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Anthocyanins - dietary natural products with a variety of bioactivities for the promotion of human and animal health

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Anthocyanins are water-soluble pigments contained in numerous food plants. This study provides an overall quantitative literature analysis on anthocyanins. Bibliometric data were collected through the search string TOPIC = anthocyan*, which yielded 44,121 publications indexed within the Web of Science Core Collection. Term maps were generated using VOSviewer software to visualize frequently mentioned terms alongside their citation data. The literature has been growing fast since the 2000s and predominantly consists of original articles, with a ratio of 13.8:1 compared to reviews. The most productive author was Professor Victor de Freitas from the University of Porto, whereas the most productive countries were China and the United States. Many publications were published in food science & technology and plant sciences journals. Frequently mentioned chemicals/chemical classes included anthocyanin, flavonoid, cyanidin, phenolic compound, and polyphenol. Recurring food items of the anthocyanin papers were grapes, many berries, and specific varieties of rice, maize, potato, and tomato.

KEY WORDS: anthocyanin / antioxidant / grape / *Vitis vinifera* (L.) / bibliometrics / Web of Science / VOS viewer

Introduction

Anthocyanins are naturally occurring pigments belonging to the flavonoid group compounds [Smeriglio *et al.* 2016, Huminiecki and Horbańczuk 2018, Mozos *et al.* 2018, 2021, Wang *et al.* 2018, Yeung *et al.* 2019, 2020a, 2022]. Chemically, anthocyanins are glycosides of flavonoids. They consist of two main components: the flavonoid nucleus called anthocyanidin, with variations in the aglycone structures contributing to the vast array of colors observed in nature, and sugars such as glucose or galactose contribute to the stability and solubility of the compound. Many anthocyanins can occur in plants and are responsible for the red, purple, and blue colors in fruits, vegetables, flowers, and leaves [Fossen and Andersen 2006]. These pigments are water-soluble and have antioxidant properties [Nascimento *et al.* 2022].

The basic structure of anthocyanidin consists of three rings: an aromatic ring (designated as ring A), condensed with a benzopyrylium (flavylium) cation (designated as ring C), and a second aromatic ring (designated as ring B). The variations in the structure of these rings, and the types and positions of the sugars attached, are responsible for distinct colors [Castañeda-Ovando *et al.* 2009].

Common anthocyanidins include cyanidin (produces red to purple colors), delphinidin (has blue colors), pelargonidin (delivers orange to red colors), petunidin (produces purple to black colors), and malvidin (produces red to purple colors). These anthocyanidins can be glycosylated, meaning that sugar molecules are attached [Pascual-Teresa and Sanchez-Ballesta, 2008]. In turn, the most common sugars found in anthocyanins include glucose, galactose, arabinose, and rhamnose. Combining specific anthocyanidins with different sugars results in various anthocyanin compounds. The diversity of anthocyanin structures contributes to the range of colors observed in plants [Harborne and Williams 2001].

Anthocyanins play several important roles in plants, contributing to various aspects of their growth, development, and survival. The most obvious role of anthocyanins is related to pigmentation. They give plants vibrant colors, such as red, purple, blue, or black, which can attract pollinators, such as bees and butterflies [Lev-Yadun and Gould 2009]. This pigmentation can also serve as a visual signal for the ripeness of fruits, making them more appealing to seed dispersers. Anthocyanins can act as natural sunscreens, absorbing and dissipating ultraviolet (UV) light, and this protects plant tissues from the harmful effects of excessive UV radiation, which can cause damage to DNA and disrupt cellular processes. Moreover, anthocyanins possess antioxidant properties, helping plants combat oxidative stress [Landi *et al.* 2015]. They neutralize harmful reactive oxygen species (ROS) produced during various metabolic processes and environmental stressors, contributing to cellular protection. Some studies suggest that anthocyanins may play a role in defending plants against herbivores and pathogens. The bitter taste of these compounds may deter herbivores, and their antimicrobial properties could help protect plants from certain diseases [Quina *et al.* 2009]. Anthocyanins are involved in regulating various aspects of plant growth and development, including seed development, root initiation, and responses

to environmental cues. They may act as signaling molecules in these processes. Anthocyanin production often increases in response to environmental stressors, such as drought, high light intensity, and extreme temperatures. This suggests a protective role in helping plants cope with adverse conditions. Anthocyanins can change color in response to changes in pH, and this property is sometimes used as a pH indicator in plant tissues, allowing researchers to monitor the acidity or alkalinity of cellular environments [Chalker-Scott 1999, Quina *et al.* 2009, Mannino *et al.* 2021].

Anthocyanins are widely present in the plant world [Brouillard 1982]. The occurrence of anthocyanins is not limited to specific plant parts; they can be found in various tissues throughout the plant. The familiar sources of anthocyanins are fruits (e.g., blueberries, strawberries, raspberries, blackberries, cranberries, sweet cherries, tart cherries, black currants, red and purple grapes, some apple varieties, especially those with red or purple skin, and pomegranates), vegetables (for example, red cabbage, red onions, red pepper, red beet, and eggplant), herbs (e.g., varieties of basil, such as purple basil, perilla leaves, especially the purple varieties), flowers (such as petunias, roses, pansies, tulips, violets, and daisies), leaves (e.g., red lettuce, red spinach, red leaves of certain tree species, especially in the autumn season), cereal grains (for example, purple corn, red rice), tea: (such as hibiscus tea), wine (e.g., red wine: the color of the red wine comes from the presence of anthocyanins extracted from grape skins during the fermentation process), and others [Pascual-Teresa and Sanchez-Ballesta 2008, Huminiecki *et al.* 2017, Fernandes *et al.* 2017, Tewari *et al.* 2017, Pieczyńska *et al.* 2020, Wang *et al.* 2020, Yeung *et al.* 2020bc, 2021ab, 2023, Chao *et al.* 2021, Chopra *et al.* 2022].

