Proceedings of the Nutrition Society (2023), **82 (OCE2)**, E118 doi:10.1017/S0029665123001271

46th Annual Scientific Meeting of the Nutrition Society of Australia, 29 November – 2 December 2022, Sustainable nutrition for a healthy life

Polyphenols and depression: exploring the potential mechanisms of action

E. Gamage[1], M.M. Lane[1], N. Travica[1], F. Jacka[1], R. Orr[1] and W. Marx[1]
[1]*Food & Mood Centre, The Institute for Mental and Physical Health and Clinical Translation (IMPACT), School of Medicine, Deakin University, Geelong, Vic., Australia*

Polyphenols are compounds synthesised exclusively in plants, of which more than 8,000 structural variants have been identified. Dietary polyphenol intake is associated with a reduced risk of chronic illnesses including cardiovascular diseases, type 2 diabetes, some forms of cancer and neurological diseases. Due to their ability to modulate relevant pathophysiological pathways, dietary polyphenols have more recently been suggested to lower the risk of depression diagnosis or depressive symptoms.[(1)] Indeed, observational studies have demonstrated that dietary polyphenol intake is associated with reduced depression risk,[(2)] while interventional studies have reported that polyphenols may decrease depressive symptoms.[(3)] However, mechanistic data supporting polyphenols' possible antidepressant effects have not been extensively synthesised. Hence, the aim of this review was to provide a synthesis of the available evidence exploring polyphenols' mechanisms of action in reducing the risk of depression diagnosis or depressive symptoms. This review includes a systematic search strategy conducted using a series of databases including PubMed, EMBASE, The Cochrane Library (Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials (CENTRAL), Cochrane Methodology Register), CINAHL, PsycINFO. Eligible articles include animal, observational, and intervention studies, as well as systematic reviews and meta-analyses of human studies. Polyphenol metabolites are thought to target several pathways implicated in depression, including inflammation, oxidative stress, hypothalamic–pituitary–adrenal axis, neurogenesis, and the kynurenine pathway. Synthesis of animal studies suggests that polyphenol interventions reduce depressive-like behaviours and affect these pathophysiological pathways by: 1) reducing circulating and brain concentrations of pro-inflammatory mediators; 2) acting as indirect antioxidants, thereby reducing oxidative stress; 3) regulating the hypothalamic–pituitary–adrenal axis via the reduction of circulating glucocorticoids; 4) promoting hippocampal neurogenesis; 5) enhancing brain-derived neurotrophic factor; 6) decreasing the kynurenine to tryptophan ratio; and, 7) shifting production from neurotoxic metabolites towards neuroprotective metabolites along the kynurenine pathway. Furthermore, while human mechanistic data are limited, polyphenol intake has been shown to improve mood and enhance circulating brain-derived neurotrophic factor and to reduce salivary cortisol concentrations. Polyphenol's potential mechanisms of action that underly the antidepressant potential of polyphenols have extensively been explored in animal studies while, human studies are lacking. Furthermore, although these animal studies provide preliminary evidence for the possible mechanisms of action, their results may not necessarily be translatable or generalisable to humans. Hence, more observational, specifically longitudinal, studies and interventional studies that specifically target pathways and biomarkers of depression, are required to better understand polyphenols' relevant mechanisms of action in humans. Such information may further support novel dietary interventions for the prevention and treatment of depression.

References

1. Morris G, Gamage E, Travica N, *et al.* (2021) *Free Radic Biol Med* **172**, 101–122.
2. Godos J, Castellano S, Ray S, *et al.* (2018) *Molecules* **5**, 23.
3. Fusar-Poli L, Vozza L, Gabbiadini A, *et al.* (2020) *Crit Rev Food Sci Nutr* **15**, 2643–2653.

Proceedings of the Nutrition Society

https://doi.org/10.1017/S0029665123001271 Published online by Cambridge University Press