Journal of Population Therapeutics & Clinical Pharmacology

REVIEW ARTICLE
DOI: 10.53555/jptcp.v29i04.2948

ANTHOCYANIN EXTRACTION, PURIFICATION AND THERAPEUTIC PROPERTIES ON HUMAN HEALTH - A REVIEW

Shivi Tyagi[1]*, Srishtishree Mani[2], Neelam Chaturvedi[3]

[1*,2]Research Scholar, Food Science and Nutrition, Banasthali Vidyapith -304022, Jaipur, India
[3]Associate Professor, Department of Food Science and Nutrition, Banasthali Vidyapith -304022, Jaipur, India

***Corresponding author:**
*Research Scholar, Food Science and Nutrition, Banasthali Vidyapith -304022, Jaipur, India
Email: shivityagi2609@gmail.com

Abstract:
Flowering and fruiting plants as well as vegetative organs contain the water-soluble vacuolar pigments known as anthocyanins. They impart the distinctive red-to-blue color to fruits and vegetables. The foundation of anthocyanin use is the extraction and purification of anthocyanins from natural plants. To advance our understanding of anthocyanins, it is necessary to continually analyze the studies as well as their potential applications. The impact of various extraction and purification methods on the rate and purity of anthocyanin extraction were examined in this paper along with the most recent advancements in anthocyanin extraction and purification research. The review's findings can serve as a basis for scientific and industrial research. Due to their health advantages, such as the ability to combat oxidative stress, possessing antibacterial qualities, and preventing noncommunicable illnesses, they are frequently utilized as natural food colorants and have the potential to be nutraceutical additions

INTRODUCTION

Anthocyanins (ACNs) are a class of naturally occurring, water-soluble flavonoids that are found in abundance in the vacuoles of plant flowers, fruits, stems, and leaves (Alvarez et al., 2021; Zhao and Yuan, 2021). ACNs, which give fruits and vegetables their unique red-to-blue color, have a major impact on the sensory properties of food. They are red pigments in an acidic environment, blue in a basic environment, and unstable in a basic environment, degrading to dark brown oxidized compounds. They are necessary for pollination in plants and protect them from cold stress and UV damage by absorbing light (Qin et al., 2016). ACNs are the glucosides of anthocyanidins, which are flavonoid derivatives generated from phenylpropanoids. The six anthocyanidins most typically present in foods, according to Khoo et al. (2017) are cyanidin, delphinidin, pelargonidin, peonidin, petunidin, and malvidin.

Currently, anthocyanins are extracted mostly from fruits, vegetables, colored grains, and by-products of fruit and vegetable processing (Ockermann et al., 2021). Anthocyanins are abundant in fruit remnants such as grape, mulberry, and raspberry. China is a major fruit producer, with an annual output of 24 million tons of fruit and about 10 million tons of fruit leftovers (Huang et al., 2017). Fruit and remnants have an abundance of anthocyanins. An important area in food processing and development is the high-value exploitation of fruit residual trash. As a result, using fruit residues to extract anthocyanins not only improves the overall utilization rate of fruit residues, solves the problem

of industrial waste treatment, and reduces the pressure of environmental protection, but also obtains high value-added products, which improves their economic benefits (Kozlowaska et al., 2021).
Given their unusual chemical composition and distinctive aroma, anthocyanins may offer health benefits. ACNs have various biological properties, including scavenging free radicals, acting as antibacterials, slowing cancer cell growth, protecting eyes, and acting as a nutraceutical additive. They also counteract oxidative stress, act as antimicrobial substances, and prevent noncommunicable diseases like neurodegenerative, cardiovascular, metabolic, and cancer (Khoo et al., 2017; Jiao et al., 2018). Additionally, *in vitro* and *in vivo* investigations (Zeilinska and Michalaska, 2016) were used to confirm anthocyanins' low toxicity and good safety as a result, anthocyanins are widely used in a variety of industries, including food, medicine, and cosmetics. ACNs color stability and durability are affected by pH, co-pigmentation, light, temperature, oxygen and metal ions (Khoo et al., 2019). Since no adverse effects of anthocyanin derivatives have been recorded, even after extremely high dosages, their use in the prevention or treatment of a variety of disorders is an enticing option (Santos et al., 2016).
The aim of this study was to highlight the latest research on anthocyanin extraction and purification, as well as to examine the benefits and drawbacks of each approach. These findings provide a solid scientific foundation for the future research and application of anthocyanins.