The occurrence of anthocyanins can vary between plant species and even within different cultivars of the same species. The concentration and types of anthocyanins present in plants may be influenced by factors such as genetics, environmental conditions, and maturity of the plant. These pigments not only provide vibrant colors to plants but also contribute to their antioxidant and health-promoting properties [Li *et al.* 2017]. Different types of plants contain different types of anthocyanins, influencing their color. The color of anthocyanins can also change depending on the pH of the environment, adding additional variability to the colors [Smeriglio *et al.* 2016].

In recent years, numerous investigations have focused on examining the diverse aspects associated to health benefits of anthocyanins. The consumption of colorful fruits and vegetables is often associated with promoting overall health and well-being due in part to the presence of anthocyanins [Prior and Wu 2006, He and Giusti 2010, Fang 2014]. In addition to their biological roles in plants, anthocyanins have been recognized for their diverse bioactivities and potential health-promoting effects in both humans and animals.

The critical aspects of their bioactivities are antioxidant properties (helping to neutralize harmful free radicals in the body), anti-inflammatory effects (conferring benefits in managing inflammatory conditions or supporting recovery from various

health challenges), cardiovascular benefits (helping to reduce blood pressure, improve blood vessel function, lower the risk of heart disease and also have positive effects on cholesterol levels), joint and musculoskeletal benefits, cancer prevention, neuroprotective effects (helping protect the brain from oxidative stress and inflammation, potentially reducing the risk of neurodegenerative diseases, e.g., Parkinson's disease [Açar *et al.* 2023], diabetes management (improving insulin sensitivity and reducing blood sugar levels), immune system support (enhancing the body's defense mechanisms), gut microbiota benefits: (support role in gut bacteria metabolism [Wattanathorn *et al.* 2023, Oteiza *et al.* 2023], eye health (protection against age-related macular degeneration and improving overall vision) and cancer prevention [Pascual-Teresa and Sanchez-Ballesta 2008, Khoo *et al.* 2017, Li *et al.* 2017, Krga and Milenkovic 2019, Speer *et al.* 2020, Hair *et al.* 2021]. In respect to anti-cancer action in particular, evidence suggests that anthocyanins possess anticarcinogenic properties by inhibiting proinflammatory pathways and inducing apoptosis, potentially making them valuable in breast cancer chemoprevention and therapy [Li *et al.* 2022]. Anthocyanins have also garnered attention for their potential in impacting oncogenes and the activity of ATP-binding cassette (ABC) and solute carrier (SLC) transporters, especially in the realm of cancer treatment. Concerning drug transporters, ABC transporters like ABCB1 and ABCG2 are implicated in multidrug resistance (MDR) by expelling chemotherapeutic agents from cancer cells, diminishing drug efficacy [Silbermann *et al.* 2019, Huang and Sadée 2006]. The strategy to reverse anticancer drug resistance via the inhibition of ABC transporters remains a high priority and a focus of cancer research. On the other hand, the SLC transporter superfamily consists of over 60 families with more than 400 genes, new transporter genes continuously being discovered (<http://slc.bioparadigms.org/>, (accessed on 4th March 2024)). In contrast, SLCs have been shown to be down-regulated in cancer cells, leading to a reduced accumulation of drugs and chemotherapy efficiency [Puris *et al.* 2023]. While direct evidence of anthocyanins modulating these transporters is lacking, general literature acknowledges diverse natural products as potential inhibitors, substrates, inducers, or activators of drug transporters, raising the prospect of natural product-drug interactions and new combination treatments [Bi *et al.* 2022].

Anthocyanins are generally considered safe and beneficial when consumed as part of a balanced diet. However, there are some considerations regarding their potential adverse effects or interactions. Allergic reactions, for example, could include symptoms such as itching, swelling, or hives [Khoo *et al.* 2017]. Anthocyanins, like other bioactive compounds in foods, may interact with medications. For example, they could interfere with blood clotting or interact with drugs used to manage blood pressure. In some cases, individuals may experience gastrointestinal discomfort, such as bloating or stomach upset, when consuming large quantities of certain fruits or vegetables rich in anthocyanins. People may respond differently to anthocyanins based on factors such as genetics, overall health, and individual sensitivities [Gonçalves *et al.* 2021]. Some foods rich in anthocyanins, such as certain berries and fruits, may

also contain oxalates. In individuals with a history of kidney stones or kidney issues, a diet high in oxalates could be a concern. However, not all anthocyanin-rich foods are necessarily high in oxalates. Anthocyanins are sometimes used as natural food colorings. While these compounds themselves are generally safe, some processed foods or beverages may contain added ingredients or preservatives that could cause sensitivities in some individuals [Liu *et al.* 2021].

It is important to emphasize that adverse effects related to anthocyanin consumption are relatively rare, especially when these compounds are obtained through the consumption of a balanced diet. The potential risks are often associated with excessive intake of supplements or highly concentrated extracts. As with any dietary component, moderation and variety are crucial factors that make up a healthy diet [Burton-Freeman *et al.* 2016].

In the past few years, there has been a growing emphasis on the intake of foods derived from natural sources such as fruits, vegetables, spices, and whole grains. This shift is primarily attributed to the presence of bioactive phytochemicals, with phenolic compounds, notably anthocyanins, being particularly noteworthy. Numerous studies have delved primarily into examining the health benefits of anthocyanins from various angles. In the work of Ayvaz *et al.* [Ayvaz *et al.* 2023] an analysis of anthocyanins, sustainable sources, and waste relationships found in the literature has been given. Considering the vast scope of knowledge on anthocyanins, the optimal solution is to use bibliometric analysis, which is a quantitative approach used to explore and evaluate the impact of scientific publications. It involves the statistical analysis of written publications to uncover patterns, trends, and relationships within the scientific literature. This method is particularly beneficial in the context of scientific article writing for several reasons such as trend analysis, research impact, network analysis or understanding the dynamics of scientific knowledge. This method is especially useful to explore fields where many publications are available [Yeung *et al.* 2023].

On this background, the aim of this study is to explore the extensive literature on anthocyanins, focusing on their diverse bioactive functionalities and their promising contributions to promoting health in humans and animals.

