

eISSN: 2581-9615 CODEN (USA): WJARAI Cross Ref DOI: 10.30574/wjarr Journal homepage: https://wjarr.com/

	WJARR W	USEN 2591-9915 CODEN (1984) HEAREA
	World Journal of Advanced Research and Reviews	
		World Journal Series INDIA
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(RESEARCH ARTICLE)

Synthesis and structural elucidation of bioactive compounds in fruits and their applications

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World Journal of Advanced Research and Reviews, 2025, 25(02), 1737-1745

Publication history: Received on 10 January 2025; revised on 15 February 2025; accepted on 18 February 2025

Article DOI: https://doi.org/10.30574/wjarr.2025.25.2.0557

# Abstract

Natural selection and processes of evolution have influenced the beneficial effects of natural products over hundreds of thousands of years, giving them a high degree of structural variety and distinctive pharmacological or biological activity. Natural products have therefore been used to cure illnesses in both traditional and modern medicine. Nowadays, natural materials are frequently utilised as a basis for medication development, with synthetic alterations made to aid in decreasing adverse effects and boosting absorption. In addition to medicine, natural products and their derivatives are frequently employed as food additives, such as herbs and spices, antibacterial agents, and antioxidants, to preserve the durability and quality of food. Bioactive compounds such as phenolic acids, flavonoids, anthocyanins, stilbenes, and lipids are abundant in grapes, mangoes, berries, and pineapple peels. These are the substances that give fruits and products made from them their health advantages. They are widely used in the food and nutraceutical industries and have anti-inflammatory, anti-carcinogenic, anti-microbial, and antioxidant properties. Utilising grape extracts that are high in these bioactive components has been connected with a lower prevalence of cardiovascular disease and its primary risk factors, such as hypertension, a medical condition that has a high global death rate. The citrus fruits are also a rich source of poly-methoxylated flavones (PMFs), a special type of bioactive flavonoid. Furthermore, because of its strong antibacterial, flavouring, and antioxidant qualities, citrus essential oil, which is abundant in limonoids and terpenes, is a valuable commodity from a commercial standpoint. The antioxidant capacities of pineapple peel extracts and these polyphenolic compounds were determined using (2,2-diphenyl-1-picrylhydrazyl) DPPH. The positive health impacts of polyphenols derived from berries and their potential use as a treatment for illnesses linked to the gut microbiota, such as cancer and inflammation. According to these findings, berries' polyphenols are a promising source of bioactive substances that can alter the gut microbiota and hence control cancer and related metabolic disorders.

Keywords: Bioactive compounds; Phenolic acids; Flavonoids; Health; Diseases

# 1. Introduction

Natural products, the small organic molecules produced by many microbes, plants, and invertebrates, are the source of some modern drugs. The best method for determining a molecule's structure is X-ray crystallography. Since most natural products do not yield crystals of appropriate X-ray quality, integrated spectroscopic techniques remain the most practical way to elucidate structures. Nevertheless, by "pushing the limits" of the then-current NMR technique, remarkable achievements in the structure determination of minuscule sample amounts of natural products have been achieved. The worldwide dietary guidelines recommend a daily consumption of fruits due to their contributions in providing vitamins, minerals, and phytochemicals to the body. Berries are particularly significant among fruits since they often contain more bioactive chemicals. According to botany, berry fruits are a group of tiny, fleshy fruits with red, purple, and blue hues that are generated from a single ovary. The most popular ones include gooseberry, blackberry, rosehip, raspberry, blueberry, white and black mulberry, strawberry, currant, and barberry. Asia, Europe, Anatolian and Mediterranean nations, and North African nations are home to a large number of them. In addition to being eaten fresh

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and frozen, these fruits are also frequently used to make processed and derived goods such as drinks, jams, dried and canned fruits, and jellies.

The high-value crop known as pistachio (Pistacia vera L.) is a member of the Anacardiaceae family and is native to dry parts of Central and West Asia. According to its degree of ripeness, the pistachio fruit is a semidry drupe with a single edible seed (kernel), a thin, soft coat (testa), and a creamy, lignified shell (endocarp) encased in a fleshy hull (mesocarp and epicarp) that ranges in colour from green to yellow-red. PGH (Pistachio green hull) is utilised as animal feed in some places, which results in nutritional issues for cattle because of the high concentration of tannins and phenolic chemicals that interact with minerals, protein, and carbs (Mokhtarpour et al., 2014). The primary carotenoids found in pistachios are lutein and zeaxanthin. Polyphenols found in pistachios may have antiviral effects against the type 1 herpes simplex virus (HSV-1). Tocopherols are bioactive substances with antioxidant qualities that are found in pistachio hulls. Phytosterols found in pistachio grains may lower the risk of cardiovascular disease. Dietary fibre, found in pistachio grains, may lower the risk of cardiovascular disease. Essential oils found in pistachio hulls may have antifungal and antibacterial qualities. Pistachio hulls can be used to create high-value dishes and are also a good source of bioactive chemicals.

