

DIETARY INTAKE OF PLANT POLYPHENOLS: EXPLORING TREND IN THE CZECH POPULATION

Pavel Sedláček¹, Monika Bludovská¹, Iveta Plavinová¹, Anna Zavadřáková¹, Luděk Müller², Dana Müllerová¹

¹Department of Hygiene and Preventive Medicine, Faculty of Medicine in Pilsen, Charles University, Pilsen, Czech Republic

²Department of Cybernetics, NTIS, University of West Bohemia in Pilsen, Pilsen, Czech Republic

SUMMARY

Objectives: This study aimed to determine trend in polyphenol consumption in the Czech Republic during the last three decades. Additionally, it provides a brief overview of the beneficial effects of polyphenols in several body systems.

Methods: Data from the Phenol-Explorer 3.6, a specialized database of polyphenolic substances, were assigned to the resources of the Czech Statistical Office on the consumption of food and beverages in the Czech Republic for the years 1989–2022. The average daily intake of polyphenols was determined by multiplying the average annual consumption of each type of food by the polyphenol content obtained from the database; results were given in milligrams of polyphenols per inhabitant and day. Since the food items in the data sources are not identical, it was necessary to create an extensive model of food categories.

Results: The current value of polyphenol intake is 1,673 mg per day per inhabitant; however, this level most likely reflects methodological underestimation. The favourable increase in dietary polyphenol intake in the Czech population – doubling, to be precise – which we observed from 1989 to 2007, has been replaced by the opposite trend in the last 15 years. The current intake of polyphenols corresponds to the level that was already achieved in 2004. Hydroxycinnamic acids (from the group of phenolic acids) are the most prevalent dietary polyphenols, followed by flavanols (from the group of flavonoids). The most frequent source of polyphenols in the Czech population are non-alcoholic beverages such as coffee, tea and juices, followed by fruits, cereals, and vegetables, respectively.

Conclusion: Current trend of dietary polyphenol intake in the Czech population is slightly decreasing. This tendency, lasting since 2008, is indisputably negative. Plant polyphenols offer opportunities for inexpensive interventions in health promotion.

Key words: polyphenols, dietary habits, prevention, non-communicable diseases, phytochemicals

Address for correspondence: P. Sedláček, Department of Hygiene and Preventive Medicine, Faculty of Medicine in Pilsen, Charles University, alej Svobody 76, 323 00 Pilsen, Czech Republic. E-mail: pavel.sedlacek@lfp.cuni.cz

<https://doi.org/10.21101/cejph.a7994>

INTRODUCTION

Plant polyphenols (PP) belong to the broad group of non-nutritional, biologically active natural compounds ubiquitously occurring in food of plant origin. Their chemical structure is characterized by one or more hydroxylated benzene rings that are usually linked to a sugar unit by a glycosidic bond. PP are believed to be secondary physiological products of plants. The basic and the largest group of PP is represented by flavonoids (including anthocyanidins). They are followed by phenolic acids, stilbenes and other phenolics, polyphenol dimers, and polymerisation products (e.g., tannins) (1).

The beneficial effect of nutrition rich in vegetables and fruits is widely accepted. In addition to fibre, vitamins, minerals, and trace elements, these food groups contain polyphenolic substances which are traditionally classified as phytochemicals. They show positive effects in several body systems and are involved in prevention of many diseases. From a public health perspective, non-communicable diseases, including ischaemic heart disease or type 2 diabetes, as well as common mental illnesses, such as anxiety disorders and major depression, account for enormous global disease burden. In recent years, we have learned about the

health benefits of PP not only from epidemiological studies, but also from clinical studies and meta-analyses. Many researchers are aware of their potential role in primary prevention and management of numerous, including the above-mentioned, diseases (2). Considering their ubiquity in plant-based food, they offer opportunities for inexpensive interventions.

It is not the purpose of this article to provide an exhaustive overview of the effects of PP, which would require a monograph of hundreds of pages. Rather, we give a brief overview with a focus on the most widespread health ailments and presentation of the trends pertaining to PP consumption during the last decades in the Czech Republic.

Biological Activity of Polyphenolic Substances – An Overview

PP are traditionally associated with their antioxidant properties (3, 4). Nevertheless, this is no longer perceived as the only or dominant mechanism of their positive effects, as other mechanisms have been discussed recently, including their ability to reduce the pro-inflammatory state of the organism and elicit other protective processes (concerning DNA, cells, tissue structures,

etc.), regeneration and resistance that support adaptability including protection of mitochondrial function, all of which contribute to maintaining health (5, 6). The effect of PP is not limited to soft tissues; phytochemicals can also be applied in specialized medical fields, e.g., in dentistry. In the following text, we will discuss some beneficial effects in detail.

