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Literature Review: The effect of modification diet and antioxidant on inflammatory and oxidative stress concentration in obesity

Studi literatur: Pengaruh modifikasi diet dan antioksidan terhadap kadar inflamasi serta stres oksidatif pada individu obesitas

Hanifah Mardhotillah[1], Diana Nur Afifah[2*], Adriyan Pramono[3]

[1] Departemen Ilmu Gizi, Program Studi Magister Ilmu Gizi, Fakultas Kedokteran, Universitas Diponegoro, Semarang, Jawa Tengah, Indonesia.
E-mail: hani.nifahmardhotillah@gmail.com
[2] Departemen Ilmu Gizi, Program Studi Magister Ilmu Gizi, Fakultas Kedokteran, Universitas Diponegoro, Semarang, Jawa Tengah, Indonesia.
E-mail: diananurafifah@live.undip.ac.id
[3] Departemen Ilmu Gizi, Program Studi Magister Ilmu Gizi, Fakultas Kedokteran, Universitas Diponegoro, Semarang, Jawa Tengah, Indonesia.
E-mail: adriyanpramono@fk.undip.ac.id

***Correspondence Author:**
Departemen Ilmu Gizi, Program Studi Magister Ilmu Gizi, Fakultas Kedokteran, Universitas Diponegoro. Tembalang, Kec. Tembalang, Kota Semarang, Jawa Tengah 50275, Indonesia.
Email: diananurafifah@live.undip.ac.id

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Abstract

Obesity is also associated with increased inflammation and oxidative stress. Mediterranean and dash diets, as well as antioxidants, can reduce the levels of inflammation and oxidative stress in obesity. This study aimed to determine the effects of dietary modifications and antioxidants on inflammatory and oxidative stress levels in obesity. This study was carried out using the literature review method using PubMed, Science Direct, and Google Scholar databases with the keywords Mediterranean Diet, DASH Diet, Antioxidant, Obesity, Inflammation, and Oxidative Stress. The inclusion criteria in this literature are articles published in the last 5 years (2018-2023) using RCT, in English, subjects >18 years old with obesity, interventions providing Mediterranean and dash diet, antioxidants derived from natural ingredients, and articles that can be accessed online. Articles were selected individually through a double process, considering the three main research quality criteria. The results of this study showed that the application of a modified diet and antioxidant can reduce inflammatory biomarkers and oxidative stress in obesity by suppressing NF-κB signaling and protecting against DNA damage. In conclusion, the application of a modified diet and antioxidants can reduce inflammatory and oxidative stress in obesity.
Keywords: Dash diet, inflammation, meddiet, obesity, oxidative stress

Abstrak

Obesitas dikaitkan dengan peningkatan inflamasi dan stres oksidatif. Diet mediterania dan diet dash serta antioksidan mampu menurunkan kadar inflamasi dan stres oksidatif pada obesitas. Studi literatur ini bertujuan untuk mengetahui pengaruh modifikasi diet dan antioksidan terhadap tingkat inflamasi dan stres oksidatif pada obesitas. Kajian ini dilakukan dengan metode *literature review* dengan menggunakan database Pubmed, Science Direct, dan Google Scholar dengan kata kunci *Mediterranean Diet*, DASH Diet, *Antioxidant*, *Obesity, Inflammation*, dan *Oxidative Stress*. Kriteria inklusi pada literatur ini ialah artikel yang terbit 5 tahun terakhir yaitu 2018 - 2023 dengan metode RCT, berbahasa inggris, subjek penelitian >18 tahun dengan status gizi obesitas, adanya intervensi pemberian diet mediterania dan diet dash, intervensi antioksidan yang berasal dari bahan alami, serta artikel yang dapat diakses secara online. Artikel diseleksi secara tunggal melalui proses ganda dengan memperhatikan tiga kriteria utama kualitas penelitian. Hasil kajian menunjukkan bahwa penerapan diet modifikasi dan antioksidan dapat menurunkan biomarker inflamasi dan stres oksidatif pada individu obesitas dengan menekan pensinyalan Nf-kβ dan melindungi kerusakan DNA. Kesimpulan, penerapan modifikasi diet serta antioksidan dapat menurunkan inflamasi dan stres oksidatif pada obesitas.
Kata Kunci: Dash diet, inflamasi, meddiet, obesitas, stres oksidatif.