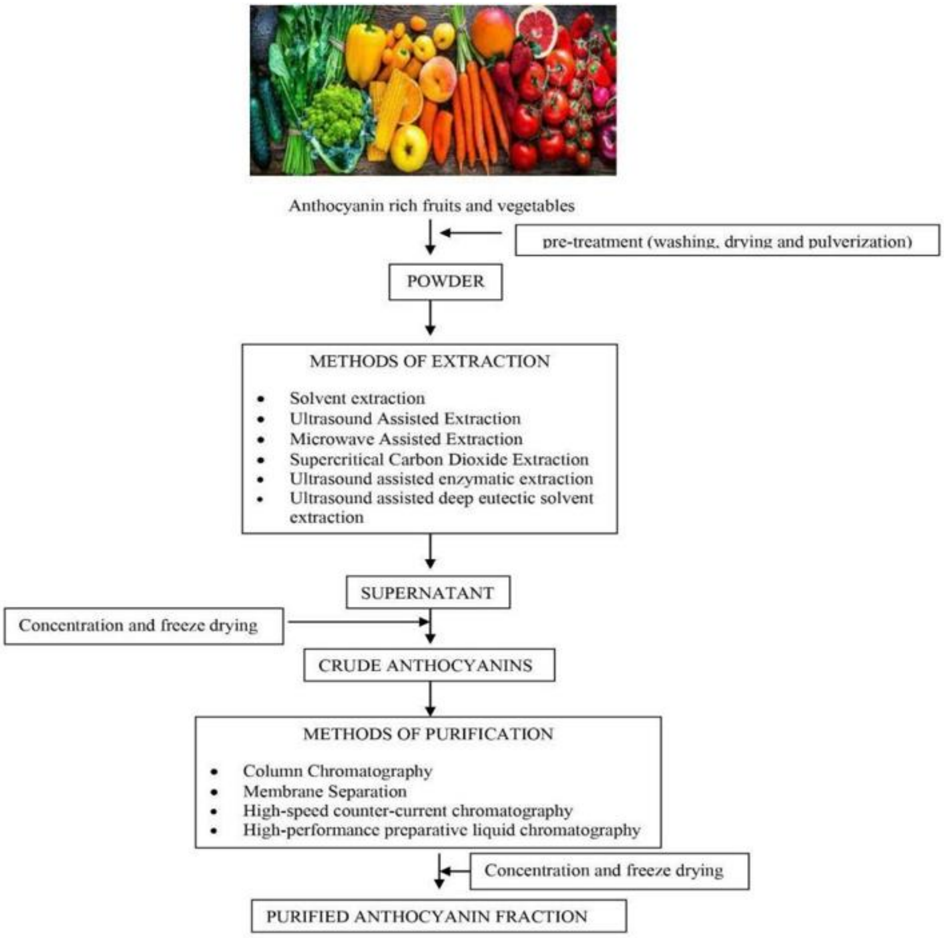

Figure 1: Techniques used in extraction and purification of anthocyanin

CHEMISTRY AND SOURCES OF ANTHOCYANIN

Chemistry of anthocyanins

Anthocyanins have a distinct chemical structure, with a carbon chain (C6—C3—C6) that separates two aromatic rings by an intermediate heterocyclic ring. The number of hydroxyl groups in anthocyanin molecules can vary, as can the degree of methylation (Vincete et al., 2016). The nature, amount, and location of sugar molecules coupled to aromatic rings, as well as the nature and number of aliphatic or aromatic acids connected to sugars, all contribute to the wide structural variety of anthocyanins. Anthocyanin sugars are often conjugated to the anthocyanidin skeleton via the C3-hydroxyl group in ring C (Trouilles et al., 2016).

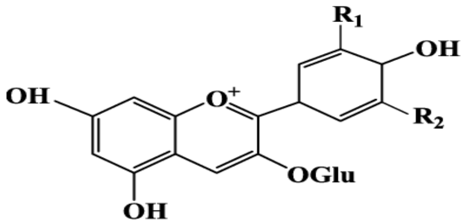

Figure 2: Chemical Structure of Anthocyanin

Anthocyanins undergo structural rearrangements in aqueous solution in four molecular configurations in response to pH changes: the flavylium cation, quinoidal base, carbinol, and chalcone forms. Anthocyanins exist largely as flavylium cations in acidic solutions (pH 1-3). When the pH rises above 4, anthocyanins take on the carbinol and chalcone forms. Chalcone can then be chemically degraded to yield phenolic acids (Jim, 2014).

Sources of Anthocyanin

Anthocyanins, natural plant flavonoids, are responsible for the orange, red, purple, and blue hues of many vegetables and fruits. These pigments may be found in fruits, stems, flowers, roots, and leaves, and they are evenly dissolved in epidermal cells. (Smeriglio et al., 2016). Their composition, however, fluctuates as a result of environmental conditions such as agronomic and genetic factors, light intensity, and temperature, which in turn determine the concentration of anthocyanins in certain fruits (Table 1) and vegetables (Song et al., 2021). Anthocyanin derivatives, including malvidin, pelargonidin, cyanidin, delphinidin, petunidin, and peonidin, are prevalent in plants. Pelargonidin, delphinidin, and cyanidin glycosides are abundant non-methylated anthocyanidins, accounting for 50% of flower colors, 69% of fruit pigments, and 80% of leaf pigments. Cyanidin-3-glucoside is a prevalent anthocyanin in fruits (Moein et al., 2016).

