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Symposium Introduction

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Polyphenols and Health: Current State and Progress

ABSTRACT: During the 5th International Conference on Polyphenols and Health that was held in Sitges (Spain) in October 2011, the latest advances in this area of active research were presented. Sessions on polyphenol effects on cardiovascular disease, polyphenols as ingredients of functional foods, the role of polyphenols in preventing obesity and diabetes, the interaction of polyphenols with gut microbiota, bioavailability and metabolism of polyphenols in humans, the mechanisms of action of these metabolites in different models, new methodologies for the study of the role of polyphenols in health, polyphenols and cancer, recent developments in phenolic compounds and neuroscience, and polyphenols in epidemiology and public health were organized. This highlight issue presents a selection of papers from invited speakers, oral presentations, and poster prize winners. The perspectives for this exciting area of very active research were also discussed at the meeting and are summarized in this introductory paper.

KEYWORDS: *polyphenols, health, biological activity, flavonoids, proanthocyanidins, anthocyanins, phenolic compounds*

The role of dietary polyphenols on human health has been intensively studied during the past 15 years. Polyphenols are universally present in plant-derived food products. These metabolites have been associated with the health benefits that plant-derived food provide to humans when consumed as part of a balanced diet.

During the past 10 years, an International Conference on Polyphenols and Health has been organized to present and discuss the recent advances in this topic. The first conference took place in Vichy (France) in 2003[1] and was organized by Augustin Scalbert. This meeting was scientifically and technically so successful that new conferences have been held in different parts of the world every two years. The second conference took Place in Davis, CA (USA), in 2005, the third in Kyoto (Japan) in 2007,[2] and the fourth in Harrogate (England) in 2009.[3] In October 2011, from the 17th to 20th, the beautiful Mediterranean town of Sitges, Spain, hosted the 5th International Conference on Polyphenols and Health. More than 700 delegates attended sessions from 110 speakers on different topics related to polyphenols and health. Sessions on polyphenol effects on cardiovascular disease, polyphenols as ingredients of functional foods, the role of polyphenols in preventing obesity and diabetes, the interaction of polyphenols with gut microbiota, bioavailability and metabolism of polyphenols in humans, mechanisms of action of these metabolites in different models, new methodologies for the study of the role of polyphenols in health, polyphenols and cancer, recent developments in phenolic compounds and neuroscience, and polyphenols in epidemiology and public health were organized.

This highlight issue presents a selection of papers from invited speakers, oral presentations, and poster prize winners.

The scientific evidence presented in the conference confirms the relevance of polyphenols as bioactive components of plant-derived food products that contribute to reducing the risk of chronic diseases.

The perspectives on polyphenols and health research were discussed during the meeting. In a general way these perspectives coincided with those recently highlighted in the American Chemical Society meeting on Food Bioactives that was held in Denver in August 2011.[4]

The results presented at the conference showed that the advances in analytical and bioinformatic methods enable a deeper characterization of the polyphenols present in food products and lead to the identification and quantification of many unknown natural metabolites in food and changes in the human metabolome as a consequence of the polyphenol intake. Advances in the discovery of polyphenol intake biomarkers were presented (Tulipani et al., in this issue). It was agreed that there is a necessity to complete food polyphenol databases, such as the Phenol Explorer database (http://www.phenol-explorer.eu),[5,6] with specific evaluation of the effects of food processing and storage in polyphenol composition and the addition of new foods from specific geographical areas (Speisky et al., in this issue). In this area the study and quantification of nonextractable phenolics and oligomeric and polymeric polyphenols and the development of new analytical methods for this purpose will be essential.[7,8] Polyphenols are extensively metabolized in the body. The metabolism module of Phenol-Explorer, the first database that allows the recall of identities and concentrations of polyphenol metabolites in biological fluids after the consumption of polyphenol-rich sources (http://www.phenol-explorer.eu/metabolites), was also presented in Sitges.

New analytical methods allow the phenolic characterization of the foods used in intervention studies. The use of HPLC-MS-SPE-NMR has permitted the identification of 180 different phenolic compounds in green, black, and white teas (Van der Hooft et al., in this issue). These advanced methods provide instruments for the complete characterization of the extracts used and for the identification of their metabolites in biological fluids and tissues (targeted metabolomics studies) (Caputi et al., in this issue). The application of UPLC-QTOF methodologies with the appropriate bioinformatics tools provides an excellent methodology to complement human intervention studies. Nutrimetabolomic strategies in the discovery of new biomarkers in human nutritional research are reviewed (Llorach et al., in this issue).

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In the development of functional foods and ingredients containing polyphenols, the relevance of the food matrix and the solubility of the polyphenols were discussed (Roopchand et al., in this issue). Technological treatments to mask nondesirable sensory aspects often associated with some polyphenols (bitterness, astringency, etc.) or to ensure the stability of the active metabolites in the food during storage and processing or during the transit of the gastrointestinal tract have been developed. The interaction of food constituents with polyphenols that affect their absorption and metabolism has also been a relevant topic of research. New nanotechnological methods offer an excellent way to discover these possibilities,[9] and these will be explored during the next years.

