

A BRIEF REVIEW ON EMERGING TRENDS IN GLOBAL POLYPHENOL RESEARCH. JOURNAL OF FOOD BIOCHEMISTRY

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A brief review on emerging trends in global polyphenol research

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Abstract

This article is focused on the global trend in research with special emphasis on the economic importance of polyphenols. We examined some of the media used for the formulation of polyphenol-enriched products. The levels of polyphenol extract production, international research funding, and number of published research work were determined from various databases and publicly available reports. The quantity of industrially extracted polyphenols was estimated to be 16,380 tons in 2015 and this is anticipated to reach a total of 33,880 tons by the end of 2024 with an estimated monetary value of USD 1.33 billion. Industrial utilization of polyphenol is dominated by the functional beverages sector (44%), followed by functional foods (33%) primarily due to high demands for polyphenol-rich consumables. Within a 10-year period, the number of polyphenol-related publications doubled from 2006 (1,574) to 2012 (3,330) and almost tripled in 2015 (4,213).

Practical applications

Polyphenols remain one of the most researched bioactive food compounds because of their wide distribution in nature and also due to their versatility as agents that can improve human health and enhance the shelf-life of foods. This report combines available scientific knowledge on the various factors that dictate polyphenol synthesis in plants, extraction methods, and utilization. The report also provides information on global polyphenol research and project funding history, which could serve as a critical reference for researchers all over the world.

KEYWORDS

functional foods, health benefits, polyphenols, research funding, solvent extraction, vegetables

1 | INTRODUCTION

Emphasis on the nutritive values of under-utilized indigenous vegetables is gaining prominence within food security programs globally because of the need for dietary interventions in human health management. In many rural areas of Africa, Asia, and Latin America, which are often characterized by low income, poor health management systems and general lack of infrastructure, the human population depends on under-utilized indigenous edible plants, especially vegetables for their daily supplies of basic nutritional needs such as proteins, micro-nutrients, vitamins, and other bioactive compounds (Adebooye & Opabode, 2004; Aworh, 2015; Barbieri, Gomes, Alercia, & Padulosi, 2014; Bioversity International, 2011; Ebert, 2014; Frison, Smith, Johns, Cherfas, & Eyzaguirre, 2006; Kongkachuichai, Charoensiri, Yakoh, Kringkasemsee, & Insung, 2015). In most parts of the developing world, in addition to being used directly as food, many edible plants are also

utilized in herbal medicine formulations for human health management traditionally. These medicinal uses are attributed to polyphenolic compounds, the major non-nutrient constituent that epidemiological studies and associated meta-analyses have proven to possess anti-glaucoma, anti-ageing, antitumor, and anti-carcinogenic properties. They are also effective in the treatments of high blood pressure, high cholesterol, complications related to diabetes, nerve or eye damage, and vision problems (Callaghan & Wilhelm, 2008; Cheynier, 2005; Chung, Wong, Wei, Huang, & Lin, 1998; Kong, Mat-Junit, Ismail, Aminudin, & Abdul-Aziz, 2014; Santos-Buelga & Scalbert, 2000; Zillich, Schweiggert-Weisz, Eisner, & Kerscher, 2015). In foods, polyphenols have been shown to contribute to bitterness (tannins), astringency (tannins), color (anthocyanins and chlorophylls), flavor (phenolic amino acids and polymerized catechins), odor (tea catechins and wine phenolics), and oxidative stability (phenolic acids and flavonoids) (Pandey & Rizvi, 2009). Aluko (2012) postulated that the mechanism of anticancer and