Introduction

Obesity is a serious health problem in both developed and developing countries including Indonesia (Blüher, 2019; Setyaningrum et al., 2021). Obesity triggers inflammatory conditions by increasing pro-inflammatory cytokines, inflammatory signal activity, and macrophage infiltration through monocyte chemoattractant protein-1 (MCP-1) and intracellular protein molecule-1 (ICAM-1) in adipocytes (DiNicolantonio et al., 2018; Wang et al., 2020). Continuous inflammation causes metabolic disorders and an imbalance in the body's immune system, thereby reducing antioxidant levels in the body, increasing oxidative stress, production of reactive oxygen species (ROS), and the risk of developing non-communicable diseases such as diabetes mellitus, heart disease, stroke, cancer, and neurodegenerative diseases (Blüher, 2019; Setyaningrum et al., 2021).

World Health Organization (WHO) has stated that 1,9 billion adults aged >18 years were overweight, with obesity reaching 650 million in 2018. Children and teenagers aged 5-19 years have been found to be obese, reaching 340 million. Interestingly, as many as 50% of overweight children are found in Asia, one of which is Southeast Asia. Over the last 20 years, the number of obese individuals in Southeast Asia has increased from 1,2 million to 2,5 million in 2020 (Raheem et al., 2022). The results of the National Baseline Health Survey (RISKESDAS) in 2018 showed that the obesity rate in Indonesia has reached 23,1% (Kemenkes RI, 2018).

The increasing prevalence of obesity remains a serious public health concern. There is a need for a series of environmental interventions to prevent obesity. One intervention that can be used is lifestyle changes to achieve and maintain healthy and ideal body weight. Lifestyle changes by improving dietary patterns can be used as interventions for obesity management. Macronutrient composition is an important factor that must be considered when improving dietary patterns (Yannakoulia et al., 2019; Rahmad et al., 2020).

A ketogenic diet with low or very low carbohydrates, a high-protein diet, and intermittent fasting are examples of diets that can be applied to help reduce weight in obesity. However, apart from paying attention to the macronutrient composition, micronutrient balance also needs to be considered. Fruits and vegetables are non-energy-dense food ingredients but have high fiber and anti-inflammatory contents, which can help reduce weight and the negative effects of obesity. Therefore, improving dietary patterns by focusing on the composition of macronutrients and micronutrients as food sources rich in antioxidants can help improve the negative effects of obesity (Yannakoulia et al., 2019) (Yılmaz et al., 2019).

Diet modifications, such as the Mediterranean diet (MedDiet) and dietary approaches to stop hypertension (dash diet), can be used as a strategy in weight management and prevention of obesity-related diseases (Kim, 2021). These two have been proven to provide positive benefits in preventing obesity-related diseases as well as providing beneficial effects in reducing inflammation and oxidative stress (Castro-Barquero et al., 2020; Schwingshackl et al., 2020). These two diets focus on increasing the consumption of fruits, vegetables, protein sources, and unsaturated fats such as olive oil, omega-3, nuts, and seeds, reducing the consumption of processed foods, and limiting added sugar and salt (Benson & Hayes, 2020; Castro-Barquero et al., 2020; Wickman et al., 2021).

Natural ingredients derived from plants rich in bioactive compounds as functional foods can also be used as an alternative to reduce inflammation and oxidative stress (Fitrah & Suwondo, 2022). Research on plant-derived functional foods has increased significantly. This is because polyphenol compounds, which are widespread and are found in many fruits, vegetables, cereals, tea, coffee, and other plants, provide extraordinary positive benefits (Grzesik et al., 2018).

Polyphenols are known to possess anti-inflammatory, antioxidant, and anticancer properties. Consuming food sources rich in polyphenols has been proven to improve the condition of several degenerative diseases and has a lower risk of side effects than using medication. Polyphenols originating from food are often used as ingredients in the diet to provide maximum effects (Grzesik et al., 2018; Yahfoufi et al., 2018).

There is a lack of literature on the mechanism of how to apply modifications to diet and the use of polyphenols on

inflammation and oxidative stress in obese conditions.

