

ANTHOCYANINS FROM BERRIES: CHEMISTRY AND ROLES IN INFLAMMATION AND DIABETES

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Keywords: açai, anthocyanins, antioxidants, bilberry, blackberry, black currant, blueberry, boysenberry, chokeberry, cranberry, diabetes, elderberry, gooseberry, health benefits, inflammation, maqui berry, mortiño, mulberry, raspberry, red currant.

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Summary

Diets insufficient in the consumption of fruits and vegetables and that are low in flavonoids have been associated to higher incidence of inflammatory-related chronic diseases. Worldwide, the number of people with diabetes is projected to increase to over 360 million by 2030. Type 2 diabetes mellitus occurs when the body loses the capacity to deal with glucose in the diet, as a result of insulin resistance or beta-cell dysfunction, resulting in high blood glucose levels. Anthocyanins belong to the flavonoid family, a class of compounds considered to provide antioxidant activity. Found naturally in a number of foods, anthocyanins are the pigments that give berries, grapes, pomegranates and kidney beans their rich colors. In addition, anthocyanins are natural pigments that may provide anti-inflammatory and anti-diabetes benefits. The present chapter offers an overview of the effect of anthocyanins on the reduction of inflammation and diabetes complications in human subjects, in animal models, and their potential mechanisms of action.

In this chapter, the botanical definitions of popular berry fruits, their common uses, and the major class of berry pigments, anthocyanins, will be introduced. An overview of absorption, metabolism, and antioxidant capacity of anthocyanins will be presented,

followed by an overview of what causes inflammatory diseases and diabetes, and the biological activities associated to anthocyanins that can overcome these health concerns. The objective will be to present an up to date overview of science-based evidence on the chemistry and health benefits of anthocyanins from berries and their roles in prevention of inflammation and diabetes. Other health benefits of anthocyanins will be briefly introduced.

1. Introduction to Berries

The purpose of this section is to clarify the definition of ‘berry’, to evaluate the horticultural significance and uses of major berry crops, and to explain the geographical significance of berries around the world. Berry fruits are of interest due to recent health claims and promotion for increased fruit and vegetable consumption in the human diet. In general, berries are readily available for consumption by many groups of people around the world. Usually consumed fresh or in processed forms, minimal preparation and varied recipe choices make berries a quick and easy addition to daily eating. Native people in many parts of the world have consumed berries throughout history. Today, berries are a common commercial crop with worldwide demand and potential for health benefits. These plants have been used historically for medicinal purposes especially in rural areas, and have traditionally been consumed as treatment for diarrhea or dysentery. Locally harvested fruits are being used in traditional medicine in India, Bangladesh, and China. In the Amazon region, in addition to being used for nourishment, açai berry oil has been used for its anti-diarrheic action, and the root for its anti-malarial activity. The Chilean maqui berry has been used as an anti-inflammatory agent and as treatment for kidney pains, fever, and stomach ulcers and tumors.

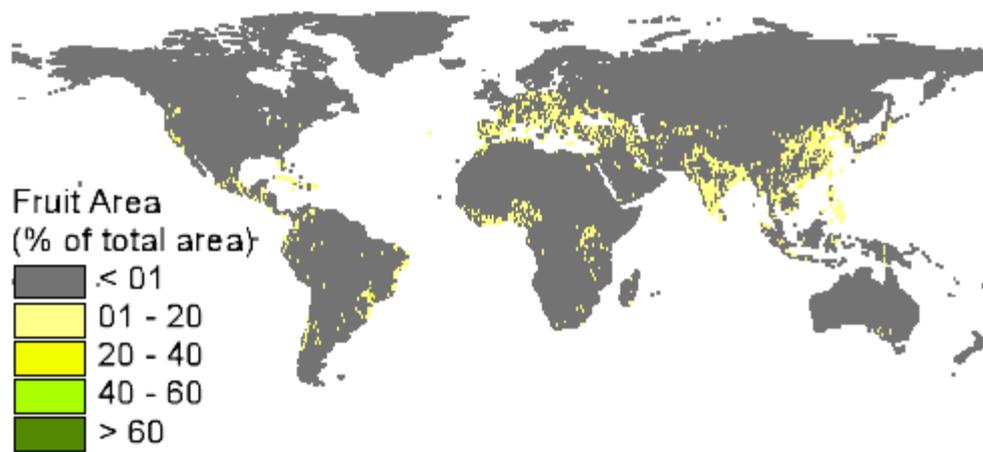
There are currently many areas in the world without access to modern pharmaceutical solutions to chronic diseases that would benefit from increased evaluation of the potential for berry fruits to prevent the pathogenesis of chronic diseases. Investigating the composition of berries and their role as antioxidants helps to establish the basis for their potential health benefits. It is important to understand the scientific background that provides the basis to promote berry fruit consumption for the potential health benefits and use of anthocyanins as functional foods.

