounts roughly equivalent to 100 g of blackcurrants reduced postprandial glycemia, insulinemia and incretin secretion.	Castro-Acosta., *et al.* [18]
	Apple and blackcurrant polyphenol-rich drinks	Combinations of polyphenols may be particularly effective through complementary mechanisms	A randomized, controlled, double-blinded cross-over trial was conducted in healthy volunteers.	Ingestion of apple and blackcurrant polyphenols decreased postprandial glycemia, which may be partly related to inhibition of intestinal glucose transport.	Castro-Acosta., *et al.* [20]
	Blackcurrant nectars	Polyphenols	A total of 18 healthy volunteers participated in a randomized, controlled, cross-over study. Blood samples were collected at fasting and six times postprandially during 120 min.	The attenuated glycemic response after the blackcurrant nectar may be explained by inhibition of intestinal absorption of glucose by blackcurrant anthocyanins.	Torronen., *et al.* [137]
	Blackcurrant nectars	Polyphenols	The effects of daily New Zealand blackcurrant intake over 7 days on fasting glucose and insulin levels and the responses of glucose and insulin during an oral glucose tolerance test.	A trend for lower fasting insulin with normal glucose and lower areas under the curve for glucose and insulin suggests that repeated intake of New Zealand blackcurrant powder increased insulin sensitivity. Regular intake of New Zealand blackcurrant powder may be beneficial for the postprandial responses in people with type 2 diabetes or metabolic syndrome.	Willems., *et al.* [151]

	Blackcurrant extract	Anthocyanins	25 overweight (BMI > 25) sedentary individuals participated in a double-blinded, randomized controlled trials	Repeated intake, rather than a single dose of New Zealand blackcurrant extract, was required to induce beneficial effects on insulin sensitivity and postprandial glucose handling in individuals with overweight or obesity. Continuous glucose monitoring enabled an effect of New Zealand blackcurrant extract to be observed under free-living conditions and highlighted the potential of anthocyanin-rich supplements as a viable strategy to reduce insulin resistance.	Nolan., *et al.* [98]

Table 1: Clinical report.

Sport	Materials	Effective factors	Conclusions	Reference
Undefined sports	Blackcurrant extract	Anthocyanins	The present study provided insight into the potential mechanisms for enhanced exercise performance with intake of blackcurrant.	Cook., *et al.* [25]
Football	Blackcurrant extract	Anthocyanins	New Zealand blackcurrant extract seemed to benefit repeated sprint performance only in trained football players.	Godwin., *et al.* [44]
Cycling	Blackcurrant extract	Anthocyanins	New Zealand blackcurrant extract seemed to be beneficial in repeated short distance cycling time trials for overall performance.	Murphy., *et al.* [93]
Cycling	Blackcurrant extract	Anthocyanins	Intake of New Zealand blackcurrant extract for 7 days elevated resting concentrations of plasma glycerol, indicative of higher lipolytic rates. This may underpin the observed increase in fat oxidation during prolonged cycling in endurance-trained females.	Strauss., *et al.* [128]
Exercise	Blackcurrant extract	Anthocyanins	This study provided data to underpin a larger study designed to evaluate the efficacy of timed blackcurrant anthocyanins consumption on post-exercise recovery and innate immunity.	Hurst., *et al.* [55]
Cycling	Blackcurrant extract	Anthocyanins	7 days intake of New Zealand blackcurrant extract does not change exercise-induced metabolic responses and 16.1 km cycling time trial performance for moderately endurance-trained men in normobaric hypoxia.	Willems., *et al.* [150]

Exercise	Blackcurrant extract	Anthocyanins	Blackcurrant had a small, but significant, effect on sport performance, with no known detrimental side effects.	Braakhuis., *et al.* [13]
Exercise	Blackcurrant extract	Anthocyanins	Daily consumption of blackcurrant anthocyanins for 5 weeks served to enhance the exercise recovery effectiveness of a single consumption of blackcurrant anthocyanins and promoted beneficial/protective antioxidant/anti-inflammatory cellular events that facilitated exercise recovery.	Hurst., *et al.* [56]
Climbing	Blackcurrant extract	Anthocyanins	Blackcurrant anthocyanin-derived metabolites seemed to affect physiological responses that facilitate sport climbing performance.	Potter., *et al.* [113]

TABLE 2: Blackcurrant anthocyanins for exercise.

Blackcurrants contain different compositions of anthocyanin and therefore generate possible biological and metabolic impacts [65]. The chemical profiles and functionality of blackcurrant juice (concentrate) and pomace are mainly decided at blackcurrant growing stages and processing strategies.

The intrinsic chemical compositions profiles (vitamins, minerals, and polyphenols) of blackcurrant berry fruits depends on various factors at the growing stage, including, most importantly, genotypes [1,59,84,100,126,134,103], geographical conditions [84,134,155], whether conditions [2]. For instance, blackcurrant cultivars in New Zealand have about 1.5 times more anthocyanins due to their exposure to UV light. Interestingly, Khoo., *et al.* [63] found that the application of pesticide treatment impacted the phytochemical profiles of blackcurrant berry fruits. Piechowiak, Balawejder [112] reported that ozonation treatment could change the total phenolic content of blackcurrant berry fruit after exposure at different concentrations for a specific duration.

For all the blackcurrant-containing products, their chemical components are affected by different processing strategies. Enzyme treatment [68], high-pressure treatment [141], microwave treatment [89], ozonation treatment [112], pulse electric field treatment [42], supercritical carbon dioxide extraction [7], and ultra sound treatment [41], in singular or in combination [7,8,118], were reported as promising strategies to improve the rate of juice or the recovery of the bioactive compounds from the matrix.

