Meeting Report

Symposium on Plant Polyphenols: Nutrition, Health and Innovations, June 2009

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Reported here is a summary of the proceedings of the Symposium on Plant Polyphenols: Nutrition, Health and Innovations, which was cosponsored by the Southeast Asia Region branch of the International Life Sciences Institute and the Nutrition Society of Malaysia in Kuala Lumpur, Malaysia, June 22–23, 2009. The symposium provided a timely update of research regarding the protective effects of polyphenols in chronic diseases, such as cardiovascular disease and cancer, as well as the development of innovative polyphenol-containing food products with enhanced nutritive and health properties. Presentations covered polyphenols from a wide range of food sources such as tea, coffee, nuts and seeds, cocoa and chocolate, soy, and Asian fruits, vegetables, and spices. The symposium was attended by a large and diverse group of nutritionists, dietitians, researchers and allied health professionals, as well as management, research and development, and marketing personnel from the food and beverage industry. Their enthusiastic participation was a testament to the increasing awareness and interest in polyphenols in the prevention and control of chronic diseases. Presented here are some of the highlights and important information from the symposium.

INTRODUCTION

Polyphenols are naturally occurring compounds found abundantly in fruits, vegetables, and beverages such as tea and coffee; they are widely studied for their protective effects against cardiovascular disease and certain types of cancer in humans. Scientific interest in polyphenols and their role in preventing chronic diseases has increased over the past 10 years, especially with regard to their anti-inflammatory and antioxidative properties. For the food industry, interest in polyphenols has led to the development of technology and product innovation to increase the supply of polyphenol-containing food products with enhanced nutritive and health properties. These developments made it timely for the Southeast Asia Region branch of the International Sciences Institute and the Nutrition Society of Malaysia to organize a symposium entitled, "Plant Polyphenols: Nutrition, Health and Innovations," which was held June 22–23, 2009, in Kuala Lumpur, Malaysia. The event was attended by more than 120 nutritionists, dietitians, researchers, and allied health professionals, as well as management, research and development, and marketing personnel from the food and beverage industry. The enthusiastic response from the participants testified to the increasing awareness and interest in polyphenols for the prevention and control of chronic diseases. Presented here are some of the highlights and important information from the symposium.

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PLANT POLYPHENOLS AND HEALTH – CURRENT STATE OF THE SCIENCE

In the opening plenary, Gary Williamson of the University of Leeds reviewed extensive data showing the ability of polyphenols to lower cardiovascular disease risk through their effects on related factors or markers of the disease. For example, in a meta-analysis of the effects of polyphenols in humans, it was found that polyphenols provided protective effects on cardiovascular disease risk in humans through the reduction of low-density lipoprotein (LDL) cholesterol and blood pressure, as well as through the improvement of flow-mediated dilation, an indication of endothelial function and a marker of cardiovascular risk.[1]

However, the effects of polyphenols are related to their bioavailability following absorption and metabolism in the body. A review of 97 bioavailability studies showed that isoflavones are the most well-absorbed polyphenols, followed by catechins and flavanones; the least well-absorbed polyphenols are the proanthocyanidins and the anthocyanins.[2] Since the exact mechanism of absorption differs greatly from one polyphenol to another, the most abundant polyphenols in our diet do not necessarily achieve the highest concentrations of active metabolites in target tissues.

A major difficulty in studying the benefits of the antioxidant properties of flavonoids is the lack of a reliable approach towards evaluating oxidative stress status in humans.[3] For determining the effects on lipid peroxidation, for example, Kevin Croft of the University of Western Australia mentioned that specific biomarkers of oxidative damage could be more useful than simple non-specific assays. Furthermore, flavonoids may inhibit the development of atherosclerosis via multiple pathways. For example, quercetin and epicatechin can augment nitric oxide status and reduce endothelin-1 concentrations, and may thereby improve endothelial function.[4]

In conclusion, the opening plenary noted that the chemical structure of flavonoids affects the absorption and metabolism of these compounds, and hence limits their bioavailability in the body. Such scientific information should be considered in the interpretation of data from in vitro experiments. Different flavonoids may also exert similar health benefits via different mechanistic pathways in the human body.

TEA

Tea, which is the most widely consumed beverage next to water, is an important source of flavonoids for a significant proportion of the world's population. Tea may reduce the risk of cardiovascular disease through its high concentrations of polyphenols or flavonoids.

