CRITICAL REVIEWS IN FOOD SCIENCE AND NUTRITION
2020, VOL. 60, NO. 5, 873–886
https://doi.org/10.1080/10408398.2018.1540969

REVIEW

Impact of plant extracts upon human health: A review

Mariana Veiga, Eduardo M. Costa, Sara Silva, and Manuela Pintado

CBQF – Centro de Biotecnologia e Química Fina – Laboratório Associado, Escola Superior de Biotecnologia, Universidade Católica Portuguesa/Porto, Porto, Portugal

ABSTRACT
With the increase in evidences directly linking diet and health, several foodstuffs, such as phenolic rich fruits and vegetables, have emerged as possessing potential health benefits. Plants, given their fiber and phenolic content (and their intrinsic biological potential), have long been considered as contributing to health promotion. Therefore, the present work aimed to review the existing evidences regarding the various potential benefits of plant extracts' and plant extract-based products' consumption, with emphasis on *in vivo* works and epidemiological studies whenever available. Overall, the information available supports that, while there are indications of the potential benefits of plant extracts' consumption, further human-based studies are still needed to establish a true cause-effect.

KEYWORDS
Health promotion; plant extracts; functional foods; phenolic compounds; dietary fiber

Introduction

Plants have been used by humanity for centuries and, while various applications could be referenced (e.g. food source, raw materials for clothing production, shelter construction or simply decoration), their use as herbal medicine is one of the oldest forms of healthcare known to mankind. In fact, the study of plants goes back hundreds of years and it has permitted them to be explored not only for food, but also to obtain non-food products. From a technical standpoint, a medicinal plant is characterized as possessing pharmacologically active components that allow it to be used, directly or indirectly, in a therapeutic treatment to prevent or cure a certain disorder (Boscolo and de Senna Valle 2008, Briskin 2000, Djeridane et al. 2006). Several works have focused on characterizing the potential medicinal properties of plants which may include anti-inflammatory, anti-tumoral, antidiabetic and antioxidant effects (Jung et al. 2006, Watt and Breyer-Brandwijk 1962, Ekor 2014, Roleira et al. 2015). Moreover, several of the drugs commonly used today in medicine are of herbal origin, with their beneficial/therapeutic effects thought to be due to the presence of several different compounds that can be found in numerous plants, such as terpenoids, alkaloids, flavonoids, phenolics, and some others. The World Health Organization estimates that more than 80% of the world's population relies on traditional medicine using plants to satisfy their primary healthcare needs (Raskin et al. 2002, Farnsworth et al. 1985, Ekor 2014, Who 2013).

The past decades have seen an increase in life expectancy, as well as in the general public's concern with life quality. The connection between health and diet has been reported by several authors, with some foodstuffs being regarded as more beneficial than others. Nutrition plays a very important role on one's health, with a balanced diet being fundamental to maintain homeostasis and therefore the proper functioning of the human organism. The consumption of fruits and vegetables has been viewed as an important part of a healthy diet, as they have high contents of dietary fiber and phenolic compounds, which are known to exert potentially beneficial effects, such as antioxidant, immunomodulatory and anti-tumoral activity, as described by several different epidemiological studies (Conlon and Bird 2014, Parkar, Stevenson, and Skinner 2008, Rodriguez-Casado 2016, Liu 2013, Slavin 2013, Anderson et al. 2009, Brown et al. 1999, Willcox, Scapagnini, and Willcox 2014, Lopez-Legarrea et al. 2014, Dreher 2018, Ganesan et al. 2018, Veiga et al. 2017).

Additionally, another factor that is perceived has having a great impact upon human health is the intestinal microbiota, with this connection having been shown through several reports (Quigley 2013, Marchesi et al. 2015, Claesson et al. 2012, Sekirov et al. 2010, Round and Mazmanian 2009, Dreher 2018, Alkasir et al. 2017, Holscher 2017). In fact, imbalances in gut microbiota composition, for instance changes in the types and numbers of bacteria in the gut, have been associated with the development of several disorders. This disturbance is known as dysbiosis and may lead to cardiovascular diseases, inflammatory bowel disease and other gastrointestinal disorders as well as mental health disorders. The modulation of the gut microbiota has been studied as a possible alternative to current treatments used, with plant extracts being a focal point due to their constitution (Hu, Wang, and Jin 2016, Morais et al. 2016,

CONTACT Manuela Pintado mpintado@porto.ucp.pt CBQF – Centro de Biotecnologia e Química Fina – Laboratório Associado, Escola Superior de Biotecnologia, Universidade Católica Portuguesa/Porto, Rua Arquiteto Lobão Vital, 172, 4200-374, Porto, Portugal.

Kashtanova et al. 2016, O'Callaghan and van Sinderen 2016, Finegold et al. 2017, Holscher 2017, Tremaroli and Bäckhed 2012, Million et al. 2013, Marchesi et al. 2015). As such, this review aims to provide some insights into how different plant extracts may have a positive, or a detrimental, impact upon human health and the microbiota, recurring to epidemiological evidences whenever possible.

Plant extracts' composition

Biological active compounds present in plants are not, normally, easily accessible. Therefore, plants have been the target of several works focusing on the extraction of these natural compounds, as well as in the removal of the fractions with lower biological relevance, thus originating extracts which may have several applications, such as medical (for example, extracts have been studied as cancer treatment alternative, treatment of diabetes and dermatological disorders, among others) or agricultural (repellent effects and antifeedant, control of diseases in plants) while being a source of bioactive compounds for the cosmetic and food industries (Djeridane et al. 2006, Hassan et al. 2009, Hilou, Nacoulma, and Guiguemde 2006, Sasidharan et al. 2011, Silva et al. 2013, Seeram et al. 2006, Armendáriz-Barragán et al. 2016, Salem et al. 2015, Ribeiro et al. 2015).

The production of an extract allows for the removal of the compounds which showcase no relevant benefit to the host. In turn, this leads to the attainment of the bioactive components, in a concentrated form, whose incorporation into other products is easier than the inclusion of the whole plant. However, the extractions usually require the use of organic solvents which may originate some concerns when considering their use/consumption by humans. There are several reports describing the advantages and disadvantages of different extraction methods for different target compounds, ranging from phenolic compounds to carbohydrates and phospholipids (Nicoue, Savard, and Belkacemi 2007, Sasidharan et al. 2011, He et al. 2016, Naczk and Shahidi 2006, Hendrix 1993, Lapornik, Prošek, and Wondra 2005, Escarpa and González 2001, Kolarovic and Fournier 1986, Silva, Costa, Calhau, et al. 2017). Furthermore, the production of plant extracts may be an interesting alternative for waste reduction (particularly at the agro-food level) as these byproducts may function as a low cost, renewable source of biologically relevant compounds and therefore contribute to a more efficient management of resources and the development of circular economy models (Armendáriz-Barragán et al. 2016, Ross 2014, Sasidharan et al. 2011, Hassan et al. 2009, Ribeiro et al. 2015).

Different extracts, obtained from different plants, can exhibit a vast array of potentially beneficial effects such as hepatoprotection, anti-tumoral, antioxidant, antimicrobial, antidiabetic, anti-inflammatory and antimalarial activity among several others. In these cases, it is perceived that the overall activity of the extract results from the synergistic action between its different constituents, particularly as tests performed with only the perceived "active principle" frequently yield poorer results than those observed for the complex chemical matrix which is the extract (Jung et al. 2006, Balasundram, Sundram, and Samman 2006, Hilou, Nacoulma, and Guiguemde 2006, Hassan et al. 2009, Islam and Choi 2009, Djeridane et al. 2006, Omoregbe, Ikuebe, and Ihimire 1996).

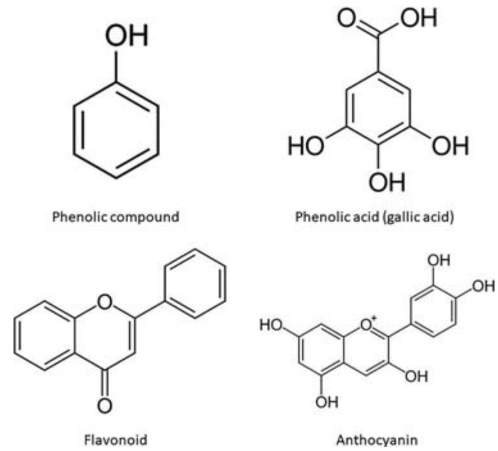

Figure 1. Basic chemical structure of a phenolic compound, phenolic acid, flavonoid and anthocyanin.

Plants' bioactive compounds

Diet has long been associated with positive, or negative, impacts upon the health and wellbeing, with foodstuff of plant origin being strongly associated with a healthier status. Fruits and vegetables are generally rich in water, sugar, fiber, several phytonutrients and vitamins, all of which are essential for the body's homeostasis. Most importantly, the potential benefits of their consumption have been frequently associated with their vitamin, phenolic and fiber contents (Fuller et al. 2016, Lv et al. 2015, Nile and Park 2014, Bosscher et al. 2009, Liu 2003, Willcox, Scapagnini, and Willcox 2014, Tiihonen, Ouwehand, and Rautonen 2010, Conlon and Bird 2014, Dillard and German 2000, Raskin et al. 2002, Trinidad et al. 2010).

Phenolic compounds

Fruits and vegetables represent the primary sources of phenolics in the human diet although they can sometimes be found in other organisms, *e.g.* bacteria, fungi and algae. They are secondary plant metabolites which exert a photoprotective function and several other roles that are crucial for the plants' metabolism and survival, such structural support and protection against pathogen's infection. In nature, *ca.* 8000 different phenolic compounds have been reported so far. According to their chemical structures, they can be divided into several groups, that range from relatively simple phenolic acids (an example is shown in Fig. 1) to highly polymerized tannins. Moreover, they are also responsible for the pigmentation and some of the organoleptic characteristics showcased by plants, such as flavor and color (Djeridane et al. 2006, Balasundram, Sundram, and Samman 2006, Landete 2012, Cheynier 2012, Lattanzio 2013).

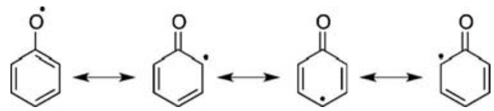

Figure 2. Formation of phenoxyl radicals.

Overall, chemically wise, phenolic compounds may be defined as molecules comprised of at least one phenol unit (an aromatic ring with one hydroxyl substitution, as seen in Fig. 1), with molecules containing more than one of these subunits being conventionally classified as polyphenols. In fruit and vegetables, phenolic compounds are frequently found in glycosylated forms (*i.e.* associated with a sugar moiety) as the free forms often present more toxicity than the glycosylated ones (Das et al. 2012, Hollman and Arts 2000, Landete 2012, Vermerris and Nicholson 2008a, b).

Phenolics have been systematically reported as being beneficial for human health and wellbeing. One of the properties most commonly associated with phenolics is antioxidant activity as, due to the position of the hydroxyl group bound to the aromatic ring, they are efficient proton donors. Moreover, phenol groups can also accept electrons resulting in the formation of relatively stable phenoxyl radicals (Fig. 2). This allows for the disruption of oxidation reaction chains that can be detrimental in biological systems and, when in foods help limit the oxidative damage of the matrix itself (allowing for longer shelf life). Moreover, after ingestion, they may be absorbed by the body and act as local antioxidants. For instance, anthocyanins (seen in Fig. 1) (water soluble flavonoid pigments that are abundant in red and purple fruits) have been described as capable of protecting liver and red blood cells against *in vitro* and *in vivo* oxidative damage and several phenolic rich extracts have been associated with the reduction of plasmatic antioxidant levels and oxidation stress markers. Additionally, these compounds have been used in order to increase functionality of some foods (Duda-Chodak et al. 2015, Youdim, Martin, and Joseph 2000, Liu et al. 2013, Sevgi, Tepe, and Sarikurkcu 2015, Wang et al. 2010, Yan et al. 2018, Silva, Costa, Vicente, et al. 2017, Olas 2017). Functional foods are defined as foodstuff or food ingredients which exert some benefit upon health, helping to prevent or ameliorate the symptoms of certain diseases, including diabetes, osteoporosis, cardiovascular diseases, among many others. Taking into account the possible health benefits shown by phenolic compounds, several studies have demonstrated how their addition or the addition of phenolic-rich extracts to certain foodstuff could be beneficial to one's health (Dissanayake et al. 2018, Quirós-Sauceda et al. 2014, Mohamed 2014, Charalampopoulos et al. 2002, Abuajah, Ogbonna, and Osuji 2015, Çam, İçyer, and Erdoğan 2014). For example, Akhtar et al. (2015) showed how a phenolic-rich pomegranate peel extract could be used as food ingredient and as potential food preservative, contributing to prevent certain diseases as well. Moreover, studies by Junior and Morand (2016) and Gao et al. (2013) showed that supplementation of phenolic-rich mate extracts in rats' diet contributed to prevent endothelial dysfunction and to regulate the expression of lipid metabolic regulators, preventing hepatic fatty deposition. Additionally, besides the potential health benefits, the use of byproducts also contributes to reduce waste (Putnik et al. 2017, Moncada and Aristizábal 2016).