Therefore, there is a need for a literature review on the mechanism of how the application of diet in the form of dietary modifications and the use of natural ingredients rich in antioxidants can reduce the levels of inflammation and oxidative stress in obesity. This study aimed to determine the effects of dietary modifications and antioxidants on the levels of inflammation and oxidative stress in obesity.

Methods

The method used was literature study or literature review using three databases: PubMed, Science Direct, and Google Scholar. The keywords used were mediterranean diet, dash diet, antioxidants, polyphenols, obesity, inflammation, and oxidative stress. Inclusion criteria included articles published within the last 5 years (2018 – 20203), using the method of Randomized Controlled Trial (RCT), english language, subjects aged >18 years with obesity nutritional status, intervention in the form of MedDiet, Dash diet, and antioxidants derived from natural ingredients, minimum intervention durations of one month with a minimum sample size of 20 people, as well as articles that can be accessed online. To simplify the study, the exclusion criteria included experimental animal subjects and pregnant women due to the risk of data bias in anthropometry, breastfeeding, and menopause.

The article search process uses techniques Boolean Search with the keywords mediterranean diet AND obesity AND inflammation AND oxidative stress, dash diet AND obesity AND inflammation AND oxidative stress, antioxidant OR polyphenols AND obesity AND inflammation AND oxidative stress. Based on the search process, obtained a total of 185 articles were selected singly by one researcher with double selection, which included the selection process and review process of the selected articles.

The articles obtained were then grouped by researchers for the selection process. Researchers grouped articles related to diet modification interventions in the form of a medium diet, dash diet, and interventions using natural ingredients against inflammation and oxidative stress in obese individuals. Articles that have undergone the selection process are then reviewed by focusing on three main criteria for research quality: interesting topics, articles relevant to the purpose of the literature review, and article suitability. Apart from paying attention to the three main criteria, the article review process also focused on the completeness of the text, articles that answered the research objectives, and articles based on the inclusion criteria, resulting in eight articles used in this literature study. The analytical approach used in this literature study is a descriptive method based on the topic used to explain and narrate the results of various studies outlined in the literature in narrative form. The search flow for this article is presented in the PRISMA diagram.

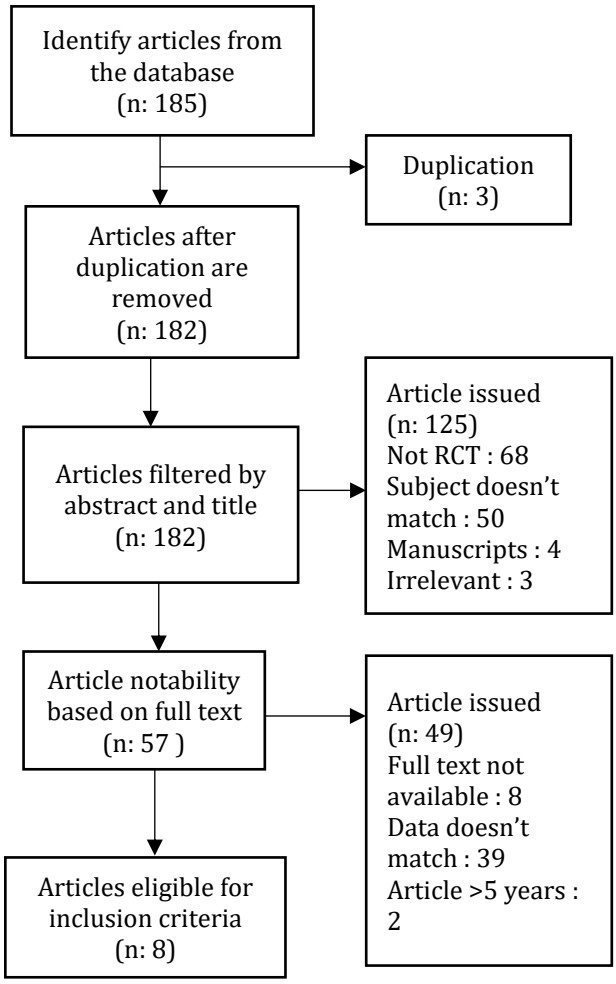

Figure 1. Literature search flow

Result and Discussion

Based on an article search through three databases and a selection process, eight articles met the inclusion criteria, including four articles discussing diet modification and four articles discussing the sources of antioxidants on inflammation and oxidative levels in obesity.