The key flavonoids present in tea are the catechins (epicatechin, epicatechin gallate, epigallocatechin, epigallocatechin gallate), quercetin, and theaflavins. As noted in the presentation by Jonathan Hodgson of the University of Western Australia, thearubigens are the predominant flavonoids in black tea (7–15% by dry weight), followed by theaflavins (4% by dry weight); in green tea, however, catechins (12–18% by dry weight) such as epigallocatechin gallate (9–13% by dry weight) predominate. A study by Loke et al.[4] showed that quercetin and epicatechin, which are flavonoids with higher concentrations in green tea than black tea, can augment nitric oxide status, cause vasodilation, and may thereby improve endothelial function. As for the effects of tea on blood pressure, results of population-based studies suggest there is an inverse association between tea intake and risk of hypertension. One such study examined the relationship between a biomarker of a tea-derived polyphenol, 4-O-methylgallic acid, and blood pressure in a cross-sectional study of 218 women aged 70 years and older. This study found that higher 4-O-methylgallic acid excretion was associated with significantly lower systolic and diastolic blood pressures, and that an intake of one cup of tea a day could lower systolic blood pressure by 2.2 mmHg and diastolic blood pressure by 0.9 mmHg.[5] However, a meta-analysis of five studies on tea consumption involving a total of 343 subjects followed for a median duration of 4 weeks showed that tea intake had no significant effects on blood pressure.[6] This implies that short-term consumption of tea appears to have little impact on blood pressure and longer-term intervention trials are needed to study the effects of tea in lowering blood pressure. In addition to improving endothelial function and lowering blood pressure, tea polyphenols may reduce cardiovascular disease risk by inhibiting lipoprotein oxidation. However, human evidence that tea polyphenols can reduce lipoprotein oxidation remains weak.[7]

According to Yu-Tang Gao of the Cancer Institute of Shanghai Jiaotong University, a number of epidemiological studies on tea drinking and cancer conducted in Shanghai, a city in which tea drinking is highly prevalent, have shown that the drinking of green tea may have a protective effect against some cancers of the digestive tract, as well as against cancers of the lung and breast. One such study involved a cohort of 18,244 men in Shanghai and examined the associations between biomarkers of specific tea polyphenols and risk of developing colorectal cancer. The study found that individuals with high prediagnostic levels of urinary epigallocatechin had a lower risk of colon but not rectal cancer.[8] A meta-analysis of epidemiologic studies on green tea, black tea, and colorectal cancer risk, which included 25 studies conducted in 11 countries on three continents, was also described during the symposium.[9] For green tea, the summary odds

ratio (OR) of 0.82 [95% confidence interval (CI), 0.69–0.98] from eight studies indicated a reduced risk of colorectal cancer with tea intake. This significant association was mainly driven by case-control findings while cohort studies did not support an association between green tea and colon cancer. Another meta-analysis indicated that green tea intake was associated with a lower risk of breast cancer.[10] The combined results from four studies (three cohort studies from Japan and one population-based case-control study from Los Angeles) indicated a reduced risk of breast cancer for the highest versus lowest intake (OR, 0.78; 95% CI, 0.61–0.98). For black tea, the summary OR of 0.98 (95% CI, 0.88–1.09) based on all studies indicated no association between black tea consumption and breast cancer risk.[10] Inconsistencies in these epidemiologic studies can be due to differences in study design, definition of tea drinking, cultural differences in tea drinking habit, and the variety and amount of tea consumed.

Manoj Joshi of the Unilever Research Center highlighted some critical factors that determine the flavonoid composition of tea as well as the bioavailability and metabolism of tea flavonoids after consumption. Changes in flavonoid composition are mediated by the methods used to process tea. Freshly plucked tea shoots are rich in flavonol monomers known as catechins, and during the manufacture of green tea, polyphenol oxidase (PPO), which drives oxidation of polyphenols, is inactivated to limit enzymatic oxidation. Conversely, oxidation is maximized in the manufacture of black tea, resulting in the formation of theaflavin and thearubigin flavonoids from the catechins. Hence, a typical cup of green tea contains native catechins at levels approximating 30–40% weight of the water-extractable materials. In comparison, a cup of black tea contains 3–10% catechins, 2–6% theaflavins, and 20% thearubigins. Nevertheless, the plasma antioxidant potential in black tea is similar to that in green tea because the conversion of catechins to oxidized flavonoids in black tea does not appear to decrease its antioxidant activity, as shown by comparable production of thiobarbituric acid-reactive substances (TBARS) and conjugated dienes in a human model of LDL oxidation.[11] Furthermore, brewing methods and the inclusion of additives such as lemon and milk may influence the composition of flavonoids and their absorption in the gut.[12,13] Further understanding of the ways in which tea flavonoids are assimilated in humans would be useful for maximizing the health benefits of tea.