Almonds are a popular and healthy snack food that are rich in nutrients, including protein, fibre, healthy fats, vitamins, and minerals. Additionally, they contain bioactive substances that may be beneficial to health, like phytosterols and polyphenols. However, in order to comprehend the possible health impacts of these components, it is crucial to take into account their metabolism and bioavailability in almonds. The nutrients and bioactive substances in almonds can have varying levels of bioavailability according to processing, cooking, and mixing with other meals. According to one study, eating raw almonds instead of roasted or blanched ones greatly increased the bioavailability of vitamin E in the almonds. The highest concentration of total phenolic compounds (66.02 mg/100 g FW) was found in the peel of a Chilean Pica cultivar. The peel and pulp of the Pica and Tommy Atkins cultivars contained four xanthones, including homo-mangiferina, mangiferin, and mangiferin gallate; three procyanidin dimers; and seven phenolic acid derivatives; only dimethyl mangiferin was found in the pulp of the Tommy Atkins cultivar (Ramírez et al., 2013). Bioactive compounds such as phenolic acids, flavonoids, anthocyanins, stilbenes, and lipids are abundant in grapes. They are widely used in the food and nutraceutical industries and have anti-inflammatory, anti-carcinogenic, anti-microbial, and antioxidant properties. Utilising grape extracts that are high in these bioactive components has been connected with a lower prevalence of cardiovascular disease and its primary risk factors, such as hypertension, a medical condition that has a high global death rate. As a result, products made from grapes have received a lot of attention as a way to treat and relieve hypertension. This review's objective is to provide an overview of the bioactive substances found in grapes, the variations in composition among various grape extracts, and the possible advantages in lowering blood pressure.

## 2. General Properties of Bioactive Compounds in Fruits

#### 2.1. Chemical Composition

Numerous health benefits associated with berry fruits include antioxidant, anti-inflammatory, antimicrobial, anticancer, and antidiabetic effects; they also contribute to plant growth and protection against biotic and abiotic stressors. The distribution of these polyphenols varies significantly depending on a number of factors, including plant genotype, environmental conditions, growing location, and fruit processing and storage. Berries are a rich source of phytochemicals, particularly phenolic compounds. Berries are known to contain a lot of flavonoid chemicals, especially anthocyanins (up to 5000 mg/kg), which give them their blue, purple, and red hues and contribute to their popularity. It seems that anthocyanins are highly unstable and prone to deterioration. In actuality, a number of variables can impact the chemistry of anthocyanins and, consequently, their stability, including oxygen, enzymes, temperature, light, and pH. Chemically speaking, anthocyanins are water-soluble glycosides of 2-phenylbenzopyrylium derivatives that are polyhydroxylated and polymethoxylated. Anthocyanidins, which are derived from delphinidin, cyanidin, pelargonidin, petunidin, malvidin, and peonidin anthocyanidins, are generally found in berries as glycosides of their respective aglycones. These anthocyanidins form O-linked conjugates with specific sugars, primarily glucose, galactose, rhamnose, arabinose, and rutinose. The primary forms of these compounds are 3,5-diglucosides, 3-monosides, and 3-biosides.

Berries are also known to contain phenolic acids, such as hydroxycinnamates and hydroxybenzoate. Caffeic, ferulic, pcoumaric, vanillic, chlorogenic, neochlorogenic, sinapic, and protocatechuic acids, along with the  $\beta$ -D-glucosides of pcoumaric and caftaric acids, are the primary phenolic acids found in berries.

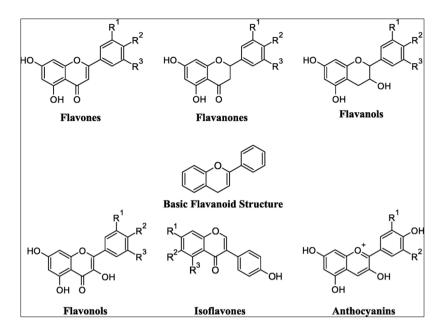


Figure 1 Chemical structures of major flavonoids contained in fruits.



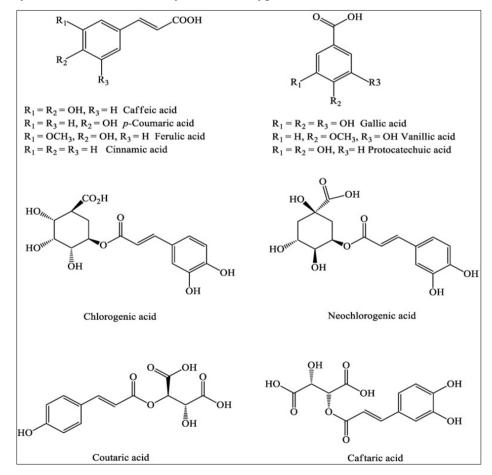


Figure 2 Chemical structures of phenolic acids contained in fruits.