Table 1. Concentration of anthocyanins in fruits.

Fruits	Anthocyanin(mg/100g)
Apple, Red	1.7
Bilberry	300-698
Black currant	130-476
Black olives	42-228
Blackberry	82.5-325.9
Cherry	25-495
Chokeberry	2-450
Cranberry	410-1480
Crowberry	67-140
Elderberry	360
Gooseberry	200-1816
Peach	2-43.3
Pomegranate	4.2
Port wine	6–0765
Purple corn	1642
Raspberry	20-687
Red grape	30-750
Strawberry	19-55

(Adapted from De Pascual-Teresa and Sanchez-Ballesta, 2018)

ANTIOXIDANT AND ANTI INFLAMMATORY PROPERTIES OF ANTHOCYANIN

Antioxidant Properties

Anthocyanin is a potent antioxidant with health and therapeutic advantages due to its capacity to scavenge free radicals. Its glycosylated B-ring structure leads to its strong antioxidant activity, which is further enhanced by ortho-hydroxylation and methoxylation. Anthocyanidin, a pigment with a higher ORAC value, might be one of the causes of its instability and reactivity. Anthocyanins offer other therapeutic benefits, such as delphinidin, an active pharmaceutical component recognized for its ability to fight melanoma cells. Cyanidin and cyanidin-3-glucoside have the greatest inhibitory impact on copper-induced low-density lipoprotein oxidation, whereas delphinidin is in the middle (Brown et al., 2017).

Anti-inflammatory Properties

Inflammation is a normal physiological reaction of the innate immune system to infections and injuries, and it is a protective mechanism that can lead to persistent damage and illness. Anthocyanins are secondary metabolites found in plant cell fluid that are present in plants such as berries, soybean seed, purple potato, purple cabbage, and black carrot (Belawal et al., 2020). At varied pH levels, these compounds exhibit diverse hues, with blue in alkaline surroundings and purplish red in acidic conditions. Anthocyanins may be found in plant fruits, flowers, and leaves, and their hypoglycemic impact has been proven (Oliveira et al., 2021). They can also influence nitric oxide synthase and potassium channel activity to modulate blood vessel relaxation and contraction. general, anthocyanins play an important role in general health and well-being (Vilhenna et al., 2020).

TECHNIQUES USED IN EXTRACTION AND PURIFICATION OF ANTHOCYANIN

Extraction of Anthocyanin

Anthocyanins are recovered from plant materials using solid-liquid extraction procedures such as methanol, ethanol, or water since they are soluble in polar solvents. Under moderate circumstances, cold acidified solvents are employed to denature cell membranes, dissolving and stabilizing anthocyanins. The acid employed is typically acetic acid (7% or TFA 3%), with organic solvent concentration ranging from 50 to 100%. The nutritional and medicinal advantages of anthocyanins have garnered attention as extraction technology has advanced, with several traditional and possible extraction techniques presented (Teixeira et al., 2021).

Solvent extraction method (SEM)

Choosing the correct organic solvents for anthocyanin extraction is critical. Methanol, ethanol, acidified water, and acidified ethanol are examples of common solvents (Biata et al., 2018). Under certain conditions, SEM can extract anthocyanins, but its long duration, low efficiency, significant solvent consumption, and high temperature limit its applicability (Azman et al., 2020).

Ultrasound-assisted extraction (UAE)

The UAE employs ultrasound to improve anthocyanin extraction by increasing cavitation and shear pressures. However, the elevated concentration and extraction time may cause anthocyanin structure to be destroyed (Belawal et al., 2020). To optimize the benefits of ultrasonic extraction, ultrasonic conditions (power, temperature, solid-to-liquid ratio, and extraction duration) must be strictly controlled (Tan et al., 2021).

Microwave Assisted Extraction (MAE)

MAE is an intriguing approach for obtaining bioactive chemicals from natural plant resources such as purple sweet potato, red cabbage, blackberry, cranberry, Lonicera edulis, and sour cherry (Enaru et al., 2021). Microwave radiation improves its efficiency by reducing the viscosity of the solvent and promoting the solubility of target components. This technique is commonly employed in the extraction process (Liu et al., 2019).

Supercritical Carbon Dioxide Extraction (SCDE)
SCDE is increasingly being utilized in research to extract anthocyanins from natural sources such as Boletus edulis, blueberry pomace, and blueberry. SCDE extraction provides great efficiency, environmental friendliness, safety, and pollution-free extraction (Qin et al., 2019). Its expensive equipment costs, technical commitment, and difficulties managing extraction parameters, however, make it a distant technology for large-scale food industry applications (Tan et al., 2021).