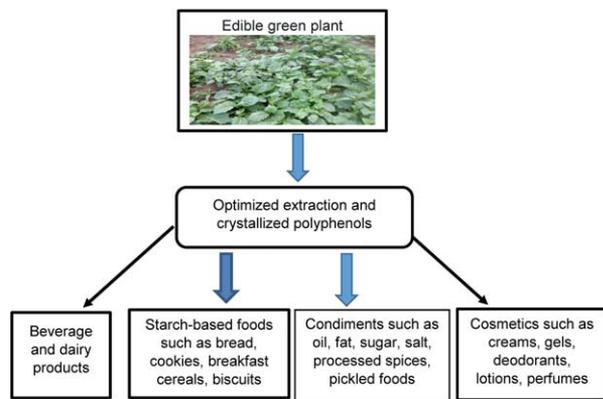


FIGURE 1 Media for polyphenol-enriched foods and products

antihypertensive effects of polyphenols could be due to its direct action on cellular metabolism or indirect through stimulation of immune system. Polyphenols have been reported to be the most prevalent antioxidant phytochemicals in the plant kingdom and reportedly possess both singlet oxygen quenching activity and radical scavenging activity (Guo, Zhao, Shen, Hou, & Xin, 1999). Polyphenols are also known to be included in brewing products, that is, liquors and wines and as food additives. The nutritional and health relevance of polyphenols are based on their abilities to act as reaction chain breakers and scavengers of harmful free radicals and reactive oxygen species, which are over produced under conditions of oxidative stress (Quideau, Deffieux, Douat-Casassus, & Pouysegou, 2011). Figure 1 shows some aspects of polyphenol usage in the food and nonfood sectors. Polyphenol-enriched extracts infused into cosmetics have been shown to be effective in the prevention and therapy for premature skin ageing, some cutaneous damages and skin cancer, which are provoked by oxidative stress especially ultraviolet (UV) irradiation (Farage, Miller, Elsner, & Maibach, 2008; Rabe, Mamelak, McElgunn, Morison, & Sauder, 2006). Polyphenol extracts have also been shown to improve skin moisture and smoothness with accompanying reductions in roughness and wrinkles (Zillich et al., 2015).

More important is the recent increase in the application of polyphenols as food additives (e.g., in baked products, noodles, and pasta), which has given rise to an expansion of the global polyphenol economy (Koca, Tekguler, Yilmaz, Hasbay, & Koca, 2018; Pasqualone et al., 2017; Ranawana et al., 2016; Schmidt, Geweke, Struck, Zahn, & Rohm, 2017; Świeca, Sęczyk, Gawlik-Dziki, & Dziki, 2014). However, it is arguable that consideration should be given to bio-accessibility, bio-availability, and efficacy of polyphenols before being considered for inclusion in foods and food products. Several authors have posited that the bioavailability would need more detailed scientific work (Andreotti, Ravaglia, & Ragaini, 2008; Bouaziz, Jemai, Khabou, & Sayadi, 2010; Cheynier, 2005; Chuah et al., 2008; D'Archivio, Filesi, Vari, Scaccocchio, & Masella, 2010; Hayta & Gamze, 2011; Manach, 2004). This is because available evidence have shown that bioavailability of polyphenols depends on food processing methods, host organism (sex, age, composition of intestinal microflora), and interactions between polyphenols and other molecules (such as salivary proteins and

digestive enzymes). Indeed, the effect of food processing on polyphenol profile of food is a major issue because cooking procedures, extent of heating, leaching into the cooking medium, pH of the cooking medium, and surface area exposed to water and oxygen, all affect polyphenol composition (Wachtel-Galor, Wong, & Benzie, 2008).

Irrespective of the question of bioavailability, the polyphenol market continues to grow globally. It has been reported that the global polyphenols market was valued at USD 757 million in 2015 because of the favorable food safety regulations, and increasing awareness of health benefits associated with the consumption of polyphenolic compounds (Allied Market Research, 2017). Based on current trends, there is anticipation of further boosts in the market from 2016 to 2024 due to increasing usage of polyphenol extract in the food, beverages, pharmaceutical, and cosmetic industry (Allied Market Research, 2017). According to Transparency Market Research (2017), the polyphenols market recorded 16,380 tons in 2015 and with an 8.4% annual growth rate. Total polyphenol consumption is anticipated to reach 33,880 tons by the end of 2024 with a monetary value of USD 1.33 billion, according to the recent report by Grand View Research (2016). The market trend suggests that global polyphenol economy in 2024 would be led by Asia Pacific, with about 40.3% of the global demand, followed by 27.8% in Europe. In terms of utilization, the global polyphenols economy was led by the functional beverages sector (44%), followed by functional foods (33%) primarily as a result of the strong demand for polyphenol-rich beverages in the form of juices, energy drinks, and enhanced water in most developed countries (Grand View Research, 2016).