Effect of Polyphenolic Substances in the Field of Cardiovascular Health

Globally, cardiovascular diseases are the major cause of morbidity and mortality, accounting for 32% of all-cause mortality and for 44% of all deaths related to non-communicable diseases. Of these deaths, 85% are due to ischaemic heart disease and stroke (7). The role of oxidative stress as a promoter of endothelial dysfunction, that in turn is a driver of early atherosclerosis and consequent cardiovascular disorders, is no longer in doubt and provides space for the anti-inflammatory and antioxidant strategy in the field of cardioprotection. “Beyond the inhibition of oxidative stress, PP also display indirect antioxidant effects, occurring through the activation of the transcription nuclear factor erythroid 2-related factor 2 (Nrf2). This process induces endogenous antioxidant systems and is likely to be responsible also for PP-mediated maintenance of the correct redox balance of cells, achieved through the equilibrium of phase I and II enzyme activity” (8). “The anti-inflammatory properties of PP are strictly connected with the modulation of oxidative stress and of the balance of redox cellular homeostasis” (9). “Multiple mechanisms, most of which are mediated by the inhibition of the nuclear factor kappa-light-chain-enhancer of activated B cells (NF- κ B), account for PP’s anti-inflammatory activity. These compounds are able to decrease the cellular production of pro-inflammatory mediators (10–12) and to inhibit the expression of adhesion molecules (13), thus impairing the chemotaxis of monocytes within the inflamed tissues” (14). “Additional mechanisms accounting for the cardioprotective action of PP target lipid metabolism; its impairment represents a causative factor of atherosclerosis development” (15). The reduction of cholesterol synthesis, the increase of LDL receptor expression and activity (16), and the increase in expression of the cholesterol transporters ATP-Binding Cassette G5/ATP-Binding Cassette G8 (17) have been described in *in vivo* models. PP’s (i.e., epigallocatechin gallate) capacity to displace cholesterol from intestinal micelles have been associated with increased cholesterol faecal elimination *in vivo*. “The effect on triglyceride plasma level is possibly related to the reduction of apolipoprotein B48 and apolipoprotein B100 production in the liver and the intestine” (14, 18). “PP could also be able to positively influence endothelial function; its impairment is an established key factor for the development of atherosclerosis” (14). The mechanism accounting for improved flow-mediated dilatation (measurement of flow-mediated arterial dilation is an ultrasound method for detecting endothelial dysfunction) probably relies on the increase of nitric oxide (NO) synthase activity (19, 20). “This NO-mediated vasodilation, together with the influence on the renin-angiotensin system, is responsible for the reduction of blood pressure, an additional cardioprotective activity of PP. Interestingly, this effect is also evident upon consumption of low, habitual amount of PP-rich food” (21). “Finally, cardiovascular benefits of PP may be ascribed to the peculiar pharmacokinetic properties mentioned above” (14).

Effects of Polyphenolic Substances in the Field of Metabolic Disorders: Overweight, Obesity and Type 2 Diabetes

“The distinctive structural properties of PP make them capable of regulating the key molecular mechanisms involved in metabolic syndrome, particularly hyperinsulinemia, altered carbohydrate metabolism, abdominal obesity, hyperlipidaemia, and disrupted glucose homeostasis. These factors can ultimately lead to the development of serious health conditions such as cardiovascular disease and type 2 diabetes” (22). “The prerequisite interactions that can further initiate some other downstream reactions mainly occur in the intestine. Several possible mechanisms involved are inhibition of carbohydrate digesting enzyme and glucose transporters, limiting endotoxemia by increasing gut barrier function, and stimulation of enteroendocrine secretion responsible for regulating hunger and satiety” (23).

In vitro studies showed inhibitory effects of flavonoids and phenolic acids on α -amylase and α -glucosidase activities and intestinal glucose absorption by the sodium-glucose cotransporters (SGLT1) and glucose transporter 2 (GLUT2). Flavonoids protected β -cells from hyperglycaemia in *in vivo* and cell culture studies. PP promoted the uptake of glucose in cell cultures by activating insulin-mediating pathways, e.g., the (Cyclic adenosine 3',5'-monophosphate)cAMP/protein kinase A and phosphatidylinositol 3-kinases (PI3K) pathways. In the liver, PP-rich foods prevented gluconeogenesis and stimulated glycogenesis (24). The results of a German meta-analysis, which also conducted a dose-response analysis, interpret that an optimal intake of 1,000 mg total polyphenols per day corresponds to the lowest risk of type 2 diabetes (25).

