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REVIEW

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Polyphenols in obesity and weight management: Are they worth further research? An umbrella review

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Abstract
Polyphenols are widely known for their putative antioxidant and anti-inflammatory effects and their potential protective role in several diseases such as type 2 diabetes, cardiovascular disease and cancer. They have also attracted significant interest as 'anti-obesity' agents, although with mechanisms of action that have been exclusively demonstrated in animal and in vitro studies. This umbrella review aims to evaluate current evidence surrounding the role of polyphenols in obesity and weight management and to establish the usefulness of these agents in combatting obesity. A search of systematic reviews and meta-analyses of randomised controlled trials was carried out. Nine systematic reviews (of which eight included a meta-analysis) were included. Evidence of polyphenols' effects on reducing bodyweight is mixed, and where the effects are significant, they are numerically small and unlikely to be of help in reducing bodyweight or preventing weight gain. Future research should focus on establishing the anti-inflammatory and antioxidant effects of polyphenols through well-designed randomised controlled trials. Such research could be more valuable and cost-effective since it has shown potential to improve human health.

KEYWORDS
obesity, polyphenols, weight loss, weight management

INTRODUCTION

Research on polyphenols and their beneficial health effects remains a hot topic, attracting a great deal of interest in various disciplines. These phytochemicals, which are abundantly available in a variety of commonly consumed foods (such as chocolate, tea, coffee, wine, olive, apples, pomegranate and berries) (D'Archivio et al., 2007; Manach et al., 2004; Newman et al., 2007), have been reported to exert antioxidant and anti-inflammatory roles that could help in the prevention and management of cardiovascular diseases, hypertension, type 2 diabetes, cancer and neurodegenerative diseases (D'Archivio et al., 2007; Manach et al., 2004; Michalska et al., 2010; Serban et al., 2015).

Although the preventative and therapeutic effects of polyphenols have been reported in thousands of in vitro and in vivo studies, a causal association between polyphenols and health has not been yet established. This is primarily due to the lack of well-designed randomised controlled trials (RCTs) as well as the significant heterogeneity which affects direct comparison between studies; studies on polyphenols greatly vary in design, duration, population (including health state and co-morbidities), dosage and formulation of polyphenol (e.g. capsule, juice or in food) (Jennings et al., 2021; Rajha et al., 2022). Additionally, the favourable effects of polyphenols are greatly affected by interindividual differences in absorption and metabolism which makes it difficult to generalise their health effects (Zhang et al., 2022). The composition of the gut microbiome is thought to partly explain this variability and the interaction between polyphenols and gut bacteria was suggested as a crucial determinant of the health benefits of polyphenols (Jennings et al., 2021; Ramos-Romero et al., 2021). Genetic polymorphisms have been reported to further affect this association (Miller et al., 2012).

The role of polyphenols in obesity and weight management has drawn both media and research interest, with polyphenols being labelled as 'anti-obesity' agents (Boccellino & D'Angelo, 2020; Lin & Lin-Shiau, 2006) capable of reducing weight and helping in the prevention and management of obesity. Observational studies in humans have predominantly indicated a negative correlation between polyphenol consumption and weight status (Aali et al., 2022; Adriouch et al., 2018; Grosso et al., 2017). Polyphenols such as catechins, anthocyanins, curcumin and resveratrol have been suggested to exert beneficial effects on lipid and energy metabolism (Meydani & Hasan, 2010; Min et al., 2013) and potentially on weight status. The proposed mechanisms of action have been mostly shown in animal and in vitro studies and included inhibition of the differentiation of adipocytes (Min et al., 2013), increase in fatty acid oxidation (Dulloo et al., 1999), decrease in fatty acid synthesis (Matsui et al., 2005), increase in thermogenesis and energy expenditure (Nagao et al., 2007), inhibition of digestive enzymes (Gu et al., 2011) and attenuation of the disruption of the composition of the gut microbiome noted in people with obesity (Duarte et al., 2021; Yen et al., 2020).

Nevertheless, the existing body of evidence regarding the impact of polyphenols on weight status in humans lacks robustness. In a previous systematic review of intervention studies looking at the effect of polyphenols on weight, we reported that the effects of polyphenols on obesity remain inconclusive (Farhat et al., 2017). In light of this, this review aims to evaluate more recent evidence derived from systematic reviews and meta-analyses of RCTs examining the effects of polyphenols on obesity and weight loss to see whether the evidence has strengthened.