Additionally, solvents applied for extraction, and providing acidic conditions were decisive factors for the chemical components and extracts stability [4,40,72,100,117]. Nour., *et al.* [100] compared the effects of the different ratio (40%, 60%, and 90%) of organic solvent (ethanol) on the blackcurrant anthocyanins extraction rates and concluded that 60% was of the highest number in terms of the concentration of the four major anthocyanins. Lee., *et al.* [72] reported that ethanol was favored than methanol to extract anthocyanins from blackcurrant. For the stability of anthocyanins, it is important to control the pH (acidic condition). The low stability of anthocyanins in pasteurized juice and frozen pulp causes a difficulty when the juice is being stored due to pigment degradation [31]. The reduction of the pigment degradation can be prevented with the addition of anthocyanin co-factors [14] and the presence of ascorbic acid [43,77]. The stabilization of the anthocyanin pigments with pH control needs to be taken into consideration to prevent discoloration and pigment degradation during manufacturing the blackcurrant berries concentrate.

Unfavorable existence of bitterness and astringency, and sugar addition

Blackcurrants are known for their characteristic bitter and astringent flavor, which is associated with proanthocyanins and anthocyanins [70]. Blackcurrants with substantial quantity of added sugar are often found with pectinolytic enzyme treatments, which increased the perception of bitterness and astringency. The enzymes additionally enhance the average degree of proanthocyanins polymerization [70], while greater levels of proanthocyanins were undesirable owing to their taste. Liu., *et al.* [79] reported the direct binding of proanthocyanins to oral epithelial cells *in vitro*. This binding occurs more intensively at higher concentrations, lower pH, and a higher temperature.

Furthermore, the addition of sugar to the blackcurrant juice influences the perception of the consumers in terms of acidity. Laaksonen., *et al.* [70] reported the most abundant sugars in the blackcurrant juices are fructose and glucose, and the degradation of sugars was caused by enzymatic treatment. On the other hand, the enzyme-aided juices contain more citric acid, which dominates the acid content in the juices, followed by malic and quinic acids with minor contents, than the non-enzymatic juices. These issues lead to companies concern about gaining health-conscious consumers' attention. In relation to consumer health and liking, therefore, it is important to consider those factors by manipulating the enzymes added during the processing as this compound also has more benefits for the health of consumers.

Anthocyanins, anthocyanidins, and proanthocyanidins

Blackcurrant has a high concentration of flavonoids, in particular anthocyanins, which give a purple color for the blackcurrant [4]. Anthocyanins are a group of water-soluble polyphenols with glycosides, while anthocyanidins are sugar free counterparts of anthocyanins [99]. The edible parts of the fruits include six main anthocyanidins, namely cyanidin (50%), pelargonidin (12%), peonidin (12%), delphinidin (12%), petunidin (7%), and malvidin (7%) [66]. The anthocyanin properties vary depending on the type of berry. The majority of anthocyanidins found in blackcurrant berry fruit are cyanidin and delphinidin, which are glycosylated with glucose or rutinoside during the process of ripening, resulting in the formation of the four major anthocyanins, namely delphinidin 3-O-rutinoside (D3R), delphinidin 3-O-glucoside (D3G), cyanidin 3-O-glucoside (C3G), and cyanidin 3-O-rutinoside (C3R), accounting for approximately 90% of blackcurrant total polyphenols content [110]. Figure 2 shows the molecular structures of the four main blackcurrant anthocyanin. This categorization relies on the hydroxyl and methoxyl groups' number and position on the flavanic nucleus. The bulk of anthocyanins are obviously found in rutinoside forms of delphinidin and cyanidin [110]. Proanthocyanidins, often referred to as condensed tannins, are also an important polyphenolic component in the blackcurrants [125].

Anthocyanins have monomeric flavan-3-ols units as common structural units and can be found as oligomers or polymers. The monomers are commonly (+)-catechin or (-)-epicatechin (referred to procyanidins) or (+) -gallocatechin or (-)-epigallocatechin (prodelphinidins). Proanthocyanidin monomers and oligomers are sometimes referred to catechins. The component is characterized as having biochemical and pharmacological actions "pleiotropically", including antioxidant, anti-inflammatory, immune-stimulative, anti-apoptotic, cell cycle arrest inducing, anti-invasive, and anti- angiogenic properties through modulation of multiple signal transduction pathways [29,92].

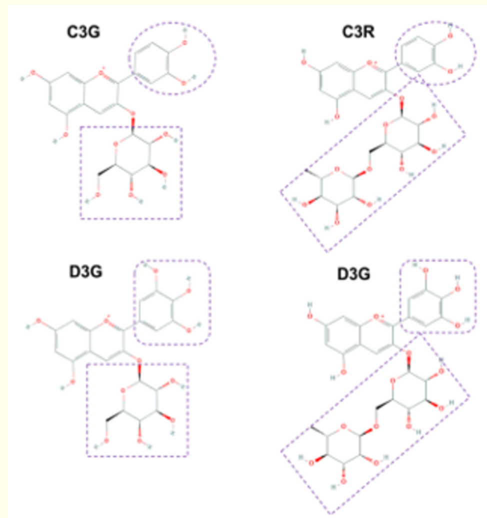

Figure 2: The molecular structures of the four main blackcurrant anthocyanins. Delphinidin 3-O-rutinoside (D3R), Delphinidin 3-O-glucoside (D3G), Cyanidin 3-O-glucoside (C3G), Cyanidin 3-O-rutinoside (C3R).

The main phytochemicals in the blackcurrant are these anthocyanins and proanthocyanidins [47], which are effective to be antioxidants [145]. These two classes of flavonoids represent a large part of the total flavonoids consumed in Western foods and have a nutrition and medical interest of their potential protective effects against diseases [145]. The average daily consumption of anthocyanins in the United States is estimated to be ~200 mg per person, and the average consumption of proanthocyanidins in the United States is estimated to be 58 mg/day [47].

Enzymatic treatments are often employed in the manufacture of juice, particularly in the processing of blackcurrant juices as the juice produces up to 91% [69]. These treatments also reduce the viscosity of the juice, and enhance bioactive components extraction, such as phenolics. Procyanidins and prodelphinindins in enzymatic maceration are significantly greater with than maceration without enzymes. One potential reason is that the bioactive compounds trapped in the pectin networks are extracted with the enzyme effects.

