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LITERATURE REVIEW **Open Access**

The Role of Phenolic Compounds in Antioxidant Enhancement in Obese Individuals: A Systematic Literature Review

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ABSTRACT

Background: Chronic inflammation and oxidative stress are complications of obesity. Consuming phenolic compounds found in plant-based foods can reduce inflammation and oxidative stress. Phenolic compounds are phytochemicals with antioxidant properties that play an important role in health.
Objectives: This article aims to examine the role of phenolic compounds in obese individuals.
Methods: This article uses a literature review method with predetermined inclusion and exclusion criteria. Articles were searched for in several electronic databases, namely PubMed and Wiley Online Library.
Results: Phenolic compounds can reduce inflammation and oxidative stress through several mechanisms. One of these is that fermented flaxseed extract improves neural health and reduces obesity markers in experimental models. Polyphenolic compounds from pigmented rice effectively reduced lipid peroxidation and pro-inflammatory cytokines. The findings highlight the anti-adipogenic, anti-inflammatory, and metabolic regulation properties of phenolic compounds.
Conclusion: Phenolic compounds play an important role in reducing oxidative stress and inflammation in obesity. Their effectiveness varies depending on the source of the compounds, with promising results from pigmented rice, fermented black beans, and fermented flaxseed. However, most results are from in vitro or animal studies, so further clinical trials are needed to validate these benefits in humans.

Keywords: Antioxidant, Health and Well-Being, Obesity, Oxidative Stress, Phenolic Compounds

INTRODUCTION

Based on WHO data, degenerative diseases are the biggest cause of 73% of deaths in 2020 (Rakainsa, Widhihastuti and Efrilianda, 2023). Degenerative disease is a condition of disease occurrence caused by a decrease in cell function. Degenerative diseases or commonly referred to as non-communicable diseases, such as diabetes mellitus, hypertension, kidney failure disease, obesity, cardiovascular disease, stroke, and other diseases (Marwiati, Setyawati and Fahrurozi, 2022). In Indonesia, these diseases have increased from 2013 to 2018, with the largest disease incidence being heart disease, chronic renal failure disease, which increased by 1.8%, diabetes mellitus, cancer, which increased by 0.4%, obstructive pulmonary disease which increased by 2.1% and vascular diseases such as hypertension and stroke. Meanwhile, diabetes mellitus also reached 2% and stroke reached 10.9% in the population aged more than 15 years (Ministry of Health of the Republic of Indonesia, 2018).

One of the main factors contributing to the increased risk of degenerative diseases is obesity. In addition, the incidence of these diseases is also prevalent in the population aged more than 15 years, as evidenced by the increase in central obesity in the age of more than 15 years, from 26.6% in 2013 to 31% in 2018. Obesity is a growing health problem associated with several chronic diseases such as type

2 diabetes, heart disease, and several other metabolic syndromes. The Indonesian Health Survey (IHS) reported that by 2023, Indonesia will have a prevalence of obesity cases in the adult population of 23.4%. This percentage was higher than the 21.8% recorded in 2018 (Ministry of Health of the Republic of Indonesia, 2018).

Chronic inflammation and oxidative stress are the causes of obesity-related problems. According to Jha et al. (2023), these disorders impair general bodily functions and lower the quality of life for obese people. To lessen the detrimental effects of obesity, a variety of dietary techniques can be employed to lower oxidative stress and inflammation. Eating foods high in antioxidants is one efficient way to combat free radicals and lower inflammation in the body (Arulselvan et al., 2016).

Phenolic compounds are phytochemicals that have nearly 8000 molecules, including flavonoids, phenolic acids, stilbenes, and lignans (Mutha et al., 2021). Phenolic compounds also have antioxidant properties, enabling them to neutralize reactive oxygen species (ROS) and participate in inflammatory signaling (Saji et al., 2019; Qiu et al., 2021). They have shown greater stability and broader effects on oxidative and inflammatory markers, which are central in obesity-related complications. However, there are limited studies examining their mechanisms specifically in obese populations. Given the increasing number of individuals with obesity, investigating how phenolic compounds can help them is very important.