Combined Extraction Method
The Ultrasound assisted enzymatic extraction (UAEE) and Ultrasound assisted deep eutectic solvent extraction (UADESE) procedures are two extraction technologies that work together to extract active components from natural sources (Tan et al., 2020). For grape skins, raspberry wine residues, and mulberry wine residues, the UAEE technique is commonly utilized. Organic solvents are prone to toxicity and are costly, making them unsuitable for anthocyanin extraction. Deep eutectic solvents (DESs) are being investigated as a low-carbon alternative. DESs are a new type of liquid salts that use inexpensive, readily accessible components to provide effective and ecologically acceptable alternatives to older approaches. For maximal anthocyanin production, the UADESE technique is applied (Turker and Dogan, 2022).

Purification of Anthocyanins
The extraction of anthocyanins contains contaminants such as sugar, protein, and organic acid that has an impact on their physiological activities, stability, and quality. Purification and separation of crude extracts are critical for high stability, activity, and purity (Tan et al., 2022).

Column chromatography method
Due to its capacity to separate contaminants and anthocyanins due to differing distribution coefficients in solid and mobile phases, column chromatography is a commonly utilized purification technique for anthocyanins separation (Nunes et al., 2022). It is commonly composed of macroporous resins, sephadex-100, and polyamide resins, which provide quick adsorption rates, huge adsorption capacity, and cheap manufacturing costs (Wang et al., 2017).

Membrane separation method
Membrane separation technique separates and purifies substances based on molecular weights using artificial and natural synthetic membranes. Micro-filtration membranes, ultra-filtration membranes, and nanofiltration membranes are now in use (Martin et al., 2017). Sample pretreatment increases extraction rate, purity, time efficiency, and environmental protection. Rapid separation and purification of anthocyanins can be facilitated by the use of suitable equipment and purification technologies (Tena and Asuero, 2022).

High-speed counter-current chromatography (HSCCC) method
HSCCC (high-speed counter-current chromatography) is a popular technology for extracting bioactive chemicals from natural plant resources. It increases sample loading capacity, enables speedy and large-scale preparation, decreases target fraction contaminants, and enhances separation success rate greatly (Xue et al., 2021).

High-performance preparative liquid chromatography (HPPLC) method
The physicochemical qualities of components are used to separate and purify crude extracts using HPPLC. To achieve greater separation, it comprises two immiscible phases that move at separate rates (Liu et al., 2018). HPPLC provides benefits such as excellent separation and purification, high detection accuracy, and automated continuous separation. However, large-scale industrial applications need substantial equipment investment and planning (Yang et al., 2016).

FACTORS AFFECTING ANTHOCYANIN STABILITY

ACNs' limited solubility and durability make them unsuitable for therapeutic usage. They can, however, be glycosylated or acylated by molecular, enzymatic, or chemoenzymatic mechanisms, boosting their biological activity and safeguarding organic molecules (Enaru et al., 2020).

pH

The color of anthocyanins is regulated by pH since it is the first parameter assessed. They exist in four chemical forms, with pH = 1 producing red and purple hues (Khoo et al., 2017). Quinoidal blue species are prevalent at pH 2-4, whereas carbinol pseudobase and chalcone occur at pH 5-6. Anthocyanins breakdown according to substituent groups at pH levels greater than 7 (Ayvaz et al., 2022).

Co-pigmentation

Anthocyanins and co-pigments interact to produce various color tints and intensities. They produce a hyperchromic effect and a bathochromic shift in absorption spectra when combined with anthocyanins, resulting in longer absorption wavelengths (Sendri et al., 2023). The efficacy of this interaction is determined by the steric organization and size of the substance. Because of their electron-rich structure and association with weakly charged flavylium cations, anthocyanins' color is stabilized through co-pigmentation (Trouillas et al., 2016). Intermolecular copigmentation, intramolecular copigmentation, and self-association between anthocyanidin nuclei and aromatic acyl groups are all examples of this interaction (Fernandes et al., 2015).

Temperature

Heat processing can cause anthocyanins, a pigment present in foods, to be lost and degraded (Rodriguez et al., 2019). Temperature also influences the stability of these chemicals' molecular structures, producing browning in the presence of oxygen. The chemical structure of anthocyanins is directly connected to their stability, with sugar fraction being a crucial determinant (Riaz et al., 2016). According to research, anthocyanins held at different temperatures are more stable than non acylated anthocyanins. Anthocyanins have a lower half-life at ambient temperature than in cold storage. Room temperature storage is not advised for long-term conservation (Hellstrom et al., 2013).

Oxygen

Anthocyanins are vulnerable to oxygen reactions due to their unsaturated structure, which affects their stability and degradation (Siroski et al., 2018). Through direct oxidative processes or oxidizing enzymes, oxygen can hasten the breakdown process. Anthocyanin stability rises when stored under vacuum, nitrogen, or argon, but decreases when stored at high oxygen concentrations. By removing oxygen from anthocyanin solutions, thermal deterioration is avoided. Hot grape juice and other anthocyanin-containing liquids can help to postpone color degradation. Anthocyanins also have antioxidant capabilities, making them useful in the prevention of cardiovascular disease (Hung., 2016).