Effect of Polyphenolic Substances in the Field of Oncology

The benefits of PP can be applied in the prevention of malignant diseases. As an example, we can mention colorectal adenoma (CRA), which is a premalignant lesion eventually resulting in colorectal cancer (CRC). The prevalence of colorectal adenoma increases with age, 25% of men and 15% of women who undergo colorectal screening have an adenoma. In patients over 60 years of age, adenomatous polyps are present in more than 40% (26). The annual rate of adenoma progression to colorectal cancer (CRC) is ~0.25% (27). PP can reduce the risk of malignant transformation with the reduction of oxidative damage to DNA and enzymes in cells and tissues and through a number of physiological activities – antibacterial, antioxidant, anti-inflammatory, antiviral, antitumor and immunomodulating functions. A number of studies have shown that PPs have inhibitory effects on CRAs and are also considered as an important source of natural medicines for the treatment of a number of other diseases due to their efficacy and safety (28).

Effect of Polyphenolic Substances in the Field of Mental Health

“Strikingly, the role of PP in improving brain vascular function, thus maintaining cerebral blood flow underpinning cognitive activity, has been well established in young and old adults. The potential anti-inflammatory mechanisms have been described

in glial and neuronal cells exposed to supraphysiological concentrations of flavonoids and some studies on humans revealed flavonoid ability to reduce plasma levels of several inflammatory markers (C-reactive protein and NF- κ B, and interleukins such as IL4, IL8 and IL13). An additional mechanism explaining the neuroprotective action of PP is the inhibition of cholinesterases, resulting in increased cholinergic activity and improved cognitive performance.” “Recent evidence suggests that PP, in particular flavonoids, may influence specific processes, the reduction of neuropathological proteins accumulation, and the improvement of synaptic plasticity.” The below described inter-relationships between PP and gut microbiota also have relevant implication in the setting of neuroprotection (14).

“Studies have also demonstrated that PP’s antioxidant properties may help improve depression through targeting neuronal survival, regeneration and development. Further, as a lipid-rich organ, the brain is highly susceptible to oxidative damage, meaning that improved antioxidant status from PP supplementation may further aid in countering depression-induced disturbances in neurotransmission. Meta-analyses results found no significant association between PP use and anxiety; and PP use did not improve the quality of life. Nevertheless, all types of PP supplementation analysed in this study produced a significant improvement in depression score.”(29). Antioxidant effect, interaction with intestinal microbiome glucoregulation, and improvement of cerebrovascular functions through a key effect on synthesis and bioavailability of NO seem to be the main mechanisms behind the improvement of brain functions (30).

Effect of PP on Immune Health and the Gut Microbiota

In addition to the above-mentioned scavenger functions and anti-inflammatory effect, PP display interesting pharmacokinetic features. Although these compounds reach the distal tract of gastrointestinal tract unchanged they are modified by the gut microbes to substances with prebiotic-like activity, which support growth of beneficial and suppress growth of potentially harmful microbes (14). The microbial diversity and stability plays an essential role in maintaining the host’s metabolic and immune response homeostasis (23). The human gastrointestinal tract contains approximately 100 trillion bacteria, which have more than three million gene functions (31). Intestinal microbes influence the host physiology by producing thousands of metabolites (32–34). The dietary composition significantly influence the gut microbiome; nutritional components, e.g., indigestible carbohydrates such as oligosaccharides or phytochemicals such as PP (35). Moreover, gut microbiome is a part of the gut–brain axis, therefore neurotransmitters and other metabolites produced by gut microbes act on the brain. The brain and the gut bidirectionally interact via the central nervous system, the hypothalamic–pituitary–adrenal (HPA) axis, the endocrine system, and the immune system. Responding to stress, emotions and other factors, the HPA axis secretes hormones which alter gut motility, digestion, and the ecosystem of the gut microbiota in general. The important neurotransmitters and metabolites such as serotonin and γ -aminobutyric acid (GABA) are also produced by the gut microbes. These molecules modulate behaviour and have an impact on the neuronal signalling, digestive function, and the

immune system of the host (36). As evident from the above, there is a generally accepted connection between mental health and the health of the gut microbiome.

Effect of Polyphenolic Substances in the Field of Dental Health

In case of tooth decay, the protective effect of PP is, *inter alia*, based on a direct interaction with the oral microbiome: They block vital functions of bacteria by acting upon intracellular membranes and forming complexes with metal ions. In addition, PP influence saliva proteins and pellicles, thereby prevent certain bacteria from the adhesion and inhibit biofilm formation. Some PP form protein-polyphenol aggregates that strengthen the pellicle of the tooth and support the afore-mentioned mechanisms. PP thus enrich proteins with potential protective mechanisms against tooth decay and erosion (37). Dietary PP have been shown to effectively reduce gingival bleeding as well as alveolar bone loss by suppressing osteoclastogenesis and inhibiting inflammatory cytokines (38). Therefore, some PP can counter the most common diseases of the oral cavity and are also involved in the prevention of oral cavity cancer (39).

Despite the above-mentioned biological effects, PP are not given particular attention in most nutritional recommendations. Regular and abundant intake of polyphenolic substances is desirable for maintaining good health. The goal of this study is to describe the trend of consumption of these phytochemicals in the Czech Republic over the past few decades. Relevant resources cover the last 30 years, although data on food consumption were collected in former Czechoslovakia from the 1950s. Unfortunately, the oldest available data do not contain all the items needed for a correct calculation; therefore, we present the development in the last three decades.