Dietary fiber

Dietary fiber, found in vegetables, fruits, grains, and legumes has been described as a group of complex non-starch carbohydrates and lignin, which include polysaccharides, oligosaccharides, lignin, and associated plants substances. These compounds are not affected by the digestive process and are not absorbed in the small intestine. However, they may be metabolized in the colon by local microorganisms, resulting in several secondary products that can be absorbed into the bloodstream. The different types of dietary fiber may be categorized according to their sources, solubility (soluble and insoluble dietary fiber), fermentability and physiological effects (Adam et al. 2014, Kendall, Esfahani, and Jenkins 2010).

The intake of fiber has gradually decreased for the past 200 years, regardless of the fact that its consumption has been associated with an array of important health benefits. It binds to substances (such as sugar and cholesterol) preventing or slowing their absorption into the bloodstream therefore contributing to the regulation of blood sugar levels and protecting against cardiovascular problems by lowering the levels of blood cholesterol. For instance, soluble dietary fiber (*e.g.* non-cellulosic polysaccharides, oligosaccharides, β-glucans, pectins and gums) has been described as being responsible for an increase in gut content viscosity and is, therefore, frequently associated with the regulation of blood glucose levels, reduction in serum cholesterol and a delay in bowel movements. Additionally, some dietary fibers may contribute to the modulation of the gut microbiota due to their fermentability, contributing to an increase in beneficial genres, such as *Bifidobacterium* which, in turn, has been associated with colon, stomach, breast and prostate cancer prevention. Furthermore, dietary fiber has been shown to significantly reduce the risk of gaining body weight and fat, notwithstanding the quantity of fat ingested or the amount of physical exercise performed, as it reduces the overall energetic intake. On the other hand, it diminishes some antibiotics' bioavailability. Rich sources of soluble fiber include fruits, vegetables, oats and pulses (Brown et al. 1999, Slavin 2008, Wu et al. 2015, Ye et al. 2015, Adam et al. 2014, Smith and Tucker 2011, Trinidad et al. 2010, Fuller et al. 2016, Tucker and Thomas 2009, Zinman et al. 2015).

Insoluble fiber is poorly broken down by the gut and absorbed into the bloodstream (such as cellulose, hemicellulose and lignin). However, given their bulking capacity and their (although low) fermentability by gut microbiota, insoluble fiber has often been associated with a reduction of bowel transit time and an improvement of laxation, while their fermentation may also contribute to the modulation of the gut microbiota. Since soluble and insoluble fibers are present in different proportions in food, and considering that both have different biological potentials, it is important to eat a variety of fiber rich foodstuffs in order to ingest both types of dietary fiber at sufficient levels (Brownawell et al. 2012, Fuller et al. 2016, Kaczmarczyk, Miller, and Freund 2012, Mudgil and Barak 2013, Slavin 2005, Trinidad et al. 2010, Ross et al. 2017, Dreher 2018, Holscher 2017).

Other compounds

All plants exposed to the atmosphere are coated with layers of a lipidic material that helps to reduce water loss and functions as a barrier to prevent pathogens' entry. The main constituents of these coatings are fatty acids polymers (joined by ester linkages) such as cutin, suberin and waxes (Duke et al. 2016, Fich, Segerson, and Rose 2016). Moreover, plants produce a large array of organic, non-phenolic, compounds that have no connection to their development or function but confer them some protection against herbivores, insects and microbes or function as attractants for pollinators and seed-dispersing animals. Terpenes represent the largest class secondary plant metabolites although some have well defined roles in plant growth and/or development and can be considered primary metabolites. The compounds belonging to this class are usually insoluble in water and are biosynthesized from acetyl-CoA or glycolytic intermediates (Duke et al. 2016, Daniel 2016).

Carbohydrates are the basis of the formation of plants. Their complexity varies between a simple monosaccharide to homogeneous and heterogeneous polysaccharides. Some of the biological properties of heterogenous polysaccharides include a protective action of mucosa and irritated skin, anti-inflammatory effect and immunomodulating activity (Hardy et al. 2015, Hendrix 1993, Duke et al. 2016).

Other compounds of interest that can be found in plants include phytosterols (promising agents in hormonal therapy), salicylates (are used for the development of aspirin), terpenoids (that have anti-inflammatory and antimicrobial activity) and alkaloids (compounds that, despite their pharmacological activity such as anesthetic, antitumoral, antiarrhythmic and antimalarial activity, showcase a high level of toxicity) (Ras et al. 2015, Racette et al. 2015, Malakar 2017, Baye et al. 2017, Tholl 2015, Cushnie, Cushnie, and Lamb 2014, Aniszewski 2015).

Plants' and plant extracts' biological potential

As mentioned previously, plants have been associated with an abundance of epidemiological evidences supporting an array of potential health benefits (Hollman 2001, Neto 2007, Graf, Milbury, and Blumberg 2005, Asif 2015, Jung et al. 2006, Omoregbe, Ikuebe, and Ihimire 1996, Pandey and Rizvi 2009, Ribeiro et al. 2015, Roleira et al. 2015, Runnie et al. 2004, Salem et al. 2015, Sasidharan et al. 2011, Osman et al. 2008, Vendrame et al. 2011, Wang et al. 2010). Therefore, it stands to reason that plant's constituents are, at least in part, responsible for the benefits observed. Dietary fiber and phenolic compounds are two abundant classes of plant components that have been widely recognized as exerting a positive influence upon human health (Cheynier 2012, Maria de Lourdes Reis 2013, Anderson et al. 2009, Kaczmarczyk, Miller, and Freund 2012). For instance, phenolic compounds have been reported as contributing to the prevention of neurodegenerative diseases (*e.g.* Parkinson and Alzheimer) as well as with the amelioration and/or prevention of other neurological pathologies such as memory loss, posttraumatic stress disorder (PTSD) and ischemic brain damage. Furthermore, several epidemiological studies have also linked phenolic compound's ingestion to a reduction of the risk of developing diabetes, cancer, cardiovascular and inflammatory diseases (Albishi et al. 2013, Bulotta et al. 2014, Nohynek et al. 2006, Ranilla et al. 2010, Rodríguez-Roque et al. 2013, Selma, Espin, and Tomas-Barberan 2009, Sevgi, Tepe, and Sarikurkcu 2015, Valdés et al. 2015, Wallace 2011). On the other hand, dietary fiber has also been associated with an array of potential health benefits, including a reduction of the risk of developing coronary heart disease, hypertension and of suffering a stroke (due to dietary fiber's potential to aid in the control of blood pressure). Moreover, it has also been reported to help prevent obesity and certain gastrointestinal disorders, such as duodenal ulcer, constipation and hemorrhoids (Anderson et al. 2009, Eswaran, Muir, and Chey 2013, Fuller et al. 2016, Kaczmarczyk, Miller, and Freund 2012, Slavin 2013, Wu et al. 2015, Ye et al. 2015). A concrete example of this biological potential is blueberry, as this fruit has been associated with many health benefits, with existing works reporting on its antioxidant, antimicrobial, antitumoral and anti-inflammatory activity, as well as gut modulating capacity (Bränning et al. 2009, Carey, Gomes, and Shukitt-Hale 2014, Dulebohn et al. 2008, Guglielmetti et al. 2013, Molan et al. 2009, Neto 2007, Piljac-Žegarac, Belščak, and Piljac 2009, Vendrame et al. 2013, Silva et al. 2016, Jo et al. 2015, Vendrame et al. 2014, Taverniti et al. 2014, Ren, Huang, and Cheng 2014).

The use of dietary fiber and phenolic compounds as ingredients capable of enhancing technological and nutritional properties of food, thus increasing the functionality of food products has been described by several authors. Furthermore, non-extractable polyphenols, which are not released from the food matrix during the digestive process and therefore manage to reach the colon nearly intact, have been shown to exhibit health promoting properties as well, namely in relation to gastrointestinal health. The gut microbiota converts these compounds into small size phenolics that are better absorbed and that persist in the blood for more than 48 hours, showcasing antioxidant and anti-inflammatory activity (Landete 2012, González-Sarrías, Espín, and Tomás-Barberán 2017, Pérez-Jiménez, Díaz-Rubio, and Saura-Calixto 2013, Yan et al. 2018, Holscher 2017).

Gut microbiota: function and modulation

Polyphenols and fibers, two of the most important plants' constituents, have both been studied regarding their microbiota modulating potential. The human gut harbors a complex microbial community, denominated intestinal microbiota, composed of over 1000 different bacterial species. Its development begins at birth and is strongly influenced by diverse factors which include immunological factors, antibiotic usage, host genetics and dietary habits. The normal gut flora is constituted by several different genera and species, which range from bacteria known to be beneficial to the host to potentially harmful bacteria such as *Clostridium* and *Salmonella*. The most predominant phylum in the human gut are Firmicutes (which includes genera of bacteria such as *Lactobacillus*, *Enterococcus* and *Clostridium*) and Bacteroidetes (which includes *Prevotella* and *Bacteroides* genera), which together represent 90% of the known phylogenetic categories existing in the gut flora. (Marchesi et al. 2015, Bernalier-Donadille 2010, Boulangé et al. 2016, Claesson et al. 2012, Conlon and Bird 2014).

Gut microbiota is essential for the normal functioning of the body and its health, besides contributing to maximize the absorption of nutrients. In fact, the connection between its composition and the overall health and wellbeing has been widely and systematically reported by the scientific community (I Naseer et al. 2014, Zhao 2013, Alkasir et al. 2017, Boulangé et al. 2016, Carabotti et al. 2015, Claesson et al. 2012, Hu, Wang, and Jin 2016, Mangiola et al. 2016). Overall, the microbiota is responsible for fermenting dietary polysaccharides (that have not been previously absorbed into the bloodstream) which, in turn allows for the removal of calories from indigestible dietary compounds. Therefore, the gut microbiota fermentation results in the production of several metabolites that can be absorbed by the host. In fact, the presence of certain species of bacteria in the gut microbiota fermentative process have been shown to improve the processing and absorption of nutrients. Additionally, there are evidences that the beneficial effects attributed to dietary polyphenols depend on their biotransformation by the gut microbiota. (Boulangé et al. 2016, Carabotti et al. 2015, Quigley 2013, Conlon and Bird 2014).

An imbalance in the normal flora has been described to contribute to intestinal disorders such as chronic inflammatory bowel, cardiovascular diseases, as well as obesity and mental health problems. This imbalance, dubbed dysbiosis, occurs due to a loss of diversity of the species present in the microbiota with a strengthening of the presence of a specie previously not predominant or even due to the depletion of a specie (or several). For instance, the depletion of *Faecalibacterium prausnitzii* (Firmicutes phylum), has been associated with inflammatory bowel disorder even though it is just a single specie (Cardona et al. 2013, Conlon and Bird 2014, Laparra and Sanz 2010, Marchesi et al. 2015, Million et al. 2013).

Modulation of the microbiota towards a perceived beneficial phenotype has been studied as an alternative treatment for some pathologies, including liver conditions and inflammatory bowel disease. This modulation may be caused by, for instance, probiotics, prebiotics or polyphenols, since these can influence the composition and/or metabolic activity of the intestine's normal flora, contributing to reduce pathogenic species such as *Clostridium* (whose reduction has been associated with ameliorating autistic related symptoms), while increasing the presence of others such as *Lactobacillus* and *Bifidobacterium* while also stimulating the production of beneficial compounds, such as butyric acid, by these bacteria. Prebiotics are food constituents that promote the growth of microorganisms that exert a positive effect on the host. Essentially, they are a specific type of dietary fiber that, when fermented by the gut microbiota, allow for both the selective growth of beneficial bacteria such as bifidobacteria, as well as an increase of the production/accumulation of beneficial metabolites (Dueñas et al. 2015, Faria et al. 2014, Guglielmetti et al. 2013, Pequegnat et al. 2013, Eswaran, Muir, and Chey 2013, Slavin 2013).