1.1. Botanical and Common Definitions

In broad terms, a fruit is the structure of a plant that contains its seeds. Figure 1 presents maps indicating the cultivated areas and yields of fruits around the world. When investigating the health benefits and claims attributed to berries, it is important to first define which fruits qualify as a ‘berry’. Botanically, true berries are those which have edible pulp produced from a single ovary.

Major ‘berry’ crops are defined as those produced on a shrub or vine that have economic importance. For the purpose of this review, berries will be considered as those in common parlance, as small fruits that can be eaten whole. These include the true berries: black currant, red currant, and gooseberry; the “false” or epigenous berries: cranberry and blueberry; the aggregate berries: blackberry, raspberry, and hybrid boysenberry (*Rubus ursinus* x *idaeus*, Rosaceae); and the multiple berry mulberry

(*Morus atropurpurea* Roxb., Moraceae). Blackberry, black raspberry, blueberry, cranberry, and red raspberry are the most commonly consumed berries in North America. Also, berries commonly consumed in other parts of the world or consumed by traditional tribal communities will be discussed. These include açai (*Euterpe oleracea*, Araceae), Andean mora berry (*Rubus glaucus* Benth, Rosaceae), Chilean maqui berry (*Aristotelia chilensis*, Elaeocarpaceae), bilberry (*Vaccinium myrtillus* L., Ericaceae), chokeberry (*Aronia melanocarpa*, Rosaceae), elderberry (*Sambucus canadensis* L. and *nigra* L., Caprifoliaceae), mortiño (*Vaccinium floribundum* Kunth, Ericaceae), sea buckthorn (*Hippophae rhamnoides*, Elaeagnaceae), and wolfberry, also called goji berry (*Lycium barbarum*, Solanaceae). These commonly consumed berries or exotic berry-type fruits have seen an increase in consumption that may have potential to improve human health. Berries positively modulate chronic diseases such as cardiovascular disease, neurodegeneration, cancer, and diseases related to aging because they contain vitamins, minerals, folate, and fiber in addition to several phytochemicals. It is important to first look at the horticultural and geographical significance of berries commonly consumed in North America and around the world before discussing berry composition and biological activity that suggests their benefits to human health.



