## Advances in Polyphenol Research: A Journal of Agricultural and Food Chemistry Virtual Issue

The term polyphenols embraces several thousand compounds ranging from small compounds that contain only a single aromatic ring bearing one to three hydroxyls up to those containing multiple such structural units with molecular masses exceeding 2000 Da. Polyphenols are commonly divided into flavonoids and non-flavonoids. Flavonoids, characterized by a C6-C3-C6 skeleton, include anthocyanins, chalcones, dihydrochalcones, dihydroflavonols, flavanols (flavan-3-ols or catechins), condensed tannins or proanthocyanidins, flavanones, flavones, flavonols, and isoflavones. Non-flavonoids include simple phenols, phenolic acids, phenolic amino acids, curcuminoids, stilbenes, lignans, and hydrolyzable gallo- and ellagitannins. Polyphenols are widespread and are almost ubiquitous in unprocessed plant material. Polyphenols are much less common in animals, generally occurring as metabolites and catabolites of dietary polyphenols. Crustaceans and molluscs, which have significant contents of phenolic amino acids, are notable exceptions. The polyphenol profile of foods of plant origin varies extensively with source and tissue within a source and total content from mg/kg to some 100 g/kg of dry mass. Processing of foods produces yet more polyphenols through various transformations. These transformations may be purely chemical in nature, as seen during coffee and cocoa roasting. Enzyme-driven oxidative changes may be desirable, as in black tea production, where many thousand thearubigins are produced, or undesirable, as in cut fruits and vegetables, i.e., through browning reaction. Matured wines, both red and white, contain polyphenol transformation products, arising both enzymatically and chemically during maceration and aging. In processed food, native and transformed polyphenols contribute critically to color, astringency, and odor. Scientists have investigated polyphenols since at least the start of the 19th century, and these compounds continue to be the subject of intense activity, with some 500 papers published in just the Journal of Agricultural and Food Chemistry (JAFC) between January 2016 and July 2017. Early studies on polyphenols focused on structure determination, and while structural characterization of the more complex polyphenols continues, since the end of the 20th century, there has been an increasing emphasis on biological activity, both in planta and after consumption by humans and domesticated animals. Studies on biological activity have been driven by epidemiological studies associating better health with the greater long-term consumption of fruits and vegetables as well as beverages, such as tea, coffee, and red wine. A serious limitation of this line of study is the difficulty of accommodating the variation of polyphenols in a dietary portion of such fruits and vegetables, because this variation might be 10-fold as a result of plant variety, agronomical, food processing, and storage conditions. Recent studies are making it increasingly clear that plants are extremely variable in their polyphenol content, which hinders the interpretation of epidemiologic correlations. Therefore, a better understanding of the causes and magnitude of such variation is essential if valid correlations between diet and health are to be achieved. Catabolites/metabolites excreted in urine have been sought as a possible means to circumvent this problem, but major individual differences clearly indicate a non-normal, probably bimodal distribution and significantly constrain this approach. Such variation seems most pronounced with the gut microbiota catabolism, as clearly illustrated by Guttierez-Diaz et al., but human genomic factors are also to be expected. Much has been learned through in vitro and animal studies about the mechanisms and extent of intestinal absorption of polyphenols. Clinical trials have defined the basic metabolic pathways for polyphenols and have provided some indication of the effect of different ways of inclusion of those polyphenols in the diet on their absorption and distribution in the body; however, more data are still required. Also needed are data for repeat consumption at short intervals, as in tea and coffee drinking, and on long-term consumption of vegetables and fruits as part of a normal diet. Intestinal absorption of plant polyphenols is low, sometimes below 0.1% of dose, and the majority of the dietary polyphenols pass to the large bowel, where they are transformed by the gut microbiota.

Interestingly, the thousands of native polyphenols occurring in the diet are converted to a comparatively small number of catabolites that appear in the plasma either unchanged or as mammalian conjugates. These catabolites not only appear at concentrations exceeding those for the native polyphenols and their associated mammalian conjugates but are also found in the plasma for a much longer period. This extended appearance in plasma might arise for two reasons. First, some polyphenols that bind strongly to mucosal proteins are retained longer in the large bowel than the general digesta, and thus, their release is delayed. Second, repeat food consumption at 2-3 h intervals places several bolus doses in the gastrointestinal track simultaneously, extending the metabolic process that produces those catabolites. Studies designed to seek beneficial effects and define the associated mechanisms have taken two approaches: human trials or animal studies relating intake to one or more biomarkers or in vitro tissue culture studies. Selection of biomarkers of the effect is problematic; crude antioxidant activity is of little value, but the more sophisticated methods to measure protein or mRNA levels are expensive, relatively insensitive, imprecise, and often contentious. The lack of precision, with the coefficient of variation (CV) usually exceeding 10% of the mean (and sometimes approaching 50%), makes it virtually impossible to detect subtle effects, and a subtle effect, repeated daily or several times daily for, say, 30 years, might be what the epidemiological studies are detecting when consumption is linked to benefit. It is important in this sense to bear in mind the fact that polyphenols are consumed in humans at dietary concentrations and not at pharmacological concentrations, and thus, the expected effect should be in accordance with the doses used, that is, subtle. In contrast, the use of cell or tissue culture studies allows for the use of higher polyphenol concentrations, exacerbating those effects, but then in many cases working at unphysiological concentrations of polyphenols. Downward extrapolation to a weaker effect taking place in humans at dietary concentrations is assumed; however, many effects are thresholded, and the in vivo relevance is impossible to judge. With this context, JAFC has organized a Virtual Issue to highlight recent notable advances in our understanding of polyphenol chemistry, metabolism, and health benefits. Fromsome 500 papers published in JAFC in the last 18 months, we selected 22 that excel in terms of their excellence and novelty in their hypothesis and methodology. Collectively, these papers highlight the importance of agronomical and climatological conditions on the polyphenol concentration, identify new plant sources of polyphenols16,18 and new genetic targets to increase or select for specific polyphenols present in plant material, elucidate the mechanisms and products of polyphenol transformations during food processing, and study the possible mechanisms by which polyphenols can provide nutritional protection againstabiotic and biotic toxicity or chronic diseases in humans andanimals. The gut microbiota interaction with polyphenols and the potential of nanotechnology for enhanced delivery of polyphenols are also illustrated. It is clear from the varying emphasis of these selected papers that polyphenols impact many areas of interest to both agricultural and food chemists and that they are of directrelevance to consumers, whether by a contribution to long-termhealth through protection of (pro)vitamins, defense againsttoxic products of rancidity, or direct impact on human physiology via their metabolites and/or gut microbiota catabolites.For 65 years, JAFC has been a leader in publishing the mostimportant advances in polyphenol research, and we invite thecommunity to continue this tradition and help to fill gaps in our understanding of polyphenol chemistry and potential healthimpacts by publishing your highquality research in JAFC.

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