METHODS

A search of the literature review was carried out in September 2023 and included PubMed, Scopus and Medline (EbscoHost) using combinations of the following keywords: polyphenols AND bodyweight OR overweight OR obesity OR BMI. The inclusion criteria consisted of systematic reviews and meta-analyses of human RCTs published between 2018 and 2023 in the English language. Reviews on polyphenols as a complementary approach to exercise and/or low-calorie diet were excluded. Systematic reviews including animal studies were also excluded. Main outcomes included indicators of weight status (e.g. bodyweight, BMI and waist circumference). The methodological quality of the systematic reviews was assessed using the AMSTAR 2 checklist, a critical appraisal tool to assess the quality of systematic reviews (Shea et al., 2017). The overall rating in the confidence of results was assessed as high, moderate, low and critically low, as indicated by Shea et al. (2017).

RESULTS

Fourteen systematic reviews were assessed for eligibility, and five of them were excluded due to their lack of examination of any outcomes related to weight status. The search identified nine eligible systematic reviews; eight of which carried out a meta-analysis. Characteristics of the studies are presented in Table 1. The meta-analyses included studies on healthy populations as well as on populations with different co-morbidities (notably obesity, type 2 diabetes and nonalcoholic fatty liver disease). Three reviews looked at resveratrol, two at green coffee extract, one each at green tea, pomegranate, blueberry or bilberry and one at multiple interventions. Studies lasted between 1 and 52 weeks.

Meta-analysis on resveratrol showed the most promising results with two out of three meta-analyses reporting a small but significant decrease in weight ([−0.17 kg {95% CI: −0.33, −0.01}, $p = 0.03$] and [−0.51 kg, {95% CI: −0.94, −0.09}, $p = 0.02$]) (Mousavi et al., 2019; Tabrizi et al., 2020). Pomegranate supplementation (in juice, extract and vinegar) and blueberry extract did not report a significant effect on weight status in the meta-analyses of Gheflati et al. (2019) and De Oliveira et al. (2022), respectively. Meta-analyses on green coffee extract also showed inconsistent results (Asbaghi et al., 2020; Gorji et al., 2019), while green tea reported the largest decrease in weight among different polyphenols-rich constituents (−1.78 kg [95% CI: −2.8, −0.75], $p = 0.001$) (Lin et al., 2020). Meta-analysis including multiple polyphenols subtypes reported a small but significant effect on weight (−0.36 kg [95% CI: −0.68, −0.05], $p = 0.02$) (Zhang et al., 2023).

Assessment of the methodological quality of reviews using the AMSTAR 2 checklist showed that the majority of systematic reviews adequately reported research questions, inclusion criteria and outcomes (items 1 & 11) and assessed risk of bias (item 9). However, most reviews did not account for the risk of bias when interpreting and discussing results (item 13) (Figure 1). The overall interpretation of the confidence in results ranged from low to high with five reviews scoring high, one review scoring moderate and three reviews scoring low (Table 1).

DISCUSSION

This umbrella review aims to evaluate current evidence surrounding the effects of polyphenols on obesity and weight loss by looking at evidence from systematic reviews and meta-analyses published since 2018. The purpose is to determine whether there is a justification

TABLE 1 Characteristics of systematic reviews included in the review.