METHODS

This systematic review was written based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The Population, Intervention, Control and Outcome (PICO) questions used in this paper are: P (Population): obesity, I (Intervention): phenolic compounds, C (Control): none and O (Outcome): antioxidants (Wallace *et al.*, 2016). Oxidative stress is a key mechanism underlying obesity-related complications. Measuring antioxidant outcomes provides direct evidence of how phenolic compounds can modulate redox balance, which subsequently influences inflammation, insulin resistance, and metabolic disorders. Inclusion and exclusion criteria included articles that evaluated the content of phenolic compounds in rice, rice is one of the most consumed staple foods globally and a source of phenolic compounds, especially in its pigmented varieties—red, black, and purple rice. Pigmented rice is rich in anthocyanins and flavonoids, which have shown strong antioxidant and anti-inflammatory effects in previous studies, making it a relevant and accessible dietary source for populations at risk of obesity, assessed antioxidant effects and articles that involved participants with obesity or animal models of obesity. Articles will be excluded if they have inappropriate topics, are not published in English and Indonesian, are more than 10 years, are not available free full text, and not a randomised controlled trial type of research. Articles were searched in several electronic databases, including PubMed and Wiley Online Library. The keywords used in the search included: 'Phenolic compounds', "Antioxidant", "Obesity", and keyword combinations such as "phenolic compounds AND antioxidant AND obesity"