2 | WHY DO PLANTS PRODUCE POLYPHENOLS?

Given the wide array of chemicals that have been extracted and identified within the Kingdom Plantae, and indeed still many more to be extracted and identified, it may be accurate to describe the green plants as the greatest chemists in nature. The question then is: why do plants produce and accumulate these groups of phytochemicals? Chemicals that are produced through series of metabolic and biochemical pathways within the green plant systems are termed phytochemicals. The phytochemicals are known to contribute to giving plants their color, flavor, and smell, and could also function as phytonutrients or antinutrients. Among the phytonutrients are the natural products that are largely responsible for the medicinal properties and health benefits of green plants while the antinutrients are phytochemicals that interfere with or reduce the body's ability to absorb essential nutrients (Manach, Scalbert, Morand, Rémésy, & Jimenez, 2004). There are also a good number of phytochemicals in plants that are poisonous and toxic, which confer on plants the principles of defence against pathogens, insects and herbivores while some of them serve as protection against solar ultra violet B (UV-B) radiation that causes severe oxidative damage in plants. In essence, therefore, these chemicals served as a determining factor in early terrestrial plant evolution (Quideau et al., 2011). Extensive scientific investigations have shown that some of the antinutrients including phytate and tannins also have beneficial health

effects in humans (Chung et al., 1998; Santos-Buelga & Scalbert, 2000; Zhou & Erdman, 1995). A major member of the phytonutrient family is the “plant phenol,” often referred to as polyphenols (Quideau et al., 2011). Polyphenols play key roles in the growth, regulation and structure of plants and vary widely in types and structures within different plants. In self-defence during periods of stress, which may be caused by radiation, heat, drought, salinity, flooding, etc., plant species modify polyphenol structure for survival. The significant roles of polyphenols in plants’ natural systems have been summarized to include release and suppression of growth hormones such as auxin. Polyphenols also function as UV-B screens to protect against ionizing radiation and enrich plant pigments. Plants synthesize polyphenols to deter (through toxicity) consumption by herbivores, prevent microbial infections (phytoalexins) and act as signaling molecules that are involved in fruit ripening and other growth processes (Huber, Eberl, Feucht, & Polster, 2003; Lattanzio, Lattanzio, & Cardinali, 2006).

3 | METHODS FOR OPTIMIZING POLYPHENOLS EXTRACTION FROM PLANT MATERIALS

A major step required for taking optimal advantage of the benefits offered by polyphenols is to optimize their recovery during extraction and to identify the bioactive compounds that constitute the polyphenol extract. It is known that the phenolic compounds of different plants differ structurally, hence it is expected that the recovery, yield and type of polyphenolics in an extract will differ depending on the plant and the extraction solvents (Sreeramulu, Reddy, Chauhan, Balakrishna, & Raghunath, 2013). Escribano-Bailon and Santos-Buelga (2003) and Nacz and Shahidi (2006) stated that water, methanol, ethanol, or propanol and their mixtures in water are the most popular extraction systems while acetone, ethyl acetate, and dimethylformamide are also used in some popular laboratories for the extraction of phenolic compounds from plant materials. Studies have shown that the amount of polyphenol extracted in a medium is influenced by the type and polarity of extracting solvent, time and temperature of extraction system as well as physical characteristic of the samples (Nacz & Shahidi, 2006). In a study of the phenolic profile of *Barringtonia racemosa* (leaves and stems), Kong et al. (2014) used deionized water for the extraction of either freeze-dried or air-dried samples and reported that freeze-drying was better because air-drying caused 5–41% reduction of polyphenols. An investigation by Sun, Mu, Xi, and Song (2014) on the effects of boiling, steaming, microwaving, baking, and frying on proximate composition, total and individual polyphenol contents, and antioxidant activity of sweet potato leaves revealed an increase of 9.44% in total polyphenol content after steaming, whereas decreases of 30, 25, and 15% were noted after boiling, microwaving, and frying, respectively. Sakakibara, Honda, Nakagawa, Ashida, and Kanazawa (2003) developed a method that detected the natural forms of all the polyphenols in vegetables, fruits, and teas at once directly without hydrolysis using HPLC system and a photodiode array detector. The method involved homogenization of the plant product in liquid nitrogen, lyophilization, and extraction with 90% methanol, which is