Naturally hydrophilic anthocyanins have limited potential in foods and cosmetics that include fats or oils. Artificial structure alter hydrophilicity by increasing lipophilicity, making them preferable for lipid-based foods and cosmetics [4,154]. Further studies on t bioactivity alteration are required.

Biokinetic of blackcurrant anthocyanins - from *in vitro* bioaccessibility to *in vivo* bioavailability

Bioaccessibility along with bioavailability are two related but often misunderstood concepts. Bioaccessibility is commonly used to evaluate the amount of nutrient or compound available for absorption after undergoing the digestion process, while bioavailability is the proportion of the nutrient or compound which, after being metabolized and distributed via tissues, reaches the systemic circulation and exerts its effect [3,46]. Thus, *in vitro* simulated gastric intestinal models evaluate bioaccessibility, whereas bioavailability is valued through *in vivo* studies.

The key issue in investigating the bioavailability of food biocomponents and pharmaceuticals is assessing methods for the three major bioavailability limiting factors: bioaccessibility, absorption, and biomolecule transformation [34]. Variability is considerable between *in vitro* studies obtained from different methodologies, highlighting the need for standardization. The *in vitro* methodologies can determine the bioavailability and bioaccessibility of bioactive compounds (simulated gastrointestinal digestion), ex-vivo methodologies (under controlled laboratory conditions, gastrointestinal organs), in-situ methodologies (intestinal perfusion in animals), and *in vivo* methodologies (studies of humans and animals) [17]. Although *in vitro* digestion methodologies are most frequently used, *in vitro* methods have low accuracy compared to *in vivo* methods because the differences between the biological and actual biological processes in the human body have different conditions. For full measurement of absorption, distribution, metabolism, and excretion of bioactive substances into the human body, *in vitro* conditions are not accessible, while conditions *in vivo* tests have biological mechanisms similar to the human body [109]. The *in vivo* tests are known as initial and most effective tests performed on humans and animals, and are considered as "gold standard" for the assessment of the adsorption, distribution, metabolism, excretion, and toxicity (ADMET) processes.

In order to investigate the bioavailability and potential health impacts of phenolic compounds, in particular anthocyanins, their absorption, metabolism, tissue distribution and excretion, as well as their biochemical activities and interactions with other nutrients are essential to be assessed.

Bioavailability, absorption, and metabolism

It is arguable in several studies that anthocyanins are absorbed but their absorption rate is depending on their chemical structure, by the dose ingested/administered, and by the food source matrix, one of the main variables impacting stability of anthocyanins. The bioavailability of anthocyanins to absorb the intestines is quite difficult and changes according to processing circumstances and interaction with other compounds, chemical status of the nutrient, release from the food matrix, the food suppressors or co-factor composition, the formation of stable, gradually metabolizing complexes [109]. Mazza., *et al.* [87] discovered that the human body's absorption of anthocyanin was studied after of a high fat diet was consumed with the ground freeze-dried blueberry in which 75% of the anthocyanins were identified in blood serum and the presence of them is linked with the rise in serum antioxidant capacity. This study indicates that the anthocyanin can be absorbed in the intact glycosylated form and potentially acylated in human subjects. Exposure to variations in pH, oxygen and a heating combination *in vitro* significantly reduces the availability of raspberry anthocyanins (extracts) to the serum fraction, although co-digestion with popular foodstuffs (e.g., bread, cooking cereals, ice cream, and cooked mince) may help. Protects the labile anthocyanins and definitely does not decrease the level of serum bioavailability polyphenols [87]. The polyphenols bind the food matrix within the digestion that protecting the unstable anthocyanins from degradation [24]. The artificial food matrix may enhance nutritional stability during storage, boost digestive effectivity, and guarantee optimal dose. Therefore, the selection of food matrix where the compounds are incorporated is important to give an optimal dosage in the human body.

Many investigations have shown that the absorption rate of total or individual anthocyanin was virtually undetected in either humans or animals. This may vary in the level of processing of the anthocyanin-containing fruit (freeze-dried blueberry powder versus spray-dried elderberry juice concentrate) and/or in the dietary variations supplemented with anthocyanin-rich material. Table 3 presented the current studies of anthocyanins' absorption from the Vaccinium species derivation. Another stage, that is the quantity of food source or extract supplied, should be addressed to assess the absorption of anthocyanins since the simultaneous intake of other substances may impact the absorption of certain nutrients, xenobiotics, and medicines. Moreover, it was recognized that sources rich in phenolic compounds regulate organic cation intestinal absorption, which was an excellent illustration of food-food interactions, taking into consideration the fact that most vitamins, nutrients, and xenobiotics cross intestinal barriers as organic cations.

On the other hand, bioavailability of anthocyanins related to the dietary sources, in relation to the glycoside type in the molecule. Several studies demonstrated that in rats and humans, anthocyanins are mainly absorbed in their intact forms of glycoside. However, other studies indicated that they were maintained in their aglycone forms [124,143]. A review study indicates that aglycones may be absorbed faster than glycosidic forms. Besides, the bioavailability of nonacylated anthocyanins is greater than that of acylated anthocyanins [21]. It is also stated that the glucose transporters such as the glucose transporter 2 (GLUT2) may absorb anthocyanins into the intestinal epithelial cells [39], potentially the cotransporter Na+/glucose 1 (SGLT1) [144], and actively transported from the intestine and endothelia, where their bioavailability is restricted in circulation [36].