MATERIALS AND METHODS

Data from the Phenol-Explorer 3.6 (PE) (40), a specialized database of polyphenolic substances containing thousands of chemical individuals divided according to occurrence in primarily plant sources, including honey as well as non-alcoholic and alcoholic beverages, were assigned to the data of the Czech Statistical Office (CSO) on the consumption of food and beverages in the Czech Republic for the years 1989–2022. The average daily intake of PP was determined by multiplying the average annual consumption of each type of food (from CSO) by the PP content obtained from the PE database and by the coefficient from extensive model. Results were given in mg PP/inhabitant and day. Because the food groups in the CSO and PE databases are not identical – for example, one food group in the CSO data corresponds to several plant species (subtypes of food) in the PE database – it was necessary to create an extensive model which considered the proportions of individual subtypes in plant species listed in Czech consumption. For example, one item of soy in the statistical records corresponds to 20 subtypes and products from soy in PE. For each plant species (from PE database), the extensive model assigns a coefficient reflecting its popularity – the market share of corresponding food in annual consumption (from CSO). Available resources or current market research conducted by the authors of the article were used to create this model. The method itself is not suitable for determining

the exact value of PP consumption, as it summarizes the particular chemical individual listed in PE. On the other hand, PE contains items summarizing the occurrence of PP in the food, e.g., total polyphenols, which had to be deliberately excluded from the calculation in order to avoid duplication or overestimation of PP intake. When all individual PP in one type of food are added, the resulting sum is always lower than the value of total polyphenols for this food. We believe that the calculated PP consumption per inhabitant per day is significantly underestimated compared to reality. Another inaccuracy of the method lies in the extensive model of constant food subtypes proportions which does not consider the gradually improving availability of more exotic and rare food products over the years, owing to the fact that data on the market share of all 350 subtypes of food and beverages listed in PE related to the past 30 years of the Czech market for each year separately are unavailable. Therefore, the model of food subtypes remains constant for the calculation, and the PP intake trend primarily reflects only the consumption of food and beverages, not the gradually improving availability of special items. The other inaccuracy lies in the distortion that, according to the CSO's methodology, the average consumption of the population is related to the total number of inhabitants, including children and the elderly whose consumption varies. The last inaccuracy is the heterogeneity of data on concentrations in PE pertaining to one chemical individual, it led us to operate with the average concentration of the active substance from several studies, which also provided data on lower and upper limits. For example, the average concentration of quercetin in strawberry is 0.54 mg/100 g, the maximum is 1 mg/100 g and the minimum is 0.3 mg/100 g. Put another way, the actual value can be in fact even many times lower or higher than the average concentration. Furthermore, PP values in foods fluctuate as a result of climate, soil, ripeness, processing, and storage (41). The authors of Phenol-Explorer have already factored and calculated these influences into their average, and we have adopted it. Both, the food subtypes model (extensive model) and the average concentration of active substances remain constant in the calculation. The calculation summarizes 7,020 items in 350 food types from PE applied to 65 foods and beverages in Czech consumption statistics.

RESULTS

The resulting trend in the consumption of polyphenolic substances is shown in Figure 1.

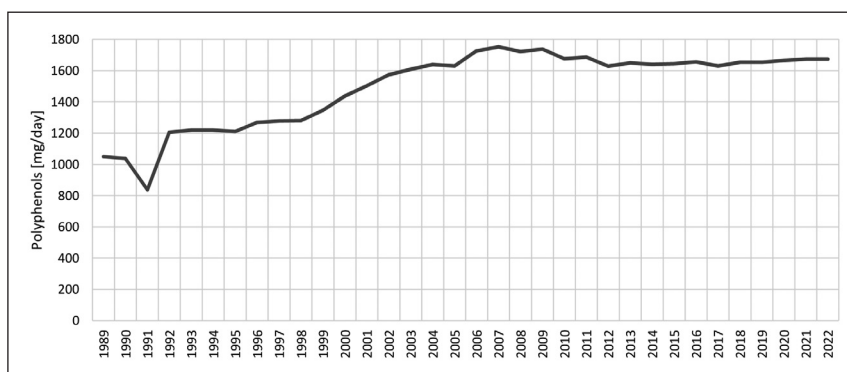


Fig. 1. Trend of daily intake of PP in mg/day per 1 inhabitant in the Czech Republic.

A favourable increase in the PP intake that can be seen from 1989 to 2007, which almost doubled compared to initial intake, is currently replaced by the opposite trend. Since 2007, we have observed a slight decreasing tendency in PP consumption. The current intake of PP thus corresponds to the value reached around 2004; it is now 5% lower than the maximum from 2007.