Material and methods

The online academic literature database, Web of Science (WoS) Core Collection, was queried on 3 January 2024 with the following search string: TS = anthocyan*. This search string identified publications listing anthocyanin and its derivatives in their titles, abstracts, and/or keywords. The query returned 44,121 papers. No additional filter was applied to limit the search, such as publication year, document type or language. The primary publication and citation data were directly acquired from the WoS platform, and then the full records of the 44,121 papers were exported to a bibliometric software called VOSviewer [van Eck and Waltman 2009] for further bibliometric analyses. In particular, VOSviewer was used to generate a term map

that visualized terms that appeared in $>1\%$ ($n = 442$) of the titles and abstracts of the 44,121 papers to reveal which terms had higher publication count or citations per paper (CPP) than others. A similar term map was generated to visualize author keywords that appeared in $>0.1\%$ ($n = 45$) of the papers. Except for these threshold settings being customized, all other settings used in VOSviewer to generate the term maps were by default.

Results

The analyzed literature set contained 44,121 papers, which has experienced exponential growth since the 2000s (Fig. 1). Most of the papers were classified as original articles by WoS ($n = 38,626$, 87.5% , $CPP = 32.1$) and the rest were mainly reviews ($n = 2798$, 6.3% , $CPP = 76.3$). The original article-to-review ratio was 13.8:1. The top 5 most productive authors, affiliations, countries, journals, and journal categories are listed in Table 1.

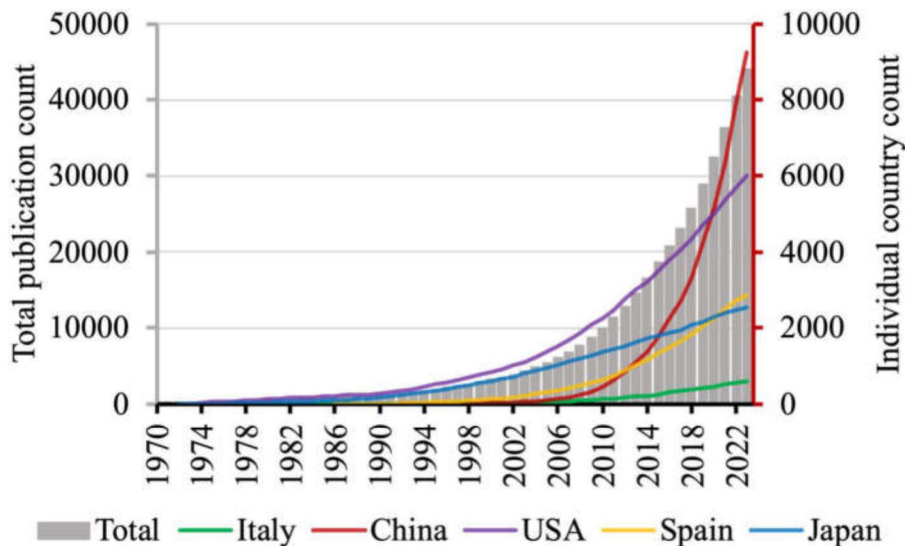


Fig. 1. Cumulative publication counts for the overall literature and the top 5 most productive countries.

The most productive author was Professor Victor de Freitas ($n = 202$, $CPP = 38.9$) from the University of Porto. China ($n = 9297$, $CPP = 24.0$) and the United States ($n = 5997$, $CPP = 54.6$) each contributed to over 10% of the papers, with their leading affiliations being the Chinese Academy of Science ($n = 818$, $CPP = 31.9$) and United States Department of Agriculture (USDA, $n = 896$, $CPP = 63.9$), respectively. Among the top 5 most productive countries, the United States, Italy, and Japan began to

Table 1. The top-five most productive authors, affiliations, countries, journals, and journal categories

Item	Number of papers (% of 44,121)	Citations per paper (CPP)
Author		
Victor de Freitas	202 (0.5)	38.9
Nuno Mateus	174 (0.4)	39.9
Fumi Tatsuzawa	107 (0.2)	16.0
Mary Ann Lila	103 (0.2)	44.9
Fernando Pina	103 (0.2)	22.2
Affiliation		
United States Department of Agriculture (USDA)	896 (2.0)	63.9
Chinese Academy of Sciences	818 (1.9)	31.9
Spanish National Research Council (CSIC)	811 (1.8)	48.6
Ministry of Agriculture Rural Affairs, China	787 (1.8)	23.2
French National Research Institute for Agriculture, Food and Environment (INRAE)	614 (1.4)	78.9
Country		
China	9297 (21.1)	24.0
United States	5997 (13.6)	54.6
Italy	3008 (6.8)	36.2
Spain	2880 (6.5)	40.3
Japan	2550 (5.8)	36.3
Journal		
Food Chemistry	1970 (4.5)	59.6
Journal of Agricultural and Food Chemistry	1792 (4.0)	84.8
Molecules	849 (1.9)	26.2
Frontiers in Plant Science	763 (1.7)	21.6
Scientia Horticulturae	761 (1.7)	24.6
Journal category		
Food Science & Technology	15,401 (34.9)	39.2
Plant Sciences	9227 (20.9)	39.1
Chemistry, Applied	5750 (13.0)	58.1
Biochemistry & Molecular Biology	5211 (11.8)	41.8
Horticulture	5016 (11.4)	19.4

publish in this field in the 1970s, whereas Spain and China were relatively newcomers that began to publish in 1986 and 1992, respectively (Fig. 1). Since then, Spain and China have remained productive especially in the 2010s. Food Chemistry was the most productive journal (n = 1970, CPP = 59.6), but the Journal of Agricultural and Food Chemistry had the highest CPP among the top 5 (n = 1792, CPP = 84.8). Each of these two journals published twice as many as the 3rd most productive journal. Overall, Food Science & Technology was the most productive journal category (n = 15,401, CPP = 39.2) whereas Chemistry, Applied had the highest CPP among the top 5 (n = 5750, CPP = 58.1).