Effect of Diet Modification in Inflammation and Oxidative Stress Levels

Four articles were reviewed regarding dietary modifications on inflammation and oxidative stress levels (Table 1). The results showed positive benefits in improving the markers of inflammation and oxidative stress in obesity.

Fat accumulation and excessive energy intake are both involved in the development of obesity (Lin & Li, 2021). Diet modification is often used as a strategy to reduce and prevent the impact of obesity with several approaches such as reducing food energy consumption to lose weight (Fitrah & Suwondo, 2022; Dewantari & Sukraniti, 2020; Yannakoulia et al., 2019). Implementing the MedDiet can provide positive benefits in reducing the risk of cardiometabolic diseases. This is because the bioactive components of these food ingredients are known to be anti-inflammatory (Finicelli et al., 2022).

Research conducted (Jovanovic et al., 2020) after administering the MedDiet for 24 weeks showed improvements in cardiometabolic status and inflammatory markers such as Tumor Necrosis Factor Alpha (TNF-α), interleukin-6 (IL-6), and hs-CRP. The MedDiet is known in the community because of its potential as an anti-inflammatory agent, improving health, and preventing chronic diseases. MedDiet is characterized by high consumption of vegetables, fruits, grains, nuts, and olive oil as the main source of fat, seafood, and dairy products in the form of yogurt and cheese, poultry, and eggs, as well as limited consumption of red meat, processed foods, and sugar. The composition of these food ingredients plays a role in modulating pro- and anti-inflammatory, oxidative stress, antioxidants, and therapeutics in treating obesity through complex and interrelated mechanisms (Dominguez et al., 2023; Finicelli et al., 2022; Koelman et al., 2022).

Monounsaturated fatty acids (MUFAs) have a higher ratio than saturated fatty acids (SFAs) and act as anti-inflammatory agents. Excessive consumption of SFA induces IL-1β, IL-6, and TNF-α and activation of the NF-κB inflammatory signaling pathway. In contrast to SFA, MUFA reduces inflammation by inhibiting the NF-κB pathway, thereby reducing the pro-inflammatory concentrations of C Reactive protein (CRP), IL-6, TNF-α, MCP-1, IFN-γ, and IL-18. Bioactive compounds, such as flavonoids, carotenoids, and polyphenols, are also present in the MedDiet and contribute to pro- and anti-inflammatory properties (Schwingshackl et al., 2020).

Table 1. Mediterania diet and dash diet in lowering inflammation and oxidative stress

Researcher and Year	Title	Method	Result and Conclusion
Kendel et al. (2020).	The efficacy of an energy-restricted anti-inflammatory diet for the management of obesity in younger adults.	Two-arm randomized controlled trial Intervention: Isocalorie administration in control group and mediterranean diet with anti-inflammatory diet (AID).	Interventions with anti inflammatory diet (AID) reduce body weight and visceral adipose tissue and improve cardiometabolic status and inflammatory levels.
Quetglas-Llabrés et al. (2023).	Mediterranean diet improves plasma biomarkers related to oxidative stress and inflammatory process in patients with non-alcoholic fatty liver disease.	Randomized controlled trial Intervention: Provision of conventional diet group and group with mediterranean diet high meal frequency (MD-	There was a decrease in alanine aminotransferase (ALT) and C Reactive Protein (CRP), improved physical fitness, and decreased malondialdehyde (MDA) levels in group with

		HMF) for 12 months.	mediterranean diet.
Marin-Alejandre et al. (2019).	The metabolic and hepatic impact of two personalized dietary strategies in subjects with obesity and nonalcoholic fatty liver disease: The fatty liver in obesity (FliO) randomized controlled trial.	Randomized controlled trial Intervention: Standard diet referring to American Heart Association (AHA) and FLiO group referring to Mediterranean diet for 6 months.	There were no significant differences between the two groups in metabolism and liver markers. The group with a mediterranean diet showed weight loss, fat content of up to 40.9%, and increased antioxidant capacity.
Rooholahzadegan et al. (2023).	The effect of DASH diet on glycemic response, meta-inflammation, and serum LPS in obese patients with NAFLD: A double-blind controlled randomized clinical trial.	Double-blinded controlled randomized clinical trial Intervention: Providing calorie-restricted and 20 samples with dash diet for 8 weeks.	There was a decrease in obesity index in both groups but the reduction in weight, BMI, and waist circumference was greater in dash group. There was a decrease in fasting glucose levels in both groups but there was no significant difference. Serum HbA1C, TLR-4, MCP-1, and LPS were found to decrease significantly in dash diet group.