The main two most represented groups of PP are flavonoids and phenolic acids. These groups are also the most representative of the health effects mentioned in the introductory section. In the group of flavonoids, the first two places are occupied by flavanols contained primarily in drinks such as coffee and tea, followed by anthocyanins mainly from fruits. The group of phenolic acids is dominated by hydroxycinnamic acids, which are abundant in all monitored food and beverage groups (starting with coffee) and spices. Biologically important stilbenes, the main of which is resveratrol, contribute to the total intake of polyphenols in the Czech Republic by only one per mille, they are found in red wine, but the lingonberry and European cranberry is also a rich source as a non-alcoholic source. Lignans were ahead of stilbenes mainly due to their presence in edible oils. Among PP substances, hydroxycinnamic acids (from the group of phenolic acids) are consumed most frequently, followed by flavanols (from the group of flavonoids). Complete overview is shown in Figures 2 and 3.

From the first group, it is primarily ferulic acid and caffeoyl-quinic acid; from the group of flavanols, epicatechin and catechin are the most common.

Flavanols, anthocyanins, flavones, flavanols, and flavanones are included among flavonoids. Hydroxycinnamic acids and hydroxybenzoic acids together with hydroxyphenylacetic acids

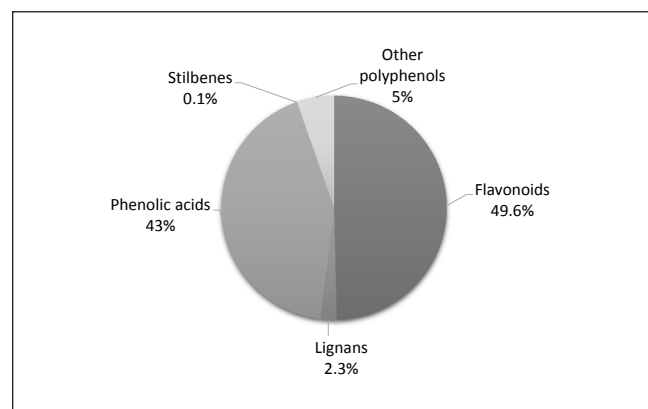


Fig. 2. Proportions of the main PP groups consumed in the Czech Republic.

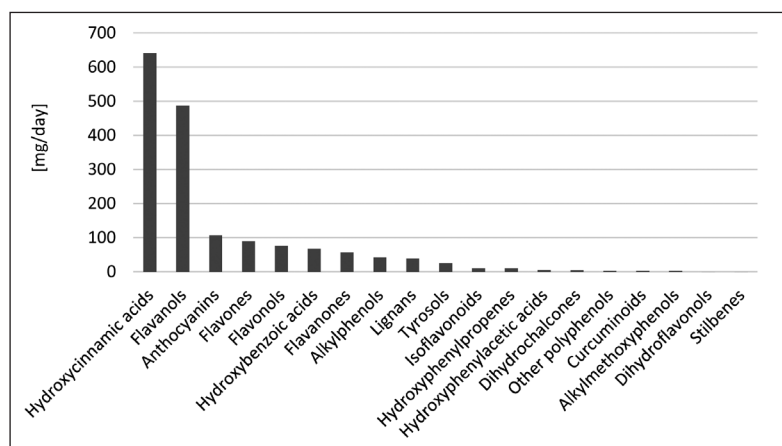


Fig. 3. Most common polyphenolic substances in daily intake.

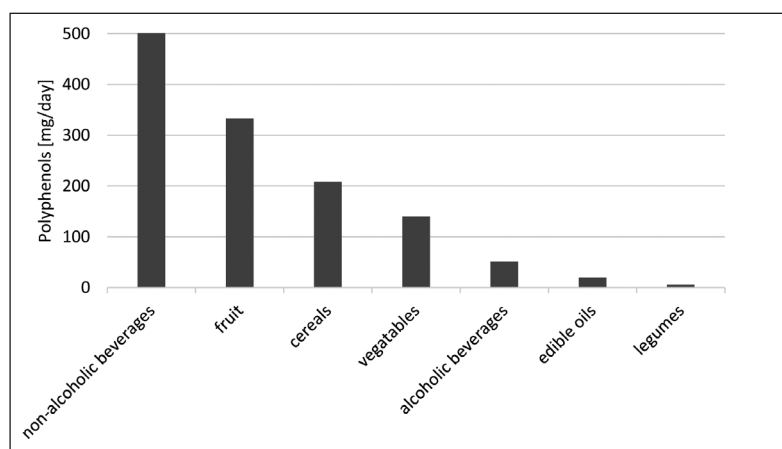


Fig. 4. Most frequent PP sources consumed by the Czech population.

are included in phenolic acids. Alkyl- and methoxy-phenols, alkylphenols, tyrosols, and curcuminoids are grouped under heading “other polyphenols”. Lignans form a separate group, as do stilbenes.