A. Fruits areas.

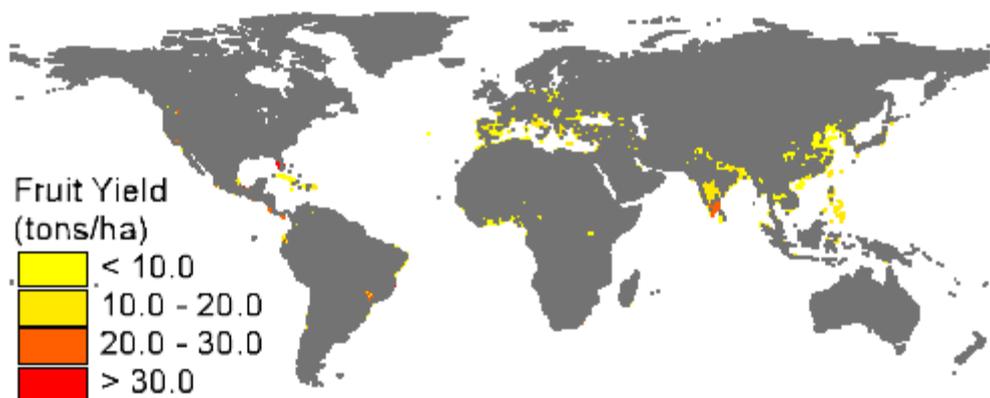


Figure 1. Availability of fruit crops worldwide: A. areas and B. yields

1.2. Horticulture and Geographical Significance: Berries around the World (Figure 2)

True berries are simple fruits produced from a single ovary having seeds and an edible pulp, and contain the *Ribes* genus of berries. Generally, the entire ovary wall of the fruit ripens into an edible outer layer. True berries include black currant, red currant and gooseberry, and have been widely adapted to grow in many soil types and regions. They have been used both fresh and processed into juice, jellies, preserves or pies. Black currants (*Ribes nigrum* L., Grossulariaceae) are perennial plants native to central and Northern Europe and Northern Asia. They grow on a small shrub reaching 1-2 m in height. Most commonly, blackcurrants are used in juice, jellies, and purees, and have a distinctive sharp sweet taste. ‘Superfruit’ is a marketing term used to refer to fruits with appealing taste and exceptionally high nutrient richness and antioxidant quality. Black currants have this special status among consumers, with many health benefits attributed to their high antioxidant levels. Red currants (*Ribes rubrum* L., Grossulariaceae) are similar to the black currant but are bright red translucent berries. The red currant is mostly used in juice, jelly and purees. This small deciduous shrub is native to parts of Western Europe, though Poland is a large producer. Gooseberry (*Ribes uva-crispa* L., Grossulariaceae) grows on a bush from 1-3 m tall with sharp spines on the branches. Gooseberries are usually green and slightly hairy, but may also be deep purple in color. They are indigenous to Europe and Western Asia, growing naturally in thickets and rocky woods in many countries. Though there are many uses in foods and cakes, gooseberries have a slightly sour taste and are recently losing sales. The Indian gooseberry (*Phyllanthus emblica*, Euphorbiaceae) is also a botanically true berry, having light green to yellow fruit that is sour, bitter and fibrous.

The epigenous or false berries include the *Vaccinium* species of cranberry and blueberry. These are termed false berries as they are not true berries botanically speaking due to the fact that there are many seeds inside, rather than just one. Cranberries (*Vaccinium macrocarpon* Ait., Ericaceae) grow on evergreen creeping shrubs or vines growing to 2 m long and 5-20 cm tall in cooler parts of the Northern hemisphere. The berry turns deep red when ripe and is slightly acidic, leading to almost all being processed into products such as juice, sauce, and sweetened dried cranberries. Sales have increased recently due to recognition of the potential for health benefits, making cranberries a commercially important crop grown mostly in the United States and Canada. Blueberry (*Vaccinium corymbosum* L., *angusifolium* Ait., *ashei* Reade, Ericaceae) fruits are round blue berries with flared crowns at the end, and grow on shrubs that vary in size depending on the variety. They are native to North America but are also cultivated in Argentina, Chile, Australia, and New Zealand. American blueberries include the low-bush, or “wild” blueberry and the high-bush or “cultivated” blueberry. Blueberries can be used in many applications due to their sweet taste, including beverages and snack foods, and are perceived to be generally healthy. Cranberries and blueberries were widely used in the New England area for trading between Native Americans and Colonial settlers.