In the small intestine, polyphenols including flavonoid aglycones and phenolic acids are easily absorbed. However, phenolic compounds must be hydrolysed by intestinal enzymes or the gut bacteria before they can be absorbed because they are mostly found in berry fruits in ester, glycoside, or polymer forms (such as anthocyanins, ellagitannins, and

flavan-3-ols). Lactase phlorizin hydrolase (LPH), a  $\beta$ -galactosidase enzyme found in enterocyte brush border membranes, is primarily involved in the metabolic process that takes place in the small intestine. Phenolic glycosides are hydrolysed by this enzyme to aglycones, which have a higher lipophilicity and can passively diffuse into intestinal cells.

Other studies, however, showed that the sodium-dependent glucose transporter (SGLT) could also carry glycosides into enterocytes, where a cytosolic glucosidase would hydrolyse them. Both enzymes may be implicated, according to reports, but further research is needed to fully understand how they relate to different phenolic glycosides.

## 2.3. Bioavailability and Metabolism of Almond Components

Additionally, studies have demonstrated the anti-inflammatory and antioxidant properties of almond polyphenols, which may help prevent chronic illnesses like diabetes and cancer. Almonds are a useful tool for managing weight because of their high fibre content, which can also support satiety and digestive health.

## 2.4. Bioactive Compounds of Guava

Guava contains phytochemicals called bioactive compounds, such as alkaloids, saponins, terpenoids, tannins, phenols, and flavonoids, which may have uses in human health. These substances are referred to as primary and secondary metabolites since they can be created in plants as byproducts of metabolic and biochemical processes. Guava plants' phytochemical production offers defence against invasive diseases like bacteria, fungus, and viruses. In order to produce the phytochemicals required for defence against external pathogens, a pool of nutrients and amino acids will be utilised by the mechanism following pathogen invasion. The formation of phytochemicals follows several biosynthetic pathways depending on the bioactive component. Alkaloids, for example, are made from the aliphatic amino acids that are created during the citric acid cycle; mevalonic acid metabolism through the mevalonate pathway produces terpenoids and saponins, but only the latter travels through the methyl erythritol pathway.

## 2.5. Bioactive Compounds of Citrus Fruits

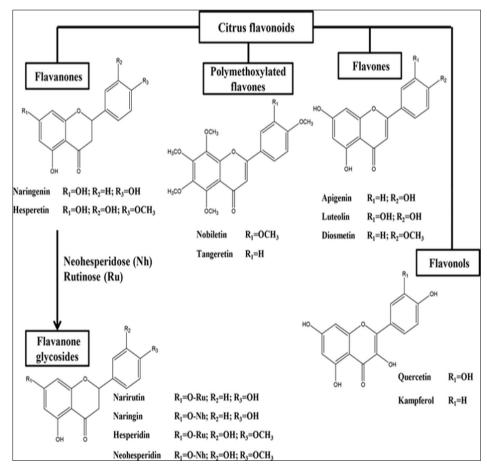


Figure 3 Chemical structure of major flavonoids of citrus fruits.

The citrus genus is well-liked all over the world due to its richness of nutrients and bioactive compounds, as well as its delicious flavour. Bioactive chemicals, primarily phenolic compounds (flavonoids, phenolic acids, and coumarins), terpenoids (limonoids and carotenoids), and pectin, are abundant in citrus fruits. Citrus fruits are also high in minerals (selenium, zinc, copper, iron, and manganese), ascorbic acid, and tocopherols and tocotrienols (vitamin E). Recent years have seen the publication of several excellent reviews on the bioactive makeup and health advantages of citrus, with a primary focus on flavonoids and essential oils (terpenes and limonoids). There isn't, however, a thorough analysis of all the main bioactive ingredients in citrus fruits. Therefore, this review offers a thorough understanding of the flavonoid, carotene, terpene, and limonoid content of citrus fruits as well as the health advantages that go along with them. According to the substitution patterns of a heterocyclic ring, flavonoids can be divided into subgroups, such as flavones, flavonols, flavanones, flavanols (flavan-3-ols), isoflavones, and anthocyanins. Citrus fruits contain a substantial amount of flavanone-7-O-glycosides (e.g., naringin, eriocitrin, hesperidin, and narirutin), flavones, polymethoxylated flavones (PMFs, e.g., nobiletin, tangeritin, and 5-demethyl nobi-letin), flavonols (quercetin, rutin, and kaempferol), and anthocyanin.