Among foods (Fig. 4), non-alcoholic beverages – coffee and tea – contribute the most to PP intake. As expected, fruit ranked second, followed by cereals and cereal products. Vegetables ranked fourth, followed by alcoholic beverages, edible oils and legumes.

DISCUSSION

Current slightly decreasing trend in PP consumption of the Czech population since 2008, especially when facing deterioration of socioeconomic situation requiring increased adaptability, is considered unfavourable. However, the modest rise in PP intake seen in the last few years is promising. The current value of PP intake of 1,673 mg per day per inhabitant cannot be considered accurate or comparable with other countries due to the shortcomings of the method described in the methodology section. Considering the methodological underestimation, it can be assumed that the real average intake of PP in the Czech Republic is in fact higher.

The method is suitable for determining foods that are sources of PP and their relative contribution to the total PP intake. As

can be seen from Figures 3 and 4, non-alcoholic beverages, dominated by coffee and tea, contribute the most to PP intake, while the proportion related to alcoholic beverages, on the other hand, is low despite the traditionally high consumption in the Czech Republic, which typically has third to fourth highest per capita alcohol intake from OECD countries (42). This is mainly due to the consumption of beer – eight times higher than wine in the Czech Republic – which is low in PP content. The intake of vegetables or fruits per person in kg is about the same, but fruits provide more PP. Cereals are consumed by Czechs about 30% more than fruits or vegetables, which is why they have ranked between fruits and vegetables as an important source of PP. Although it would be recommended to increase the consumption of red wine, due to the high representation of PP including stilbenes such as resveratrol, further consumption of alcoholic beverages or replacing beer with wine cannot be recommended, as the WHO does not consider any dose of alcohol to be safe (43).

CONCLUSION

Polyphenolic substances have several multisystemic effects that can be exploited at a low cost to promote population health and to improve markers of various diseases and health status in general. The favourable increase in dietary PP intake in the Czech

population – doubling, to be precise – which we observed from 1989 to 2007, has been replaced by the opposite trend in the last 15 years. The current intake of PP corresponds to the level that was achieved in 2004; it is lower than the maximum from 2007 by 5%. The decreasing tendency in the intake of polyphenolic substances lasting since 2008 is indisputably negative. Therefore, it is necessary to promote the availability and dietary intake of phytochemicals, especially those contained in vegetables, which ranked as the 4th most frequent source of PP, despite the generally acknowledged health benefits. Similarly, it is advisable to promote the consumption of fruit and to maintain a significant proportion of non-alcoholic beverages such as tea and coffee in the diet. By contrast, due to the adverse effects of alcohol and the high consumption of alcoholic beverages in the Czech Republic, we cannot recommend promotion of alcoholic beverages in agreement with the WHO.

Acknowledgement

This research was funded by the Cooperatio No. 207032 – Immunity and Infection; by the project No. CZ.02.1.01/0.0/0.0/17_048/0007267.