It is recognized that the efficiency of transport and absorption of anthocyanins differed in each type. Other influence variables were the dosage ingested/administered and the period of exposure, depending on the organ/tissue, in addition to the chemical structure were studied. The efficiency of transport may be characterized by more free hydroxyl groups and less OCH3 groups, reducing the bioavailability of anthocyanins. Talavéra., *et al.* [132] demonstrated that aglycone structure influenced intestinal absorption of anthocyanin induced by the presence of methoxylated groups that reduced intestinal absorption. In addition, a previous study revealed that anthocyanins glycosides were highly absorbed in the stomach due to the favorable environmental condition for their stability. A recent *in vitro* study using a stomach cell line verified the absorption of anthocyanin and that M3G was evaluated with better transport efficiency in the anthocyanin. Anthocyanins come in touch with various pH conditions during the passage of anthocyanins via the gastrointestinal tract and may thus occur in different forms. This translates into a rate-limiting step to comprehend the forms of anthocyanin in different parts of the body. Ziberna., *et al.* [158] suggested that bilitranslocase (organic anion carrier) expressed in the gastric epithelium of rats may be involved in stomach anthocyanin absorption. On the other hand, the transport route of sugar movement may be involved in the absorption of anthocyanins. In human studies, Drakou., *et al.* [35] concluded that the sugar moiety is a major source of human absorption of dietary flavonoid glycosides, i.e., absorption of aglycones via glucose enhanced, may be through sodium-dependent glucose transport system absorption (SLGT1). Furthermore, an *in vitro* study suggested the involvement of GLUT2 (the facilitative glucose transporter) in intestinal absorption of anthocyanins.

The cation group's existence seems to affect their intestinal metabolism. Anthocyanins are present in the stomach and intestine in different forms, which are anthocyanins absorption sites [88]. The red flavylium cation form is the form with greater stability in the acidic gastric environment. The flavylium cation, however, is most likely converted to carbinol pseudo, which, after entering the basic environment of the upper small intestine has a limited absorption rate [28]. Their glycosidic forms are hydrolyzed into the colon via microflora, and the aglycones into phenolic acids and/or other unidentified metabolites metabolized [62]. Therefore, the labeling of isotopes of anthocyanins is suggested to evaluate their absorption and metabolism more effectively [81].

In addition, the anthocyanin structure's electron deficit renders anthocyanidins extremely reactive and its stability depends on the pH and temperature. The nutrients in the gut lumen interact with the anthocyanins and other polyphenols, and create stable complexes with non-heme dietary iron, limiting its absorption in the gut [130]. Nevertheless, the length of time that the anthocyanins are exposed to via food or incubation period in cell experiments seems to be a crucial component in their bioavailability [97]. Despite the fact that anthocyanins have a poor bioavailability when compared to other blackberry polyphenols, these modest amounts of anthocyanins may be bioavailable and well maintained in tissues. Nonetheless, the metabolites produced by the consumption of anthocyanin-rich meals have yet to be fully characterized [49]. There is a chance that undiscovered anthocyanin metabolites are contributing to the observed biologic effects of anthocyanins. However, urine and serum studies [104] (after an oral dosage of 120-230 g of whole berries (fresh weight)) revealed that parent chemicals and their metabolites exhibited comparable kinetic characteristics. Anthocyanins discharged in the urine account for less than 1% of the entire eaten dosage, according to studies. Relatively urinary excretion is usually employed to establish the minimum absorption rate but, when phenolic chemicals appear in the blood circulation or are strongly excreted in bile and in urine, this parameter for quantitative assessment might lead to an underestimated absorption. Since many of these studies were carried out in animals and cell cultures, further studies including the metabolites of anthocyanins are needed to fully characterize biokinetics of anthocyanins.

Biotransformation

Prior to consumption, anthocyanins can be biotransformed, which occurs naturally during processing and storage. This transformation resulted in conjugates of anthocyanin-flavan-3-ol. Consequently, the anthocyanins ingested in processed foods might contain different compounds in plants utilized for manufacturing. Anthocyanins are rapidly absorbed into the stomach wall as glycosides after ingestion [132]. The glycosidic forms of anthocyanins can begin metabolic alteration before they are absorbed owing to bacterial digestion of the glycosidic linkage of anthocyanins by the gastrointestinal system. Biological fluids include metabolites of anthocyanins occur predominantly in methylated, glucuronidated, and sulfoconjugated forms.

Certain studies have identified glucuronidated and methylated anthocyanins in human and animal models' urine and blood. The intact glycosidic form reaches the circulatory system rapidly (6 to 20 min), and is eliminated in the urine [88]. Anthocyanins are absorbed and distributed as metabolites in human serum and urine. The predominant metabolic reaction with anthocyanins is O-methylation after gastric absorption [142]. There was no analysis of anthocyanin metabolites in urine, including aglycons and conjugates. The intact substance and its 4'-O-methyl derivatives were only detected [83]. A 721 mg oral C3G dosage was observed in humans, 32.7% of intact C3G were identified, and an average of 67.3% of conjugated metabolites were identified in the serum. Bile samples showed that methylated conjugated metabolites of C3G were present, absorbed and further metabolized rapidly [34]. Nevertheless, whereas D3G was the most recovered anthocyanin in bile, it was not discovered in plasma even after 30 min from the aorta. Consequently, C3G gained the methylated form in the liver and tended to be eliminated by bile rather than being distributed into the blood. While rat liver had significant levels of methylated anthocyanins, no [48]traces were found in plasma.

The anthocyanins in blackcurrants may be digested in the gastrointestinal tract, then absorbed into the blood, and finally metabolized. The small intestine only absorbed lower quantities, and most of the anthocyanins are present in the large intestine, where they are metabolized and altered. During the intestine, different enzymes can also modify anthocyanins before entering the blood circulation [120]. Phase I metabolites have been identified as chloroglucinaldehyde,3,4-dihydroxybenzaldehyde, and glucuronidated and methylated cyanidins have been mainly recognized as phase II metabolites [9]. The *in vitro* and live cell biotransformation of anthocyanins is crucial for evaluating the bioavailability of blackcurrant anthocyanins to maximize their potential for health promotion.

In vitro and *in vivo* studies of metabolic syndrome

Blackcurrants are connected to diets high in anthocyanins and have a vital role in health, as well as in treatment and prevention of diseases, such as cardiovascular and metabolic syndrome incidence, including glucose tolerance, dyslipidemia, high blood pressure, abdominal obesity, and insulin resistance, this increases the risk of diabetes and cardiovascular diseases. Most investigations are *in vitro* studies and only a few studies have been conducted *in vivo* [30]. This section will review the *in vitro* and *in vivo* metabolic syndrome studies as indicated in (Table 3,4).