## 2.6. Bioactive Compounds in Mangoes

The flesh and skin of nine different types of mangoes grown in China were found to contain various phenolic acids (Abbasi et al., 2015). Ferulic acid (33.75 mg) was the most abundant phenolic acid in 100 g FW of pulp, followed by protocatechuic (0.77 mg), gallic (0.93–2.98 mg), vanillic (0.57–1.63 mg), protocatechuic (0.77 mg), and caffeic (0.25–0.10 mg) acids (Abbasi et al., 2015). Protocatechuic acid (0.48–1.1 mg/100 g dry weight (DW)), vanillic acid (16.9–24.4 mg/100 g DW), gallic acid (94.6–98.7 mg/100 g DW), and chlorogenic acid (28–301 mg/100 g DW) were the main phenolic acids found in Ataulfo mangos from Mexico (Palafox-Carlos et al., 2012).

However, due to their low concentrations, these authors were unable to measure the other well-known phenolic acids, namely p-hydroxybenzoic, p-coumaric, and ferulic acids. High levels of phenolic acids and their derivatives, including gallic, methyl digallate ester, methyl gallate, gallotannins, galloyl glucose, theogallin, protocatechuic, and ferulic acid, have been detected in the peel extracts of the mango cultivars Ataulfo, Keitt, Osteen, and Sensation (López-Cobo et al., 2017).

## 2.7. Bioactive Compounds in Grapes

Although grapes are a rich source of bioactive compounds, certain factors, such as variety, maturity, post-harvest storage, and environmental factors like location, light conditions, temperature, nutrition, water, microorganisms, and viticulture practices, can affect how much of these compounds accumulate in grapes (Chen et al., 2020, Colombo et al., 2020, Perestrelo et al., 2012). According to Gouot et al. (2019), the primary phenolic compounds found in grape berries are flavonoids, which include anthocyanins and proanthocyanidins, hydroxycinnamic acids, and stilbenes. Phenolic substances like hydroxycinnamic acids, anthocyanins, proanthocyanidins, and stilbenes are among the bioactive phytochemicals found in grapes.

## 3. Results and Discussion

Numerous bioactive substances, each with specific health advantages, are found in fruits, such as polyphenols, carotenoids, flavonoids, anthocyanins, vitamins, and phytoestrogens. Many bioactive substances included in fruits function as antioxidants, shielding cells from the harm that free radicals can do and possibly lowering the chance of developing chronic illnesses. According to research, eating fruits high in bioactive chemicals may strengthen the immune system and help against cancer, heart disease, and neurological illnesses.

Phenolic chemicals are abundant in the rinds, peels, and seeds of fruits. Since the peel of citrus fruits contains more polyphenols than the edible part, citrus trash is a rich source of phenolic compounds. It has been reported that apple peels can contain up to 3300 mg of phenol per 100 g of dry matter. The juice and wine industries produce mono-, oligo-, and polymeric pro-anthocyanidins (phenolics), which are abundant in grape skins and seeds. Bioactive flavonoids, particularly polyethoxylated flavones (PMFs), such as nobiletin, tangeritin, and 5-demethyl nobiletin, are abundant and remarkable in citrus fruits. Citrus fruits are also rich in provitamin A, carotenoids (like  $\beta$ -citraurin), and bioactive xanthophylls. By lowering the body's levels of inflammatory mediators and reactive oxygen species (ROS), these bioactive substances lower the risk of metabolic syndrome, which includes cancer, diabetes, cardiovascular disease (CVD), and neurodegenerative diseases. Furthermore, because of its flavouring, antimicrobial, antioxidant, and other health-promoting qualities, citrus essential oil, which is high in terpenes (like D-limonene) and limonoids (like limonin)—is a valuable product from an economic standpoint.

Research on the makeup, content, and health-promoting properties of citrus fruit bioactive has advanced significantly. All over the world, guava (Psidium guajava Linn.) is widely recognised for its culinary and nutritional benefits. Due to their high levels of dietary fibre, potassium, folic acid, and dietary minerals, guavas were also listed as super fruits. The guava plant contains a variety of bioactive compounds, including terpenes, tannins, polyphenols, quercetin, quercitrin, ursolic acid, linoleic acid, myristic acid, guajavanoic acid, arabinose, ascorbigen, and destructive. In traditional medicine, guava fruit, leaves, and other plant parts are also well known for their therapeutic qualities. The guava tree is cultivated on a commercial basis because every part of it has economic value. The fruit is considered the poor man's apple of the tropics, and the guava plant has reached a key point in terms of biological action and restorative usage. According to this review, an abundance of bioactive compounds, including polyphenols, carotenoids, carbs, proteins, and minerals, may be found in many sections of mango trees, including the bark, leaves, fruit pulp, peel, and stone. The genotype of the mango and its growing conditions affect the amounts of these compounds. These compounds) scavenging intermediates work in concert to produce the total antioxidant activity (AoA) of mango fruit. For the treatment of a wide range of conditions, including autoimmune diseases, the bioactive compounds in mango may be a viable source for logical drug design and the identification of mechanism-based inhibitors.