Light

Light enhances the production and concentration of anthocyanins in plants, influencing their stability. Light is necessary for creation but also hastens their decomposition. The rate of light-induced breakdown is affected by the quantity of molecular oxygen present. Fluorescent light causes significant anthocyanin loss (Siroski et al., 2019). Colors of plants such as grapes and berries are determined by anthocyanins, which are regulated by the aglycon's B-ring substitution pattern. According to research, preserving grape juice at 20°C in the dark eliminates 30% of the anthocyanin, whereas light exposure destroys nearly half (Muche et al., 2018) .

THERAPEUTIC PROPERTIES

Anthocyanins and Eyesight

Smartphone use has resulted in an increase in ocular disorders such as discomfort, impaired vision, strain, and pain. Bilberry fruit contains anthocyanin, which helps enhance night vision and improve eye health. In negative lens-induced chick myopia models, it relaxes ciliary muscles, increases rhodopsin regeneration, and inhibits axial and ocular length elongation (Nomi et al., 2019).

Anthocyanin and Cancer

Anthocyanins have recently sparked interest as possible antitumoral medications due to their ability to treat cancer by decreasing cell growth, increasing apoptosis, and lowering invasion. These chemicals exhibit a wide range of biological actions, including antioxidant, anti-inflammatory, mutagenesis, differentiation, and anti-invasion capabilities (Lin et al., 2017).

Anthocyanins and Cardiovascular Disease

Cardiovascular disease is a primary cause of death globally, and its health is dependent on endothelial function, arterial stiffness, and atherosclerotic plaques. Anthocyanins, dietary antioxidants, have been proven in rodent models to prevent cardiovascular disease (CVD) (Mozos et al., 2017). They lower triglyceridemia, cholesterol, and platelet hyperactivity. Anthocyanins have antiatherogenic, antihypertensive, antiglycation, antithrombotic, and anti-inflammatory properties, as well as the ability to improve dyslipidemia and vascular stiffness. They also help to defend against oxidative stress and atherosclerosis (Liu et al., 2016).

Anthocyanins and Diabetes

Edible berries exhibit antiglycemic properties in both people and animals, showing that anthocyanins limit glucose transport in intestinal cells (Hidalgo et al., 2016). The Caco-2 cell line is used to research small intestine barrier function and cellular biology. Anthocyanin extract from red grape skins decreased glucose absorption by 60%, whereas polyphenol extracts from strawberry and apple juice inhibited basolateral glucose transport by a factor of five (Faria et al., 2019). Pelargonidin-3-Glucoside in strawberry juice might account for 25% of its inhibitory activity, whereas particular apple flavonoids could account for 85% (Manzano *et al*., 2020).

Anthocyanin and Degenerative Issues.

Anthocyanins have a high oxygen radical absorption capability and a significant antioxidant activity, making them useful in neurodegenerative disorders (Krishna et al., 2018). They bind to free radicals and inhibit ROS production in cells. Anthocyanins have a significant affinity for DPPH, alkyl, and hydroxyl free radicals and do so in a dose-dependent manner (Rehman et al., 2017). Anthocyanins and the gut microbiome have been studied as independent health influencers with positive effects on cardiovascular and bone health, as well as potentially overlapping mechanisms in the prevention and treatment of cardiovascular disease, cancer, neurodegenerative disorders, and aging-related bone loss (Zhu et al., 2020).

FUTURE PERSPECTIVES

Standardized analytical processes are critical for future investigations since they offer more homogeneous data and allow for speedier comparisons. Because red flavilyum cations, the predominant form of anthocyanin at physiological pH, cannot be detected by current technologies, Observing and quantifying the quinoidal base form may give further pictures of anthocyanin metabolism. Further research is needed to understand anthocyanins mechanisms of illness prevention and their effects on various age-related disorders, such as Alzheimer's disease, as well as the isolation techniques of anthocyanins along with its impact on value added products. Before anthocyanins may be widely employed in clinical applications to lower tumor and cancer risk, further research is needed to understand the mechanisms and evaluate their bioavailability.

CONCLUSIONS

Anthocyanins have been proven in studies to have beneficial benefits on a variety of ailments, including diabetes, cardiovascular disease, and cancer. Berries are high in anthocyanins, which have been demonstrated to help prevent degenerative illnesses. The features of the sample matrix and the extraction process parameters impact the extraction of anthocyanins from berries and fruit leftovers. Deep eutectic solvent extraction, ultrasonic aided extraction, microwave-assisted extraction, and supercritical fluid extraction are all current extraction technologies. These methods provide benefits in terms of extraction rate, energy consumption, extraction time, and environmental protection. They do, however, have stringent equipment requirements and process optimization norms. The expense of equipment makes industrialization of these procedures difficult. The focus of research is on improving various extraction methods and determining the best approach based on overall anthocyanin extraction rate. upgrading extraction equipment, studying new extraction technologies, upgrading laboratory equipment, optimizing sample pretreatment procedures, and developing extraction and purification processes for diverse purities are all future research objectives.