In vitro studies

Table 3 summarizes the numerous alleged health advantages of blackcurrant conducted *in vitro*. Kim., *et al.* [64] revealed the hypocholesterolemia effect of blackcurrant extract, by modulating the genes involved in intestinal cholesterol transport. utilizing Caco-2 cells as an *in vitro* model. Antibacterial activities on bacteria that ruin food, including Listeria monocytogenes [114], and Salmonella [110]. Blackcurrant extract with rich anthocyanin has an excellent perspective as an antibacterial additive in food. Parkar., *et al.* [110] has found the inhibitory function of intestinal epithelial cells adhesion *in vitro* and an increase in the proliferation of gut probiotics (Lactobacillus rhamnosus). Blackcurrant juice can therefore be utilized to control intestinal health.

Main benefits	Materials	Effective factors	Methods	Conclusions	Reference
Promoting gut health	Blackcurrant juice	Cyanidin rutinoside	A gut epithelium model	Blackcurrant juice inhibited salmonella proliferation and adhesion to gut cells	Parkar., *et al.* [110]
Neuroprotective activity	Blackcurrant extract	Anthocyanin and proanthocyanidin	Rotenone treated dopaminergic cell	Blackcurrant extract alleviated neurodegeneration in Parkinson's disease via enhancement of mitochondrial function	Strathearn., *et al.* [127]
Hypocholesterolemic effect	Blackcurrant extract	Anthocyanins	Caco-2 cells model	Blackcurrant extract modulated genes involved in intestinal cholesterol transport	Kim., *et al.* [64]
Antibacterial effect	Blackcurrant extract	Anthocyanins	Listeria monocytogenes and other food-spoiling bacteria	Anthocyanin-rich berries would have potential as both antibacterial additives in food	Raudsepp., *et al.* [114]
Hypoglycemic effects	Blackcurrant enriched cookies	bioactive compounds	*In vitro* glycemic glucose equivalent assay	A significant ($p < 0.05$) decrease in glucose release was observed in blackcurrant enriched cookies after *in vitro* digestion compared to the control.	Mofasser Hossain., *et al.* [91]
	Blackcurrant extract	Anthocyanins and their acid hydrolysates (anthocyanidins)	*In vitro* enzymes inhibitory activities assay	Anthocyanidins had a better α-glucosidase inhibitory activity than their corresponding anthocyanins after acid hydrolysis	Zhang., *et al.* [156]
Cardiovascular protection	Blackcurrant juices	Total anthocyanin or individual anthocyanin contents	Endothelium-dependent relaxation of isolated coronary arteries can be related to their antioxidant capacity and/or phenolic content.	Correlations between relaxation amplitude and total anthocyanin or individual anthocyanin contents are of interest for the development of functional blackcurrant beverages with the potential to promote vascular protection.	Tabart., *et al.* [131]
	Blackcurrant juices	Total polyphenol content and/or individual phenolic compound contents	Rat aorta segments immersed in an organ bath	Blackcurrant juice caused the most marked vasorelaxation. Kaempferol, epigallocatechin gallate and peonidin-3-O-glucoside seemed to emerge as the interesting phenolic compounds likely to be responsible for the potent vasorelaxation	Matute., *et al.* [86]
	Blackcurrant extract and anthocyanins	Blackcurrant extract and anthocyanins	The effects of blackcurrant extract on the regulation of eNOS expression and NO synthesis in human endothelial cells as key regulators in cardiovascular disease	Blackcurrant extract and anthocyanin may regulate NO synthesis via eNOS expression.	Horie., *et al.* [52]

Main benefits	Materials	Effective factors	Methods	Conclusions	Reference
Anti-inflammation	Blackcurrant juice	Anthocyanins and ascorbic acid	RAW 264.7 macrophages	Anthocyanins and ascorbic acid in blackcurrant juice repressed inflammatory biomarkers	Huebbe., *et al.* [53]
	Blackcurrant extract	Delphinidin-3-rutinoside (44%)	RAW 264.7 macrophages	Blackcurrant extract partly inhibited nuclear translocation of NF-kB independent of the Nrf2-mediated pathways.	Lee et al. [71]
	Blackcurrant extract	Anthocyanins	A two-component cell culture system of intestinal epithelial cells and macrophages	Blackcurrant extract downregulated the expression of inflammatory mediators	Olejnik., *et al.* [106]
	Purified blackcurrant anthocyanin samples	Anthocyanins	Human endothelial cells	Blackcurrant anthocyanins reduced the expression of endothelial inflammatory antigens	Blando., *et al.* [12]
	Blackcurrant extract	Blackcurrant extract	Mouse bone marrow-derived macrophages and human THP-1 macrophages	Blackcurrant extract metabolites inhibited the production of obesity-associated inflammatory factors.	Lee, Lee [74]
	Blackcurrant enriched cookies extract	Phenolic extracts	Cancer cell line, HepG2 model	Phenolic extracts suppressed the regulation of inflammatory cytokine IL-1β (about 3 to 4-fold), IL-6 (about 2-fold) and transcription signalling factor NF-kB (about 2-fold).	Mofasser Hossain., *et al.*. [90]
Anticancer	Blackcurrant extract	Phenolic compounds	*In vitro* simulated upper intestinal tract digestion and subsequent fecal fermentation	Phenolic compounds metabolites retained biological activity and modulated cellular processes associated with colon cancer.	Brown., *et al.* [15]
	Blackcurrant juice	Anthocyanins	Murine melanoma (B16F10), ovarian cancer (A2780) and cervical cancer (HeLa) cell lines	Blackcurrant anthocyanins antioxidant potential was associated with their antiproliferative potential	Diaconeasa., *et al.* [33]
	Blackcurrant	Blackcurrant juice, blackcurrant extract and anthocyanins	Jurkat cells	The blackcurrant juice and blackcurrant extract induced activation of caspase 3 was markedly inhibited by pretreatment with N-acetylcysteine. Blackcurrant extract and the two active anthocyanins induced the formation of reactive oxygen species. Blackcurrant juice and its major anthocyanins induced a redox-sensitive caspase 3-dependent apoptosis in Jurkat cells, involving a dysregulation of the Akt/Bad/Bcl-2 pathway	Leon-Gonzalez., *et al.* [76]