Fruit extracts

Fruits are often associated with a healthier lifestyle. For instance, berries are often considered "superfruits", due to their high anthocyanin and phenolic content. Phenolic compounds have long been regarded as one of the classes of compounds, present in whole plant foods, which are most likely capable of affecting physiological processes that may grant some protection against chronic diet-associated diseases. The gut microbiota plays a very important part in the release of polyphenols that are bound to dietary fiber and that would otherwise not be absorbed into the blood serum. In fact, the majority of polyphenols are not absorbed at the upper gastrointestinal level and, therefore, reach the colon and may be metabolized by the microbiota, altering the original compound's bioactivity and bioavailability. This happens through the enzymatic activity of the gut microbial community (Faria et al. 2014, Marchesi et al. 2015, Cardona et al. 2013, Etxeberria et al. 2013).

Recent studies have shown that the intake of polyphenolic extracts, such as the ones obtained from the consumption of a blueberry powder drink, can help modulate the human gut microbiota, increasing the abundance of *Bifidobacterium* and *Lactobacillus* and diminishing the presence of *Clostridium histolyticum* which, considering that the latter has been associated with inflammatory bowel disease, contributes to a healthier profile of the gut. Moreover, different studies have shown that phenolics can alter the *Bacteroides/Firmicutes* balance, with *Firmicutes* being more predominant in people who suffer from obesity and *Bacteroides* being reported as contributing significantly to the reduction of blood pressure and high-density lipoprotein cholesterol. Furthermore, it is thought that *Bacteroides* are the genera mostly involved in the reactions necessary for anthocyanins' metabolization, since they express all the enzymes needed. Likewise, in a 16 weeks long study with mice, the dietary administration of proanthocyanidin-rich extracts led to a shift in the predominance of *Bacteroides*, *Clostridium* and *Propionibacterium* spp. to a predominance of *Bacteroides*, *Lactobacillus* and *Bifidobacterium* spp. In another study, a proanthocyanidin-rich extract from grape seeds given to healthy adults (for 2 weeks) was shown to significantly increase the presence of bifidobacteria in the gut. Thus, polyphenols may be capable of modulating the microbial community present in the gut and potentially improve the health of the host, through host-microbial interactions.

One of the mechanisms involved in the modulation, is due to the presence of microbial enzymes, which can alter phenolics and other compounds through hydrolysis, cleavage and decarboxylation, among others. For instance, the gut microbiota is responsible for hydrolyzing glycosides into their aglycones counterparts and their subsequent degradation into simple phenolic acids. Other possible mechanism involved in the modulation of the gut microflora is thought to be associated with the fact that polyphenols act differently upon distinct microbial colonies, affecting their viability differently. For example, an anthocyanin rich blueberry extract has been shown to have antimicrobial activity against different food pathogens, but no action upon probiotic bacteria. Additionally, phenolic compounds have been reported to exert selective antimicrobial activity against intestinal pathogens such as *Salmonella*, but also against *Staphylococcus*, by generating hydrogen peroxide and by altering the permeability of the cellular membrane. (Selma, Espin, and Tomas-Barberan 2009, Duda-Chodak et al. 2015, Etxeberria et al. 2013, Laparra and Sanz 2010, Marchesi et al. 2015, Puupponen-Pimiä et al. 2005, Cardona et al. 2013, Boulangé et al. 2016, Million et al. 2013, Fernandes et al. 2014, Dueñas et al. 2015, Boto-Ordóñez et al. 2014, Vendrame et al. 2013, Hidalgo et al. 2012, Faria et al. 2014, Valdés et al. 2015).

Anthocyanins have been widely associated not only with gut microbiota modulation, and with strong anti-inflammatory and antioxidant activities, with several epidemiological studies suggesting that the increased consumption of berries and anthocyanin rich berry extracts may lead to a reduction of the risk of developing cardiovascular disease, with anthocyanins exerting a beneficial impact upon related proinflammatory biomarkers and upon endothelial function (Mursu et al. 2008, Wallace 2011, Du et al. 2016, Olas 2017). However, to better support these claims, more studies are needed to assess the involving metabolism of anthocyanins by the gut microbiota and their subsequent impact upon cardiovascular health.

Citrus fruits have lower phenolics content than berries, possessing mainly flavonoids as well as fiber, pectins, vitamins and sugar. While citric extracts have been studied mainly for their antioxidant potential, reports on their potential antimicrobial, anti-diabetic, anti-inflammatory and cardiovascular protective effects have been published. Additionally, two phenolic compounds present in citrus peels (polymethoxyflavones and hydroxylpolymethoxyflavones) have shown anti-obesity potential in studies conducted *in vitro* and *in vivo*, by decreasing lipid accumulation as well as showing gut modulating capacity (Zou et al. 2016, Ghasemi, Ghasemi, and Ebrahimzadeh 2009, Lv et al. 2015, Gorinstein et al. 2001, Goulas and Manganaris 2012, Park et al. 2015, Alu'datt et al. 2017, Tung et al. 2018).

Leaf extracts

Although fruits are known to be rich in several bioactive compounds, leaves also represent a rich source of potentially beneficial compounds, with some authors reporting that leaves possess a significantly higher amount of total phenolics than the fruit (Jiménez-Aguilar and Grusak 2017, Salem et al. 2015, Piljac-Žegarac, Belščak, and Piljac 2009, da Silva et al. 2013). This difference may be due to the function of leaves, since these are responsible for the photosynthetic pathway and consequent O_2 production, which also lead to the production of reactive oxygen species that are detrimental to tissues. As such, taking into account the known antioxidant activity of phenolic compounds, these may be present in larger amounts in leaves to exert a protective effect upon its tissues, as well as to protect against the stress caused by solar exposure. For instance, aqueous and ethanolic extracts of passion fruits' leaves have been shown to possess higher antioxidant activity than the fruit itself, with this also happening with the leaves of berry bushes when comparing with the fruit themselves, including berries such as blackberry and strawberry. Chlorophyll is responsible for the leaves' usually green color, while carotenoids and flavonoids (such as anthocyanins) can also be present contributing to leaves' red/orange color during autumn. Additionally, some leaves extracts have been shown to possess some antimicrobial activity due to the presence of flavonoids (Jaakola et al. 2004, Riihinen et al. 2008, Ehlenfeldt and Prior 2001, Bendini et al. 2006, da Silva et al. 2013, Wang and Lin 2000).

Moreover, leaf extracts have also been studied for their microbiota modulating capacity. A particular example is the strong link existing between leaves extracts and obesity amelioration. Obesity has been shown to be connected to an imbalance in the gut microbiota, with reports showing predominance of the phylum *Firmicutes* in obese people. Previous works have shown that green tea extract may not only contribute to an amelioration of obesity related complications through gut microbiota modulation, but also exert a beneficial effect upon lipid metabolism. Moreover, rats fed a green tea powder in association with a *Lactobacillus* strain exhibited an increased presence of *Lactobacillus* genera in the gut and attenuated the inflammation resulting from the high fat diet given to the mice in the experiment. Additionally, black tea led to changes in a gut model microbiome, shifting the Firmicutes/Bacteroidetes ratio, and showing the possible modulation of select bacteria genera of the intestinal flora (Seo et al. 2015, Million et al. 2013, Zhao 2013, Axling et al. 2012, Kemperman et al. 2013).

Rosemary extracts have been investigated for their metabolism and inflammation regulatory properties in animal models, with some extracts leading to changes in rat's microbiota composition of rats, that translated into an increase of *Bifidobacterium* and short chain fatty acids' levels. Rhubarb extract has been shown to have interesting microbiota modulating properties. The supplementation of mice's diet with this extract led to an increase of the Verrucomicrobia phylum, associated with potential health benefits (although further studies are still required), in detriment of the Firmicutes phylum. Additionally, besides the gut microbiota modulating effect, rhubarb has shown renal-protective and hepaprotective effects in several *in vivo* experiments, as well as potential as acting as an antiproliferative compound against pancreatic cancer cells (Neyrinck et al. 2017, Arosio et al. 2000, Wang et al. 2009, Cai et al. 2008, Clementi and Misiti 2010, Romo-Vaquero et al. 2014, Vallverdú-Queralt et al. 2014). On the other hand, da Silva et al. (2013) described how passion fruit leaves promoted an increase in the total bacteria found on gut without being selective, unlike what has been described about some leaf extracts, which are able to inhibit pathogenic bacteria growth, while augmenting the presence of potentially beneficial bacteria such as *Lactobacillus* and *Bifidobacterium* (Cueva et al. 2010, Puupponen-Pimiä et al. 2005, Nohynek et al. 2006, Silva et al. 2013).

Olive leaves are the byproducts of olive production, with its extracts showing high potential for incorporation into different matrixes. As olive leaves possess high amounts of phenolic compounds, their potential health benefits have been studied, with authors describing olive leaf extracts as having antimicrobial, antioxidant and antidiabetic activity, as well as exerting cytotoxicity activity against breast cancer cells. Olive leaves possess phenolics belonging to the secoiridoids family, such as secoiridoid oleuporein, a bioactive compound which is thought to contribute to the leaves' potential health benefits (Paiva-Martins et al. 2007, Ribeiro et al. 2015, Pereira et al. 2007, Talhaoui et al. 2015, Taamalli et al. 2012, De Marino et al. 2014).

Root and tuber extracts

Root and tuber crops have been studied for their potential health benefits and as a source of functional ingredients. Some of their potential health benefits include antioxidant, hypoglycemic, antimicrobial and immunomodulatory activities, which are thought to be associated to the presence of phenolic compounds, some proteins, phytic acids and glycoalkaloids, their usually high fiber content that may help modulate microbiota composition and consequently ameliorate metabolic disorders in obese people, as well as cardiovascular diseases and other maladies (Delzenne, Neyrinck, and Cani 2011, Holscher 2017, Eswaran, Muir, and Chey 2013, Slavin 2013, Anderson et al. 2009).

Solanum jamesii tuber extracts have been shown to exert antiproliferative activity upon intestinal cancer cells. When the main components of the extract were tested for their antiproliferative activity, they did not prove to be effective, corroborating the hypothesis that the compounds present in extracts possess higher biological activity when interacting synergistically among themselves (Chandrasekara and Josheph Kumar 2016, Imam et al. 2014, Nzaramba et al. 2009).

A popular plant in India, nagarmotha (*Cyperus rotundus*) has been described as having diuretic, anti-inflammatory, antimicrobial, analgesic and anti-dysenteric activities, among several others, with essential oils being prepared from the tuber of the plant. Infusions of these tubers, as well as extracts prepared from the plant, have also been associated with antimicrobial, antioxidant, apoptotic and cytotoxicity activities. Additionally, reports have shown that when nagarmotha extracts were administered to obese mice, it prevented weight gain. However, reports connecting the gut microbiota modulation and this plant are still scarce, with results being inconclusive (Imam et al. 2014, Kilani et al. 2008, Lemaure et al. 2007, Torres-Fuentes et al. 2015).

Yacon tubers, rich sources of fructooligosaccharides and phenolic compounds, have shown potential to treat hyperglycemia, kidney problems, as well as reduce the risk of colon cancer. Yacon tuber extracts have also been studied regarding their potential prebiotic effect and gut modulating properties, since they are able to increase numbers of health promoting bacteria while decreasing the levels of potentially pathogenic bacteria. For instance, the prebiotic effect of yacon extract has been assessed with a guinea pig model, with yacon enhancing beneficial bacteria such as *Lactobacillus* and promoting the production of short chain fatty acids. Furthermore, yacon sirup, when administered for a period of 120 days led to increased satiety levels and a decrease in body weight. As such, yacon roots are considered to be potential dietary supplement that may prevent and/or ameliorate some diseases (Sousa et al. 2015, Campos et al. 2012, Delgado et al. 2013, Caetano et al. 2016, Valentová and Ulrichová 2003, Delzenne, Neyrinck, and Cani 2011).