Conflicts of Interest

None declared

REFERENCES

- Rathod NB, Elabed N, Punia S, Ozogul F, Kim SK, Rocha JM. Recent developments in polyphenol applications on human health: a review with current knowledge. *Plants*. 2023 Mar;12(6):1217. doi: 10.3390/plants12061217.
- Rana A, Samtiya M, Dhewa T, Mishra V, Aluko RE. Health benefits of polyphenols: a concise review. *J Food Biochem*. 2022 Oct 1;46(10):e14264. doi: 10.1111/jfbc.14264.
- Shahidi F, Ambigaipalan P. Phenolics and polyphenolics in foods, beverages and spices: antioxidant activity and health effects – a review. *J Funct Foods*. 2015 Oct 1;18:820-97.
- Carrizzo A, Forte M, Damato A, Trimarco V, Salzano F, Bartolo M, et al. Antioxidant effects of resveratrol in cardiovascular, cerebral and metabolic diseases. *Food Chem Toxicol*. 2013 Nov 1;61:215-26.
- Del Rio D, Rodriguez-Mateos A, Spencer JPE, Tognolini M, Borges G, Crozier A. Dietary (poly)phenolics in human health: Structures, bioavailability, and evidence of protective effects against chronic diseases. *Antioxidants Redox Signal*. 2013 May 10;18(14):1818-92.
- Abbaszadeh H, Keikhaei B, Mottaghi S. A review of molecular mechanisms involved in anticancer and antiangiogenic effects of natural polyphenolic compounds. *Phyther Res*. 2019 Aug 1;33(8):2002-14.
- GBD 2017 Mortality Collaborators. Global, regional, and national age-sex-specific mortality and life expectancy, 1950–2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet*. 2018 Nov 10;392(10159):1684-735.
- Iranshahy M, Iranshahi M, Abtahi SR, Karimi G. The role of nuclear factor erythroid 2-related factor 2 in hepatoprotective activity of natural products: a review. *Food Chem Toxicol*. 2018 Oct 1;120:261-76.
- Rahman I, Biswas SK, Kirkham PA. Regulation of inflammation and redox signaling by dietary polyphenols. *Biochem Pharmacol*. 2006 Nov 30;72(11):1439-52.
- Vitale M, Vaccaro O, Masulli M, Bonora E, Del Prato S, Giorda CB, et al. Polyphenol intake and cardiovascular risk factors in a population with type 2 diabetes: The TOSCA.IT study. *Clin Nutr*. 2017 Dec 1;36(6):1686-92.
- Yu W, Tao M, Zhao Y, Hu X, Wang M. 4'-Methoxyresveratrol Alleviated AGE-Induced Inflammation via RAGE-Mediated NF- κ B and NLRP3 Inflammasome Pathway. *Molecules*. 2018 Jun 14;23(6):1447. doi: 10.3390/molecules23061447.
- Callcott ET, Thompson K, Oli P, Blanchard CL, Santhakumar AB. Coloured rice-derived polyphenols reduce lipid peroxidation and pro-inflammatory cytokines ex vivo. *Food Funct*. 2018 Oct 17;9(10):5169-75.
- Medina-Remón A, Casas R, Tresserra-Rimbau A, Ros E, Martínez-González MA, Fitó M, et al. Polyphenol intake from a Mediterranean diet decreases inflammatory biomarkers related to atherosclerosis: a substudy of the PREDIMED trial. *Br J Clin Pharmacol*. 2017 Jan 1;83(1):114-28.
- Poti F, Santi D, Spaggiari G, Zimetti F, Zanotti I. Polyphenol health effects on cardiovascular and neurodegenerative disorders: a review and meta-analysis. *Int J Mol Sci*. 2019 Jan 16;20(2):351. doi: 10.3390/ijms20020351.
- Hurtubise J, McLellan K, Durr K, Onasanya O, Nwabuko D, Ndisang JF. The different facets of dyslipidemia and hypertension in atherosclerosis. *Curr Atheroscler Rep*. 2016 Dec;18(12):82. doi: 10.1007/s11883-016-0632-z.
- Sae-Tan S, Grove KA, Lambert JD. Weight control and prevention of metabolic syndrome by green tea. *Pharmacol Res*. 2011 Aug 1;64(2):146-54.
- Hirsova P, Kolouchova G, Dolezelova E, Cermanova J, Hyspler R, Kadova Z, et al. Epigallocatechin gallate enhances biliary cholesterol secretion in healthy rats and lowers plasma and liver cholesterol in ethinylestradiol-treated rats. *Eur J Pharmacol*. 2012 Sep 15;691(1-3):38-45.
- Dash S, Xiao C, Morgantini C, Szeto L, Lewis GF. High-dose resveratrol treatment for 2 weeks inhibits intestinal and hepatic lipoprotein production in overweight/obese men. *Arterioscler Thromb Vasc Biol*. 2013 Dec;33(12):2895-901.
- Fisher ND, Hughes M, Gerhard-Herman M, Hollenberg NK. Flavanol-rich cocoa induces nitric-oxide-dependent vasodilation in healthy humans. *J Hypertens*. 2003;21(12):2281-6.
- Leikert JF, Räthel TR, Wohlfart P, Cheynier V, Vollmar AM, Dirsch VM. Red wine polyphenols enhance endothelial nitric oxide synthase expression and subsequent nitric oxide release from endothelial cells. *Circulation*. 2002 Sep 24;106(13):1614-7.
- Taubert D, Roesen R, Lehmann C, Jung N, Schömig E. Effects of low habitual cocoa intake on blood pressure and bioactive nitric oxide: a randomized controlled trial. *JAMA*. 2007 Jul 4;298(1):49-60.
- Zhang X, Song X, Hu X, Chen F, Ma C. Health benefits of proanthocyanidins linking with gastrointestinal modulation: an updated review. *Food Chem*. 2023 Mar 15;404(Pt A):134596. doi: 10.1016/j.foodchem.2022.134596.
- Das T, Chatterjee N, Capanoglu E, Lorenzo JM, Das AK, Dhar P. The synergistic ramification of insoluble dietary fiber and associated non-extractable polyphenols on gut microbial population escorting alleviation of lifestyle diseases. *Food Chem X*. 2023 May 2;18:100697. doi: 10.1016/j.fochx.2023.100697.
- Hanhineva K, Törrönen R, Bondia-Pons I, Pekkinen J, Kolehmainen M, Mykkänen H, et al. Impact of dietary polyphenols on carbohydrate metabolism. *Int J Mol Sci*. 2010 Mar 31;11(4):1365-402.
- Rienks J, Barbaresco J, Oluwagbemigun K, Schmid M, Nöthlings U. Polyphenol exposure and risk of type 2 diabetes: dose-response meta-analyses and systematic review of prospective cohort studies. *Am J Clin Nutr*. 2018 Jul 1;108(1):49-61.
- Conteduca V, Sansonno D, Russi S, Dammacco F. Precancerous colorectal lesions (review). *Int J Oncol*. 2013 Oct;43(4):973-84.
- Zhiqiang F, Jie C, Yuqiang N, Chenghua G, Hong W, Zheng S, et al. Analysis of population-based colorectal cancer screening in Guangzhou, 2011–2015. *Cancer Med*. 2019 May 1;8(5):2496-502.
- Ma F, Lin Y, Ni Z, Chen T, Wang X. Therapeutic effects of natural polyphenols on colorectal adenomas: focus on preclinical studies (review). *Oncol Rep*. 2023 Jun;49(6):112. doi: 10.3892/or.2023.8549.
- Lin K, Li Y, Toit ED, Wendt L, Sun J. Effects of polyphenol supplementations on improving depression, anxiety, and quality of life in patients with depression. *Front Psychiatry*. 2021 Nov 8;12:765485. doi: 10.3389/fpsy.2021.765485.
- Ammar A, Trabelsi K, Boukhris O, Bouaziz B, Müller P, Glenn JM, et al. Effects of polyphenol-rich interventions on cognition and brain health in healthy young and middle-aged adults: systematic review and meta-analysis. *J Clin Med*. 2020 May 25;9(5):1598. doi: 10.3390/jcm9051598.
- Guinane CM, Cotter PD. Role of the gut microbiota in health and chronic gastrointestinal disease: understanding a hidden metabolic organ. *Therap Adv Gastroenterol*. 2013 Jul;6(4):295-308.
- Valdes AM, Walter J, Segal E, Spector TD. Role of the gut microbiota in nutrition and health. *BMJ*. 2018 Jun 13;361(Supp1):36-44.
- Negi S, Das DK, Pahari S, Nadeem S, Agrewala JN. Potential role of gut microbiota in induction and regulation of innate immune memory. *Front Immunol*. 2019 Oct 25;10:2441. doi: 10.3389/fimmu.2019.02441.
- Zheng D, Liwinski T, Elinav E. Interaction between microbiota and immunity in health and disease. *Cell Res*. 2020 Jun;30(6):492-506.