	Blackcurrant extract	Phytoestrogenic effects of black-currant extract	Breast cancer (MCF-7) and human endome-trial cancer (Ishikawa) cell lines	Blackcurrant anthocyanins acted as phytoestrogens *in vitro*.	Nanashima., *et al.* [96]
	Blackcurrant fruit wine	Blackcurrant fruit wine	Human breast (MCF-7), colon (CaCo-2) and cervical (HeLa) cancer cell lines	Blackcurrant fruit wine could act as an effective anti-proliferative agent.	Ljevar., *et al.* [80]
	Blackcurrant extract	Blackcurrant extract digested in an artificial gastrointestinal tract	Colon cancer HT-29 cells	The anticancer effect of the black-currant extract was related to the dose-dependent modulation of intracellular ROS accumulation.	Olejnik., *et al.* [105]

Table 3: *In vitro* investigations.

Main benefits	Materials	Effective factors	Methods	Conclusions	Reference
Cardiovascular protection	Blackcurrant extract	Anthocyanins	Ovariectomized (OVX) rats, a widely used animal model of meno-pause.	Anthocyanin-rich blackcurrant extract significantly upregulated eNOS mRNA levels and NO synthesis through phytoestrogenic activity and therefore promoted blood ves-sel health in OVX rats as a postmenopausal model.	Horie., *et al.* [52]
Hepatoprotec-tion	Blackcurrant extract	Anthocyanins	Acetaminophen induced acute hepatic damage in rat models	Treatment with anthocyanins normalized blood activities of glutamate oxaloacetate and glutamate pyruvate transaminase and prevented APAP-induced plasmatic and tis-sular alterations in biomarkers of oxidative stress	Cristani., *et al.* [27]
Neuroprotec-tive effects	Blackcurrant extract	Anthocyanins	19-month-old male Fischer rats	Blackcurrant extract enhanced neuronal functioning and restored the brain's ability to generate a neuroprotective response to stress.	Shukitt-Hale., *et al.* [123]
Obesity	Blackcurrant pomaces	Blackcurrant pomaces extract	20 male New Zealand white rabbits	A polyphenol-rich extract from blackcurrant pomace ingested at relatively high amounts may be a useful therapeutic option in the reversal of dysfunctions related to obesity and its complications.	Jurgonski., *et al.* [61]
	Whole blackcurrant powder	-	Male C57BL/6J mice	Blackcurrant consumption prevented obesity-induced steatosis, inflammation, and fibrosis in the liver.	Lee., *et al.* [75]
Bone health	Blackcurrant extract	Anthocyanins	An estrogen deficiency mouse model.	Blackcurrant may be effective in mitigating osteoclast-induced postmenopausal bone loss	Zheng., *et al.* [157]
	Blackcur-rants	Anthocyanins	A mouse model of age-related bone loss.	Early consumption of blackcurrant may pro-tect from aging-associated bone loss.	Sakaki., *et al.* [119]
Hypocholes-terolaemic	Blackcurrant extract	Anthocyanins	High fat/high cho-lesterol diet-induced metabolic disturbances in mice.	Blackcurrant extract supplementation de-creased glucose, and inhibited liver steatosis, suggesting that this berry may be consumed to prevent metabolic dysfunctions induced by diets high in fat and cholesterol.	Benn., *et al.* [10]

	Blackcurrant pomaces	Blackcurrant pomaces containing variable level of phenolic compounds	Wistar rats	Better hypocholesterolemia effect was observed after supplementation of the diet with unprocessed preparation of blackcurrant pomaces.	Jaroslawska., *et al.* [58]
	Blackcurrant pomaces	66.5% dietary fibers and 4.9% polyphenols	Rats fed a high-fat diet	The 8-week supplementation with blackcurrant fiber decreased body weight, whereas both fibers decreased epididymal fat mass, increased the fecal concentration of short-chain fatty acids, prevented hyperinsulinemia and decreased cholesterolaemia.	Jurgonski., *et al.* [60]
Hypoglycaemic	Blackcurrant extract	Anthocyanins	High fat/high cholesterol diet-induced metabolic disturbances in mice.	Blackcurrant extract supplementation decreased plasma total cholesterol and glucose, and inhibited liver steatosis.	Benn., *et al.* [10]
	Blackcurrant extract	Delphinidin 3-rutinoside	Rats fed a high-fat diet	The novel biological function of delphinidin 3-rutinoside-rich blackcurrant extract as a GLP-1 secretagogue. An increase in endogenous GLP-1 secretion induced by blackcurrant extract may help to reduce the dosages of diabetic medicines and prevent diabetes.	Tani., *et al.* [133]
	Blackcurrant extract	Delphinidin 3-rutinoside	Type 2 diabetic mice (KK-A(y)).	Delphinidin 3-rutinoside-rich blackcurrant extract may help prevent diabetes and allow the dosages of diabetes drugs to be reduced.	Iizuka., *et al.* [57]

Main benefits	Materials	Effective factors	Methods	Conclusions	Reference
Anti-inflammation	Blackcurrant extract	Four major anthocyanins	Stimulated human alveolar epithelial cells.	All blackcurrant polyphenolic extracts suppressed CCL26 secretion by lung alveolar cells Delphinidin glycosides to cyanidin glycosides in the blackcurrant cultivars was an important determinant in influencing CCL26 suppression in lung cells. The development of specific cultivars as functional foods/ingredients with beneficial biological activities	Nyanhanda., *et al.* [101]
	Freeze-dried blackcurrant	Anthocyanins	A diet-induced obesity (DIO) mouse model.	Blackcurrant significantly reduced F4/80 mRNA and the number of CLS in the epididymal fat pad, indicative of less macrophage infiltration. Varying anthocyanin composition differentially affect plasma lipids and adipose macrophage infiltration in DIO mice, but with no differences in their antioxidant capacity and anti-inflammatory potential.	Kim., *et al.* [65]

