Proceedings of the Nutrition Society (2024), **83 (OCE1)**, E134 doi:10.1017/S0029665124001526

47th Annual Scientific Meeting of the Nutrition Society of Australia and Nutrition Society of New Zealand, 28 November – 1 December 2023, Nutrition & Wellbeing in Oceania

Effect of dietary polyphenols on chronobiology in mammalian cells in vitro

N. Sulaimani[1,2], M.J. Houghton[1,2], M.P. Bonham[1] and G. Williamson[1,2]
[1]*Department of Nutrition, Dietetics and Food, Monash University, Notting Hill, 3168, Australia*
[2]*Victorian Heart Institute, Monash University, Clayton, 3168, Australia*

Circadian clocks play a key role in metabolic homeostasis, and disruption of circadian rhythms is inextricably intertwined with metabolic disorders [1]. Emerging evidence in the literature suggests that polyphenols possess the potential to modulate metabolic processes associated with circadian rhythms. This review aims to evaluate the effects of polyphenols on metabolic homeostasis via circadian rhythms and their potential mechanism(s) of action on circadian rhythmicity of clock components and linked metabolic processes, by critically assessing the literature on mammalian cells *in vitro*. To ensure that all relevant studies in this area were included, a systematic search protocol was developed by defining the inclusion and exclusion criteria based on the population, intervention, comparator and outcome framework, along with limiting the source of evidence to original research written in English. Three databases (Ovid Medline, Web of Science, and Scopus) were searched with no time constraints. The search identified 5842 studies and, after duplicate removal and initial screening, 48 studies were reviewed in full. Of those, 38 were eligible for inclusion. The included studies were published between 2008-2023, with a notable surge in publications after 2016, which is indicative of the growing attention towards polyphenols and circadian biology. 33 polyphenols were examined for their effects on circadian cellular processes (n = 16 papers), expression of clock genes and/or proteins (n = 26), or circadian rhythm features of clock genes (n = 10). A handful of studies examined the role of polyphenols in regulating disrupted glucose and lipid metabolism through clock components. The findings suggested that the underlying mechanisms were BMAL1-dependent. It must be noted that the effects of the reported polyphenols were elucidated at concentrations exceeding the normal range found in human plasma and target tissues (⊠ 10 μM). However, a single study revealed that (−)-epigallocatechin-3-gallate (EGCG) at a physiologically-relevant concentration (10 μM), improved hepatic glucose metabolism [2]. Further, the polyphenols reported in this review exhibited the potential to influence numerous clock components, mainly BMAL1, PER2 and RORα/γ, at mRNA and/or protein levels when administered at physiologically-relevant concentrations. These polyphenols include nobiletin, tangeretin, curcumin, bavachalcone, cinnamic acid, (−)-epigallocatechin-3-gallate, resveratrol and Urolithin A. Polyphenols have the potential to regulate circadian oscillators and associated metabolic processes in various types of cells. However, there is significant methodological heterogeneity among the studies, which makes it difficult to compare outcomes. Thus, this review will help future research in the field of circadian impacts of polyphenols to integrate standardised approaches, in aspects such as utilisation of a synchronisation method and physiologically-relevant concentrations of polyphenols (≤ 10 μM) in cultured cells. This is critical for understanding how polyphenols might modulate circadian-metabolic health in humans.

Keywords: flavonoid; circadian rhythms; metabolism; clock genes

Ethics Declaration

Yes

Financial Support

King Abdulaziz University PhD scholarship.

References

1. Poggiogalle E, Jamshed H & Peterson CM (2018) *Metabolism* **84**, 11–27.
2. Mi Y *et al.* (2017) *Mol Nutr Food Res* **61**(12), 1700440.