Inulin extracted from Jerusalem artichoke (*Helianthus tuberosus* L.) tubers was shown to have a higher prebiotic capacity than a commercial prebiotic with inulin having been associated with colorectal cancer inhibition and a decrease of intestinal pH (Rubel et al. 2014, Shoaib et al. 2016). An extract of Chinese yam flour (*Dioscorea batatas*) was tested to evaluate its effects upon the gastrointestinal tract of rats, with results showing it appeared to improve digestive capacity, but it did not affect the growth of bacteria belonging to the gut. However, other reports have shown an increase of butyrate, acetate and propionate after the administration of Chinese yam polysaccharide to rats and there was shift in the predominant groups of bacteria of the gut microflora, with *Lactobacillus* and *Ruminococcus* species increasing and *Salmonella typhimurium* and *Clostridium perfringens* decreasing after 21 days of supplementation (Jeon et al. 2006, Kong et al. 2009).

Conclusion

A healthy diet is considered to be rich in fruits and vegetables, with these foodstuffs being strongly associated with overall wellbeing mainly due to the presence of phenolic compounds and fiber. As such, the addition of extracts rich in potentially biologically active compounds might confer some added benefits to certain foodstuffs, contributing to an improvement of the overall health and wellbeing. For example, the supplementation of phenolic compounds in the diet, either through fruits or leaves extracts, might lead to an increase of *Bacteroidetes* and a reduction of *Firmicutes*, as well as an increase in *Bifidobacterium* and *Lactobacillus* species, changes considered positive for one's health and associated with the amelioration of obesity, inflammation and other disorders, and also contributing to the prevention of cardiovascular and neurological problems.

Although several studies have shown the biological potential of the extracts consumption, mostly extracts derived from fruits, further human based studies are still needed to establish a true cause effect, with roots and tubers extracts impact upon health being the least explored.

Funding

This work was supported by National Funds from FCT (grant number UID/Multi/50016/2013).

ORCID

Mariana Veiga http://orcid.org/0000-0002-1815-3270
Eduardo M. Costa http://orcid.org/0000-0003-3121-4514
Sara Silva http://orcid.org/0000-0002-0896-9946
Manuela Pintado http://orcid.org/0000-0002-0760-3184

References

Abuajah, Christian Izuchukwu, Augustine Chima Ogbonna, and Chijioke Maduka Osuji. 2015. Functional components and medicinal properties of food: A review. *Journal of Food Science and Technology* 52 (5):2522–2529.

Adam, Clare L., Patricia A. Williams, Matthew J. Dalby, Karen Garden, Lynn M. Thomson, Anthony J. Richardson, Silvia W. Gratz, and Alexander W. Ross. 2014. Different types of soluble fermentable dietary fibre decrease food intake, body weight gain and adiposity in young adult male rats. *Nutrition & Metabolism* 11 (1):36

Akhtar, Saeed, Tariq Ismail, Daniele Fraternale, and Piero Sestili. 2015. Pomegranate peel and peel extracts: Chemistry and food features. *Food Chemistry* 174:417–425.

Albishi, Tasahil, Jenny A. John, Abdulrahman S. Al-Khalifa, and Fereidoon Shahidi. 2013. Antioxidant, anti-inflammatory and DNA scission inhibitory activities of phenolic compounds in selected onion and potato varieties. *Journal of Functional Foods* 5 (2): 930–939.

Alkasir, Rashad, Jing Li, Xudong Li, Miao Jin, and Baoli Zhu. 2017. Human gut microbiota: The links with dementia development. *Protein & Cell* 8 (2):90–102.

Alu'datt, Muhammad H., Taha Rababah, Mohammad N. Alhamad, Majdi A. Al-Mahasneh, Khalil Ereifej, Ghazi Al-Karaki, Mohammed Al-Duais, Juan E. Andrade, Carole C. Tranchant, Stan Kubow, and Kawther A. Ghozlan. 2017. Profiles of free and bound phenolics extracted from citrus fruits and their roles in biological systems: Content, and antioxidant, anti-diabetic and anti-hypertensive properties. *Food & Function* 8 (9):3187–3197.

Anderson, James W., Pat Baird, Richard H. Davis, Stefanie Ferreri, Mary Knudtson, Ashraf Koraym, Valerie Waters, and Christine L. Williams. 2009. Health benefits of dietary fiber. *Nutrition Reviews* 67 (4):188–205.

Aniszewski, Tadeusz. 2015. *Alkaloids: Chemistry, biology, ecology, and applications*. Amsterdam: Elsevier.

Armendáriz-Barragán, Brenda, Nadiah Zafar, Waisudin Badri, Sergio Arturo Galindo-Rodríguez, Dounia Kabbaj, Hatem Fessi, and Abdelhamid Elaissari. 2016. Plant extracts: From encapsulation to application. *Expert Opinion on Drug Delivery* 13 (8):1165–1175. doi: 10.1080/17425247.2016.1182487.

Arosio, Beatrice, Nicoletta Gagliano, Lorena Maria Pia Fusaro, Luciano Parmeggiani, Jacopo Tagliabue, Paola Galetti, Diego De Castri, Claudia Moscheni, and Giorgio Annoni. 2000. Aloe-emodin quinone pretreatment reduces acute liver injury induced by carbon tetrachloride. *Pharmacology and Toxicology* 87 (5):229–233.

Asif, Mohammad. 2015. Chemistry and antioxidant activity of plants containing some phenolic compounds. *Chemistry International* 1 (1):35–52.

Axling, Ulrika, Crister Olsson, Jie Xu, Céline Fernandez, Sara Larsson, Kristoffer Ström, Siv Ahrné, Cecilia Holm, Göran Molin, and Karin Berger. 2012. Green tea powder and *Lactobacillus plantarum* affect gut microbiota, lipid metabolism and inflammation in high-fat fed C57BL/6J mice. *Nutrition & Metabolism* 9 (1):105

Balasundram, Nagendran, Kalyana Sundram, and Samir Samman. 2006. Phenolic compounds in plants and Agri-industrial by-products: Antioxidant activity, occurrence, and potential uses. *Food Chemistry* 99 (1):191–203.

Baye, Estifanos, Negar Naderpoor, Marie Misso, Helena Teede, Lisa J. Moran, and Barbora de Courten. 2017. Treatment with high dose salicylates improves cardiometabolic parameters: Meta-analysis of randomized controlled trials. *Metabolism: Clinical and Experimental* 71 :94–106.

Bendini, Alessandra, Lorenzo Cerretani, Luca Pizzolante, Tullia Gallina Toschi, Flavia Guzzo, Stefania Ceoldo, Andrea Maria Marconi, Filippo Andreetta, and Marisa Levi. 2006. Phenol content related to antioxidant and antimicrobial activities of *Passiflora* spp. extracts. *European Food Research and Technology* 223 (1):102–109.

Bernalier-Donadille, A. 2010. Fermentative metabolism by the human gut microbiota. *Gastroenterologie Clinique et Biologique* 34:S16–S22.

Boscolo, Odara Horta, and Luci de Senna Valle. 2008. Plantas de uso medicinal em quissamã, Rio De Janeiro, Brasil. *Iheringia. Série Botânica* 63 (2):263–278.

Bosscher, D., A. Breynaert, L. Pieters, and N. Hermans. 2009. Food-based strategies to modulate the composition of the microbiota and their associated health effects. *Journal of Physiology and Pharmacology/Polish Physiological Society.-Kraków, 1991, Currens* 60 (S: 6):5–11.

Boto-Ordóñez, María, Mireia Urpi-Sarda, María Isabel Queipo-Ortuño, Sara Tulipani, Francisco J. Tinahones, and Cristina Andres-Lacueva. 2014. High levels of *Bifidobacteria* are associated with increased levels of anthocyanin microbial metabolites: A randomized clinical trial. *Food & Function* 5 (8):1932–1938.

Boulangé, Claire L., Ana Luisa Neves, Julien Chilloux, Jeremy K. Nicholson, and Marc-Emmanuel Dumas. 2016. Impact of the gut microbiota on inflammation, obesity, and metabolic disease. *Genome Medicine* 8 (1):42

Bränning, Camilla, Åsa Håkansson, Siv Ahrné, Bengt Jeppsson, Göran Molin, and Margareta Nyman. 2009. Blueberry husks and multi-strain probiotics affect colonic fermentation in rats. *British Journal of Nutrition* 101 (06):859–870.

Briskin, Donald P. 2000. Medicinal plants and phytomedicines. Linking plant biochemistry and physiology to human health. *Plant Physiology* 124 (2):507–514.

Brown, Lisa, Bernard Rosner, Walter W. Willett, and Frank M. Sacks. 1999. Cholesterol-lowering effects of dietary fiber: A Meta-analysis. *The American Journal of Clinical Nutrition* 69 (1):30–42.

Brownawell, Amy M., Wim Caers, Glenn R. Gibson, Cyril W. C. Kendall, Kara D. Lewis, Yehuda Ringel, and Joanne L. Slavin. 2012. Prebiotics and the health benefits of fiber: Current regulatory status, future research, and goals. *The Journal of Nutrition* 142 (5):962–974.

Bulotta, Stefania, Marilena Celano, Saverio Massimo Lepore, Tiziana Montalcini, Arturo Pujia, and Diego Russo. 2014. Beneficial effects of the olive oil phenolic components oleuropein and hydroxytyrosol: Focus on protection against cardiovascular and metabolic diseases. *Journal of Translational Medicine* 12 (1):219.

Caetano, Brunno F. R., Nelci A. de Moura, Ana P. S. Almeida, Marcos C. Dias, Kátia Sivieri, and Luís F. Barbisan. 2016. Yacon (*Smallanthus sonchifolius*) as a food supplement: health-promoting benefits of fructooligosaccharides. *Nutrients* 8 (7):436.

Cai, Jun, Anthony Razzak, Justin Hering, Abdul Saed, Tricia A. Babcock, Scott Helton, and N. Joseph Espat. 2008. Feasibility evaluation of emodin (rhubarb extract) as an inhibitor of pancreatic cancer cell proliferation in vitro. *Journal of Parenteral and Enteral Nutrition* 32 (2):190–196.

Çam, Mustafa, Necattin Cihat İçyer, and Fatma Erdoğan. 2014. Pomegranate peel phenolics: microencapsulation, storage stability and potential ingredient for functional food development. *LWT-Food Science and Technology* 55 (1):117–123.

Campos, David, Indira Betalleluz-Pallardel, Rosana Chirinos, Ana Aguilar-Galvez, Giuliana Noratto, and Romina Pedreschi. 2012. Prebiotic effects of Yacon (*Smallanthus sonchifolius* poepp. & Endl), a source of fructooligosaccharides and phenolic compounds with antioxidant activity. *Food Chemistry* 135 (3):1592–1599.

Carabotti, Marilia, Annunziata Scirocco, Maria Antonietta Maselli, and Carola Severi. 2015. The gut-brain axis: interactions between enteric microbiota, Central and enteric nervous systems. *Annals of Gastroenterology: Quarterly Publication of the Hellenic Society of Gastroenterology* 28 (2):203.

Cardona, Fernando, Cristina Andrés-Lacueva, Sara Tulipani, Francisco J. Tinahones, and María Isabel Queipo-Ortuño. 2013. Benefits of polyphenols on gut microbiota and implications in human health. *The Journal of Nutritional Biochemistry* 24 (8): 1415–1422.

Carey, Amanda N., Stacey M. Gomes, and Barbara Shukitt-Hale. 2014. Blueberry supplementation improves memory in Middle-aged mice fed a high-fat diet. *Journal of Agricultural and Food Chemistry* 62 (18):3972–3978.

Chandrasekara, Anoma, and Thamilini Josheph Kumar. 2016. Roots and tuber crops as functional foods: A review on phytochemical constituents and their potential health benefits. *International Journal of Food Science* 2016:1.

Charalampopoulos, D., R. Wang, S. S. Pandiella, and C. Webb. 2002. Application of cereals and cereal components in functional foods: A review. *International Journal of Food Microbiology* 79 (1–2):131–141.

Cheynier, Véronique. 2012. Phenolic compounds: From plants to foods. *Phytochemistry Reviews* 11 (2–3):153–177.