	Blackcurrants	Anthocyanins.	A mouse model of acute allergic lung inflammation.	Oral supplementation with New Zealand blackcurrant was effective in reducing lung inflammation, and highlighted the potential benefit of developing cultivars with specific polyphenolic profiles for the creation of functional foods with desirable biological activity	Shaw., *et al.* [122]
Promoting gut health	Blackcurrant pomaces	Blackcurrant pomaces containing variable level of phenolic compounds	Wistar rats	Blackcurrant pomaces selectively modulated the enzymatic activity of the colon microflora, reduced the activity of enzymes with potentially harmful properties and promoted activities of enzymes that might increase the use of carbohydrates that escaped digestion in the upper gastrointestinal tract	Jaroslawska., *et al.* [58]
	Blackcurrant	Mono- and di-glycosylated cyanidins and delphinidins	C57BL/6 mouse model of polygenic obesity	Consumption of berries resulted in a strong shift in the gastrointestinal bacterial communities towards obligate anaerobes that correlated with decrease in the gastrointestinal luminal oxygen and oxidative stress.	Overall., *et al.* [107]
	Blackcurrants	Anthocyanin-rich blackcurrant extract and dietary fibers individually and their combinations	The effects of anthocyanin-rich blackcurrant extract and dietary fibers individually and their combinations on biomarkers of large intestinal health in rats.	Blackcurrants significantly altered the bacterial populations by increasing the abundance of *Bacteroides-Prevotella-Porphyromonas* group and *Lactobacillus spp*., while decreasing the abundance of *Bifidobacterium spp*. and *Clostridium perfringens*. Dietary fiber increased the number of goblet cells in the colon.	Paturi., *et al.* [111]
	Blackcurrant	Anthocyanins	3-8 months old female mice Gut microbiome profiles using 16S sequencing of their feces.	Blackcurrant supplementation favorably modulated gut microbiome, but there were distinct age-specific differences	Cao., *et al.* [16]

Table 4: *In vivo* (mouse) investigations.

Vascular protection

The potent vasorelaxation effects of anthocyanins-rich blackcurrant juice on porcine coronary artery rings was tested by Tabart., *et al.* [131]. The authors have found that blackcurrant anthocyanins induced vasorelaxation by improving the endothelial function. Most recently, Matute., *et al.* [86] investigated the vasorelaxation effects of anthocyanin-rich fruit juices under *in vitro* experimental conditions and highlighted that blackcurrant peonidin-3-O-glucoside was probably responsible for powerful vasorelaxation. Further clinical studies are required to properly explore the favorable endothelium-dependent cardiovascular benefits after the consumption of vegetable and fruit juice.

Hypoglycemic effects

The treatment of diabetes mellitus could benefit from a diet rich in delphinidin and/or cyanidin. Mofasser Hossain., *et al.* [91] added blackcurrant powder, which is high in anthocyanins, to cookies, and it was found that reduced sugar level after *in vitro* digestion was substantial ($p < 0.05$). This study has demonstrated the hypoglycemic effects of blackcurrant powder, which may be used to develop functional food, such as cookies, pasta, and other high starch matrix foods. Zhang., *et al.* [156] discovered the α-glucosidase inhibition activities of blackcurrant anthocyanins and anthocyanidins. Similarly, Hui., *et al.* [54] reported the inhibitory activities of blackcurrant powder extract towards α-amylase and α-glucosidase. More precisely, Hui., *et al.* [54] also concluded that the inhibition of Cya-3-Glu and Del-3-Glu from blackcurrant powder extract exhibited stronger inhibitory activities towards α-amylase and α-glucosidase when compared to Mal-3-Glu and Cya-3-Rut.

Anticancer effects

Blackcurrant polyphenol breakdown products and metabolites are beneficial against colon cancer, as Brown., *et al.* [15] reported. Olejnik., *et al.* [105] further explored the anticancer effects of blackcurrant fruits on colorectal cancer cell line. The gastrointestinal digested blackcurrant extract could still deliver a variety of biological effects, including suppression of cancer cell proliferation, cancer cell cycle arrest, and induction of apoptosis, as well as a reduction in MMP-2 and MMP-9 activities that reduces cancer cell invasion. Diaconeasa., *et al.* [33] indicated that blackcurrant extract rich in anthocyanin might potentially inhibit the proliferation of tumor cell lines. Leon-Gonzalez., *et al.* [76] have further studied the blackcurrant antiproliferative effect on Jurkat cells at molecule levels and the precise mechanism. The growth of Jurkat cells was suppressed by blackcurrant-derived products and anthocyanins in a redox-sensitive fashion by triggering apoptosis through the activation of p73 and caspase 3, and the downregulation of UHRF1, which altered the p-Akt/ p-Bad/Bcl-2 pathway. One of the factors responsible for the pro-apoptotic action is the delphinidin-3-O-glucoside and delphinidin-3-O- rutinoside, and its significantly dependent on a prooxidant event. Blackcurrant wine has found to be anti-proliferative tested cancer cells [80]. In addition, Nanashima., *et al.* [95] reported that blackcurrant extract had the potential to prevent breast cancer at gene level.

Anti-inflammatory effect

A hydroalcoholic blackcurrant extract (Ribes nigrum) has been reported to exhibit considerable anti-inflammatory efficacy without its ulcerative potential, even at high doses during chronic treatment [32]. In rats, the anti-inflammatory effect of the ethanol Ribes nigrum extract was obtained by the conventional anti-inflammatory medication indomethacin on carrageen-induced hind leg edema. Interestingly, none of the 10 extract-treated rats developed stomach ulcers for 21 days. Proanthocyanidins are also known to have anti-inflammatory properties [67].