Aggregate berries include blackberries, raspberries and boysenberries. Aggregate berries are composed of many small individual drupes, called drupelets, which are the small fleshy parts forming around individual ovules of the fruit. There are many

varieties of blackberries (*Rubus* sp. Rosaceae), which have naturally sharp spines that reach 3-6 m in height, and grow throughout the Northern hemisphere. Blackberries are one of the most widely available and widespread berries, having many species and hybrids, and are becoming one of the most economically important berries following more common strawberry (*Fragaria ×ananassa* Duch.), blueberry (*Vaccinium* spp.), and red raspberry (*R. idaeus* L.) (Finn and Clark 2011). Mostly popular for its use in desserts, jams, and jellies, blackberries can also be made into wine. Raspberries (*Rubus idaeus*, Rosaceae) are similar to blackberries but are smaller, softer, and have a different color. They can be easily grown in many parts of the world and are commercially important for the fresh fruit market and for processing into frozen products, juices, or dried fruit. Fruits of the raspberry plant grow on woody brambles and are usually red in color, but may also be black or yellow. Black raspberries (*Rubus occidentalis* L., Rosaceae) are not the same plant as the red raspberry, but a North American species grown mostly in the state of Oregon and used for juice and jam production. Boysenberries (*Rubus ursinus x idaeus*, Rosaceae) are a hybrid between a red raspberry and a blackberry, which was discovered in California and is now widely produced in the state of Oregon, as well as in New Zealand. The berry has similar fruit to blackberries with purple fruit, though usually are larger and have larger drupelets.

The last group of berries used in common parlance are multiple fruit berries, which include mulberries (*Morus atropurpurea* Roxb., Moraceae). Black mulberry (*Morus nigra*, Moraceae) is native to western Asia but has been cultivated in Europe for hundreds of years. The fruits are 2-3 cm long and are found on medium sized deciduous trees growing to 10-15 m tall. The fruit is usually eaten fresh and may be important to horticultural production of other berry fruits as they are in high demand by birds.

The berries just discussed are the most commonly referred to as berries; however, there are many exotic or rare berries less common to North American consumers with unique characteristics and horticultural interest. Some of these berries have become more common to the general public due to the introduction to grocery stores of the popular marketing term 'superfruits'. One very popular berry in the market today is açai (*Euterpe oleracea*, Arecaceae). This berry is the fruit of the açai palm that grows in tropical Central and South America mainly in floodplains and swamps. The palm is a small bushy evergreen similar to cherry trees growing to 15 m or more, and the berries are dark purple fruits. Known mostly because of its antioxidant properties, açai berries are used mostly in processed form or as juice or preserves because of poor shelf-life.

Acerola (*Malpighia glabra*, Malpighiaceae) is a berry that grows on widespread fruit-bearing shrubs thought to be native to the Caribbean Islands or Central America. The berry looks like a common cherry and is known to lose its flavor and nutritional content very rapidly after harvest due to a thin delicate skin, making it ideal to eat fresh, but not suitable for commercial production. They may also be sold to be used in juices and jellies, as well as for medicinal purposes.

The Andean mora berry, or Andes berry (*Rubus glaucus* Benth, Rosaceae), is a climbing perennial shrub native that grows year round in the Andes in northern South America. It is known for its dark-red color, tartness, and juiciness in comparison to other cultivated blackberries and raspberries in the *Rubus* genus. The Andes berry is highly perishable

with 30% of harvest being discarded (Garzon 2009) and therefore is usually processed into juice, preserves, and liquors.

Chilean wild blackberry or maqui berry (*Aristotelia chilensis*, Elaeocarpaceae) grows on an evergreen shrub that reaches 3-5 m high in temperate forests of central to southern Chile and western Argentina. Both the leaves and the fruits have been used in folk medicine to treat several ailments, and have potential to be used in dietary supplements or as functional foods.

Bilberry (*Vaccinium myrtillus* L., Ericaceae), also called European blueberry or whortleberry, is found on low-growing shrubs in Finland, Sweden, Russia, Scotland, Poland, and Belarus, with history in European folk medicine. It has a very strong color and is known to be beneficial for eye health and has potential for other health benefits due to its anthocyanin content. The small size of bilberries makes them hard to commercialize and are rarely cultivated, but usually eaten fresh or made into jams, juices, or pies.