Acknowledgement This review paper is written with sincere efforts under the guidance of Dr. Neelam Chaturvedi, Associate Professor (Food Science and Nutrition) College of Home Science, Banasthali Vidyapith.

Conflict of interest: All authors declare that they do not have conflict of interest.

REFERENCES

1. Alvarez-Suarez, J. M., Cuadrado, C., Redondo, I. B., Giampieri, F., González-Paramás, A. M., & Santos-Buelga, C. (2021). Novel approaches in anthocyanin research-Plant fortification and bioavailability issues. Trends in Food Science & Technology, 117, 92-105.
2. Ayvaz, H., Cabaroglu, T., Akyildiz, A., Pala, C. U., Temizkan, R., Ağçam, E., Ayvaz, Z., Durazzo, A., Lucarini, M., Direito, R., & Diaconeasa, Z. (2022). Anthocyanins: Metabolic Digestion, Bioavailability, Therapeutic Effects, Current Pharmaceutical/Industrial Use, and Innovation Potential. Antioxidants (Basel, Switzerland), 12(1), 48
3. Azman, E. M., Charalampopoulos, D., & Chatzifragkou, A. (2020). Acetic acid buffer as extraction medium for free and bound phenolics from dried blackcurrant (Ribes nigrum L.) skins. Journal of Food Science, 85(11), 3745-3755.
4. Belwal T., Singh G., Jeandet P., Pandey A., Giri L., Ramola S., Bhatt I.D., Venskutonis P.R., Georgiev M., Clément C., et al. Anthocyanins, multi-functional natural products of industrial relevance: Recent biotechnological advances. Biotechnol. Adv. 2020; 43:107600.
5. Biata, N. R., Mashile, G. P., Ramontja, J., Mketo, N., and Nomngongo, P. N. (2019). Application of ultrasound-assisted cloud point extraction for preconcentration of antimony, tin and thallium in food and water samples prior to ICP-OES determination. J. Food Comp. Anal. 76, 14–21.
6. Brown JE, Kelly MF. Inhibition of lipid peroxidation by anthocyanins, anthocyanidins and their phenolic degradation products. Eur J Lipid Sci Technol. 2017;109(1):66–71
7. Enaru, B., Drețcanu, G., Pop, T. D., Stănilă, A., & Diaconeasa, Z. (2021). Anthocyanins: Factors Affecting Their Stability and Degradation. Antioxidants (Basel, Switzerland), 10(12), 1967
8. Faria A., Pestana D., Azevedo J., Martel F., De Freitas V., Azevedo I., Mateus N., Calhau C. Absorption of anthocyanins through intestinal epithelial cells-Putative involvement of GLUT2. Mol. Nutr. Food Res. 2009; 53:1430–1437.
9. Fernandez-Aulis F., Hernandez-Vazquez L., Aguilar-Osorio G., Arrieta-Baez D., Navarro-Ocan A. Extraction and Identification of Anthocyanins in Corn Cob and Corn Husk from Cacahuacintle Maize. J. Food Sci. 2019; 84:954–962.
10. Hellström, J., Mattila, P., & Karjalainen, R. (2013). Stability of anthocyanins in berry juices stored at different temperatures. Journal of Food Composition and Analysis, 31(1), 12-19.
11. Hidalgo I.J., Raub T.J., Borchardt R.T. Characterization of the human-colon carcinoma cell-line (Caco-2) as a model system for intestinal epithelial permeability. Gastroenterology. 1989; 96:736–749.
12. Huang W., Yan Z., Li D., Ma Y., Zhou J., Sui Z. Antioxidant and Anti-Inflammatory Effects of Blueberry Anthocyanins on High Glucose-Induced Human Retinal Capillary Endothelial Cells. Oxid. Med. Cell. Longev. 2016; 2016:1862462.