In vivo - Animal studies

Table 4 depicts the various putative health benefits of blackcurrant using the *in vivo* investigation. Rich anthocyanins in berries might dramatically upregulate eNOS mRNA levels and NO synthesis along with phytoestrogenic activity in OVX rats as a postmenopausal model [51]. Anthocyanin-rich in blackcurrant may offer health advantages in postmenopausal women in the blood vessels. Another study utlizing an *in vivo* model of coronary occlusion and reperfusion has shown that rats who had a diet rich in anthocyanin have decreased infarct in their hearts (with Cy and Pg glycosides) [82]. Greater levels of myocardial glutathione and higher endogenous cardiac antioxidant defense systems might be associated with the observed cardio-protection.

The liver affects the metabolic removal of toxic substances that cause damage and decreased liver function. Anthocyanin-rich diet substantially lowered liver malondialdehyde levels, elevated the antioxidant enzyme, e.g., superoxide dismutase, and eliminated enhanced indicators of liver damage, i.e., alanine and aspartate aminotransferase [9]. Anthocyanins normalized blood activities of glutamate oxaloacetate and glutamate pyruvate transaminase, as well as prevented acetaminophen-induced plasmatic and tissue changes in biomarkers of oxidative stress [27]. Furthermore, blueberry anthocyanins reduced the production of reactive oxygen species (ROS) and oxidative tissue damage, as well as suppressed the activity of hepatic stellate cells.

Anthocyanins and anthocyanidins also exert neuroprotective activities. Anthocyanins improve neuronal function and restore the capacity of the brain to create neuroprotective stress response [123]. Anthocyanins can have effects in rats treated with D-galactose (D-gal). A lower receptor for advanced glycation end products (RAGE), decreased oxidative stress. Lower levels of inflammatory markers were produced by anthocyanins [9]. Therefore, under ischemic brain damage, the role of the anthocyanins becomes more important to provide neuroprotection instead of antioxidant properties of anthocyanins.

Encapsulation of blackcurrant anthocyanins

Blackcurrant anthocyanins are compounds that sensitive to external factors and interactions with food components such as enzymes pigment stability, sugars, co-pigments, and ascorbic acid, due to their chemical structure [25]. The color and stability of anthocyanins are dependent on pH, due to changes in the concentration of the four species, including chalcone, pseudo base, flavylium cation, and quinonoid base. Besides, oxidation, light, metal ions, oxygen, temperature, acylation, and enzymes are factors that affect the rate of decomposition of anthocyanin [11,152]. Several recent studies have shown that the human digestive system can absorb intact anthocyanins in the blood and are beneficial to human health by reducing the risk of cardiovascular disease and improving vision [25]. In order to maintain the physical and chemical properties of the anthocyanin complex, providing controlled release of the functional ingredients in the human body, and building a functional barrier between the anthocyanins and external environmental factors such as light, water, reactive compounds, oxygen, heat, and enzyme, it was necessary to encapsulate the anthocyanins [152]. One of the most widely used methods for encapsulating anthocyanins is the drying method. There are also other techniques such as complexation, liposomal encapsulation, emulsification, and gelation. The drying method includes two types, the first is spray drying, where low particles are used in water activities and have wall matrices that slow down the decomposition of anthocyanins in the presence of moisture, heat, and light such as maltodextrin, modified starch, gums, proteins, and their mixtures and contains. This method applies to biopolymers, polymeric compounds, and metal ions. The proteins have high surface activity properties, which ensure the stability of anthocyanins during spray drying by forming a glass film around the particles. Another example, spray-dried pectin molecules with a high degree of esterification showed higher stabilizing effects on anthocyanins [153]. The second, freeze-drying, is a suitable encapsulation method for heat-sensitive bioactive such as anthocyanins. many works compared this method with spray drying one. The results showed that the lyophilized particles confer higher and more stable antioxidant activity for anthocyanins. However, this method still has limitations, which are presented by the higher permeability of the lyophilized particles generated by ice sublimation during the freeze-drying process, and the difficulty of controlling the particle size due to grinding or clumping of the material after drying technique [108]. Each encapsulation technique has advantages and disadvantages in relation to the applicable equipment, the feasibility of large-scale production, preparation conditions, and encapsulation wall materials. Some studies revealed that the encapsulation could impair the color quality of anthocyanins, owing to the thick encapsulated outer walls, the interactions between encapsulating agents, as well as the increased turbidity derived from emulsion-based delivery systems. There is still an urgent need to develop new strategies to manufacture robust delivery systems for anthocyanins, which can not only improve the color stability but also maintain food matrix quality [153]. Incorporating pigmentation and encapsulation may overcome the limitations of using a single technique. It has been shown that the combined use of fitting agents and encapsulation agents enables the simultaneous achievement of color intensification, and higher encapsulation [6]. The development of these strategies is necessary to meet consumer demand for both health awareness and benefits to achieve sustainable food engineering.

Concluding remarks and future perspectives

This study provides an insight into the bioavailability and biokinetics of blackcurrant anthocyanins, with specific emphasis on its implications in metabolic diseases. The main approach of this review is focusing on the metabolism of the anthocyanins from the blackcurrant, including the bioavailability, bioaccessibility, and bioactivity, by summarizing factors affecting phytochemical profiles of blackcurrant-based products, including growing and processing and biokinetic of blackcurrant anthocyanins. Anthocyanin absorption into the human body has been examined following intake of high-fat meals along with ground freeze-dried blackcurrant. However, in humans and animals, the absorption rate of total or individual anthocyanins was estimated to be extremely low because there were differences in the degree of anthocyanin processing of fruit product, and/or differences in diets supplemented by anthocyanin rich matter. Therefore, anthocyanins need to be biotransformed to anthocyanin-flavan-3-ols conjugates before consumption. In addition, the biotransformation of anthocyanins *in vitro* and living cells is important to assess the bioavailability of blackcurrant anthocyanins to optimize their health promotion effectiveness. Further studies using metabolites of anthocyanins are required for the comprehensive characterization of biokinetics of anthocyanins. Furthermore, the involvement of practical food processing, food matrices, and food digestion processes need to be taken into consideration.

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Conflicts of Interest

There are none to declare.

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