The MedDiet also plays a role in reducing the concentration of oxidative stress biomarkers and increasing the concentration of antioxidants. This is supported by research conducted by Quetglas-Llabrés et al. (2023) and Marin-Alejandre et al. (2019), which showed a decrease in alanine aminotransferase (ALT), CRP, and malondialdehyde (MDA), and increased antioxidant capacity.

The main source of fat in the MedDiet is olive oil, which is known for its health benefits. The oleic acid, vitamin E, and polyphenols found in olive oil can protect against DNA damage caused by ROS, reducing the number of free radicals by neutralizing metabolites that are potentially carcinogenic. Free radicals are associated with increased lipid peroxidation; therefore, the application of a MedDiet with a high consumption of antioxidants derived from fruits and vegetables can help protect the body from lipid peroxidation mediated by oxidative stress by reducing lipid substrates and increasing antioxidant concentrations (Castro-Barquero et al., 2020; Schwingshackl et al., 2020).

The implementation of a Dash diet is also beneficial for improving inflammatory markers. Rooholahzadegan et al. (2023) showed a decrease in body weight, BMI, serum triglycerides, very low-density lipoprotein cholesterol (VLDL-C), MCP-1, and improvements in total antioxidant capacity (TAC) and glutathione (GSH).

Dash diet is identical to being low in sodium so it is known for its potential in lowering blood pressure, but dash diet also has the potential to reduce inflammation and oxidative stress (Castro-Barquero et al., 2020; Filippou et al., 2020; Wickman et al., 2021). Low sodium levels help control body weight by reducing hunger, as evidenced by an increase in satiety hormones, such as leptin (Soltani et al., 2018). Similar to MedDiet, dash diet composition is also rich in antioxidants, which supports its role as a cellular antioxidant and antioxidant system (Castro-Barquero et al., 2020).

Fruits and vegetables contain flavonoids, which act as antioxidants and help reduce free radicals, lipid peroxidation, inflammation, and weight control (Castro-Barquero et al., 2020) (Suri et al., 2019). Dash diet has a high fiber content, low glycemic index levels so it has a positive effect on the mechanism of slowing

glucose absorption, changing the gastroinstestinal microbiota thereby suppressing the production of pro-inflammatoy cytokines stimulating short-chain fatty acids (SCFA) production in the intralume resulting in lower free fatty acid (FFA) (Soltani et al., 2018; Suri et al., 2019).

Dash diets also contain high levels of Ca and Mg. Calcium and magnesium are inversely related to obesity because of their role in increasing lipolysis, thus playing an important role in weight management. Calcium and magnesium are also known to be protective agents against DNA damage and antioxidant enzymes because they influence oxidative stress levels by increasing TAC and GSH as free radical scavengers (Rooholahzadegan et al., 2023). The mechanism of the benefits of the MedDiet and dash diet in reducing inflammation and oxidative stress is presented in Figure 1.

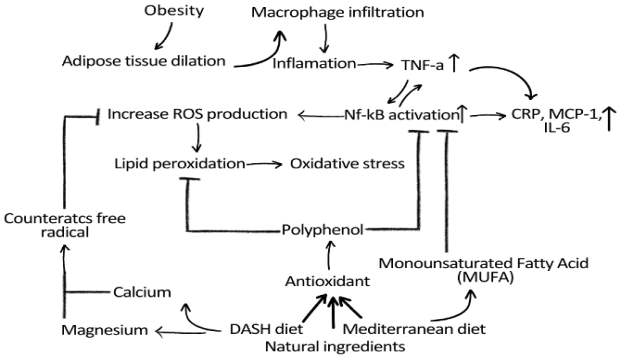

Figure 1. Mechanisms of Mediterranean diet, dash diet, and natural ingredients in lowering inflammation and oxidative stress in obesity.