Chokeberry (*Aronia melanocarpa*, Rosaceae) is a deciduous shrub that grows to 1-4 m depending on the variety, and the berry is mainly red and black. While native to the eastern part of the United States, it was introduced to Europe in the 19th century and is popular in Russia and Poland. It is considered to be a healing plant, with experimental planting being done of different cultivars. Known to have very high anthocyanin content, the chokeberry may be used as a flavoring or pigment agent, and is being increasingly used for juice, wine, jam, and as a natural food pigment.

Cloudberry (*Rubus chamaemorus*, Rosaceae) fruits grow in the Northern hemisphere and are available mostly in Finland and Sweden, but also in Alaska and Canada. The plant grows to 10-25 cm high with straight branchless stalks and hand-like lobed leaves. The berries are soft, juicy, golden-yellow in color, and have a tart taste. They are not widely used commercially, but can be made into jams, juices, tarts and liquors.

Elderberry (*Sambucus canadensis* L. or *Sambucus nigra*, Caprifoliaceae) is native to eastern North America, and was used by early settlers as a dried food or medicinal crop. The elderberry fruit is a dark purple to black berry, 3-5 mm in diameter, and may produce clusters. *S. nigra* is the European cultivar that is in demand due to its use in preserves, as a natural pigment, and for wine making, and also as a potential functional food.

Lingonberries (*Vaccinium vitis-idaea*, Ericaceae) have many common names including cowberry, and grow on small evergreen shrubs that reach only 10-40 cm high in forests of northern Eurasia and North America. They are commercially sold as a popular European crop in Nordic countries and Russia. The red berries are 6-10 mm in diameter and have a sour taste mostly used in processed and frozen forms. There is increasing interest to use lingonberries for health beneficial properties, as they are rich in vitamins and minerals.

Mortiño (*Vaccinium floribundum* Kunth., Ericaceae) is a deciduous spreading shrub that grows in many regions of northern South America such as Ecuador. Its round blue-black

edible berries are widely consumed fresh or as processed products. Local communities in Ecuador have used the plant to treat various medical conditions, including diabetes and inflammation.

<p>Black currant (<i>Ribes nigrum</i> L., Grossulariaceae)</p>  <p>vivekamexports.com</p>	<p>Blackberry (<i>Rubus</i> sp. Rosaceae)</p>  <p>Berries in the world. A report prepared for SITRA/Lapinnova Oy by: Invenire Market Intelligence. Finland. June 2008.</p>	<p>Andes berry (<i>Rubus glaucus</i> Benth)</p>  <p>biolib.cz</p>
<p>Red currant (<i>Ribes rubrum</i> L.)</p>  <p>nutritionkey.wordpress.com</p>	<p>Raspberry (<i>Rubus idaeus</i>)</p>  <p>bbcgoodfood.com</p>	<p>Acerola (<i>Malpighia emarginata</i>)</p>  <p>bewellbuzz.com</p>
<p>Gooseberry (Indian Gooseberry: <i>Emblica officinalis</i> Gaertn.)</p>  <p>pickyourown.org</p>	<p>Boysenberry (<i>Rubus ursinus</i> x <i>idaeus</i>)</p>  <p>gourmetsleuth.com</p>	<p>Bilberry (<i>Vaccinium myrtillus</i>)</p>  <p>herbalextracts.net</p>
<p>Cranberry (<i>Vaccinium macrocarpon</i> Ait.)</p>  <p>hunnylovins.blogspot.com</p>	<p>Mulberry (<i>Morus atropurpurea</i> Roxb.)</p>  <p>fruitdirectory.com</p>	<p>Chokeberry (<i>Aronia spp.</i>)</p>  <p>fruitdirectory.com</p>