As health-related molecules, bioactive chemicals have been shown to lower the risk of cancer, Alzheimer's, cataracts, Parkinson's disease, and other illnesses. Their ability to delay or prevent damage to DNA, proteins, and lipids has been linked to their antioxidant and radical scavenging qualities. These substances do in fact have antibacterial qualities, and by dividing the cell membranes of microbes and causing lysis, they help shield fruits from dangerous substances.

# 4. Conclusion

It is concluded that sustainable bioactive chemicals from fruits may be produced using innovative extraction techniques. Bioactive chemicals are being extracted from fruits using a variety of innovative approaches. As useful additives, these sustainable extracts are applied to various food products. A significant source of bioactive chemicals with a range of uses and health advantages is fruit waste. According to research, traditional extraction methods are frequently ineffective, expensive, and harmful to the environment when it comes to extracting bioactive compounds. Alternative extraction techniques are therefore required in order to efficiently and sustainably recover bioactive components of fruits. The sorts of bioactive substances found in fruit waste, including polyphenols, carotenoids, pectins, and essential oils, are compiled in this review. The many extraction methods that have been employed or suggested to value fruit waste are also covered, including enzyme-assisted extraction, ultrasound-assisted extraction, and microwave-assisted extraction. Additionally, it draws attention to the possible health advantages and uses of bioactive substances derived from fruit waste in food, medicine, and cosmetics. The regular consumption of fruits, such as berries, apples, and tropical fruits, as part of a nutritious diet has been shown to promote excellent health and help prevent chronic diseases. Berries are often a major source of antioxidant chemicals, with tropical fruits and apples coming in second and third. A major source of these health-promoting compounds is berries, which are particularly high in phytochemicals and anthocyanins. Apples have larger levels of quercetin, while tropical fruits have higher levels of  $\beta$ -carotene. The findings point to possible future directions for the utilization of the fruit species that were examined and found to have a significant amount of antioxidant activity. Additionally, this study will help customers plan diets high in antioxidants and dietitians estimate the daily intake of phenolic antioxidants and their health effects.

## **Compliance with ethical standards**

#### Disclosure of conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

#### References

- [1] Etim KAD., Isaac UE., Igiri A.O. Morphological Alterations of the Rat Testicles Following Administration of Graded Doses of Leaves of Guava (Psidium guajava Linn.) Aqueous Extract. Tropical Health and Medical Research 2020.
- [2] Adhau GW., Salvi VM. Formation and quality acceptable properties of guava cheese. International Journal of Advanced Research. 2014;2(11):665-669.
- [3] Mitra SK., Devi HL., Chakraborty I., Pathak PK. Recent development in postharvest physiology and storage of guava. In III International Symposium on Guava and other Myrtaceae. 2012; 959:89-95.