Claesson, Marcus J., Ian B. Jeffery, Susana Conde, Susan E. Power, Eibhlís M. O'Connor, Siobhán Cusack, Hugh M. B. Harris, Mairead Coakley, Bhuvaneswari Lakshminarayanan, Orla O'Sullivan, et al. 2012. Gut microbiota composition correlates with diet and health in the elderly. *Nature 488* (7410):178.

Clementi, Elisabetta M., and Francesco Misiti. 2010. Potential health benefits of rhubarb. In *Bioactive foods in promoting health*, 407–423. Elsevier.

Conlon, Michael A., and Anthony R. Bird. 2014. The impact of diet and lifestyle on gut microbiota and human health. *Nutrients* 7 (1): 17–44.

Cueva, Carolina, M. Victoria Moreno-Arribas, Pedro J. Martín-Álvarez, Gerald Bills, M. Francisca Vicente, Angela Basilio, Concepción López Rivas, Teresa Requena, Juan M. Rodríguez, and Begoña Bartolomé. 2010. Antimicrobial activity of phenolic acids against commensal, probiotic and pathogenic bacteria. *Research in Microbiology* 161 (5):372–382.

Cushnie, T. P Tim., Benjamart Cushnie, and Andrew J. Lamb. 2014. Alkaloids: An overview of their antibacterial, antibiotic-enhancing and antivirulence activities. *International Journal of Antimicrobial Agents* 44 (5):377–386.

da Silva, Juliana Kelly, Cinthia Baú Betim Cazarin, Talita C. Colomeu, Ângela Giovana Batista, Laura M. M. Meletti, Jonas Augusto Rizzato Paschoal, Stanislau Bogusz Júnior, Mayra Fontes Furlan, Felix Guillermo Reyes Reyes, Fábio Augusto, et al. 2013. Antioxidant activity of aqueous extract of passion fruit (*Passiflora edulis*) leaves: In vitro and in vivo study. *Food Research International* 53 (2):882–890.

Daniel, Mammen. 2016. *Medicinal plants: Chemistry and properties*. Boca Raton: CRC Press.

Das, Lipi, Eshani Bhaumik, Utpal Raychaudhuri, and Runu Chakraborty. 2012. Role of nutraceuticals in human health. *Journal of Food Science and Technology* 49 (2):173–183.

Marino, Simona, Carmen Festa, Franco Zollo, Antonella Nini, Lina Antenucci, Gennaro Raimo, and Maria Iorizzi. 2014. Antioxidant activity and chemical components as potential anticancer agents in the olive leaf (*Olea europaea* L. cv leccino.) decoction. *Anti-Cancer Agents in Medicinal Chemistry* 14 (10):1376–1385.

Delgado, Grethel Teresa Choque, Wirla Maria da Silva Cunha Tamashiro, Mário Roberto Maróstica Junior, and Glaucia Maria Pastore. 2013. Yacon (*Smallanthus sonchifolius*): A functional food. *Plant Foods for Human Nutrition (Dordrecht, Netherlands)* 68 (3): 222–228.

Delzenne, Nathalie M., Audrey M. Neyrinck, and Patrice D. Cani. 2011. Modulation of the gut microbiota by nutrients with prebiotic properties: Consequences for host health in the context of obesity and metabolic syndrome. *Microbial Cell Factories* 10 (Suppl 1):S10. doi:10.1186/1475-2859-10-s1-s10.

Dillard, Cora J., and J. Bruce German. 2000. Phytochemicals: Nutraceuticals and human health. *Journal of the Science of Food and Agriculture* 80 (12):1744–1756.

Dissanayake, Amila A., Chuan-Rui Zhang, Gary L. Mills, and Muraleedharan G. Nair. 2018. Cultivated maitake mushroom demonstrated functional food quality as determined by in vitro bioassays. *Journal of Functional Foods* 44:79–85.

Djeridane, A., M. Yousfi, B. Nadjemi, D. Boutassouna, P. Stocker, and N. Vidal. 2006. Antioxidant activity of some Algerian medicinal plants extracts containing phenolic compounds. *Food Chemistry* 97 (4):654–660.

Dreher, Mark L. 2018. Insights on the role of fiber in colonic microbiota health. In *Dietary fiber in health and disease*, 41–66. Springer.

Du, Huaidong, Liming Li, Derrick Bennett, Yu Guo, Timothy J. Key, Zheng Bian, Paul Sherliker, Haiyan Gao, Yiping Chen, Ling Yang., et al. 2016. Fresh fruit consumption and major cardiovascular disease in China. *The New England Journal of Medicine* 374 (14): 1332–1343.

Duda-Chodak, Aleksandra, Tomasz Tarko, Paweł Satora, and Paweł Sroka. 2015. Interaction of dietary compounds, especially polyphenols, with the intestinal microbiota: A review. *European Journal of Nutrition* 54 (3):325–341.

Dueñas, Montserrat, Irene Muñoz-González, Carolina Cueva, Ana Jiménez-Girón, Fernando Sánchez-Patán, Celestino Santos-Buelga, M. Moreno-Arribas, and Begoña Bartolomé. 2015. A survey of modulation of gut microbiota by dietary polyphenols. *BioMed Research International* 2015:1. doi:10.1155/2015/850902.

Duke, James A., Leland J. Cseke, Sara Warber, Ara Kirakosyan, Harry L. Brielmann, and Peter B. Kaufman. 2016. *Natural products from plants*. Boca Raton: CRC Press.

Dulebohn, Rachel V., Weiguang Yi, Anita Srivastava, Casimir C. Akoh, Gerard Krewer, and Joan G. Fischer. 2008. Effects of blueberry (*Vaccinium ashei*) on DNA damage, lipid peroxidation, and phase II enzyme activities in rats. *Journal of Agricultural and Food Chemistry* 56 (24):11700–11706.

Ehlenfeldt, Mark K., and Ronald L. Prior. 2001. Oxygen radical absorbance capacity (ORAC) and phenolic and anthocyanin concentrations in fruit and leaf tissues of highbush blueberry. *Journal of Agricultural and Food Chemistry* 49 (5):2222–2227.

Ekor, Martins. 2014. The growing use of herbal medicines: Issues relating to adverse reactions and challenges in monitoring safety. *Frontiers in Pharmacology* 4:177

Escarpa, A., and M. C. González. 2001. Approach to the content of total extractable phenolic compounds from different food samples by comparison of chromatographic and spectrophotometric methods. *Analytica Chimica Acta* 427 (1):119–127.

Eswaran, Shanti, Jane Muir, and William D. Chey. 2013. Fiber and functional gastrointestinal disorders. *The American Journal of Gastroenterology* 108 (5):718

Etxeberria, Usune, Alfredo Fernández-Quintela, Fermín I. Milagro, Leixuri Aguirre, J. Alfredo Martínez, and María P. Portillo. 2013. Impact of polyphenols and polyphenol-rich dietary sources on gut microbiota composition. *Journal of Agricultural and Food Chemistry* 61 (40):9517–9533.

Faria, Ana, Iva Fernandes, Sónia Norberto, Nuno Mateus, and Conceição Calhau. 2014. Interplay between anthocyanins and gut microbiota. *Journal of Agricultural and Food Chemistry* 62 (29): 6898–6902.

Farnsworth, Norman R., Olayiwola Akerele, Audrey S. Bingel, Djaja D. Soejarto, and Zhengang Guo. 1985. Medicinal plants in therapy. *Bulletin of the World Health Organization* 63 (6):965.

Fernandes, Iva, Ana Faria, Conceição Calhau, Victor de Freitas, and Nuno Mateus. 2014. Bioavailability of anthocyanins and derivatives. *Journal of Functional Foods* 7:54–66.

Fich, Eric A., Nicholas A. Segerson, and Jocelyn K. C. Rose. 2016. The plant polyester cutin: Biosynthesis, structure, and biological roles. *Annual Review of Plant Biology* 67(1):207–233.

Finegold, Sydney M., Paula H. Summanen, Julia Downes, Karen Corbett, and Tomoe Komoriya. 2017. Detection of *Clostridium perfringens* toxin genes in the gut microbiota of autistic children. *Anaerobe* 45:133–137.

Fuller, Stacey, Eleanor Beck, Hayfa Salman, and Linda Tapsell. 2016. New horizons for the study of dietary fiber and health: A review. *Plant Foods for Human Nutrition* 71 (1):1–12.

Ganesan, Divya, Eman Al-Sayed, Abhishek Albert, Eldho Paul, Abdel Nasser B. Singab, Selvam Govindan Sadasivam, and Luciano Saso. 2018. Antioxidant activity of phenolic compounds from extracts of eucalyptus globulus and melaleuca styphelioides and their protective role on D-glucose-induced hyperglycemic stress and oxalate stress in NRK-49Fcells. *Natural Product Research* 32 (11): 1274–1280.

Gao, Hongli, Zhaochun Liu, Wenju Wan, Xiaolan Qu, and Meihua Chen. 2013. Aqueous extract of yerba mate tea lowers atherosclerotic risk factors in a rat hyperlipidemia model. *Phytotherapy Research* 27 (8):1225–1231.

Ghasemi, Kamran, Yosef Ghasemi, and Mohammad Ali Ebrahimzadeh. 2009. Antioxidant activity, phenol and flavonoid contents of 13 citrus species peels and tissues. *Pakistan Journal of Pharmaceutical Sciences* 22 (3):277–281.

González-Sarrías, Antonio, Juan Carlos Espín, and Francisco A. Tomás-Barberán. 2017. Non-extractable polyphenols produce gut microbiota metabolites that persist in circulation and show anti-inflammatory and free radical-scavenging effects. *Trends in Food Science & Technology* 69:281–288.

Gorinstein, Shela, Olga Martín-Belloso, Yong-Seo Park, Ratiporn Haruenkit, Antonin Lojek, Milan Cᵃıž, Abraham Caspi, Imanuel Libman, and Simon Trakhtenberg, 2001. Comparison of some biochemical characteristics of different citrus fruits. *Food Chemistry* 74 (3):309–315.

Goulas, Vlassios, and George A. Manganaris. 2012. Exploring the phytochemical content and the antioxidant potential of citrus fruits grown in Cyprus. *Food Chemistry* 131 (1):39–47.

Graf, Brigitte A., Paul E. Milbury, and Jeffrey B. Blumberg. 2005. Flavonols, flavones, flavanones, and human health: Epidemiological evidence. *Journal of Medicinal Food* 8 (3):281–290.

Guglielmetti, Simone, Daniela Fracassetti, Valentina Taverniti, Cristian Del Bo', Stefano Vendrame, Dorothy Klimis-Zacas, Stefania Arioli, Patrizia Riso, and Marisa Porrini. 2013. Differential modulation of human intestinal *Bifidobacterium* populations after consumption of a wild blueberry (*Vaccinium angustifolium*) drink. *Journal of Agricultural and Food Chemistry* 61 (34):8134–8140.

Hardy, Karen, Jennie Brand-Miller, Katherine D. Brown, Mark G. Thomas, and Les Copeland. 2015. The importance of dietary carbohydrate in human evolution. *The Quarterly Review of Biology* 90 (3): 251–268.

Hassan, Ammara, Salma Rahman, Farah Deeba, and Shahid Mahmud. 2009. Antimicrobial activity of some plant extracts having hepatoprotective effects. *Journal of Medicinal Plants Research* 3 (1): 020–023.

He, Bo, Ling-Li Zhang, Xue-Yang Yue, Jin Liang, Jun Jiang, Xue-Ling Gao, and Peng-Xiang Yue. 2016. Optimization of ultrasound-assisted extraction of phenolic compounds and anthocyanins from blueberry (*Vaccinium ashei*) wine pomace. *Food Chemistry* 204:70–76.

Hendrix, Donald L. 1993. Rapid extraction and analysis of nonstructural carbohydrates in plant tissues. *Crop Science* 33 (6):1306–1311.

Hidalgo, Maria, M. Jose Oruna-Concha, Sofia Kolida, Gemma E. Walton, Stamatina Kallithraka, Jeremy P. E. Spencer, Glenn R. Gibson, and Sonia de Pascual-Teresa. 2012. Metabolism of anthocyanins by human gut microflora and their influence on gut bacterial growth. *Journal of Agricultural and Food Chemistry* 60 (15):3882–3890.