Figure 2 is a term map that visualizes the recurring terms in the titles and abstracts of the papers. One could easily note that grape is broadly referred as a common source of anthocyanins, as many terms at the top of the term map are related to grapes, such as *Vitis vinifera* (L.) (i.e. grape, n = 580, CPP = 40.1), veraison (i.e. onset of

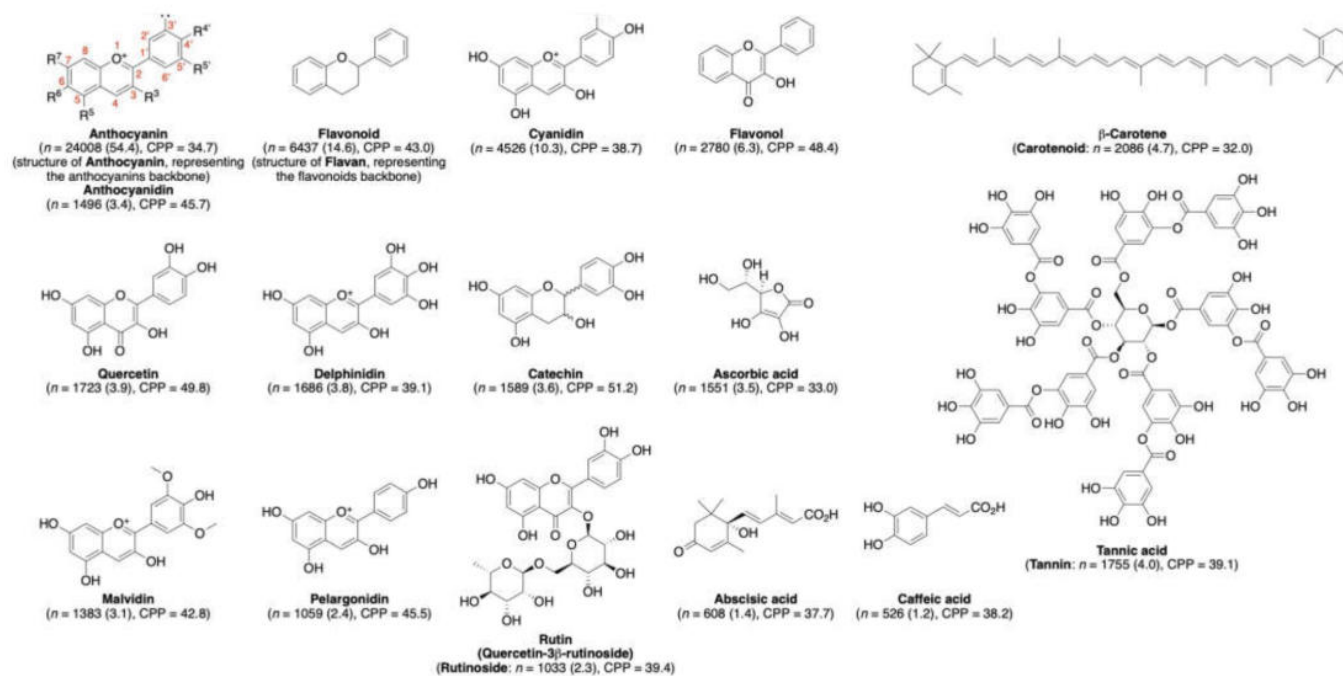


Figure 3. Chemical structures of frequently mentioned chemicals/chemical classes. In brackets are indicated the number of papers (*n*) in which the respective phytochemical was cited and the citations per paper (CPP).

Table 3. Recurring food items (n>100) mentioned in the author keywords of the anthocyanin papers

Food items	Number of papers (% of 44,121)	Citations per paper (CPP)
<i>Vitis vinifera</i>	479 (1.1)	46.3
Strawberry	478 (1.1)	47.5
Blueberry	452 (1.0)	39.6
Red wine	433 (1.0)	42.6
Grape	409 (0.9)	45.3
Apple	276 (0.6)	47.0
Grapevine	204 (0.5)	36.0
<i>Arabidopsis thaliana</i>	196 (0.4)	61.6
Bilberry	148 (0.3)	40.2
Blackberry	145 (0.3)	56.0
Black rice	142 (0.3)	34.0
<i>Hibiscus sabdariffa</i>	138 (0.3)	26.7
Purple sweet potato	130 (0.3)	25.9
Tomato	130 (0.3)	31.4
Maize	126 (0.3)	28.7
Raspberrry	125 (0.3)	55.1
Potato	123 (0.3)	30.2
Rice	123 (0.3)	33.4
<i>Aronia melanocarpa</i>	118 (0.3)	36.5
Cabernet Sauvignon	111 (0.3)	29.7
Mulberry	111 (0.3)	43.6
Blackcurrant	110 (0.2)	27.0
Cranberry	104 (0.2)	51.6

Discussion

Analyzed literature

The exponential growth in the number of papers within the analyzed literature emphasized the increasing interest and research activity regarding anthocyanins (Fig. 1). Original articles in this dataset were predominant. This indicates a substantial focus on generating new research findings and empirical data. The relatively lower percentage of reviews (only 6.3%) implies that the scholarly community is prioritizing the generation of fresh insights and primary research over synthesizing existing knowledge. The citation per paper (CPP) metrics provide additional insights into the impact and significance of the published works. Original articles, with a CPP of 32.1, demonstrate a moderate level of citation, indicating a notable influence in the academic community. On the other hand, reviews, with a higher CPP of 76.3, suggest a greater level of attention and recognition, potentially due to their comprehensive synthesis and analysis of existing literature. The observed trends in the examined literature dataset indicate a vibrant and dynamic research development, characterized by a significant emphasis on original research.