- [4] Jolhe P., Sahu GD., Kumar V. Preparation and evaluation of jelly (Psidium guajava). Journal of Pharmacognosy and Phytochemistry 2020;9(6):20612063.
- [5] Upadhyay R., Dass JFP., Chauhan AK., Yadav P., Singh RB. Guava enriched functional foods: therapeutic potentials and technological challenges. The role of functional food security in global health 2019, 365-378.
- [6] Sinha M., Mishra S. Effect of Value Addition on Guava Cheese with Medicinal Herbs under Ambient Storage Condition (Psidium gujava L.) cv. "Allahabad Safeda". International Journal of Pure and Applied Bioscience 2017;5(3):559-566.
- [7] Biswas B., Rogers K., McLaughlin F., Daniels D., Yadav A. Antimicrobial activities of leaf extracts of guava (Psidium guajava L.) on two gram-negative and gram positive bacteria. International journal of microbiology 2013.
- [8] Raihana AN., Marikkar JMN., Amin I., Shuhaimi M. A review on food values of selected tropical fruits' seeds. International Journal of food properties, 2015;18(11):2380-2392.
- [9] Vijaya Anand A., Velayuthaprabhu S., Rengarajan R L., Sampathkumar P., Radhakrishnan R. Bioactive Compounds of Guava (Psidium guajava L.). Bioactive Compounds in Underutilized Fruits and Nuts 2020, 503527.
- [10] Chen M., Yu S. Lipophilized grape seed proanthocyanidin derivatives as novel antioxidants. Journal of Agricultural and Food Chemistry. 2017;65(8):1598–1605. doi: 10.1021/acs.jafc.6b05609.
- [11] Chong M.F., Macdonald R., Lovegrove J.A. Fruit polyphenols and CVD risk: A review of human intervention studies. British Journal of Nutrition. 2010;104(S3): S28–S39. doi: 10.1017/S0007114510003922. [DOI] [PubMed] [Google Scholar]
- [12] Lapuente, M., Estruch, R., Shahbaz, M., Casas R. Relation of Fruits and Vegetables with Major Cardiometabolic Risk Factors, Markers of Oxidation, and Inflammation. Nutrients 2019, 11, 2381. https://doi.org/10.3390/nu11102381.
- [13] Zou Z., Xi W., Hu Y., Nie C., Zhou Z. Antioxidant activity of Citrus fruits. Food Chem. 2016, 196, 885–896. https://doi.org/10.1016/j.foodchem.2015.09.072.
- [14] Wu, G.A., Terol, J., Ibanez, V., Lopez-Garcia, A., Perez-Roman, E., Borreda, C., Alonso, R.; et al. Genomics of the origin and evolution of Citrus. Nature 2018, 554, 311–316. https://doi.org/10.1038/na-ture25447.
- [15] Lu, X., Zhao, C., Shi, H., Liao, Y., Xu, F., Du, H., Zheng, J. Nutrients and bioactive in citrus fruits: Different citrus varieties, fruit parts, and growth stages. Crit. Rev. Food Science Nutr. 2021, 1–24. https://doi.org/10.1080/10408398.2021.1969891.
- [16] Zhang, M., Zhu, S.Y., Yang, W.J., Huang, Q.R., Ho, C.T. The biological fate and bioefficacy of citrus flavonoids: Bioavailability, biotransformation, and delivery systems. Food Funct. 2021, 12, 3307–3323. https://doi.org/10.1039/d0fo03403g.
- [17] United States Department of Agriculture Foreign Agricultural Service. Citrus: World Markets and Trade. 2021. Available online: https://www.fas.usda.gov/data/citrus-world-markets-and-trade.
- [18] Lado, J., Gambetta, G., Zacarias, L. Key determinants of citrus fruit quality: Metabolites and main changes during maturation. Sci. Hortic. 2018, 233, 238–248. https://doi.org/10.1016/j.scienta.2018.01.055.
- [19] Bora, H., Kamle, M., Mahato, D.K., Tiwari, P., Kumar, P. Citrus Essential Oils (CEOs) and Their Applications in Food: An Overview. Plants 2020, 9, 357. https://doi.org/10.3390/plants9030357.
- [20] Gonzalez-Mas, M.C., Rambla, J.L., Lopez-Gresa, M.P., Blazquez, M.A., Granell, A. Volatile Compounds in Citrus Essential Oils: A Comprehensive Review. Front. Plant Sci. 2019, 10, 12. https://doi.org/10.3389/fpls.2019.00012.
- [21] Stevens, Y., Van Rymenant, E., Grootaert, C., Van Camp, J., Possemiers, S., Masclee, A., Jonkers, D. The Intestinal Fate of Citrus Flavanones and Their Effects on Gastrointestinal Health. Nutrients 2019, 11, 1464. https://doi.org/10.3390/nu11071464.
- [22] Barreca, D., Mandalari, G., Calderaro, A., Smeriglio, A., Trombetta, D., Felice, M.R., Gattuso, G. Citrus Flavones: An Update on Sources, Biological Functions, and Health Promoting Properties. Plants 2020, 9, 288. https://doi.org/10.3390/plants9030288.
- [23] Addi, M., Elbouzidi, A., Abid, M., Tungmunnithum, D., Elamrani, A., Hano, C. An Overview of Bioactive Flavonoids from Citrus Fruits. Appl. Sci. 2022, 12, 29.