Hilou, A., O. G. Nacoulma, and T. R. Guiguemde. 2006. In vivo antimalarial activities of extracts from *amaranthus spinosus* L. and *boerhaavia erecta* L. in mice. *Journal of Ethnopharmacology* 103 (2): 236–240.

Hollman, Peter C. H. 2001. Evidence for health benefits of plant phenols: Local or systemic effects? *Journal of the Science of Food and Agriculture* 81 (9):842–852.

Hollman, Peter C. H., and Ilja C. W. Arts. 2000. Flavonols, flavones and flavanols–nature, occurrence and dietary burden. *Journal of the Science of Food and Agriculture* 80 (7):1081–1093.

Holscher, Hannah D. 2017. Dietary fiber and prebiotics and the gastrointestinal microbiota. *Gut Microbes* 8 (2):172–184.

Hu, Xu, Tao Wang, and Feng Jin. 2016. Alzheimer's disease and gut microbiota. *Science China. Life Sciences* 59 (10):1006–1023.

Naseer, I., Fehmida Bibi Muhammad, Mohammed H. Alqahtani, Adeel G. Chaudhary, Esam I. Azhar, Mohammad A. Kamal, and Muhammad Yasir. 2014. Role of gut microbiota in obesity, type 2 diabetes and Alzheimer's disease. *CNS & Neurological Disorders - Drug Targets* 13 (2):305–311.

Imam, Hashmat, Ghulamuddin Sofi, Aziz Seikh, and Azad Lone. 2014. The incredible benefits of nagarmotha (Cyperus rotundus). *International Journal of Nutrition, Pharmacology, Neurological Diseases* 4 (1):23.

Islam, Md Shahidul, and Haymie Choi. 2009. Antidiabetic effect of Korean traditional Baechu (Chinese cabbage) kimchi in a type 2 diabetes model of rats. *Journal of Medicinal Food* 12 (2):292–297.

Jaakola, Laura, Kaisu Määttä-Riihinen, Sirpa Kärenlampi, and Anja Hohtola. 2004. Activation of flavonoid biosynthesis by solar radiation in bilberry (*Vaccinium myrtillus* L) leaves. *Planta* 218 (5): 721–728.

Jeon, Jeong Ryae, Ji Seon Lee, Chu Hee Lee, Jong Yeon Kim, Soon Dong Kim, and Doo Hyun Nam. 2006. Effect of ethanol extract of dried Chinese yam (Dioscorea batatas) flour containing dioscin on gastrointestinal function in rat model. *Archives of Pharmacal Research* 29 (5):348–353. doi: 10.1155/2009/598152.

Jiménez-Aguilar, Dulce M., and Michael A. Grusak. 2017. Minerals, vitamin C, phenolics, flavonoids and antioxidant activity of Amaranthus leafy vegetables. *Journal of Food Composition and Analysis* 58:33–39.

Jo, Yu Na., Dong Eun Jin, Ji Hee Jeong, Hyeon Ju Kim, Dae-Ok Kim, and Ho Jin Heo. 2015. Effect of anthocyanins from rabbit-eye blueberry (*Vaccinium virgatum*) on cognitive function in mice under trimethyltin-induced neurotoxicity. *Food Science and Biotechnology* 24 (3):1077–1085.

Jung, Mankil, Moonsoo Park, Hyun C. Lee, Yoon-Ho Kang, Eun S. Kang, and Sang K. Kim. 2006. Antidiabetic agents from medicinal plants. *Current Medicinal Chemistry* 13 (10):1203–1218.

Junior, Euclides Lara Cardozo, and Christine Morand. 2016. Interest of mate (Ilex paraguariensis A. St.-hil.) as a new natural functional food to preserve human cardiovascular health–A review. *Journal of Functional Foods* 21:440–454.

Kaczmarczyk, Melissa M., Michael J. Miller, and Gregory G. Freund. 2012. The health benefits of dietary fiber: Beyond the usual suspects of type 2 diabetes mellitus, cardiovascular disease and Colon cancer. *Metabolism: Clinical and Experimental* 61 (8):1058–1066.

Kashtanova, Daria A., Anna S. Popenko, Olga N. Tkacheva, Alexander B. Tyakht, Dimitry G. Alexeev, and Sergey A. Boytsov. 2016. Association between the gut microbiota and diet: Fetal life, early childhood, and further life. *Nutrition (Burbank, Los Angeles County, Calif.)* 32 (6):620–627.

Kemperman, Robèr A., Gabriele Gross, Stanilas Mondot, Sam Possemiers, Massimo Marzorati, Tom Van de Wiele, Joël Doré, and Elaine E. Vaughan. 2013. Impact of polyphenols from black tea and red wine/grape juice on a gut model microbiome. *Food Research International* 53 (2):659–669.

Kendall, Cyril W. C., Amin Esfahani, and David J. A. Jenkins. 2010. The link between dietary fibre and human health. *Food Hydrocolloids* 24 (1):42–48.

Kilani, Soumaya, Mohamed Ben Sghaier, Ilef Limem, Ines Bouhlel, Jihed Boubaker, Wissem Bhouri, Ines Skandrani, Aicha Neffatti, Ribai Ben Ammar, Marie Genviève Dijoux-Franca., et al. 2008. In vitro evaluation of antibacterial, antioxidant, cytotoxic and apoptotic activities of the tubers infusion and extracts of *Cyperus rotundus*. *Bioresource Technology* 99 (18):9004–9008.

Kolarovic, Ladislav, and Nestor C. Fournier. 1986. A comparison of extraction methods for the isolation of phospholipids from biological sources. *Analytical Biochemistry* 156 (1):244–250.

Kong, X. F., Y. Z. Zhang, X. Wu, Y. L. Yin, Z. L. Tan, Y. Feng, F. Y. Yan, M. J. Bo, R. L. Huang, and T. J. Li. 2009. Fermentation characterization of Chinese yam polysaccharide and its effects on the gut microbiota of rats. *International Journal of Medical Microbiology* 2009:1. doi: 10.1155/2009/598152.

Landete, J. M. 2012. Updated knowledge about polyphenols: Functions, bioavailability, metabolism, and health. *Critical Reviews in Food Science and Nutrition* 52 (10):936–948.

Laparra, José Moisés, and Yolanda Sanz. 2010. Interactions of gut microbiota with functional food components and nutraceuticals. *Pharmacological Research* 61 (3):219–225.

Lapornik, Brigita, Mirko Prošek, and Alenka Golc Wondra. 2005. Comparison of extracts prepared from plant by-products using different solvents and extraction time. *Journal of Food Engineering* 71 (2):214–222.

Lattanzio, Vincenzo. 2013. Phenolic compounds: Introduction. In *Natural products*, 1543–1580. Springer.

Lemaure, Bernard, André Touché, Irène Zbinden, Julie Moulin, Didier Courtois, Katherine Macé, and Christian Darimont. 2007. Administration of *Cyperus rotundus* tubers extract prevents weight gain in obese zucker rats. *Phytotherapy Research: PTR* 21 (8): 724–730.

Liu, Rui Hai. 2003. Health benefits of fruit and vegetables are from additive and synergistic combinations of phytochemicals. *The American Journal of Clinical Nutrition* 78 (3):517S–520S.

Liu, Rui Hai. 2013. Health-promoting components of fruits and vegetables in the diet. *Advances in Nutrition (Bethesda, Md.)* 4 (3): 384S–392S.

Liu, Wei, Xiangyi Lu, Guangyang He, Xiang Gao, Mengxian Li, Junhua Wu, Zhenjing Li, Jihui Wu, Juncheng Wang, and Cheng Luo. 2013. Cytosolic protection against ultraviolet induced DNA damage by blueberry anthocyanins and anthocyanidins in hepatocarcinoma HepG2 cells. *Biotechnology Letters* 35 (4):491–498.

Lopez-Legarrea, Patricia, Nicholas Robert Fuller, María Angeles Zulet, Jose Alfredo Martinez, and Ian Douglas Caterson. 2014. The influence of Mediterranean, carbohydrate and high protein diets on gut microbiota composition in the treatment of obesity and associated inflammatory state. *Asia Pacific Journal of Clinical Nutrition* 23 (3): 360–368.

Lv, Xinmiao, Siyu Zhao, Zhangchi Ning, Honglian Zeng, Yisong Shu, Ou Tao, Cheng Xiao, Cheng Lu, and Yuanyan Liu. 2015. Citrus fruits as a treasure trove of active natural metabolites that potentially provide benefits for human health. *Chemistry Central Journal* 9 (1): 68.

Malakar, Sreepurna. 2017. Bioactive food chemicals and gastrointestinal symptoms: a focus of salicylates. *Journal of Gastroenterology and Hepatology* 32 (S1):73–77.

Mangiola, Francesca, Gianluca Ianiro, Francesco Franceschi, Stefano Fagiuoli, Giovanni Gasbarrini, and Antonio Gasbarrini. 2016. Gut microbiota in autism and mood disorders. *World Journal of Gastroenterology* 22 (1):361

Marchesi, Julian R., David H. Adams, Francesca Fava, Gerben D. A. Hermes, Gideon M. Hirschfield, Georgina Hold, Mohammed Nabil Quraishi, James Kinross, Hauke Smidt, and Kieran M. Tuohy. 2015. The gut microbiota and host health: a new clinical frontier. *Gut* 65 (2):330–339. doi: 10.1136/gutjnl-2015-309990.

Maria de Lourdes Reis, Giada. 2013. Food Phenolic Compounds: Main Classes, Sources and Their Antioxidant Power. doi: 10.5772/51687.

Million, M.,. J. -C. Lagier, D. Yahav, and M. Paul. 2013. Gut bacterial microbiota and obesity. *Clinical Microbiology and Infection: The Official Publication of the European Society of Clinical Microbiology and Infectious Diseases* 19 (4):305–313.

Mohamed, Suhaila. 2014. Functional foods against metabolic syndrome (obesity, diabetes, hypertension and dyslipidemia) and cardiovasular disease. *Trends in Food Science & Technology* 35 (2):114–128.

Molan, Abdul Lateef, Mary Ann Lila, John Mawson, and Shampa De. 2009. In vitro and in vivo evaluation of the prebiotic activity of water-soluble blueberry extracts. *World Journal of Microbiology and Biotechnology* 25 (7):1243–1249.

Moncada, Jonathan, and Valentina Aristizábal. 2016. Design strategies for sustainable biorefineries. *Biochemical Engineering Journal* 116: 122–134.

Morais, Carina Almeida, Veridiana Vera de Rosso, Débora Estadella, and Luciana Pellegrini Pisani. 2016. Anthocyanins as inflammatory modulators and the role of the gut microbiota. *The Journal of Nutritional Biochemistry* 33:1–7.

Mudgil, Deepak, and Sheweta Barak. 2013. Composition, properties and health benefits of indigestible carbohydrate polymers as dietary fiber: A review. *International Journal of Biological Macromolecules* 61:1–6.

Mursu, Jaakko, Sari Voutilainen, Tarja Nurmi, Tomi-Pekka Tuomainen, Sudhir Kurl, and Jukka T. Salonen. 2008. Flavonoid intake and the risk of ischaemic stroke and CVD mortality in Middle-aged finnish men: The kuopio ischaemic heart disease risk factor study. *The British Journal of Nutrition* 100 (4):890–895.

Naczk, Marian, and Fereidoon Shahidi. 2006. Phenolics in cereals, fruits and vegetables: Occurrence, extraction and analysis. *Journal of Pharmaceutical and Biomedical Analysis* 41 (5):1523–1542.

Neto, Catherine C. 2007. Cranberry and blueberry: Evidence for protective effects against cancer and vascular diseases. *Molecular Nutrition & Food Research* 51 (6):652–664. doi: 10.1002/mnfr.200600279.

Neyrinck, Audrey M., Usune Etxeberria, Bernard Taminiau, Georges Daube, Matthias Van Hul, Amandine Everard, Patrice D. Cani, Laure B. Bindels, and Nathalie M. Delzenne. 2017. Rhubarb extract prevents hepatic inflammation induced by acute alcohol intake, an effect related to the modulation of the gut microbiota. *Molecular Nutrition & Food Research* 61 (1):1500899.

Nicoue, Eugene Emile, Sylvain Savard, and Khaled Belkacemi. 2007. Anthocyanins in wild blueberries of Quebec: extraction and identification. *Journal of Agricultural and Food Chemistry* 55 (14): 5626–5635.