The data presented in Table 1 offered insights into the overview of anthocyanin research, shedding light on the most prolific authors, affiliations, countries, journals, and journal categories. These observations may be discussed regarding the key contributors, geographical trends, and the impact of scholarly output in this field. Among the authors researching anthocyanins were Victor de Freitas, Nuno Mateus, Fumi Tatsuzawa, Mary Ann Lila, and Fernando Pina. Professor Victor de Freitas from the University of Porto was the most productive author, with a substantial publication count ($n = 202$) and a noteworthy Citation per Paper (CPP) score of 38.9. His top-cited articles were above all about: natural anthocyanin pigments/dyes and phenolic co-pigments/co-dyes (CPP = 339) [Trouillas *et al.* 2016]; bioavailability of anthocyanins and derivatives (CPP= 248) [Fernandes *et al.* 2014b]; wine flavonoids in health and disease prevention (CPP=138) [Fernandes *et al.* 2017]; sensorial properties of red wine polyphenols (CPP= 120) [Soares *et al.* 2017]; anthocyanin profile and antioxidant capacity of black carrots (CPP= 120) [Algarra *et al.*, 2014] and understanding the molecular mechanism of anthocyanin binding to pectin (CPP= 111) [Fernandes *et al.* 2014a].

The data analysis showed that the Food Chemistry journal was the most productive, publishing 1970 articles with citations per paper (CPP) of 59.6. Conversely, the Journal of Agricultural and Food Chemistry achieved the highest CPP, reaching 84.8 with 1792 publications. Among the top five most productive journal categories, Food Science & Technology published an impressive 15,401 articles and Chemistry, Applied attained the highest CPP at 58.1. These observations suggest that in addition to the sheer number of publications, it is also important to consider the quality and impact of publications on the further development of the scientific field. The dominance of Food Science & Technology as the most productive journal category, coupled with Chemistry, Applied which is having the highest CPP among the top 5, highlights the interdisciplinary nature of anthocyanin research and the collaborative efforts across various scientific domains in advancing our understanding of anthocyanins.

Geographically, China and the United States were major contributors, collectively accounting for over 20% of the total papers (Fig. 1). Examining the temporal aspect of anthocyanin research reveals interesting patterns among the top 5 most productive countries, in which The United States, Italy, and Japan initiated research on anthocyanins. On the other hand, Spain and China entered the scene as relative newcomers, but demonstrated consistent productivity. The predominance of articles on anthocyanins coming from China and the United States can be attributed to several factors. First, both nations possess robust research infrastructures, including highly regarded universities, research institutes, and laboratories. This environment is conducive to scientific research and progress. Secondly, there is substantial financial investment in scientific research in both countries, which is a crucial element for conducting high-quality research. Additionally, the significant markets for food and dietary supplements in China and the United States may stimulate research into nutritional components, including anthocyanins. The reason is that the economic

potential of these countries can stimulate scientific attention and funding in areas related to food and nutrition science. Furthermore, the diverse climatic and botanical landscapes of both countries contribute to the availability of various natural sources of anthocyanins. This diversity may stimulate research on these compounds due to the increased availability and variety of plant sources. Finally, international scientific cooperation, between researchers from China and the United States, increases the exchange of knowledge and experience. This can lead to a greater distribution of research results and methodologies, thus potentially increasing the number of publications on anthocyanins. However, it is important to note that these are general speculations, and the actual reasons may be more complex and diverse. Research activity in a particular area results from various factors such as scientific interests, resource availability, funding, scientific policies, and current trends in health and nutrition.

The recurring terms in the titles and abstracts of the anthocyanin papers

The map presented in Figure 2 offers visualization of the recurring terms found in the titles and abstracts of the analyzed papers. Prominently emerging at the top of the term map were “*Vitis vinifera* (L.)”, “veraison”, “grapevine”, and “vine”. This analysis highlights the substantial focus on grape-related topics as a primary source of anthocyanins and also underscores the importance of understanding their composition, properties, and potential applications.

Vitis vinifera (L.) is a plant belonging to the *Vitaceae* family, exhibits significant pigmentation mainly due to anthocyanins [Ju *et al.* 2021]. These naturally occurring compounds are crucial in determining the color of grape fruits [Trouillas *et al.* 2016]. The presence and specific composition of anthocyanins in *Vitis vinifera* (L.) are subject to various influencing factors. These include the genetic varietal characteristics of the grapes [Fournier-Level *et al.* 2011], environmental conditions such as light, temperature and soil composition [He *et al.* 2010, Gaiotti *et al.* 2018, Yan *et al.* 2020], the degree of ripeness of the grape berries [Shahab *et al.*, 2020] and the methodologies used in the production of wine [Mori *et al.* 2007]

The next word “veraison” was found at the top of words appearing in both the title and abstract of anthocyanin-related articles. As grapes ripen, enzymes responsible for anthocyanin synthesis become active, leading to the production and accumulation of these pigments in the skin [He and Giusti 2010]. The specific types and proportions of anthocyanins vary among grape varieties, contributing to the distinctive colors and flavors characteristic of different wines [Ju *et al.* 2021]. Beyond their role in coloration, anthocyanins in *Vitis vinifera* (L.) grapes have garnered attention for their antioxidant properties that may help protect against oxidative stress and inflammation, potentially reducing the risk of chronic diseases such as cardiovascular disorders and certain cancers [Fernandes *et al.* 2017]. The research focused on anthocyanins in *Vitis vinifera* (L.) encompasses a broad spectrum of disciplines, including plant physiology, biochemistry, agronomy, enology, and nutrition, tested mechanisms of

pigment stabilization during winemaking and storage, and the bioavailability and physiological effects of anthocyanins upon human consumption [Baydar *et al.* 2004, Núñez *et al.* 2004].

The following most frequently repeated words in articles about anthocyanins were “grapevine” and “vine”. These studies focused on understanding the molecular mechanisms underlying anthocyanin biosynthesis in grapevines and characterizing of the genes and enzymes involved in the biosynthetic pathway, as well as elucidating the regulatory factors that control anthocyanin production during grape ripening. Scientists examining the genetic diversity of grapevine varieties identified genetic markers associated with high anthocyanin levels and desirable color traits, facilitating breeding efforts to develop new grape varieties with improved anthocyanin profiles [Fournier-Level *et al.* 2009]. We can also find research regarding how environmental factors such as light, temperature, water availability, and soil composition influence anthocyanin accumulation in grapevines. Many authors also examined the effects of cultural practices, such as pruning, canopy management, and irrigation strategies, on anthocyanin synthesis and distribution within grapevine tissues. Research is also of great interest in post-harvest handling and processing techniques to explore ways to preserve and enhance anthocyanin stability in grape products and to evaluate the potential health benefits of anthocyanins derived from grapevine products, including their antioxidant, anti-inflammatory, and cardioprotective effects. In the area of wine technology and enology, studies focus on the impact of winemaking techniques, fermentation parameters, and ageing conditions on anthocyanin extraction, stability, and evolution in wine.