COFFEE

The main active compounds in coffee are phenolic acids, primarily chlorogenic acids, which possess antioxidant properties. For filtered coffee, the total amount of chlorogenic acids is between 100 and 200 mg per 100 mL; the most abundant form is 5-caffeoylquinic acid (5-CQA), which accounts for 35–50% of the total chlorogenic acids. The absorption and metabolism of the chlorogenic acid compounds is less well studied than that of flavonoids, since there are many different compounds in coffee and the pathway of absorption, metabolism, and excretion is complicated. However, as reported by Gary Williamson of the University of Leeds, investigative studies to quantify the absorption and metabolism of phenolic acids from coffee are ongoing, as is the collection of evidence for its effect on disease prevention.

Once again, the bioavailability (metabolism and absorption) of the phenolic acids in coffee determines the benefits of coffee consumption in humans. Current evidence shows that phenolic acids in coffee are absorbed efficiently, and that many of their metabolites (dihydrocaffeic acid-3-O-sulfate and dihydroferulic acid) can be measured in plasma after coffee consumption. An epidemiologic study on coffee consumption and cardiovascular disease from the Iowa Women's Health Study showed that, compared to non-drinkers, women who drank coffee had a lower risk of cardiovascular death, although the association was U-shaped, with the lowest risk in the category of women who drank between one and three cups a day (relative risk [RR], 0.76; 95% CI, 0.64–0.91). In addition, women who drank six or more cups of coffee a day had a statistically significant 30% reduction in the risk of mortality from inflammatory diseases.[14] Woon-Puay Koh of theNational University of Singapore also presented prospective data from the Singapore Chinese Health Study, a population-based cohort of 63,257 middle-aged and elderly Chinese in Singapore, which showed that subjects who reported drinking four or more cups of coffee per day had a 30% reduction in the risk of diabetes (RR, 0.70; 95% CI, 0.53–0.93) compared to those who reported non-daily consumption.[15] This association was strengthened upon adjustment for caffeine, suggesting that non-caffeine components, such as chlorogenic acid in coffee, are responsible.[15] The relationship between coffee and Parkinson's disease was also examined in the Singapore Chinese Health Study, and the study found that drinking at least two cups of coffee a day resulted in a 32% reduction in the risk of Parkinson's disease (RR, 0.68; 95% CI, 0.45–1.01)].[16] Total caffeine intake was also inversely related to disease risk. A meta-analysis involving eight case-control and five cohort studies also showed that daily coffee drinkers have a lower risk of Parkinson's disease compared with non-drinkers (RR, 0.69; 95% CI, 0.59–0.80),[17] and a null association with decaffeinated coffee suggests that caffeine is the putative causal agent

underpinning the observed reduction in Parkinson's disease risk related to coffee.[18]

SOY

Soy has generated much interest during the past 20 years because the legume is a unique source of isoflavones, which are diphenolic compounds that possess both hormonal and nonhormonal properties. According to Mark Messina of the Soy Nutrition Institute, isoflavones are present at an average concentration of about 2 mg/g in soybeans, although there is at least a threefold range among different soybean varieties. An earlier review of 97 bioavailability studies showed that isoflavones are the most well-absorbed polyphenols,[2] and in the soybean, the three isoflavones genistein, daidzein, and glycitein represent approximately 50%, 40%, and 10%, respectively, of the total isoflavone content. The proposed benefits of isoflavones include protection against osteoporosis, breast cancer, and heart disease, and the alleviation of hot flushes during menopause.