Nile, Shivraj Hariram, and Se Won Park. 2014. Edible berries: Bioactive components and their effect on human health. *Nutrition (Burbank, Los Angeles County, Calif.)* 30 (2):134–144.

Nohynek, Liisa J., Hanna-Leena Alakomi, Marja P. Kähkönen, Marina Heinonen, Ilkka M. Helander, Kirsi-Marja Oksman-Caldentey, and Riitta H. Puupponen-Pimiä. 2006. Berry phenolics: antimicrobial properties and mechanisms of action against severe human pathogens. *Nutrition and Cancer* 54 (1):18–32.

Nzaramba, M. Ndambe, Lavanya Reddivari, John B. Bamberg, and J. Creighton Miller. Jr. 2009. Antiproliferative activity and cytotoxicity of *Solanum jamesii* tuber extracts on human Colon and prostate cancer cells in vitro. *Journal of Agricultural and Food Chemistry* 57 (18):8308–8315.

O'Callaghan, Amy, and Douwe van Sinderen. 2016. Bifidobacteria and their role as members of the human gut microbiota. *Frontiers in Microbiology* 7:925

Olas, Beata. 2017. The multifunctionality of berries toward blood platelets and the role of berry phenolics in cardiovascular disorders. *Platelets* 28 (6):540–549.

Omoregbe, R. E., O. M. Ikuebe, and I. G. Ihimire. 1996. Antimicrobial activity of some medicinal plants extracts on *Escherichia coli, Salmonella paratyphi* and *Shigella dysenteriae*. *African Journal of Medicine and Medical Sciences* 25 (4):373–375.

Osman, Nadia, Diya Adawi, Siv Ahrné, Bengt Jeppsson, and Göran Molin. 2008. Probiotics and blueberry attenuate the severity of dextran sulfate sodium (DSS)-induced colitis. *Digestive Diseases and Sciences* 53 (9):2464–2473.

Paiva-Martins, Fátima, Rui Correia, Susana Félix, Pedro Ferreira, and Michael H. Gordon. 2007. Effects of enrichment of refined olive oil with phenolic compounds from olive leaves. *Journal of Agricultural and Food Chemistry* 55 (10):4139–4143.

Pandey, Kanti Bhooshan, and Syed Ibrahim Rizvi. 2009. Plant polyphenols as dietary antioxidants in human health and disease. *Oxidative Medicine and Cellular Longevity* 2 (5):270–278.

Park, Yong-Seo, Milena Cvikrová, Olga Martincová, Kyung-Sik Ham, Seong-Gook Kang, Yang-Kyun Park, Jacek Namiesnik, Adamo Domenico Rombolà, Zenon Jastrzebski, and Shela Gorinstein. 2015. In vitro antioxidative and binding properties of phenolics in traditional, citrus and exotic fruits. *Food Research International (Ottawa, Ont.)* 74:37–47.

Parkar, Shanthi G., David E. Stevenson, and Margot A. Skinner. 2008. The potential influence of fruit polyphenols on colonic microflora and human gut health. *International Journal of Food Microbiology* 124 (3):295–298.

Pequegnat, Brittany, Martin Sagermann, Moez Valliani, Michael Toh, Herbert Chow, Emma Allen-Vercoe, and Mario A. Monteiro. 2013. A vaccine and diagnostic target for *Clostridium bolteae*, an autism-associated bacterium. *Vaccine* 31 (26):2787–2790.

Pereira, Ana, Isabel Ferreira, Filipa Marcelino, Patricia Valentão, Paula Andrade, Rosa Seabra, Leticia Estevinho, Albino Bento, and José Pereira. 2007. Phenolic compounds and antimicrobial activity of olive (*Olea europaea* L. *Cv. Cobrançosa*) leaves. *Molecules* 12 (5): 1153–1162.

Pérez-Jiménez, Jara, M. Elena Díaz-Rubio, and Fulgencio Saura-Calixto. 2013. Non-extractable polyphenols, a major dietary antioxidant: Occurrence, metabolic fate and health effects. *Nutrition Research Reviews* 26 (02):118–129.

Piljac-Žegarac, Jasenka, Ana Belščak, and Ante Piljac. 2009. Antioxidant capacity and polyphenolic content of blueberry (*Vaccinium corymbosum* L.) leaf infusions. *Journal of Medicinal Food* 12 (3):608–614.

Putnik, Predrag, Danijela Bursać Kovačević, Anet Režek Jambrak, Francisco Barba, Giancarlo Cravotto, Arianna Binello, Jose Lorenzo, and Avi Shpigelman. 2017. Innovative "green" and novel strategies for the extraction of bioactive added value compounds from citrus wastes—A review. *Molecules* 22 (5):680.

Puupponen-Pimiä, R., Liisa Nohynek, S. Hartmann-Schmidlin, Marja Kähkönen, Marina Heinonen, Kaisu Määttä-Riihinen, and K. -M. Oksman-Caldentey. 2005. Berry phenolics selectively inhibit the growth of intestinal pathogens. *Journal of Applied Microbiology* 98 (4):991–1000. doi: 10.1111/j.1365-2672.2005.02547.x.

Quigley, Eamonn M. M. 2013. Gut bacteria in health and disease. *Gastroenterology & Hepatology* 9 (9):560

Quirós-Sauceda, A. E., H. Palafox-Carlos, S. G. Sáyago-Ayerdi, J. F. Ayala-Zavala, Luis Arturo Bello-Perez, E. Alvarez-Parrilla, L. A. De La Rosa, A. F. González-Córdova, and G. A. Gonzalez-Aguilar. 2014. Dietary fiber and phenolic compounds as functional ingredients: interaction and possible effect after ingestion. *Food & Function* 5 (6):1063–1072.

Racette, Susan B., Xiaobo Lin, Lina Ma, and Richard E. Ostlund Jr. 2015. Natural dietary phytosterols. *Journal of AOAC International* 98 (3):679–684.

Ranilla, Lena Galvez, Young-In Kwon, Emmanouil Apostolidis, and Kalidas Shetty. 2010. Phenolic compounds, antioxidant activity and in vitro inhibitory potential against key enzymes relevant for hyperglycemia and hypertension of commonly used medicinal plants, herbs and spices in Latin America. *Bioresource Technology* 101 (12): 4676–4689.

Ras, Rouyanne T., Yvonne T. van der Schouw, Elke A. Trautwein, Isabelle Sioen, Geertje W. Dalmeijer, Peter L. Zock, and Joline W. J. Beulens. 2015. Intake of phytosterols from natural sources and risk of cardiovascular disease in the European prospective investigation into cancer and nutrition-The Netherlands (EPIC-NL) population. *European Journal of Preventive Cardiology* 22 (8):1067–1075.

Raskin, Ilya, David M. Ribnicky, Slavko Komarnytsky, Nebojsa Ilic, Alexander Poulev, Nikolai Borisjuk, Anita Brinker, Diego A. Moreno, Christophe Ripoll, Nir Yakoby, et al. 2002. Plants and human health in the twenty-first century. *TRENDS in Biotechnology* 20 (12):522–531.

Ren, Tingting, Chao Huang, and Mingliang Cheng. 2014. Dietary blueberry and bifidobacteria attenuate nonalcoholic fatty liver disease in rats by affecting SIRT1-mediated signaling pathway. *Oxidative Medicine and Cellular Longevity* 2014:1.

Ribeiro, Ana, Marilene Estanqueiro, M. Oliveira, and José Sousa Lobo. 2015. Main benefits and applicability of plant extracts in skin care products. *Cosmetics* 2 (2):48–65.

Riihinen, Kaisu, Laura Jaakola, Sirpa Kärenlampi, and Anja Hohtola. 2008. Organ-specific distribution of phenolic compounds in bilberry (*Vaccinium myrtillus*) and 'northblue' blueberry (*Vaccinium corymbosum x V. angustifolium*)). *Food Chemistry* 110 (1):156–160.

Rodriguez-Casado, Arantxa. 2016. The health potential of fruits and vegetables phytochemicals: notable examples. *Critical Reviews in Food Science and Nutrition* 56 (7):1097–1107.

Rodríguez-Roque, María Janeth, María Alejandra Rojas-Graü, Pedro Elez-Martínez, and Olga Martín-Belloso. 2013. Soymilk phenolic compounds, isoflavones and antioxidant activity as affected by in vitro gastrointestinal digestion. *Food Chemistry* 136 (1):206–212.

Roleira, Fernanda M. F., Elisiário J. Tavares-da-Silva, Carla L. Varela, Saul C. Costa, Tiago Silva, Jorge Garrido, and Fernanda Borges. 2015. Plant derived and dietary phenolic antioxidants: Anticancer properties. *Food Chemistry* 183:235–258.

Romo-Vaquero, María, María-Victoria Selma, Mar Larrosa, María Obiol, Rocío García-Villalba, Rocío González-Barrio, Nicolas Issaly, John Flanagan, Marc Roller, Francisco A. Tomás-Barberán, et al. 2014. A rosemary extract rich in carnosic acid selectively modulates caecum microbiota and inhibits β-glucosidase activity, altering fiber and short chain fatty acids fecal excretion in lean and obese female rats. *PloS One* 9 (4):e94687.

Ross, K. A., D. Ehret, D. Godfrey, L. Fukumoto, and M. Diarra. 2017. Characterization of pilot scale processed Canadian organic cranberry (*Vaccinium macrocarpon*) and blueberry (*Vaccinium angustifolium*) juice pressing residues and Phenolic-Enriched extractives. *International Journal of Fruit Science* 17 (2):202–232.

Ross, Kelly A. 2014. Concepts important in understanding the health benefits of phenolics in fruits and vegetables: Extractable & Non-Extractable phenolics and the influence of cell wall polysaccharides on bioaccessibility & bioavailability. *Research in Health and Nutrition* 2:29–43.

Round, June L., and Sarkis K. Mazmanian. 2009. The gut microbiota shapes intestinal immune responses during health and disease. *Nature Reviews. Immunology* 9 (5):313

Rubel, Irene A., Ethel E. Pérez, Diego B. Genovese, and Guillermo D. Manrique. 2014. In vitro prebiotic activity of inulin-rich carbohydrates extracted from Jerusalem artichoke (*Helianthus tuberosus* L.) tubers at different storage times by *Lactobacillus paracasei*. *Food Research International* 62:59–65.

Runnie, I., M. N. Salleh, S. Mohamed, R. J. Head, and M. Y. Abeywardena. 2004. Vasorelaxation induced by common edible tropical plant extracts in isolated rat aorta and mesenteric vascular bed. *Journal of Ethnopharmacology* 92 (2–3):311–316.

Salem, Maryem Ben, Hanen Affes, Kamilia Ksouda, Raouia Dhouibi, Zouheir Sahnoun, Serria Hammami, and Khaled Mounir Zeghal. 2015. Pharmacological studies of artichoke leaf extract and their health benefits. *Plant Foods for Human Nutrition* 70 (4):441–453.

Sasidharan, S., Y. Chen, D. Saravanan, K. M. Sundram, and L. Yoga Latha. 2011. Extraction, isolation and characterization of bioactive compounds from plants' extracts. *African Journal of Traditional, Complementary and Alternative Medicines* 8 (1):1–10.

Seeram, Navindra P., Lynn S. Adams, Yanjun Zhang, Rupo Lee, Daniel Sand, Henry S. Scheuller, and David Heber. 2006. Blackberry, black raspberry, blueberry, cranberry, red raspberry, and strawberry extracts inhibit growth and stimulate apoptosis of human cancer cells in vitro. *Journal of Agricultural and Food Chemistry* 54 (25): 9329–9339.

Sekirov, Inna, Shannon L. Russell, L. Caetano M. Antunes, and B. Brett Finlay. 2010. Gut microbiota in health and disease. *Physiological Reviews* 90 (3):859–904.

Selma, Maria V., Juan C. Espin, and Francisco A. Tomas-Barberan. 2009. Interaction between phenolics and gut microbiota: Role in human health. *Journal of Agricultural and Food Chemistry* 57 (15): 6485–6501.

Seo, Dae-Bang, Hyun Woo Jeong, Donghyun Cho, Bum Jin Lee, Ji Hae Lee, Jae Young Choi, Il-Hong Bae, and Sung-Joon Lee. 2015. Fermented green tea extract alleviates obesity and related complications and alters gut microbiota composition in diet-induced obese mice. *Journal of Medicinal Food* 18 (5):549–556.