35. Yamauchi T, Koyama N, Hirai A, Suganuma H, Suzuki S, Murashita K, et al. Definition of a dietary pattern expressing the intake of vegetables and fruits and its association with intestinal microbiota. *Nutrients*. 2023 Apr 27;15(9):2104. doi: 10.3390/nu15092104.
36. Kwon C, Ediriweera MK, Kim Cho S. Interplay between phytochemicals and the colonic microbiota. *Nutrients*. 2023 Apr 20;15(8):1989. doi: 10.3390/nu15081989.
37. Flemming J, Meyer-Probst CT, Speer K, Kölling-Speer I, Hannig C, Hannig M. Preventive applications of polyphenols in dentistry-a review. *Int J Mol Sci*. 2021 May 5;22(9):4892. doi: 10.3390/ijms22094892.
38. Basu A, Masek E, Ebersole JL. Dietary polyphenols and periodontitis-a mini-review of literature. *Molecules*. 2018 Jul 20;23(7):1786. doi: 10.3390/molecules23071786.
39. Varoni EM, Lodi G, Sardella A, Carrassi A, Iriti M. Plant polyphenols and oral health: old phytochemicals for new fields. *Curr Med Chem*. 2012;19(11):1706-20.
40. Rothwell JA, Pérez-Jiménez J, Neveu V, Medina-Ramon A, M'Hiri N, Garcia Lobato P, et al. Database on polyphenol content in foods - Phenol-Explorer [Internet]. Paris: INRAE; 2015 [cited 2023 May 24]. Available from: <http://phenol-explorer.eu/>.
41. Spencer JP, Abd El Mohsen MM, Minihafe AM, Mathers JC. Biomarkers of the intake of dietary polyphenols: strengths, limitations and application in nutrition research. *Br J Nutr*. 2008 Jan;99(1):12-22.
42. OECD. Health at a Glance 2021: OECD Indicators [Internet]. Paris: OECD Publishing; 2021 [cited 2024 Jun 12]. Available from: https://www.oecd-ilibrary.org/social-issues-migration-health/health-at-a-glance-2021_ae3016b9-en.
43. WHO Regional Office for Europe. No level of alcohol consumption is safe for our health [Internet]. Copenhagen: WHO Regional Office for Europe; 2023 [cited 2023 Jun 14]. Available from: <https://www.who.int/europe/news/item/04-01-2023-no-level-of-alcohol-consumption-is-safe-for-our-health>.

Received July 28, 2023

Accepted in revised form June 14, 2024