Study/characteristics/duration	Polyphenol/food type	Population conditions	Main outcomes	Overall rating of the confidence in results[a]
Tabrizi et al. (2020)/meta-analysis of 36 RCTs/1–48 weeks	Resveratrol (extract) (8–3000 mg/day)	Healthy adults, overweight & obesity, metabolic syndrome, NAFLD, hypertension, T2DM, heart disease, schizophrenia	Bodyweight (−0.17 kg [95% CI: −0.33, −0.01], $p = 0.03$) BMI (−0.2 kg/m^2 [95% CI: −0.35, −0.05], $p = 0.01$) Waist circumference (−0.42 cm [95% CI: −0.68, −0.16], $p = 0.001$)	Moderate
Delpino et al. (2021)/meta-analysis of 19 RCTs/4–28 weeks	Resveratrol (extract) (40–3000 mg/day)	Overweight & obesity, metabolic syndrome, T2DM, NAFLD, impaired glucose tolerance	Bodyweight (0.03 kg [95% CI: −0.44, 0.49], $p > 0.05$) BMI (0.01 kg/m^2 [95% CI: −0.39, 0.41], $p > 0.05$) Waist circumference (−1.04 cm [95% CI: −1.81, −0.27], $p < 0.05$)	Low
Mousavi et al. (2019)/meta-analysis of 28 RCTs/4–52 weeks	Resveratrol (extract) (8–3000 mg/day)	Healthy, overweight and obesity, metabolic syndrome, PCOS, T2DM, NAFLD, Alzheimer's, schizophrenia	Bodyweight (−0.51 kg, [95% CI: −0.94 to −0.09], $p = 0.02$) BMI (−0.17 kg/m^2 [95% CI: −0.32, −0.03], $p = 0.02$) WC (−0.79 cm [95% CI: −1.39, −0.2], $p = 0.009$)	High
Gheflati et al. (2019)/meta-analysis of 13 RCTs/3–45 weeks	Pomegranate (juice and extract, concentrate, vinegar)	Healthy, overweight & obesity, athletes, NAFLD, metabolic syndrome, haemodialysis, heart disease, T2DM	Bodyweight (−0.23 kg [95% CI: −0.94, −0.47], $p = 0.51$) BMI (−0.12 kg/m^2 [95% CI: −0.29, −0.03], $p = 0.13$) WC (−0.08 cm [95% CI: −0.33, −0.17], $p = 0.53$)	High
Lin et al. (2020)/meta-analysis of 22 RCTs/2–12 weeks	Green tea (99–20 000 mg/day) (extract or drink)	Healthy, overweight and obesity, dyslipidaemia, metabolic syndrome, NAFLD, PCOS, prediabetes	Bodyweight (−1.78 kg [95% CI: −2.8, −0.75], $p = 0.001$) BMI (−0.65 kg/m^2 [95% CI: −1.04, −0.25], $p = 0.001$) WC (−1.5 cm [95% CI: −3.19, 0.18], $p = 0.08$)	High
Gorji et al. (2019)/meta-analysis of 16 RCTs/1–12 weeks	Green coffee extract (46–1000 mg/day)	Healthy, overweight & obesity, hypertension, metabolic syndrome, NAFLD, dyslipidaemia	Bodyweight (−0.59 kg [95% CI: −1.5, 0.33], $p = 0.21$) BMI (−0.4 kg/m^2 [95% CI: −0.8, −0.005], $p = 0.05$) WC (−0.85 cm [95% CI: −1.76, 0.07], $p = 0.07$)	High
Asbaghi et al. (2020)/meta-analysis of 12 RCTs/1–12 weeks	Green coffee bean extract (46–1000 mg/day)	Healthy, overweight & obesity, NAFLD, metabolic syndrome, impaired glucose tolerance, hypertension, dyslipidaemia	Bodyweight (−1.23 kg [95% CI: −1.64, −0.82 kg], $p < 0.001$) BMI (−0.48 kg/m^2 [95% CI: −0.78, −0.18], $p = 0.001$) WC (−1 cm [95% CI: −1.70, −0.29], $p = 0.006$)	High
Zhang et al. (2023)/meta-analysis of 38 RCTs/1–12 months	Multiple interventions (e.g. berry extract, soybean extract, tea, onion peel extract, resveratrol, curcumin)	Healthy, overweight & obesity, post-menopausal, dyslipidaemia, NAFLD	Bodyweight (−0.36 kg [95% CI: −0.68, −0.05], $p = 0.02$) BMI (−0.13 kg/m^2 [95% CI: −0.23, −0.03], $p = 0.01$) WC (−0.6 cm [95% CI: −1.01, −0.2], $p = 0.004$)	Low
De Oliveira et al. (2022)/review of 8 RCTs/1 day – 24 weeks	Blueberry or bilberry (22.5–400 g/day)	Metabolic syndrome, obesity, T2DM	No significant differences in bodyweight	Low

Note: Values represent mean post-intervention difference between intervention and control groups (95% CI).

Abbreviations: BMI, body mass index; NAFLD, nonalcoholic fatty liver disease; PCOS, polycystic ovary syndrome; RCTs, randomised clinical trials; T2DM, type 2 diabetes mellitus; WC, waist circumference.

[a]The overall rating in the confidence of results was assessed as high, moderate, low and critically low based on AMSTAR2 critical appraisal tool, as indicated by Shea et al. (2017).

FIGURE 1 Quality assessment of studies using AMSTAR2. Colours represent: green: yes; yellow: partial yes; red: no; grey: not applicable.

for carrying out further studies primarily aimed at establishing a link between polyphenols and obesity prevention and management. Research on polyphenols is very complex with around 8000 structures of polyphenols already identified (Asbaghi et al., 2020), and their health effects depend on the composition of the gut microbiome as well as host genetic polymorphisms (Zhang et al., 2022). Compiling evidence from meta-analyses is expected to potentially account for confounding factors and present a higher level of evidence compared to individual studies.