Chemicals/chemical classes identified from the titles and abstracts of the anthocyanin papers

Within the top 20, several compounds stood out with notably high CPPs (>50), indicating their significant impact and citation frequency (Tab. 2). Among these, proanthocyanidin and catechin were particularly prominent (Fig. 3).

Proanthocyanidins, also known as condensed tannins, are a group of polyphenolic compounds found in various plants [Mannino *et al.* 2021]. They are part of the larger class of flavonoids and are composed of flavan-3-ol units, such as catechin and epicatechin, linked together through carbon-carbon bonds [Qi *et al.* 2023]. Proanthocyanidins are widely distributed in nature and can be found in foods such as grapes, apples, berries, nuts, cocoa, red wine, and certain types of tea [Zhang *et al.* 2023]. These compounds have been studied for their potential health benefits such as antioxidant properties, cardiovascular health, skin health, cognitive function, anti-inflammatory effects, antimicrobial properties and dental health [Unusan 2020, Zhang *et al.* 2023]. In addition to their health benefits, proanthocyanidins play a role in the flavor, color, and astringency of foods and beverages [Qi *et al.* 2023]. They contribute to the bitterness and astringency of certain fruits, such as grapes and berries, as well as beverages like red wine and tea.

Catechin is a flavonoid compound belonging to the subclass of flavan-3-ols, having a hydroxyl (-OH) group attached to the 3-carbon position of the C ring. Its chemical structure consists of a flavan nucleus, which is a 3-ring structure with two phenyl rings (A and B rings) connected by a heterocyclic pyran ring (C ring) [Baranwal *et al.* 2022]. Catechin can exist in different forms, including epicatechin, epicatechin gallate, epigallocatechin, and epigallocatechin gallate, depending on the specific arrangement of hydroxyl groups on the flavan nucleus. The structural variations and arrangements of catechin molecules contribute to their diverse biological activities and potential health benefits [Isemura 2019]. It is present in various foods and beverages, including tea (particularly green tea), cocoa, fruits such as apples, berries, and grapes, as well as certain nuts such as hazelnuts and pecans [Yilmaz 2006]. Catechin is one of the most abundant flavonoids in the human diet. The potential health benefits of catechin are the same as proanthocyanidins [Isemura 2019].

The recurring author keywords of the anthocyanin papers

Figure 4 depicts the frequently occurring author keywords in the context of antioxidant research, excluding derivatives of the term “anthocyanin.” Among the ten most frequently recurring keywords identified, several prominent themes emerge, reflecting the focus and interests of researchers in this field.

First of all, antioxidant activity stands out as the most prevalent keyword. This underscores the primary objective of many studies, which is to investigate the antioxidant properties of various compounds and their potential health benefits. Antioxidant activity is a crucial aspect of the action of polyphenols, flavonoids, and other phenolic compounds, which are also among the most recurring keywords in our visualization. Anthocyanins exhibit significant antioxidant activity due to their chemical structure, which allows them to donate electrons or hydrogen atoms to reactive oxygen species (ROS), thus neutralizing them. They can directly scavenge various free radicals, such as superoxide anion radicals ($O_2^{\bullet-}$), hydroxyl radicals ($\bullet OH$), and peroxy radicals ($ROO\bullet$) [Smeriglio *et al.* 2016, Liu *et al.* 2021]. Anthocyanins can also chelate transition metal ions, such as iron and copper, which are involved in the generation of ROS via Fenton and Haber-Weiss reactions. Other antioxidants, such as vitamin C and vitamin E, can also regenerate other antioxidants, by anthocyanins. Anthocyanins have been shown to upregulate the expression and activity of endogenous antioxidant enzymes, including superoxide dismutase (SOD), catalase, and glutathione peroxidase. Anthocyanins can protect cell membranes from oxidative damage by incorporating into the lipid bilayer and preventing lipid peroxidation, which is a common consequence of oxidative stress [Prior and Wu 2006, Quina *et al.* 2009].

Polyphenols are a diverse group of naturally occurring compounds found abundantly in plants. They are characterized by the presence of multiple phenol (hydroxyl) groups and can be further classified into several subclasses, including flavonoids, phenolic acids, lignans, and stilbenes. Polyphenols play essential

roles in plants, serving as antioxidants, pigments, and defense compounds against environmental stressors such as UV radiation and pathogens [Han *et al.* 2007, Belščak-Cvitanović *et al.* 2018]. Polyphenols are well-known for their antioxidant activity, which helps neutralize harmful free radicals in the body and protect cells from oxidative damage. This antioxidant capacity contributes to their potential health benefits, including reducing the risk of chronic diseases such as heart disease, cancer, and neurodegenerative disorders. Polyphenols are found in a wide variety of plant-based foods, including fruits (berries, apples, citrus fruits, grapes), vegetables (onions, broccoli), whole grains, nuts, seeds, tea, coffee, cocoa, red wine, herbs, and spices [Li *et al.* 2014].

Flavonoids are a large and diverse group of polyphenolic compounds abundantly present in various fruits, vegetables, grains, herbs, spices, nuts, seeds, tea, and wine. Flavonoids are classified into several subclasses based on the degree of oxidation and the pattern of substitution on the heterocyclic ring (ring C). Major subclasses include flavonols, flavones, flavanones, flavanols (catechins), anthocyanins, and isoflavones. Each subclass has unique chemical properties and biological activities. Flavonoids are abundant in a wide range of plant-based foods, with different subclasses found in different food sources. For example, flavonols are prevalent in onions, apples, berries, and tea, while flavanones are abundant in citrus fruits. Flavonoids possess various biological activities and have been associated with numerous health benefits. These include antioxidant, anti-inflammatory, anti-cancer, cardioprotective, neuroprotective, and anti-diabetic effects [Pietta 2000, Havsteen 2002].