The study of the interaction of polyphenols and their metabolites with macromolecules (particularly proteins and lipids) will afford new evidence of their effect. In the evaluation of the bioavailability and metabolism of polyphenols the development of new analytical methods that will enable the release of the metabolites from protein, carbohydrate, and lipid molecules will help to establish the real bioavailability of phenolic compounds and their tissue distribution. The study of deconjugation processes in specific tissues will help to understand the effects of phenolic metabolites.[10]

The dual interaction between gut microbiota and polyphenols appeared as one of the main topics of innovative research in the area.[11,12] Polyphenol gut microbiota metabolites are often better absorbed than the parent food phenolics, and these microbial metabolites have specific biological effects that extend those of the food phenolic compounds. Polyphenols can also modulate the gut microbioma, promoting the development of some bacterial groups (Tuohy and Viola and Truchado et al., in this issue). There is growing evidence that many polyphenols favor the development of beneficial lactobacilli and bifidobacteria, whereas they delay the growth of coliforms and other potentially harmful bacteria in the colon. The recent discovery of human enterotypes[13] opens a new field of research that will explain in many cases the large interindividual variability observed in human intervention studies.

Human intervention studies have confirmed the effect of different dietary phenolic compounds in decreasing the risk of cardiovascular diseases. Olive oil, wine, tea, cocoa, fruit, and vegetable phenolics have been linked to these health effects. The role of polyphenols and their in vivo conjugated metabolites in reducing cardiovascular disease biomarker, and the reduction of cardiovascular inflammation was reported. Other studies described the effects of phenolics improving gut inflammation, obesity, diabetes, hypertension, and metabolic syndrome (Jiménez et al., Ueda and Ashida, Weseler and Bast, and Morand et al., all in this issue).

The health effects of food polyphenols have been repeatedly associated with their free radical scavenging and antioxidant effects, as free radicals and oxidation are among the factors that have been associated with the origin of the main chronic diseases including neurodegenerative diseases, cardiovascular diseases, and cancer. Thus, many studies have been devoted to the evaluation of the total antioxidant capacity of foods,[14−18] the correlation with the polyphenol content, and the evaluation of the changes with cultivation and processing factors. Recent evidence has, however, indicated that the effects of antioxidants are less relevant than expected, as the antioxidant polyphenols are poorly absorbed and extensively metabolized to nonantioxidant metabolites.[19,20] In addition, many of these compounds have a very low bioavailability and never reach the tissues where they have to exert their antioxidant action in sufficient amounts.[21,22] This means that much of the evidence for bioactivity of polyphenols evaluated on human cell lines may have little significance in vivo. Future studies of the mechanisms of the biological effects of polyphenols on human cell lines should use the metabolites produced in vivo (conjugates of the original aglycones or gut microbiota metabolites such as methyl ethers, glucuronides, and sulfates) and at the concentrations reached in biological fluids and tissues (nanomolar range) to provide real biological significance (Giménez-Bastida et al. and Tognolini et al., in this issue).

Animal models, as close to humans as monkeys and as simple as the worm *Caenorhabditis elegans*, have been successfully used in polyphenols and health research. These have been particularly useful in toxicological and in tissue distribution studies, which are essential to understand the metabolites that can be active in vivo. The model of *C. elegans* provides a smart methodology for testing the activity of polyphenols in a simple and repetitive manner that can be very useful for screening studies (González-Manzano et al., in this issue).

It is well established that polyphenol bioavailability is usually very low[21,22] and that the concentration of circulating metabolites of food polyphenols is usually in the nanomolar range. The concentrations of food polyphenols in the gastrointestinal tract are, however, quite high, and there is evidence of relevant effects locally. For instance, the antioxidant effects of dietary polyphenols prevent the oxidation of vitamins and other nutrients (lipids, proteins, cholesterol, etc.), thus preserving a higher quality of the nutrient intake (Kanner et al., in this issue). In addition, these polyphenols can have an effect in modulating the activity of gastrointestinal enzymes such as amylases, lipases, and proteases and therefore inhibiting the absorption of glucose and fatty acids with the associated benefits in obesity, diabetes, and metabolic syndrome (Yilmazer-Musa et al., in this issue).

Food polyphenols and their microbiota metabolites show also anti-inflammatory effects in the gut, thus improving gut health (Giménez-Bastida et al., in this issue). Some polyphenols and metabolites have also effects on the intestinal cells, promoting apoptosis in cancerous cells while having no harmful effects on normal colonocytes (Tognolini et al., in this issue). These metabolites can also interact with neuronal receptors in the gastrointestinal tract, therefore producing effects that go beyond local effects.

Because of the sustained increase in the research interest in polyphenols and health by academia and industry, we anticipate exciting results at the next conference, which will travel to South America and will be organized by Cesar Fraga in Buenos Aires (Argentina), October 16−19, 2013.

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Notes

The authors declare no competing financial interest.

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