Effect of Antioxidant Consumption on Inflammation and Oxidative Stress Levels in Obesity

There are four studies reviewed regarding the consumption of antioxidant sources on levels of inflammation and oxidative stress, which are presented in Table 2. The results of the literature show positive benefits in improving the markers of inflammation and oxidative stress in obesity.

A study conducted by Uchio et al. (2021) showed a decrease in CRP levels after capsule administration of Curcuma longa extract (CLE). CRP is a marker of inflammation; therefore, a decrease in CRP level can be a sign of improved inflammation (Mehta et al., 2023). CLE inhibits phosphorylation of B-alpha (IkBα) which is induced by TNF-α, thereby inhibiting NF-κB activation and reducing CRP levels (Uchio et al., 2021).

Research conducted by Cazzola & Rondanelli (2020) showed a decline in ox-LDL and increased antioxidant capacity after administration of N-oleoyl-phosphati-dylethanolamine and epigallo catechin-3-gallate (NOPE-EG-CG). EGCG is the main catechin and polyphenol component of green tea. Catechins are natural polyphenolic compounds found in many plants, especially in green and black tea. One gram of green tea leaf powder contained 200 mg catechins (Bae et al., 2020; Bernatoniene & Kopustinskiene, 2018).

The chemical structure of catechins, including the number and location of hydroxyl groups, plays an important role as an antioxidant (Sheng et al., 2023). The role of catechins as antioxidants consists of two mechanisms: direct counteracting free radicals, preventing lipid peroxidation by stabilizing free radicals and binding metal ions, and an indirect mechanism by producing detoxification enzyme II and antioxidant enzymes, inhibiting the formation of pro-oxidant enzymes. The role of catechins in inhibiting pro oxidant enzymes is by suppressing various inflammation and oxidative stress pathways such as suppressing nicotinamide adenine dinucleotide phosphate (NADPH) activation, TNF-α, Nf-kB, and activator protein-1 (AP-1) which plays an important role in the development of diseases related to oxidative stress (Bernatoniene & Kopustinskiene, 2018).

Machado et al. (2020) showed an increase in antioxidant capacity and a decrease in oxidative stress levels after consuming drinks with the addition of *yacon flour*. Chlorogenic acid was the main phenolic compound found in yacon, with a content of 658 mg GAE/100 g flour. The hydroxyl group in this compound can increase the antioxidant capacity, which provides protection against free radicals by neutralizing free radicals by donating electrons, reducing free radical production, and avoiding oxidation of biomolecules (Machado et al., 2020).

Another study (Ruiz-García et al., 2023) stated that there was an improvement in inflammation levels and total antioxidants after

the administration of extra virgin oil (EVOO) for 30 days. Pure juice from olives is known as EVOO and is recognized as the best-quality oil. EVOO's acidity has a low level of 0,8% and a sensory value above 6,5 points, resulting in perfect taste and aroma (Jimenez-lopez et al., 2020; Román et al., 2019). EVOO consists of 97-99% triglycerides and 1-3% minor compounds that play a role in biological properties and sensory attributes. EVOO also contains MUFA, especially oleic acid and several polyunsaturated fatty acids (PUFAs) such as linoleic acid with a content of 65-83% which is known for its benefits in lowering cholesterol (Jimenez-lopez et al., 2020; Bucciantini et al., 2021).

The bioavailability of EVOO is considered to be quite high which is around 55-60% and can be absorbed by the small intestine. Talking about EVOO cannot be separated from the MedDiet, and it is famous for its health benefits. EVOO is known for its benefits as an antimicrobial, antitumor, antioxidant, anti-inflammatory, and for modulating gene expression by protecting proteins involved in inflammatory mechanisms, oxidative stress, and lipid metabolism. The positive benefits of EVOO cannot be separated from and are related to the high proportion of MUFA, especially oleic acid and secoiridoid polyphenols. Secoiridoids are a group of phenolic compounds, especially the aglycones ligustroside and oleuropein, with their respective derivatives oleocanthal and oleacein (OLA).