- [24] Wang, Y., Liu, X.J., Chen, J.B., Cao, J.P., Li, X., Sun, C.D. Citrus flavonoids and their antioxidant evaluation. Crit. Rev. Food Science Nutr. 2021, 1–22. https://doi.org/10.1080/10408398.2020.1870035.
- [25] Pontifex, M.G., Malik, M., Connell, E., Muller, M., Vauzour, D. Citrus Polyphenols in Brain Health and Disease: Current Per-spectives. Front. Neurosci. 2021, 15, 640648. https://doi.org/10.3389/fnins.2021.640648.
- [26] Zhao, C.Y., Wang, F., Lian, Y.H., Xiao, H., Zheng, J.K. Biosynthesis of citrus flavonoids and their health effects. Crit. Rev. Food Sci. Nutr. 2020, 60, 566–583. https://doi.org/10.1080/10408398.2018.1544885.
- [27] Gandhi, G.R., Vasconcelos, A.B.S., Wu, D.T., Li, H.B., Antony, P.J., Li, H., Geng, F., Gurgel, R.Q., Narain, N., Gan, R.Y. Citrus Flavonoids as Promising Phytochemicals Targeting Diabetes and Related Complications: A Systematic Review of In Vitro and In Vivo Studies. Nutrients 2020, 12, 2907. https://doi.org/10.3390/nu12102907.
- [28] Mahmoud, A.M., Bautista, R.J.H., Sandhu, M.A., Hussein, O.E. Beneficial Effects of Citrus Flavonoids on Cardiovascular and Metabolic Health. Oxid. Med. Cell. Longev. 2019, 2019, 5484138. https://doi.org/10.1155/2019/5484138.
- [29] Bellavite, P., Donzelli, A. Hesperidin and SARS-CoV-2: New Light on the Healthy Function of Citrus Fruits. Antioxidants 2020, 9, 742. https://doi.org/10.3390/antiox9080742.
- [30] Den Hartogh, D.J., Tsiani, E. Antidiabetic Properties of Naringenin: A Citrus Fruit Polyphenol. Biomolecules 2019, 9, 99. https://doi.org/10.3390/biom9030099.
- [31] Zaidun, N.H., Thent, Z.C., Abd Latiff, A. Combating oxidative stress disorders with citrus flavonoid: Naringenin. Life Sci. 2018, 208, 111–122. https://doi.org/10.1016/j.lfs.2018.07.017.
- [32] Nakajima, A.; Ohizumi, Y. Potential Benefits of Nobiletin, A Citrus Flavonoid, against Alzheimer's Disease and Parkinson's Disease. Int. J. Mol. Sci. 2019, 20, 3380. https://doi.org/10.3390/ijms20143380.
- [33] Goh, J.X.H., Tan, L.T.H., Goh, J.K., Chan, K.G., Pusparajah, P., Lee, L.H., Goh, B.H. Nobiletin and Derivatives: Functional Com-pounds from Citrus Fruit Peel for Colon Cancer Chemoprevention. Cancers 2019, 11, 867. https://doi.org/10.3390/can-cers11060867.
- [34] Klimek-Szczykutowicz, M., Szopa, A., Ekiert, H. Citrus limon (Lemon) Phenomenon—A Review of the Chemistry, Pharmaco-logical Properties, Applications in the Modern Pharmaceutical, Food, and Cosmetics Industries, and Biotechnological Studies. Plants 2020, 9, 119. https://doi.org/10.3390/plants9010119.
- [35] Gao, Z., Gao, W., Zeng, S.L., Li, P., Liu, E.H. Chemical structures, bioactivities and molecular mechanisms of citrus polymethoxy flavones. J. Funct. Foods 2018, 40, 498–509. https://doi.org/10.1016/j.jff.2017.11.036.
- [36] Smeriglio, A., Cornara, L., Denaro, M., Barreca, D., Burlando, B., Xiao, J.B., Trombetta, D. Antioxidant and cytoprotective activities of an ancient Mediterranean citrus (Citrus lumia Risso) albedo extract: Microscopic observations and polyphenol characterization. Food Chem. 2019, 279, 347–355. https://doi.org/10.1016/j.foodchem.2018.11.138.
- [37] Mazzotti, F., Bartella, L., Talarico, I.R., Napoli, A., Di Donna, L. High-throughput determination of flavanone-Oglycosides in citrus beverages by paper spray tandem mass spectrometry. Food Chem. 2021, 360, 130060. https://doi.org/10.1016/j.food-chem.2021.130060.
- [38] Rong, X., Xu, J., Jiang, Y., Li, F., Chen, Y.L., Dou, Q.P., Li, D.P. Citrus peel flavonoid nobiletin alleviates lipopolysaccharide-induced inflammation by activating IL-6/STAT3/FOXO3a-mediated autophagy. Food Funct. 2021, 12, 1305–1317. https://doi.org/10.1039/d0fo02141e.
- [39] Wang, F., Zhao, C.Y., Yang, M.K., Zhang, L., Wei, R.J., Meng, K., Bao, Y.M., Zhang, L.N., Zheng, J.K. Four Citrus Flavanones Exert Atherosclerosis Alleviation Effects in ApoE(-/-) Mice via Different Metabolic and Signaling Pathways. J. Agric. Food Chem. 2021, 69, 5226–5237. https://doi.org/10.1021/acs.jafc.1c01463.
- [40] Song, M.Y., Lan, Y.Q., Wu, X., Han, Y.H., Wang, M.Q., Zheng, Li, F., Zhou, J.Z. The chemopreventive effect of 5demethylnobiletin, a unique citrus flavonoid, on colitis-driven colorectal carcinogenesis in mice is associated with its colonic metabolites. Food Funct. 2020, 11, 4940–4952. https://doi.org/10.1039/d0fo00616e.
- [41] World Health Organization. Antimicrobial resistance. World Health Organization; 2021 [cited Apr 26 2022]; Available from. Available from: https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance.
- [42] Díaz-de-Cerio E., Verardo V., Gómez-Caravaca AM., Fernández-Gutiérrez A., Segura-Carretero A. Health effects of Psidium guajava L. Leaves: An overview of the last decade. Int J Mol Sci. 2017;18(4):897. doi: 10.3390/ ijms18040897, PMID 28441777.