Phenolic compounds are a diverse group of organic compounds characterized by the presence of one or more phenol (hydroxyl) groups attached to aromatic rings. They are widely distributed in nature and can be found in various plant-based foods, including fruits, vegetables, grains, nuts, seeds, herbs, spices, tea, coffee, and wine. Foods rich in phenolic compounds include fruits such as berries, apples, citrus fruits, and grapes; vegetables like onions, garlic, and spinach; grains such as whole grains and legumes; nuts and seeds; herbs and spices; and beverages like tea, coffee, and wine [Wojdyło *et al.* 2007, Cheynier 2012].

Antioxidants are molecules that inhibit or neutralize the harmful effects of free radicals and reactive oxygen species (ROS) in the body. Antioxidants play a crucial role in maintaining cellular health by counteracting the damaging effects of oxidative stress and protecting against various chronic diseases and aging processes. Antioxidants can be classified into several categories based on their chemical structure and properties. Common antioxidants include vitamins (such as vitamin C, vitamin E, and vitamin A), minerals (such as selenium and zinc), phytochemicals (such as flavonoids, phenolic acids, and carotenoids), and enzymes (such as superoxide dismutase and catalase). Some of the best dietary sources of antioxidants include berries (such as blueberries, strawberries, and raspberries) [Junqueira *et al.* 2004, Fusco *et al.* 2007, E Obrenovich *et al.* 2011].

Phenolics (which are also known as “phenolic compounds”) represent a diverse group of organic compounds that contain a phenol ring. They are widely distributed in nature and are found in various plants, fruits, vegetables, and beverages such as tea, coffee, and wine. Phenolics are known for their antioxidant properties. Some common phenolic compounds include flavonoids (e.g., quercetin, kaempferol, and catechins), phenolic acids (e.g., caffeic acid, ferulic acid, and gallic acid) and stilbenes (e.g., resveratrol). All phenolics help protect the body from oxidative stress and inflammation, which are associated with various chronic diseases such as cardiovascular disease, cancer, and neurodegenerative disorders. In addition to their health benefits, phenolic compounds also contribute to the flavor, color, and aroma of foods and beverages, making them important for sensory quality [Soobrattee *et al.* 2005, Umar Lule and Xia 2005].

Additionally, the term “bioactive compounds” appears frequently (739 occurrences), indicating a broader interest in exploring the physiological effects and mechanisms of action of various bioactive substances beyond their antioxidant activity alone. Finally, the appearance of “HPLC” (high-performance liquid chromatography) with 579 occurrences highlights the significance of analytical techniques in antioxidant research. HPLC plays a crucial role in identifying, quantifying, and characterizing bioactive compounds, providing valuable insights into their presence and concentration in different samples [Abuohashish and El Sharkawy 2023, Srinivasan *et al.* 2023].

The recurring food items discussed in the anthocyanin papers

Table 3 presents the most commonly mentioned food items in the anthocyanin research papers. Alongside grapes, a variety of berries, rice, maize, potato, tomato, and other plant species were frequently highlighted in the literature.

Grapes are one of the primary sources of anthocyanins. Anthocyanins contribute to the red, purple, and blue hues of grapes, particularly in darker grape varieties such as Concord, black currant, and purple grapes. Anthocyanins are concentrated in the skin of grapes, where they serve several essential functions. Grapes boast a wealth of flavonoids, potent compounds known for their ability to combat free radicals, thereby preventing senility. They offer protection against cardiovascular and cerebrovascular ailments while alleviating fatigue, aiding digestion, bolstering immunity, and enhancing blood circulation. Notably, the presence of anthocyanins and resveratrol in grapes confers health-enhancing properties to grape-derived products, including antioxidative effects, increased elasticity of blood vessels, and the promotion of radiant skin [Ribéreau-Gayon 1982, Flamini, 2013, Flamini *et al.* 2013].

Berries are renowned for their rich content of anthocyanins. The presence of anthocyanins in berries serves multiple purposes similar to that of grapes. Various types of berries are rich sources of anthocyanins, with berries like blueberries, strawberries, raspberries, blackberries, and cranberries containing particularly high concentrations of these beneficial compounds. The king of berries is blueberries. The skin of this fruit is packed with essential nutrients such as vitamin A, vitamin E,

minerals, niacin, and trace elements. Its benefits extend across a spectrum of health functions, including anti-cancer, heart support, cardiovascular protection, relief from visual fatigue, anti-aging properties, and promotion of skin health. Blueberries, in particular, boast a remarkable anthocyanin content ranging from 3.87 to 4.87 mg/g, surpassing that of strawberries, raspberries, and blackberries. Furthermore, they are abundant in potent compounds like proanthocyanidins, earning them a reputation as one of the fruits with the highest levels of antioxidant activity [Rani and Khullar 2004, Skrovankova *et al.* 2015, Olas 2018].

White rice is not typically associated with high levels of anthocyanins compared to fruits, there are varieties of rice that do contain anthocyanins – pigmented rice varieties, such as black rice (also known as forbidden rice), red rice, and purple rice. A primary source of phenolic compounds is wild rice, and it is regarded as a whole grain with health benefits. Its remarkable antioxidant properties and health benefits have garnered significant interest, encompassing the inhibition of oxidative stress, alleviation of hyperlipidemia, and prevention of conditions such as atherosclerosis, type II diabetes, and obesity. Compared with colorless rice, the representative flavonoids in red rice are proanthocyanidins, whereas those in wild rice and black rice include both anthocyanins and proanthocyanidins [Goufo and Trindade 2014, Xia *et al.* 2021].

Maize, commonly known as corn, is not typically associated with high levels of anthocyanins in its kernels. However, there are specific varieties of maize, known as “purple corn” or “blue corn”, that contain anthocyanins. In maize, the predominant anthocyanin pigments belong to the cyanidin and pelargonidin groups. Cyanidin-based anthocyanins impart a red-to-purple color, while pelargonidin-based anthocyanins contribute to a more orange-to-red hue. Additionally, other minor anthocyanin compounds may be present in maize, but cyanidin and pelargonidin derivatives are the most commonly found types. In addition to anthocyanins, purple and blue maize varieties also contain other phytochemicals, vitamins, and minerals that contribute to their potential health-promoting properties [Salinas Moreno *et al.* 2005, Petroni *et al.* 2014].