<p>Blueberry (<i>Vaccinium corymbosum</i> L., <i>angusifolium</i> Ait., <i>ashei</i> Reade)</p>  <p>wrensoft.com</p>	<p>Elderberry (<i>Sambucus canadensis</i> and <i>S. nigra</i>)</p>  <p>blog.biottajuices.com</p>	<p>Crowberry (<i>Empetrum spp.</i>)</p>  <p>fruitipedia.com</p>
<p>Maqui berry (<i>Aristotelia chilensis</i>)</p>  <p>maquiberrytruth.com</p>	<p>Mortiño (<i>Vaccinium floribundum</i> Kunth.)</p>  <p>my.englishclub.com</p>	<p>Marionberry (<i>Rubus hybrid</i>)</p>  <p>fruitsinfo.com</p>

Figure 2. Images of berries. Berry (Scientific name) and Image Source.

Sea buckthorn (*Hippophae rhamnoides*, Elaeagnaceae) is a very thorny deciduous shrub with dense branches that can tolerate extremely harsh winters and poor soils. Native to Europe and Asia, almost all of sea buckthorn production comes from China. Increasingly used in cosmetics, supplements, and processed jams juices and liquors, sea buckthorn berries have also been used in traditional medicines and is becoming popular for potential nutritional antioxidant value.

Wolfberry, otherwise known as the Goji berry (*Lycium barbarum*, Solanaceae), has recently become popular as a superfruit, and grows as 1-2 cm ellipsoid bright orange-red berries. It grows on a 1-3 m high woody perennial plant, and is mainly cultivated in the south of China. It has been used in traditional Chinese medicine, herbal teas, and dishes such as rice congee or soups. Wolfberries are commonly sold in their dried form, and are traditionally cooked before consumption.

1.3. Production and Potential Future Markets

Berries have been used in the trading of ancient people from many different environments. Native Americans have used a wide variety of wild berries by picking them when ripe, drying them, and incorporating them into dried meat and animal fat for food and medicine year-round.

Current consumption of berries is limited to a few very popular berries, with local niche markets for other less common berries. There are also preferences for certain berries such as blueberries, raspberries and blackberries (Figure 3) that make consumption of other more expensive berry types less likely. Potential issues with handling, transportation, or storage make fresh consumption of exotic berries available only to the

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Biographical Sketches

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scientific studies introduced new materials to improve human health. President of the Association of Food Technologists (IFT, Central Mexico); Mentor of students and promoter of science among the general public for the National Academy of Science (Mexico); Head and co-founder of several programs in Food Engineering and Food Science in different Universities in Latin America including the Doctoral program in Food Science in the central part of Mexico (PROPAC) where she implemented a vigorous educational and research program in Food Toxicology. Fellow of the Mexican Academy of Sciences; recognitions awarded by the Mexican Government and Foundations for her scientific contributions to Food Toxicology; fellow of the United Nations University.

Michelle H. Johnson is a graduate student in Nutritional Sciences at the University of Illinois in Urbana-Champaign. She received her B.S. in biochemistry in 2010 from Iowa State University, where she did undergraduate research on carbohydrate enzymes and nutritional physiology. During the past three years of her graduate studies, Michelle has been conducting research evaluating the potential use of blueberry-blackberry fermented beverages on inhibition of markers of inflammation and carbohydrate utilization, leading to the publication of articles in the *Journal of Agricultural and Food Chemistry* (2011) the *Journal of Food Science* (2011), and *Molecular Nutrition and Food Research* (2013). She has received the Toshiro Nishida Research Award and the William Rose Endowed Awards for her research presented at scientific conferences including the Institute of Food Technologists Annual Meeting & Food Expo, and Experimental Biology, and has been selected as the recipient of the College of Agricultural, Consumer and Environmental Sciences 2012 Graduate Student Research Award – M.S. Michelle has worked as a teaching assistant for Food Chemistry courses and has served as a mentor to several undergraduate students in the department of Food Science and Human Nutrition at the University of Illinois.