13. Jiao, X., Li, B., Zhang, Q., Gao, N., Zhang, X., & Meng, X. (2018). Effect of in vitro-simulated gastrointestinal digestion on the stability and antioxidant activity of blueberry polyphenols and their cellular antioxidant activity towards HepG2 cells. International Journal of Food Science & Technology, 53(1), 61-71.
14. Jim Fang. 2014. Bioavailability of Anthocyanins. drug Metabolism Reviews. 46(4): 508-520.
15. Khoo H., Ng H., Yap W.-S., Goh H., Yim H. Nutrients for prevention of macular degeneration and eye-related diseases. Antioxidants. 2017; 8:85.
16. Khoo H.E., Azlan A., Tang S.T., Lim S.M. Anthocyanidins and anthocyanins: Colored pigments as food, pharmaceutical ingredients, and the potential health benefits. Food Nutr. Res. 2017; 61:1361779.
17. Kozłowska, A., & Dzierżanowski, T. (2021). Targeting inflammation by anthocyanins as the novel therapeutic potential for chronic diseases: An update. Molecules, 26(14), 4380.
18. Krishna, P.-G.-A.; Sivakumar, T.-R.; Jin, C.; Li, S.-H.; Weng, Y.-J.; Yin, J.; Gui, -Z.-Z. Antioxidant and Hemolysis Protective Effects of Polyphenol-Rich Extract from Mulberry Fruits. Pharmacogn. Mag. 2018, 14, 103.
19. Lin BW, Gong CC, Song HF, Cui YY. Effects of anthocyanins on the prevention and treatment of cancer. Br J Pharmacol. 2017 Jun;174(11):1226-1243.
20. Liu C., Sun J., Lu Y., Bo Y. Effects of anthocyanin on serum lipids in dyslipidemia patients: A systematic review and meta-analysis. PLoS ONE. 2016;11(9)
21. Liu T., Zhang L., Joo D., Sun S.-C. NF-κB signaling in inflammation. Signal Transduct. Target. Ther. 2019; 2:17023.
22. Manzano S., Williamson G. Polyphenols and phenolic acids from strawberry and apple decrease glucose uptake and transport by human intestinal Caco-2 cells. Mol. Nutr. Food Res. 2010; 54:1773–1780.
23. Martín J., Kuskoski E.M., Navas M.J., Asuero A.G. Antioxidant Capacity of Anthocyanin Pigments. In: Justino J., editor. Flavonoids—From Biosynthesis to Human Health. Science, Technology and Medicine Open Access Publisher; Rijeka, Croatia: 2017. pp. 205–255.
24. Moein, M., Zahra, S., & Fatemeh, F. (2017). Isolation and determination of antioxidant capacities of anthocyanin from Rosa canina fruits. Обзоры по клинической фармакологии и лекарственной терапии, 15(Спецвыпуск 1), 43-44.
25. Mozos I., Malainer C., Horbańczuk J., Gug C., Stoian D., Luca C.T., Atanasov A.G. Inflammatory markers for arterial stiffness in cardiovascular diseases. Front. Immunol. 2017; 8:1058.
26. Muche, B. M., Speers, R. A., & Rupasinghe, H. V. (2018). Storage temperature impacts on anthocyanins degradation, color changes and haze development in juice of "Merlot" and "Ruby" grapes (Vitis vinifera). Frontiers in nutrition, 5, 100.
27. Nomi Y, Iwasaki-Kurashige K, Matsumoto H. Therapeutic Effects of Anthocyanins for Vision and Eye Health. Molecules. 2019 Sep 11;24(18):3311.
28. Nunes, A. N., Borges, A., Matias, A. A., Bronze, M. R., & Oliveira, J. (2022). Alternative Extraction and Downstream Purification Processes for Anthocyanins. Molecules, 27(2), 368
29. Ockermann, P., Headley, L., Lizio, R., & Hansmann, J. (2021). A review of the properties of anthocyanins and their influence on factors affecting cardiometabolic and cognitive health. Nutrients, 13(8), 2831.
30. Oliveira J., Azevedo J., Teixeira N., Araújo P., de Freitas V., Basílio N., Pina F. On the Limits of Anthocyanins Co-Pigmentation Models and Respective Equations. J. Agric. Food Chem. 2021; 69:1359–1367.
31. Qin Z., Wang X., Gao J., Guo Y., Huang Z., Du Y. The tomato hoffman's anthocyaninless gene encodes a bHLH transcription factor involved in anthocyanin biosynthesis that is developmentally regulated and induced by low temperatures. PLoS ONE. 2016;11: e0151067.
32. Rehman S.U., Shah S.A., Ali T., Chung J.I., Kim M.O. Anthocyanins reversed D-galactose-induced oxidative stress and neuroinflammation mediated cognitive impairment in adult rats. Mol. Neurobiol. 2017; 54:255–271.