then subjected to HPLC analysis without hydrolysis. The authors reported a recovery of 68–92% total polyphenol, while the HPLC eluted constituent polyphenols within 95 min in the following order: simple polyphenols, catechins, anthocyanins, glycosides of flavones, flavonols, isoflavones, and flavanones, their aglycones, anthraquinones, chalcones, and theaflavins. A study by Sulaiman, Sajak, Ooi, Supriatno, and Seow (2011) reported the efficiency of using four solvent systems (70% acetone, 70% ethanol, 70% methanol, and distilled water) on extraction of polyphenols from 37 raw vegetables. The results revealed 70% acetone and 70% methanol as the most efficient media for extracting polyphenolic antioxidants from the vegetables. An assessment of the efficiency of tartaric acid and glycerol in the extraction yield of polyphenol was carried out by Makris, Passalidi, Kallithraka, and Mourtzinis (2016), and the results showed that solutions containing only glycerol (20%, w/v) were more suitable for retrieving polyphenols, flavonoids, and pigments from grape pomace, while tartaric acid exerted a negative effect even at 2% (w/v) concentration. The polyphenol contents of millet, using water, acetone, propanol, ethanol, and methanol ($30 \pm 2^\circ\text{C}$) and after refluxing was investigated by Chethan and Malleshi (2007). The authors demonstrated that optimal extraction of polyphenol was achieved when the extraction solvents were acidified with 1% HCl. In a quadratic general rotary unitized design for extraction of polyphenols from areca seed, Zhang, Huang, Chen, Han, and Zhang (2014) reported the optimum conditions to be 70% ethanol, with a liquid to solid ratio of 11:1 (v/w), a temperature of 70°C for 120 min, which gave up to 16.37% yield of polyphenols.

4 | GLOBAL INTEREST AND FOCUS ON POLYPHENOL RESEARCH

For a long time in academic literature, vegetable tannin was the terminology used to describe a plant extract that was used in the conversion of animal skin to leather and perhaps was first recorded as vegetable tannins by Theophrastus (371–286 BC) in his botany compendium, *Historia Plantarum* (Quideau et al., 2011). With the passage of time, the term “vegetable tannins” got replaced by another terminology “polyphenols”; however, literature is not explicit regarding the name(s) of scientist(s) who coined the term “polyphenols.” It is however, remarkable that scientists including German Nobel Laureate, Emil Fischer (1919), Karl Freudenberg (1920) and Theodore White (1957) carried out earliest historically significant laboratory studies on vegetable tannins, now referred to as polyphenols. Between 1950 and 1994, the trio biochemists (Edgar Charles Bate-Smith, Tony Swain and Edwin Haslam), all of the United Kingdom, carried out studies that laid the foundations for the modern studies on the defensive roles of polyphenols in plants, nutritional benefits of polyphenols and elucidation of chemical structures and properties of polyphenols (Haslam, 1998, 2007). Given the prominence that polyphenols have gained in the food industry in relation to human health management as well as the economic prospect offered by its exploitation, it is now a common knowledge that a new box has been opened for plant sciences and phytochemistry research. The possible exploitation of polyphenols in

other areas of human endeavors may soon be revealed with more research into the action, mode of action and chemistry of polyphenols.

As a result of the interests that topics related to polyphenols have generated in the areas of botany, agriculture, chemistry, and human nutrition, we evaluated the scope and depth of publications on polyphenols, and also analyzed the publications in relation to spread in the last 10 years (2010–2016), outlet of publication, continent, and funding bodies of research and publication language. For this purpose, we used the database of the Web of Science (http://apps.webofknowledge.com/WOS_GeneralSearch_input.do?product=WOS&search_mode=GeneralSearch&SID=1DM8j7efCmbkMAYBPJ4&preferencesSaved=). The database shows that there were 43,221 documented information in literature between 1900 and January 2016 (116 years) on the subject of polyphenols. Progressively, in a period of 10 years (2006 and 2016) as shown in Figure 2, there were remarkable increases in the number of publications that emerged in the general studies of polyphenols. Specifically, the number of publications doubled in 2012 when compared with 2006 and almost tripled in 2016. The implication of this is that there is a general interest in polyphenols research culminating in the massive release of scientific information from laboratories all over the world.