The estrogen-like effects of isoflavones has led to the biologic plausibility that these soybean constituents can exert benefits on bone mineral density in postmenopausal women. Two prospective epidemiologic studies looking into the risk of major osteoporotic fractures from the Shanghai Women's Health Study (24,403 women, average follow-up 4.5 years) and the risk of hip fractures from the Singapore Chinese Health Study (35,298 women, average follow-up 7.1 years) found a one-third reduction in fracture risk with the highest quintile or quartile of dietary isoflavone intake compared to the lowest intake.[18–20] Another randomized, placebo-controlled trial in Italy, in which osteopenic postmenopausal women were given 54 mg of genistein per day in aglycone form, showed a pronounced increase in bone mineral density in the treatment group.[21] Despite these promising results, recent results from three randomized, double-blind, placebo-controlled trials, each involving between 100 and 200 postmenopausal women in the United States, yielded disappointing results with null association between intakes of soy protein or mixed isoflavones and benefits on bone health.[22–24]

On the effects of soy on menopausal symptoms, Mark Messina referred to the results of a systematic review and meta-analysis of randomized controlled trials of soy isoflavones and postmenopausal hot flushes; the results indicated that, in comparison with placebo, higher isoflavone intake was associated with a 20% reduction in the frequency and 30% reduction in the severity of hot flushes as well as a clinically relevant improvement in the quality of life.[25] High-dose genistein supplements may also be more effective than low-dose genistein supplements. Other recently published meta-analyses also concluded that isoflavones had very modest effects on reproductive hormone levels in women[26] and no effects in men.[27]

There are also prospective findings suggesting that soy isoflavones may have lasting beneficial effects against breast cancer development. Epidemologic evidence from the Singapore Chinese Health Study, as reported by Woon Puay-Koh, found that mammographic density was inversely associated with soy intake in a subset of 380 women from this cohort. The difference in mammographic density, a surrogate of breast cancer risk, between women from the higher and lower quartiles of soy isoflavone intake was 4–5%, a difference that was similar in magnitude to that reported in Western populations of women undergoing menopause or commencing hormone therapy.[28] In the Singapore Chinese Health Study cohort, it was also found that postmenopausal women with higher (above median) soy intake showed a statistically significant 18% reduction in the risk (RR, 0.82; 95% CI, 0.70–0.97) of breast cancer compared to those with lower (below median) intake.[29] The inverse association between soy intake and breast cancer risk was more apparent in postmenopausal women (RR, 0.67; 95% CI, 0.51–0.88), and it strengthened further in women with a high body mass index (above median) compared to their leaner counterparts.[29] For breast cancer survivors, current epidemiologic and laboratory evidence suggests that up to three servings per day of traditional soy foods are unlikely to be harmful.[30]

Further reported by Woon-Puay Koh was an inverse relationship between the intake of soy foods (tofu products and soybean drink) and lung cancer risk among non-smoking women in the Singapore Chinese Health Study; the relative risk for the highest versus the lowest quartile of total isoflavone intake was 0.59 (95% CI, 0.38–0.91).[31] No relationship was observed between dietary isoflavones and lung cancer risk among women who smoked or among men (both smokers and non-smokers) in this cohort. The association between increased dietary soy isoflavones and decreased risk of lung cancer among non-smoking women is consistent with the ability of soy isoflavones to competitively inhibit the estrogen receptor-mediated pathway that might possibly be implicated in lung carcinogenesis in non-smoking women.

Despite all of the health benefits of soy, the consumption of soy depends on consumers' attitudes and market acceptance towards soy foods, as highlighted by Karl Weingartner of the University of Illinois. Currently, the market demand for soy foods is driven by its low cost (e.g., soy ingredients are less expensive than animal-based ingredients), high functionality (e.g., soy can improve the texture and extend the shelf-life of food products), and health benefits.

NUTS AND SEEDS

In a presentation by Oliver Chen of Tufts University, it was noted that nuts and seeds contain numerous phytochemicals that can promote health and reduce the risk of chronic diseases. Phenols, including phenolic acids, flavonoids, and stilbenes, as well as proanthocyanidins, are found in almonds, cashews, hazelnuts, pecans, pistachios, peanuts, and walnuts in varying concentrations.[32] Nut phytochemicals have been associated with numerous bioactivities known to affect the initiation and progression of several pathogenic processes. Their bioaccessibility in the human gut is a key factor in assessing their significance in human health, and the estimated nonextractable polyphenol content in nuts is almost double that of extractable polyphenols. The additional benefits of dietary fiber and unsaturated fats in nuts also justify their promotion; the regular inclusion of a handful (1.5 ounce or 40 g) of nuts every day as part of a healthy diet can be promoted for a variety of health benefits, as qualified by the USA FDA Heart Health Claim for Nuts in 2003.