There are specific varieties of potatoes that exhibit pigmentation due to the presence of anthocyanin pigments. These pigmented potatoes are commonly referred to as “purple potatoes” or “blue potatoes.” Purple sweet potatoes, extensively cultivated in China, have garnered significant attention due to their abundant anthocyanin content, offering various physiological benefits such as lowering blood lipids, antioxidative properties, and anti-aging effects. The primary chemical constituents of anthocyanins in purple sweet potatoes are predominantly cyanidin and peonidin. Notably, these potatoes boast a higher anthocyanin concentration compared to fruits like eggplant and cherries, and the anthocyanins extracted from purple sweet potatoes demonstrate greater stability against light and heat than those from other plants, such as strawberries and red cabbages. Consequently, purple sweet potatoes serve as an excellent source of robust and stable anthocyanins. In terms of antioxidant capacity, purple potatoes surpass white potatoes, containing between 3 and 4 times more anthocyanins and

exhibiting 2.5-3.0 times greater free radical scavenging ability. Research indicates many health benefits associated with purple potatoes, including liver protection, anticancer properties, blood sugar regulation, anti-aging effects, and support for weight loss efforts [Brown *et al.* 2003, Zhao *et al.* 2009].

Some specific tomato cultivars have been bred or genetically modified to contain anthocyanins, resulting in purple or blue pigmentation. These purple or blue tomatoes are often referred to as “indigo tomatoes” or “blue tomatoes”. The anthocyanins in such tomatoes belong to the cyanidin group, similar to those found in other purple-hued fruits and vegetables. Indigo tomatoes contain predominantly delphinidin-based anthocyanins. Indigo tomatoes are not as widely available as traditional red tomatoes, and their cultivation may be limited to specific regions or specialty markets. Additionally in red tomatoes the high levels of lycopene was identified. Lycopene helps protect cells from damage caused by free radicals. This can contribute to reduced risk of chronic diseases, such as heart disease and certain types of cancer. Studies suggest that lycopene may improve cardiovascular health by reducing LDL cholesterol levels and blood pressure. Additionally, their antioxidant action is believed to have a protective effect on the skin, helping to shield it from UV damage [Povero *et al.* 2011, Gonzali and Perata 2020, Yeung *et al.* 2022].

Natural feed additives as a source of antioxidants in animal farming

In livestock production, extracts from vegetables and fruits are increasingly used as feed additives, offering a dual benefit to both the animals and the end consumers [Maj *et al.* 2023, Wójcik *et al.* 2023]. Such natural additives may not only enhance the taste of the feed, making it more palatable and thereby encouraging animals to consume more, but they also may contribute significantly to improving animal health and the quality of the meat produced.

One notable example is the use of dietary resveratrol supplementation in broilers. Resveratrol, a compound found in the skin of grapes and in other fruits, is known for its potent antioxidant properties. Supplementation of broiler diets with resveratrol has been shown to prevent the impairment of meat quality associated with transport stress, a common issue in the poultry industry. This improvement in meat quality is attributed to resveratrol’s ability to decrease muscle anaerobic glycolysis metabolism and enhance muscle antioxidant capacity. This not only leads to healthier animals but also results in meat that is of a higher quality, with benefits such as improved texture, taste, and nutritional value [Zhang *et al.* 2018].

The addition of specific plant-derived compounds like Capsicum oleoresin, Carvacrol, Cinnamaldehyde, and their mixtures to broiler diets has also been shown to further enhance meat quality. These components not only improve the sensory properties of chicken meat, including taste, tenderness, juiciness, and overall acceptability, but also positively influence the physical and chemical properties of the meat. For breast meat, the inclusion of these additives has been found to affect its L* value (lightness) and toughness, along with chemical properties such as dry matter (DM), crude fiber

(CF), crude protein (CP), linoleic acid, eicosapentaenoic acid (EPA), behenic acid, monounsaturated fatty acids (MUFA), polyunsaturated fatty acids (PUFA), and total omega-6 fatty acids ($\Sigma n-6$). Similarly, for leg meat, these feed additives impact physical properties like toughness and firmness, as well as chemical properties including CF, CP, linoleic acid, eicosanoids, EPA, lignoceric acid, MUFA, and total omega-3 fatty acids ($\Sigma n-3$). The supplementation of Capsicum oleoresin, Carvacrol, Cinnamaldehyde, and their mixtures into broiler diets thereby not only makes the feed more appealing to the animals but also significantly improves the nutritional and sensory qualities of the meat [İpçak and Alçiçek 2018, Marchewka *et al.* 2023].

Incorporating such natural feed additives into livestock diets represents a forward-thinking approach to agriculture, emphasizing sustainability, animal welfare, and product quality. By leveraging the health-promoting properties of plant-based compounds, producers can achieve better outcomes across the board, from enhanced animal well-being to superior meat products for consumers.

Conclusions

The publications on anthocyanin were heavily contributed by China and the United States as well as European and Asian countries such as Italy, Spain, and Japan. Many publications focused on the areas of food science & technology and plant sciences. Frequently mentioned chemicals/chemical classes included anthocyanin, flavonoid, cyanidin, phenolic compound, and polyphenol. Recurring food items of the anthocyanin papers included grapes, many berries, and specific varieties of rice, maize, potato, and tomato. The literature has demonstrated that anthocyanins are beneficial to both animals and humans.

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Author contributions: AWKY and AGA conceived the work. AWKY performed data collection and analyses. AWKY and MS drafted the manuscript. DH contributed parts of the draft on cancer and ABC/SLC-transporter-expression-mediated drug resistance and chemotherapy efficiency. All authors critically reviewed and revised the manuscript and approved its submission for publication in the journal *Animal Science Papers and Reports*.

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