- [43] Kumar M., Tomar M., Adamowicz R., Saurabh V., Nair MS., Maheshwari C, et al. Guava (Psidium guajava L.) leaves: Nutritional composition, phytochemical profile, and health-promoting bioactivities. Foods. 2021;10(4):752. doi: 10.3390/foods10040752, PMID 33916183.
- [44] Oncho D.A., Ejigu M.C., Urgessa O.E. Phytochemical constituent and antimicrobial properties of guava extracts of east Hararghe of Oromia, Ethiopia. Clin Phytosci. 2021;7(1). doi: 10.1186/s40816-021-00268-2.
- [45] Biswas T., Dwivedi U.N. Plant triterpenoid saponins: Biosynthesis, in vitro production, and pharmacological relevance. Protoplasma. 2019;256(6):1463-86. doi: 10.1007/s00709-019-01411-0, PMID 31297656.
- [46] Habtemariam S. Introduction to plant secondary metabolites—from biosynthesis to chemistry and antidiabetic action. Medicinal Foods as Potential Therapies for Type-2 Diabetes and associated Diseases. 2019;109-32. 10.
- [47] Al Mamari H. Phenolic compounds: Classification, chemistry, and updated techniques of analysis and synthesis. Phenolic compounds – chemistry, synthesis, diversity, nonconventional industrial, pharmaceutical and therapeutic applications. 2022.
- [48] Kammerer, D.R., Saleh, Z.S., Carle, R., Stanley, R.A. Adsorptive recovery of phenolic compounds from apple juice. European Food Research and Technology 2007, 224, 5–613.
- [49] Benavente-Garcia, O., Castillo, J., Marin, F.R., Ortuno, A., Del Rio, J.A. Uses and properties of citrus flavonoids. Journal of Agricultural and Food Chemistry 1997, 45, 4505–4515.
- [50] Balasundram, N., Sundram, K., Samman, S. Phenolic compounds in plants and agri-industrial by-products: Antioxidant activity, occurrence, and potential uses. Food Chemistry 2006, 99, 191–203.
- [51] Azizi, A. F., Sethi, S., Joshi, A., Singh, A. M., Raigond, P., Singh, M. K., Yadav, R. K. Biochemical and Functional Attributes of Raw and Boiled Potato Flesh and Peel Powders for Suitability in Food Applications. J. Food Sci. Technol. 2020, 57(11), 3955–3965. DOI: 10.1007/s13197-020-04424-3.
- [52] Sumaya K., Muhamad S. A., Zubair K., Hyrije K., Sustainable novel extraction of bioactive compounds from fruits and vegetables waste for functional foods: a review. International Journal of Food Properties, Vol.25, 2022, issue 1, https://doi.org/10.1080/10942912.2022.2144884.
- [53] Cirmi S., Navarra M., Woodside J.V., Cantwell M.M. Citrus fruits intake and oral cancer risk: A systematic review and meta-analysis. Pharmacol. Res. 2018; 133:187–194. doi: 10.1016/j.phrs.2018.05.008. [DOI] [PubMed] [Google Scholar].
- [54] Kawabata A., Hung T.V., Nagata Y., Fukuda N., Suzuki T. Citrus kawachiensis Peel Powder Reduces Intestinal Barrier Defects and Inflammation in Colitic Mice. J. Agric. Food Chem. 2018; 66:10991–10999. doi: 10.1021/acs.jafc.8b03511. [DOI] [PubMed] [Google Scholar].
- [55] Martirosyan D., Von Brugger J., Bialow S. Functional food science: Differences and similarities with food science. Funct Foods Health Dis. 2021; 11:408-30.
- [56] Granato D., Barba F.J., Bursać Kovačević D., Lorenzo J.M., Cruz A.G., Putnik P. Functional foods: product development, technological trends, efficacy testing, and safety. Annu Rev Food Sci Technol. 2020; 11:93-118.
- [57] Indriyani N.N., Anshori J.A., Permadi N., Nurjanah S., Julaeha E. Bioactive components and their activities from different parts of Citrus aurantifolia (christm.) Swingle for food development. Foods. 2023; 12:2036.
- [58] Swamy M.K. Plant-derived bio actives: Chemistry and mode of action. Springer, Nature; 2020.
- [59] Walia A., Gupta A.K., Sharma V. Role of bioactive compounds in human health. Acta Sci Med Sci. 2019; 3:25-33.
- [60] Dahiya D., Terpou A., Dasenaki M., Nigam P.S. Current status and future prospects of bioactive molecules delivered through sustainable encapsulation techniques for food fortification. Sustain Food Technol. 2023; 1:500-10.
- [61] Ghosh S., Sarkar T., Pati S., Kari Z.A., Edinur H.A., Chakraborty R. Novel bioactive compounds from marine sources as a tool for functional food development. Front Mar Sci. 2022; 9:832957.