33. Riaz, M., Zia-Ul-Haq, M., & Saad, B. (2016). Anthocyanins and human health: biomolecular and therapeutic aspects (Vol. 10, pp. 978-3). Switzerland: Springer.
34. Rodriguez-Mateos A., Vauzour D., Krueger C.G., Shanmuganayagam D., Reed J., Calani L., Mena P., Del Rio D., Crozier A. Bioavailability, bioactivity and impact on health of dietary flavonoids and related compounds: An update. Arch. Toxicol. 2014; 88:1803–1853.
35. Santos-Buelga C., Mateus N., De Freitas V. Anthocyanins. Plant pigments and beyond. J. Agric. Food Chem. 2016; 62:6879–6884.
36. Sarkar, R., Kundu, A., Banerjee, K., & Saha, S. (2018). Anthocyanin composition and potential bioactivity of karonda (Carissa carandas L.) fruit: An Indian source of biocolorant. LWT, 93, 673-678.
37. Sendri, N., Singh, S., Sharma, B., Purohit, R., & Bhandari, P. (2023). Effect of co-pigments on anthocyanins of Rhododendron arboreum and insights into interaction mechanism. Food chemistry, 426, 136571.
38. Sikorski Z. Fennema's Food Chemistry (Fifth Edition)—Edited by Srinivasan Damodaran and Kirk L. Parkin. J. Food Biochem. 2018;42:e12483
39. Smeriglio A, Bareca D, Belloccoco E, Trombetta D. Chemistry, pharmacology and health benefits of anthocyanins. Phytother. Res. 2016;30(8):1256–1286.
40. Song, D. H., Gu, T. W., & Kim, H. W. (2021). Quality Characteristics of Senior-Friendly Gelatin Gels Formulated with Hot Water Extract from Red Maple Leaf as a Novel Anthocyanin Source. Foods 2021, 10, 3074.
41. Sonia de Pascual-Teresa and Maria Teresa Sanchez-Ballesta Anthocyanins: from plant to health. Phytochem Rev (2008) 7:281–299
42. Tan C., Dadmohammadi Y., Lee M.C., Abbaspourrad A. Combination of copigmentation and encapsulation strategies for the synergistic stabilization of anthocyanins. Compr. Rev. Food Sci. Food Saf. 2021; 20:3164–3191.
43. Tan, J., Han, Y., Han, B., Qi, X., Cai, X., Ge, S., & Xue, H. (2022). Extraction and purification of anthocyanins: A review Journal of Agriculture and Food Research, 8, 100306.Tan, J., Han, Y., Han, B., Qi, X., Cai, X., Ge, S., & Xue, H. (2022). Extraction and purification of anthocyanins: A review. Journal of Agriculture and Food Research, 8, 100306.
44. Tan, J., Li, Q., Xue, H., & Tang, J. (2020). Ultrasound-assisted enzymatic extraction of anthocyanins from grape skins: Optimization, identification, and antitumor activity. Journal of food science, 85(11), 3731-3744.
45. Teixeira R.F., Benvenutti L., Burin V.M., Gomes T.M., Ferreira S.R.S., Ferreira-Zielinski A.A. An eco-friendly pressure liquid extraction method to recover anthocyanins from broken black bean hulls. Innov. Food Sci. Emerg. Technol. 2021; 67:102587.
46. Tena, N., & Asuero, A. G. (2022). Up-To-Date Analysis of the Extraction Methods for Anthocyanins: Principles of the Techniques, Optimization, Technical Progress, and Industrial Application. Antioxidants (Basel, Switzerland), 11(2), 286.
47. Türker, D. A., & Doğan, M. (2022). Ultrasound-assisted natural deep eutectic solvent extraction of anthocyanin from black carrots: Optimization, cytotoxicity, in-vitro bioavailability and stability. Food and Bioproducts Processing, 132, 99-113.
48. Vicente Dragano, N.R.; Castro Marques, A.Y. Chapter 11—Native Fruits, Anthocyanins in Nutraceuticals, and the Insulin Receptor/Insulin Receptor Substrate-1/Akt/Forkhead Box Protein Pathway. In Molecular Nutrition and Diabetes; Mauricio, D., Ed.; Academic Press: San Diego, CA, USA, 2016; pp. 131–145.
49. Vilhena R., Figueiredo I., Baviera A., Silva D., Marson B., Oliveira J., Peccinini R., Borges I., Pontarolo R. Antidiabetic activity of Musa x paradisiaca extracts in streptozotocin-induced diabetic rats and chemical characterization by HPLC-DAD-MS. J. Ethnopharmacol. 2020; 254:112666.
50. Wang D., Xia M., Yan X., Li D., Wang L., Xu Y., Jin T., and Ling W. Gut microbiota metabolism of anthocyanin promotes reverse cholesterol transport in mice via repressing miRNA-10b. Circ. Res. 2012;111:967–981.

51. Xue, H., Tan, J., Li, Q., Tang, J., & Cai, X. (2021). Ultrasound-assisted enzymatic extraction of anthocyanins from raspberry wine residues: process optimization, isolation, purification, and bioactivity determination. Food Analytical Methods, 14, 1369-1386.
52. Yang, F. X., Xu, P., Yang, J. G., Liang, J., Zong, M. H., & Lou, W. Y. (2016). Efficient separation and purification of anthocyanins from saskatoon berry by using low transition temperature mixtures. RSC advances, 6(106), 104582-104590.
53. Zhao X., Feng P., He W., Du X., Chen C., Suo L., Liang M., Zhang N., Na A., Zhang Y. The Prevention and Inhibition Effect of Anthocyanins on Colorectal Cancer Curr. Pharm. Des. 2020; 25:4919–4927.
54. Zhao, X., & Yuan, Z. (2021). Anthocyanins from pomegranate (Punica granatum L.) and their role in antioxidant capacities in vitro Chemistry & Biodiversity, 18(10), e2100399.
55. Zielinska, M., & Michalska, A. (2016) Microwave-assisted drying of blueberry (Vaccinium corymbosum L.) fruits: drying kinetics, polyphenols, anthocyanins, antioxidant capacity, color, and texture Food Chemistry, 212, 671-680.