In a period of 116 years (1900–2016), 85% of the total published works on polyphenols research were in the form of peer-reviewed original research journal articles (Figure 3). In contrast, review articles, conference proceedings, abstracts and book chapters accounted for 6, 3.8, 6, and 1%, respectively of published polyphenols research. Other outlets, including notes, editorial comments, letters, news items, book reviews, and published books constituted very small proportion of the publications. The number of publications by authors from United States of America institutions significantly outnumbered those that came from any other part of the world (Figure 4). It is interesting to note that countries of the Asia Pacific (China, Japan, India, and South Korea) also published significantly high number of research articles on polyphenols when compared with African countries (South Africa, Egypt, Nigeria, and Morocco). The huge concentration of polyphenols research in the Asia Pacific and Europe is probably dictated by the fact that about 68% of the global demand for polyphenols is in this region (Grand View Research, 2016) led by the functional beverages sector (44%) and

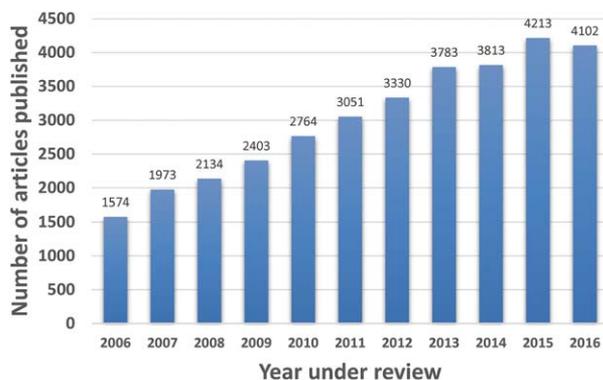


FIGURE 2 Total numbers of articles published on polyphenols between 2006 and 2016. (Source: Web of Science database)

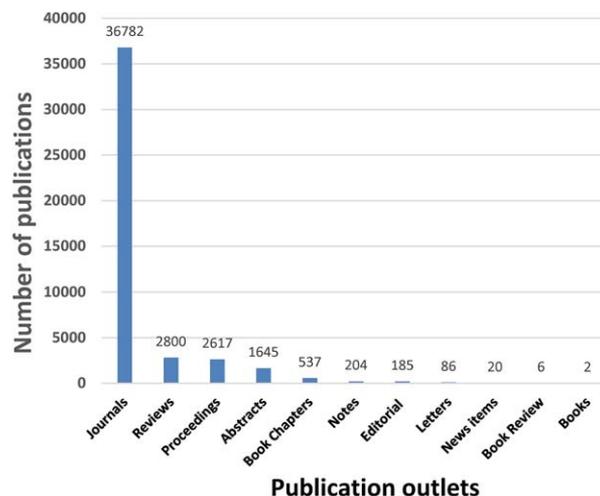


FIGURE 3 Types of publications in the general studies of polyphenols (1900–2016). (Source: Web of Science database)

functional foods (33%). It is noted that there is a strong demand for polyphenol-rich beverages in the form of juices, energy drinks, and enhanced water in most developed countries in recent times (Grand View Research, 2016). Funding institutions that are based in the United States and China (Figure 5) provided financial supports for 1,531 and 1,459 published research articles, respectively, in polyphenols studies while those based in Japan, EU, Spain, Brazil, Canada, and Germany provided funding for a total of 934 published research works. Again, this trend points to the overwhelming importance attached to polyphenols in these regions of the world. These trends in research funding are closely reflected in Figure 3 with the United States and China having significantly higher numbers of published articles compared with other regions of the world.