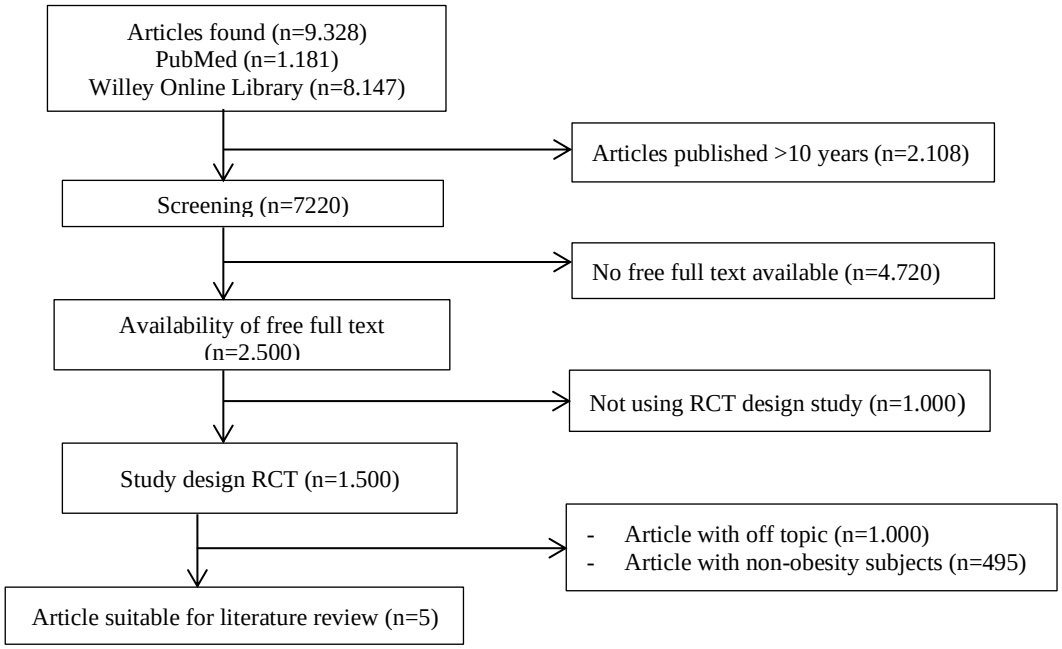

Figure 1. Literature Search Flowchart

RESULTS AND DISCUSSION

Table 1. Results of Article Review

Author	Title	Subject Criteria and Study Design	Intervention	Duration	Outcome
(de Vasconcelos *et al.*, 2022)	Extra virgin coconut oil (Cocos nucifera L.) exerts anti-obesity effect by modulating adiposity and improves hepatic lipid metabolism, leptin, and insulin resistance in diet-induced obese rats	Subjects: 32 male rats were randomly divided into four groups: healthy; healthy treated with E-VCO; obese; obese treated with E-VCO. Study Design: experimental study (in vivo)	Administration of Extra Virgin Coconut Oil (E-VCO)	16 weeks	Extra Virgin Coconut Oil (E-VCO) reduces fat mass, increases cholesterol excretion, and improves insulin resistance and inflammation in obesity.
(Rodrigues *et al.*, 2021)	Phenolic compounds from jaboticaba ameliorate intestinal inflammation and associated endotoxemia in obesity	Subject: Obese mice consuming a high-fat diet. *Study design*: experimental study (in vivo)	Administration of Phenolic compound Extract from Jaboticaba (PEJ)	14 weeks	The PEJ intervention group showed reduced weight gain, improved insulin sensitivity and dyslipidemia. In addition, PEJ also reduced inflammation and metabolic endotoxemia.
(Aloo, Barathikannan and Oh, 2024)	Polyphenol-rich fermented hempseed ethanol extracts improve obesity, oxidative stress, and neural health in high-glucose diet-induced Caenorhabditis elegans	Subjects: Caenorhabditis elegans with high glucose diet and normal diet as control. Study design: experimental study (in vivo)	Administration of flaxseed extract fermented by phenolic compounds	7 days	The study showed that flaxseed rich in phenolic compounds can improve antioxidant activity and neuronal health in obesity models.
(Flores-Medellín *et al.*, 2021)	Protein hydrolysates and phenolic compounds from fermented black beans inhibit markers related to obesity and type-2 diabetes	Subject: 3T3-L1 Cells (mouse embryonic fibroblast cell line) Study design: experimental study (in vivo)	Administration of protein hydrolysates and phenolic compounds from fermented black beans to 3T3-L1 cell culture media.	7 days	Protein hydrolysate and phenolic compounds from fermented black beans inhibit adipogenesis, reduce oxidative stress, and suppress inflammation.
(Callcott *et al.*, 2018)	Colored rice-derived polyphenols reduce lipid peroxidation and pro-inflammatory cytokines ex vivo	Subjects: Fasting blood samples of overweight/obese humans with no metabolic history. Study design: Ex vivo experimental study	Polyphenol content obtained from unpigmented rice (Reiziq) and pigmented rice samples (Yunlu29 - red, Purple - purple).	1-hour ex vivo plasma incubation	Polyphenols derived from pigmented rice (red and purple) Pigmented rice polyphenols (red & purple) reduce oxidative stress and inflammation more effectively than non-pigmented rice.

The results of the literature search were conducted using two major databases, PubMed (n=1,181) and Wiley Online Library (n=8,147), with a total of 9,328 articles identified. In the first stage, articles published more than 10 years ago (n=2,108) were excluded, leaving 7,220 articles. Next, at the screening stage, articles that did not have free full-text access (n=4,720) were excluded, leaving 2,500 articles. Articles that were not a Randomized Controlled Trial (RCT) type of research (n=1,000) were excluded, leaving 1,500 articles. Then, at the relevance stage, articles that had inappropriate topics (n=1,000) and articles with non-obese research subjects (n=495) were excluded. Based on all these selection stages, 5 articles that met all inclusion criteria were used for further analysis.

Phenolic compounds are bioactive secondary metabolite compounds that can be described as phenol-containing compounds. Phenols are benzene rings that are substituted with hydroxyl groups or can be referred to as hydroxybenzene (Mamari and Mamari, 2021). Phenolic compounds are widely distributed in plants that are utilized as a response to conditions such as infection, UV radiation, and so on (Arisandy, 2018).

Phenolic compounds can be found in vegetables and fruits, especially in berries, grapes, and tomatoes. Phenolic compounds are useful for preventing and treating diseases in humans because these compounds provide antioxidant, antimicrobial and anti-inflammatory properties (Rahman *et al.*, 2021). Based on the review, phenolic compounds can also be found in virgin coconut oil, jaboticaba, fermented flaxseed, fermented black beans, and pigmented rice, showing significant potential in reducing oxidative stress and inflammation.

The results showed that phenolic compounds can reduce the production of Reactive Oxygen Species (ROS), which play an important role in oxidative stress in obesity. This was proven by research conducted by Aloo, Barathikannan and Oh (2024) who found that fermented flaxseed extract rich in phenolic compounds can improve antioxidant activity and neural health in Caenorhabditis elegans subjects. In 3T3-L1 adipose cells, the phenolic compounds found in fermented black beans can decrease oxidative stress and suppress adipogenesis (Flores-Medellín *et al.*, 2021).