Sevgi, Kemal, Bektas Tepe, and Cengiz Sarikurkcu. 2015. Antioxidant and DNA damage protection potentials of selected phenolic acids. *Food and Chemical Toxicology: An International Journal Published for the British Industrial Biological Research Association* 77:12–21.

Shoaib, Muhammad, Aamir Shehzad, Mukama Omar, Allah Rakha, Husnain Raza, Hafiz Rizwan Sharif, Azam Shakeel, Anum Ansari, and Sobia Niazi. 2016. Inulin: Properties, health benefits and food applications. *Carbohydrate Polymers* 147:444–454.

Silva, S., E. M. Costa, C. Calhau, R. M. Morais, and M. E. Pintado. 2017. Anthocyanin extraction from plant tissues: A review. *Critical Reviews in Food Science and Nutrition* 57 (14):3072–3083. doi: 10.1080/10408398.2015.1087963.

Silva, Sara, Eduardo M. Costa, M. Mendes, R. M. Morais, Conceição Calhau, and M. M. Pintado. 2016. Antimicrobial, antiadhesive and antibiofilm activity of an ethanolic, anthocyanin-rich blueberry extract purified by solid phase extraction. *Journal of Applied Microbiology* 121 (3):693–703.

Silva, Sara, Eduardo M. Costa, Sandra Vicente, Mariana Veiga, Conceição Calhau, Rui M. Morais, and Manuela E. Pintado. 2017. DNA agarose gel electrophoresis for antioxidant analysis: Development of a quantitative approach for phenolic extracts. *Food Chemistry* 233:45–51.

Silva, Sara, E. M. Costa, M. F. Pereira, M. R. Costa, and M. E. Pintado. 2013. Evaluation of the antimicrobial activity of aqueous extracts from dry *Vaccinium corymbosum* extracts upon food microorganism. *Food Control* 34 (2):645–650.

Slavin, Joanne. 2013. Fiber and prebiotics: mechanisms and health benefits. *Nutrients* 5 (4):1417–1435.

Slavin, Joanne L. 2005. Dietary fiber and body weight. *Nutrition (Burbank, Los Angeles County, Calif.)* 21 (3):411–418.

Slavin, Joanne L. 2008. Position of the American dietetic association: health implications of dietary fiber. *Journal of the American Dietetic Association* 108 (10):1716–1731.

Smith, Caren E., and Katherine L. Tucker. 2011. Health benefits of cereal fibre: A review of clinical trials. *Nutrition Research Reviews* 24 (1):118–131.

Sousa, Sérgio, Jorge Pinto, Claúdia Pereira, F. Xavier Malcata, M. T. Bertoldo Pacheco, Ana M. Gomes, and Manuela Pintado. 2015. In vitro evaluation of yacon (*Smallanthus sonchifolius*) tuber flour prebiotic potential. *Food and Bioproducts Processing* 95:96–105.

Taamalli, Amani, David Arráez-Román, Enrique Barrajón-Catalán, Verónica Ruiz-Torres, Almudena Pérez-Sánchez, Miguel Herrero, Elena Ibañez, Vicente Micol, Mokhtar Zarrouk, Antonio Segura-Carretero, and Alberto Fernández-Gutiérrez. 2012. Use of advanced techniques for the extraction of phenolic compounds from Tunisian olive leaves: Phenolic composition and cytotoxicity against human breast cancer cells. *Food and Chemical Toxicology : An International Journal Published for the British Industrial Biological Research Association* 50 (6):1817–1825.

Talhaoui, Nassima, Amani Taamalli, Ana María Gómez-Caravaca, Alberto Fernández-Gutiérrez, and Antonio Segura-Carretero. 2015. Phenolic compounds in olive leaves: Analytical determination, biotic and abiotic influence, and health benefits. *Food Research International* 77 :92–108.

Taverniti, Valentina, Daniela Fracassetti, Cristian Del Bo', Claudia Lanti, Mario Minuzzo, Dorothy Klimis-Zacas, Patrizia Riso, and Simone Guglielmetti. 2014. Immunomodulatory effect of a wild blueberry anthocyanin-rich extract in human caco-2 intestinal cells. *Journal of Agricultural and Food Chemistry* 62 (33):8346–8351.

Tholl, Dorothea. 2015. Biosynthesis and biological functions of terpenoids in plants. In *Biotechnology of isoprenoids*, 63–106. Cham: Springer.

Tiihonen, Kirsti, Arthur C. Ouwehand, and Nina Rautonen. 2010. Human intestinal microbiota and healthy ageing. *Ageing Research Reviews* 9 (2):107–116.

Torres-Fuentes, Cristina, Harriët Schellekens, Timothy G. Dinan, and John F. Cryan. 2015. A natural solution for obesity: Bioactives for the prevention and treatment of weight gain. A review. *Nutritional Neuroscience* 18 (2):49–65.

Tremaroli, Valentina, and Fredrik Bäckhed. 2012. Functional interactions between the gut microbiota and host metabolism. *Nature* 489 (7415):242

Trinidad, Trinidad P., Aida C. Mallillin, Anacleta S. Loyola, Rosario S. Sagum, and Rosario R. Encabo. 2010. The potential health benefits of legumes as a good source of dietary fibre. *The British Journal of Nutrition* 103 (4):569–574.

Tucker, Larry A., and Kathryn S. Thomas. 2009. Increasing total fiber intake reduces risk of weight and fat gains in women. *Journal of Nutrition* 139 (3):576–581.

Tung, Yen-Chen, Wei-Tien Chang, Shiming Li, Jia-Ching Wu, Vladimir Badmeav, Chi-Tang Ho, and Min-Hsiung Pan. 2018. Citrus peel extracts attenuated obesity and modulated gut microbiota in mice with high-fat diet-induced obesity. *Food & Function* 9 (6):3363–3373. doi:10.1039/C7FO02066J.

Valdés, Lorena, A. Cuervo, N. Salazar, Patricia Ruas-Madiedo, M. Gueimonde, and S. González. 2015. The relationship between phenolic compounds from diet and microbiota: Impact on human health. *Food & Function* 6 (8):2424–2439.

Valentová, Kateřina, and Jitka Ulrichová. 2003. *Smallanthus sonchifolius* and *lepidium meyenii*-prospective Andean crops for the prevention of chronic diseases. *Biomed Papers* 147 (2):119–130.

Vallverdú-Queralt, Anna, Jorge Regueiro, Miriam Martínez-Huélamo, José Fernando Rinaldi Alvarenga, Leonel Neto Leal, and Rosa M. Lamuela-Raventos. 2014. A comprehensive study on the phenolic profile of widely used culinary herbs and spices: Rosemary, thyme, oregano, cinnamon, cumin and Bay. *Food Chemistry* 154:299–307.

Veiga, R. S., S. De Mendonça, P. B. Mendes, N. Paulino, M. J. Mimica, A. A. Lagareiro Netto, I. S. Lira, B. G. -C. López, V. Negrão, and M. C. Marcucci. 2017. Artepillin C and phenolic compounds responsible for antimicrobial and antioxidant activity of green propolis and Baccharis dracunculifolia DC. *Journal of Applied Microbiology* 122 (4):911–920.

Vendrame, Stefano, Allison Daugherty, Aleksandra S. Kristo, and Dorothy Klimis-Zacas. 2014. Wild blueberry (*Vaccinium angustifolium*)-enriched diet improves dyslipidaemia and modulates the expression of genes related to lipid metabolism in obese zucker rats. *The British Journal of Nutrition* 111 (2):194–200.

Vendrame, Stefano, Allison Daugherty, Aleksandra S. Kristo, Patrizia Riso, and Dorothy Klimis-Zacas. 2013. Wild blueberry (*Vaccinium angustifolium*) consumption improves inflammatory status in the obese zucker rat model of the metabolic syndrome. *The Journal of Nutritional Biochemistry* 24 (8):1508–1512.

Vendrame, Stefano, Simone Guglielmetti, Patrizia Riso, Stefania Arioli, Dorothy Klimis-Zacas, and Marisa Porrini. 2011. Six-week consumption of a wild blueberry powder drink increases bifidobacteria in the human gut. *Journal of Agricultural and Food Chemistry* 59 (24): 12815–12820.

Vermerris, Wilfred, and Ralph Nicholson. 2008a. Families of phenolic compounds and means of classification. In *Phenolic compound biochemistry*, 1–34. Dordrecht: Springer.

Vermerris, Wilfred, and Ralph Nicholson. 2008b. Isolation and identification of phenolic compounds. In *Phenolic compound biochemistry*, 151–196. Dordrecht: Springer.

Wallace, Taylor C. 2011. Anthocyanins in cardiovascular disease. *Advances in Nutrition* 2 (1):1–7.

Wang, Jiabo, Yanling Zhao, Xiaohe Xiao, Huifang Li, Haiping Zhao, Ping Zhang, and Cheng Jin. 2009. Assessment of the renal protection and hepatotoxicity of rhubarb extract in rats. *Journal of Ethnopharmacology* 124 (1):18–25.

Wang, Shiow Y., and Hsin-Shan Lin. 2000. Antioxidant activity in fruits and leaves of blackberry, raspberry, and strawberry varies with cultivar and developmental stage. *Journal of Agricultural and Food Chemistry* 48 (2):140–146.

Wang, Yu-Ping, Ming-Liang Cheng, Bao-Fang Zhang, Mao Mu, Ming-Yu Zhou, Jun Wu, and Cheng-Xiu Li. 2010. Effect of blueberry on hepatic and immunological functions in mice. *Hepatobiliary & Pancreatic Diseases International: HBPD INT* 9 (2):164–168.

Watt, John Mitchell, and Maria Gerdina Breyer-Brandwijk. 1962. *The Medicinal and Poisonous Plants of Southern and Eastern Africa being an Account of their Medicinal and other Uses, Chemical Composition, Pharmacological Effects and Toxicology in Man and Animal*. 2nd ed. Edinburgh: E. & S. Livingstone Ltd.

WHO. 2013. *WHO Traditional Medicine Strategy 2014–2023*. World Health Organization.

Willcox, Donald Craig, Giovanni Scapagnini, and Bradley J. Willcox. 2014. Healthy aging diets other than the Mediterranean: A focus on the Okinawan diet. *Mechanisms of Ageing and Development* 136–137 :148–162.

Wu, Yihua, Yufeng Qian, Yiwen Pan, Peiwei Li, Jun Yang, Xianhua Ye, and Geng Xu. 2015. Association between dietary fiber intake and risk of coronary heart disease: A meta-analysis. *Clinical Nutrition (Edinburgh, Scotland)* 34 (4):603–611.

Yan, Shuaishuai, Hongjun Shao, Zhihao Zhou, Qi Wang, Luhua Zhao, and Xingbin Yang. 2018. Non-extractable polyphenols of green tea and their antioxidant, anti-α-glucosidase capacity, and release during in vitro digestion. *Journal of Functional Foods* 42:129–136.

Ye, Zhong, Visalakshi Arumugam, Esther Haugabrooks, Patricia Williamson, and Suzanne Hendrich. 2015. Soluble dietary fiber (Fibersol-2) decreased hunger and increased satiety hormones in humans when ingested with a meal. *Nutrition Research (New York, N.Y.)* 35 (5):393–400.

Youdim, Kuresh A., Antonio Martin, and James A. Joseph. 2000. Incorporation of the elderberry anthocyanins by endothelial cells increases protection against oxidative stress. *Free Radical Biology and Medicine* 29 (1):51–60.

Zhao, Liping. 2013. The gut microbiota and obesity: From correlation to causality. *Nature Reviews Microbiology* 11 (9):639

Zinman, Bernard, Christoph Wanner, John M. Lachin, David Fitchett, Erich Bluhmki, Stefan Hantel, Michaela Mattheus, Theresa Devins, Odd Erik Johansen, Hans J. Woerle., et al. 2015. Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. *The New England Journal of Medicine* 373 (22):2117–2128.

Zou, Zhuo, Wanpeng Xi, Yan Hu, Chao Nie, and Zhiqin Zhou. 2016. Antioxidant activity of citrus fruits. *Food Chemistry* 196:885–896.