Table 2. Antioxidant in lowering inflammation and oxidative stress

Researcher and Year	Title	Method	Result and Conclusion
Uchio et al. (2021).	Curcuma longa extract improves serum inflammatory markers and mental health in healthy participants who are overweight: A randomized, double-blind, placebo-controlled trial.	A randomized double-blind placebo-controlled study Intervention: Intervention with the administration of two capsules of Curcuma longa extract (CLE) and a control group with two placebo capsules for 12 weeks.	Compared to the control group administration of CLE capsules for 12 weeks showed a decrease in body weight, BMI, and C-reactive protein levels.
Cazzola & Rondanelli (2020).	N-Oleoyl-Phosphatidyl-Ethanolamine and Epigallo Catechin-3-Gallate Mitigate Oxidative stress in overweight and class 1 obese people on a low-calorie diet.	Randomized double-blind and placebo controlled Intervention: Intervention with N-oleoyl-phosphatidylethanolamine and epigallo catechin-3-gallate (NOPE-EGCG) and group with placebo 200 mg soybean lecithin for 2 months.	There was a decrease in Ox-LDL and an increase in antioxidant capacity in the group with NOPE-EGCG.
Machado et al. (2020).	Effect of yacon flour associated with an energy-restricted diet on intestinal permeability, fecal short chain fatty acids, oxidative stress and inflammation markers levels in adults with obesity or overweight: A randomized double-blind placebo controlled clinical trial.	Double-blind, parallel, randomized, placebo-controlled, two-arm, clinical trial study Intervention: The intervention consumed 350 ml of drinks without yacon flour and the intervention group was given drinks given 25 grams of yacon flour for 6 weeks. Each group was also given a diet with an energy reduction of	Compared to the control group, interventions with beverage consumption supplemented with yacon flour showed an increase in antioxidant capacity and a decrease in levels of oxidative stress and short-chain fatty acids (SCFA). The use of yacon flour is beneficial in increasing

		500 kcal/day.	antioxidant capacity and decreasing oxidative stress levels in obese individuals.
Ruiz-García et al. (2023).	Rich oleocanthal and oleacein extra virgin olive oil and inflammatory and antioxidant status in people with obesity and prediabetes. The APRIL study: A randomized, controlled crossover study.	Randomized crossover double blind controlled Intervention: The study sample was divided into two groups, namely the group given extra virgin olive oil (EVOO) and the group given olive oil (OO) for 30 days.	Compared to OO intervention, there was a decrease in interferon-γ, lipid levels, body weight, BMI, and blood glucose as well as an increase in total antixodants after EVOO administration. The use of EVOO which is rich in oleocanthal and oleacein is beneficial in improving inflammatory and antioxidant levels in obese and prediabetic individuals.

Research interest in OLA is increasing because of its anti-inflammatory and antioxidant benefits by inhibiting LPS-induced inflammatory responses, increasing Nrf-2/HO-1 protein expression, and blocking the NF-κB inflammatory signaling pathway (Román et al., 2019; Bucciantini et al., 2021; Muñoz-García et al., 2022).

The mechanisms underlying the anti-inflammatory and antioxidant roles of natural ingredients are presented in Figure 1. The limitations of this literature review are the use of minimal resources, two examples of dietary modification, and the presence of comorbidities.

Conclusion

Potency MedDiet, dash diet, as well as the use of natural ingredients, can be used as a strategy in preventing disease caused by obesity by reducing inflammatory markers and oxidative stress by suppressing Nf-kB inflammatory signaling pathway, producing free radical scavengers, increasing antioxidant capacity, and protecting against DNA damage caused by free radicals.

Further research is needed on the application of MedDiet, dash diet, and natural ingredients, as well as a combination of the two on biomarkers of inflammation and oxidative stress in obesity without comorbidities to avoid bias. In addition, diet and use of natural ingredients are currently issues that are widely discussed by the public because of awareness about maintaining health. Seeing the potential of implementing diet modifications and using natural ingredients to reduce inflammation and oxidative stress can be used as a strategy and initial step for the government in obesity management, so that it can help reduce the risk of non-communicable diseases, considering that inflammation and oxidative stress in conditions of obesity are one of the triggers for non-communicable diseases.

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