While supplementation with pomegranate or grape seed extract did not show significant effects on weight (Gheflati et al., 2019), three meta-analyses, one on resveratrol, one on green coffee extract and one on green tea, found that the mean post-intervention difference between intervention and control groups in weight was 0.51, 1.23 and 1.78 kg, respectively, (all $p < 0.05$) in studies of different durations. The meta-analysis that combined different types of polyphenols also reported a small decrease in weight (mean difference: −0.36 kg, $p = 0.02$) (Zhang et al., 2023), albeit it was further limited by the different subtypes of polyphenols included. These outcomes translate to around 1% weight loss and are particularly limited by the large confidence intervals reported in all meta-analyses. While even a small reduction in weight (e.g. 1% of weight) may exert some beneficial effects on cardiometabolic risk factors (Admiraal et al., 2013), it is unlikely to be of help in combatting obesity. Additionally, a clinically relevant decrease in weight constitutes 5% of weight loss (Ryan & Yockey, 2017), which will possibly not result from polyphenol supplementation. Green tea, shown to exert the largest effects on weight loss only led to small reductions in weight. Furthermore, it is worth mentioning that some forms of polyphenol supplementation (in food or juice) are also a source of calories which if added to the usual diet may not lead to weight loss; instead, they may lead to weight gain. For instance, in the systematic review conducted by Mousavi et al. (2019), subgroup analysis revealed a significant decrease in weight at a resveratrol dosage of 500 mg/day. To provide perspective, this amount is roughly equivalent to consuming 0.5–1.4 kg/day of fresh grapes, depending on the grape cultivars (Moriartry et al., 2001).

Although some high-quality meta-analyses reported a stronger effect of polyphenols on weight loss in overweight and obese participants (Gorji et al., 2019; Lin et al., 2020; Mousavi et al., 2019; Tabrizi et al., 2020), the difference remains numerically small and does not suggest BMI to be a crucial factor in generating clinically meaningful results. Based on this evidence, polyphenols could then be suggested as complementary approaches alongside a healthy/reduced-calorie diet and regular physical activity in the prevention and management of obesity.

In our previous systematic review, we reported that the effects of polyphenols on obesity remain inconclusive, suggesting that they may exert small effects on bodyweight due to their inhibitory effects on digestive enzymes (Farhat et al., 2017). Recent evidence suggests that further research has not added additional insights into the link between polyphenols on obesity. Planning large interventions to establish whether this association is causal will not likely be cost-effective considering the minimal likely effects on weight status. Moving forward, labelling certain polyphenols as 'anti-obesity' agents is far too stretched. With the promising results of polyphenols on inflammation and oxidative stress, further research elucidating their role is timely. Randomised controlled long-term trials considering the optimal doses of polyphenols while accounting for interindividual differences (e.g. age, gender, health status and metabolic differences) may be more effective in elucidating their effects on human health. Previous research is in line with this suggestion and proposed that quercetin (a subtype of polyphenol) is more effective as an antidiabetic agent than as an effective agent in the management of obesity (Arias et al., 2014). Although obesity represents a low-grade inflammation which increases reactive oxygen species (ROS) production (Skalicky et al., 2008), which constitutes a mechanism by which polyphenols could help to reduce weight, in a systematic review, polyphenols in blueberries decreased oxidative stress without affecting bodyweight (De Oliveira et al., 2022).

Limitations

This review presents limitations in relying on evidence from systematic reviews and meta-analyses that displayed a high degree of heterogeneity with regard to study duration, polyphenol type and dosage, gender, age, disease status as well as mode of administration (e.g. capsule, food, juice). Additionally, three reviews were assessed as exhibiting low confidence in results due to critical flaws and this could affect study rigour; it is however worth noting that these reviews reported little to no significant effects on weight status outcomes. Some studies included a combination of different compounds and not merely the polyphenol in question (e.g. resveratrol with epigallocatechin; Tabrizi et al., 2020). Additionally, reviews selected only considered weight as a primary outcome, while most studies investigating the effects of polyphenols on general health assessed weight status as a secondary outcome. However, this review was effective in compiling the most recent evidence linking polyphenols to obesity and providing future directions.

CONCLUSIONS

This umbrella review collates evidence which supports the view that the effects of certain types of polyphenols on obesity are small and do not warrant further research in this regard. Research focusing on the long-term antioxidant and anti-inflammatory activities of polyphenols may be more useful in establishing their effects on human health and ultimately for recommending the appropriate intakes of polyphenols (including type, dose and duration) for disease prevention and management.

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CONFLICT OF INTEREST STATEMENT

None.

DATA AVAILABILITY STATEMENT

None.

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