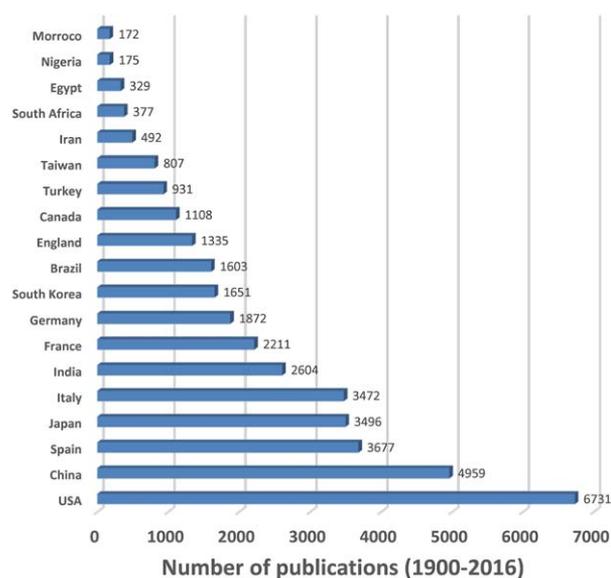


FIGURE 4 Global distributions of countries with most publications in polyphenols research (first 20 countries). (Source: Web of Science database)

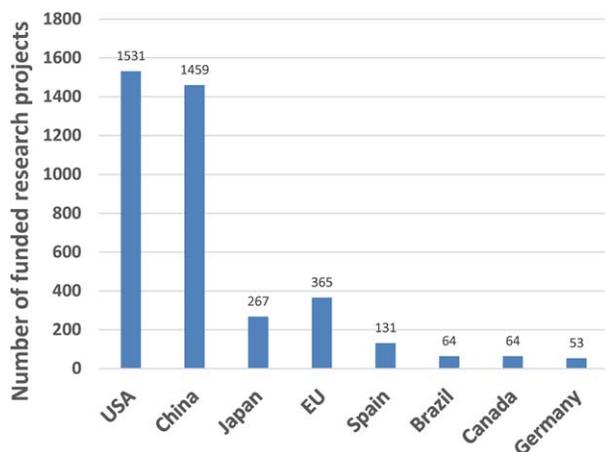


FIGURE 5 Major research funding countries for polyphenols studies. (Source: Web of Science database)

The bioavailability of polyphenols has been a major problem limiting its use as a dietary intervention for the different disease factors that polyphenols have been found to prevent or manage. Interests in studies that can elucidate the specific intake measurements are important for health claims and have gained interest in the scientific community. Research on the interactions of polyphenols with different food components such as proteins, fats, carbohydrates, and minerals have been studied (Zhang, Huang, et al., 2014; Zhang, Yu, et al., 2014). The availability of fruits and vegetables has also been studied (Woodside, Draper, Lloyd & McKinley, 2017). Metabolomics research on identifying the residual amount of polyphenols from wines and other food constituents in urine and other waste metabolites have also continued to advance from the use of single biomarkers to biomarker libraries (Noh et al., 2017; Zamora-Ros et al., 2016; Zamora-Ros et al., 2017). It is now possible to use a polyphenol database to search for polyphenol metabolites from different body fluids or submit a new research into the data base (Rothwell et al., 2016). An evident growth in this area of research has also revealed the complexities involved with the polyphenol metabolome. Therefore, an understanding of the transformations involving polyphenols in vivo is required. However, the results obtained from each study can be deposited into the phenol library as a dietary biomarker for future references.

5 | CONCLUSIONS

The current trends suggest that studies and research in polyphenols will continue to be a major part of global academic and industrial research for several years to come because of the established nutritional benefits of polyphenols to human health. This projection is backed by the abundance of vegetables and their contributions to environmental sustainability. The global market for polyphenols is growing rapidly with the possibility of contributing significantly to economic development and foreign exchange earnings for many countries. Even at the present level of progress on the health benefits, there are still areas where research needs to concentrate efforts. For example, we must be able to continue the screening of traditional edible plants that

have the potential of high yield of polyphenols, address the issues of bioavailability of polyphenols in human body system, dose and safety, optimization of extraction from plant tissue, and push for proper regulation in the use of polyphenols for fortification of foods, beverages, and cosmetics.

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