Like nuts, olives are also considered a health-promoting food due to their high lipid (monounsaturated fat) and polyphenol contents. Karin Wertz of DSM Nutritional Products Ltd, reported that olive polyphenols, the best known of which is hydroxytyrosol, have been shown to beneficially reduce plasma levels of oxidized-LDL and to improve the plasma lipid profile in human intervention trials[33,34]; the anti-inflammatory activity of olive polyphenols also help relieve the severity of arthritis.[35] However, it is important to note that olive polyphenols, due to their water solubility, are mostly lost during processing for olive oil and table olives.[36,37]

COCOA AND CHOCOLATE

Described as one of the richest sources of dietary flavonoids, it is important to differentiate natural cocoa from manufactured cocoa powders or chocolates. As highlighted by Kevin Croft of the University of Western Australia, the flavonoids present in cocoa include anthocyanins, flavones, flavanols, and flavonols. Flavanols, the most abundant flavonoids in cocoa, comprise the two monomeric flavanols (+)-catechin and (-)-epicatechin.[38] However, significant amounts of coca flavonoids can be lost during the manufacturing process; as an example, 60% of the mean total flavonoid content in the concentration of all cocoa flavonoids is lost as a result of alkalinization treatment.[38]

The health benefits of cocoa, including its cardiovascular benefits, appear to be related to the bioavailability and activity of the cocoa flavanols. A study by Heiss et al.[39] found that the daily consumption of a flavanol-rich cocoa drink over 7 days resulted in a sustained increase in flow-mediated dilation, which is an indication of endothelial function and a marker of cardiovascular risk. A meta-analysis of five randomized controlled studies involving a total of 173 subjects on diets rich in cocoa for a median duration of 2 weeks showed that cocoa-rich diets were associated with statistically significant reductions in systolic and diastolic blood pressure.[6]

ASIAN FRUITS, VEGETABLES, AND SPICES

The evidence for a protective effect of high-level consumption of fruits and vegetables is consistent for many chronic diseases, and this effect may be attributed, in part, to the antioxidants found in fruits and vegetables. In their studies, Mia Isabelle and De-Jian Huang of the National University of Singapore, analyzed the peroxyl radical scavenging capacity, total phenolic content, ascorbic acid, and various lipophilic antioxidants of 66 commonly consumed vegetables in Singapore. Most of the vegetables with high antioxidant capacity were dark-colored vegetables; e.g., matrimony vine was found to have the highest antioxidant activity, as measured by its hydrophilic oxygen radical absorbance capacity (H-ORAC), while dried seaweed had the highest corrected total phenolic content, followed by sweet potato leaves.[40] Findings from this study conducted in Singapore suggest that dark green leafy and brightly colored vegetables tend to contain high levels of antioxidant and total phenolic content, and the general public should be encouraged to consume more of such vegetables.

Myung-Hee Kang of Hannam University reported results from intervention trials investigating the benefits of consuming fruits and vegetables with high polyphenol content for reducing oxidative stress, assessed as lymphocyte DNA damage in smokers, hypertensive patients, and healthy volunteers.[41–43] The results support the hypothesis that green vegetable juice, grape juice, and carrot juice, which are high in polyphenols, may confer chemoprotective effects against cancer by decreasing DNA damage in subjects exposed to oxidative stress.

CONCLUSION

In his summary presentation, E-Siong Tee of the Nutrition Society of Malaysia noted that the scientific interest in plant polyphenols has been matched by increasing awareness among the general public regarding the role of polyphenols in reducing the risk of chronic diseases. The evidence from experimental and descriptive epidemiological studies may be regarded as substantial for justifying relevant nutritional recommendations that are in line with dietary guidelines to encourage healthy eating. It is also important that the taste and nutritional values of

foods rich in polyphenols continue to be enhanced through ongoing technologies and innovations. Trevor Webb of Food Standards Australia New Zealand mentioned there is a significant relationship between nutritional knowledge and willingness to try functional foods, since consumers with the most nutritional knowledge are those who would be most interested in the enrichment of healthy products with fiber or antioxidants. Educational strategies may, therefore, be necessary to provide consumers with greater insight into the health benefits of foods or specific bioactive components so as to encourage the consumption of functional foods.[44]

Finally, through the use of the international CODEX guidelines on nutrition and health claims,[45] as well as through national authorities in the Asian region, E-Siong Tee concluded the legal provisions for making health claims on polyphenols are sufficient; however, the regulatory framework in Asia needs to be developed further to facilitate the review and approval of such claims.

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Declaration of interest. The authors have no relevant interests to declare.

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