Based on the five articles that have been reviewed, the mechanism of phenolic compounds in enhancing antioxidants in obese populations to prevent obesity and its complications is through the prevention of oxidative stress, inhibition of inflammation, and regulation of metabolic pathways. Research conducted by Callcott et al. (2018) found that phenolic compounds from rice pigments (red and purple) can lower Malondialdehyde (MDA) levels, hence preventing oxidative stress. Lipid peroxidation is an indicator of oxidative stress that produces MDA. MDA can cause inflammation that has the potential to cause cardiovascular disease through its binding with body proteins, thereby forming Malondialdehyde Acetaldehyde (MAA) (Vehkala et al., 2013). This shows that polyphenols have the potential to reduce oxidative damage in obese people.

In obese individuals, inflammation generally occurs due to fat accumulation in the body, which triggers the production of proinflammatory cytokines that cause inflammation. This can increase the risk of cardiovascular disease. Inflammation in obese individuals can be reduced by inhibiting the production of proinflammatory cytokines through phenolic compounds. Based on research by Callcott et al. (2018), TNF-α production can be suppressed through the administration of polyphenolic extracts obtained from rice. The phenolic compounds contained in rice can reduce inflammation that can worsen the condition of obese individuals.

The mechanism of phenolic compounds in maintaining the condition of obese individuals is through the neutralization of free radicals, reduction of fat accumulation in the liver and adipose tissue, increased insulin sensitivity, regulation of the leptin hormone, and inhibition of fat cell formation or lipogenesis. This was proven by a study by de Vasconcelos et al. (2022), which showed improvements in lipid and insulin profiles or anti-adiposity effects in obese mice that were treated with E-VCO containing phenolic compounds.

According to Batista et al. (2018), phenolic compounds play a role in maintaining weight gain by increasing β-fatty acid oxidation and lipolysis, which enhances antioxidant activity in obese populations. Obese individuals generally experience intestinal dysfunction, which causes endotoxins such as lipopolysaccharides (LPS) from intestinal bacteria to enter the circulation, triggering systemic inflammation. To stop the further spread of endotoxins, phenolic compounds help improve intestinal integrity by reducing local inflammation and oxidative stress (Singh *et al.*, 2019). This was proven by the research of Rodrigues et al. (2021), who found that phenolic compounds from jaboticaba can improve insulin resistance, reduce inflammation, lower dyslipidaemia, and reduce obesity. Meanwhile, Flores-Medellín et al. (2021) found that the ability of phenolic compounds to increase antioxidants is through regulating metabolic pathways and reducing the expression of adipogenesis genes. These genes are genes that play a role in controlling fat storage. According to Aloo, Barathikannan and Oh (2024), phenolic compounds found in flaxseed fermented with Pediococcus acidilactici have the ability to block pancreatic lipase enzymes. The enzyme aids in the hydrolysis of triglycerides into fatty acids and glycerol and increases fat absorption which can lead to obesity and its attendant diseases (Yan *et al.*, 2022).

Based on the above, it suggests the potential for phenolic compounds to be therapeutic agents to address complications of obesity, such as chronic inflammation and oxidative stress. However, more thorough clinical trials are needed to verify these findings in humans, as most studies were conducted in animal models or in vitro. In addition, further research is needed to determine the best dosage and the most efficient source of phenolic compound ingredients.

CONCLUSION

Phenolic compounds can increase antioxidant activity and reduce inflammation in obese individuals. Based on an analysis of five articles, these compounds have the ability to suppress oxidative stress, reduce inflammation, and balance metabolic pathways associated with obesity complications, such as insulin resistance, adiposity, and dyslipidemia. The effectiveness of phenolic compounds depends on their source. Generally, phenolic compounds are found in brown rice, fermented black beans, and fermented flaxseed extract. This indicates the potential of phenolic compounds as anti-obesity agents through several mechanisms, namely inhibition of lipid peroxidation, reduction of pro-inflammatory cytokine levels (TNF-α, IL-6), and regulation of adipogenesis. However, most of the studies analyzed were based on animal or in vitro models, so more extensive clinical trials in humans are needed to confirm their effectiveness. In addition, it is important to determine the optimal dosage and usage strategy for phenolic compounds to be applied in effective diet programs. Further research is expected to open up opportunities for the use of phenolic compounds as dietary interventions in the management of obesity complications.

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Conflict of Interest and Funding Disclosure

None

Author Contributions

SM: data analysis, writing-original draft, writing-review, editing, visualization; FF: supervision, validation.

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