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Original Article

Antioxidant, anti-inflammatory and anti-obesity effects of onion and its by-products in high-fat fed rodents: a systematic review

Efeitos antioxidantes, anti-inflamatórios e anti-obesidade da cebola e seus subprodutos em roedores alimentados com alto teor de gordura: uma revisão sistemática

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Abstract

The effects of onion and its by-products on metabolic changes induced by excessive consumption of a high fat diet have been the focus of many studies. The aim of this study was to systematically review the effects of onion and its by-products antioxidant, anti-inflammatory and anti-obesity in rats exposed to a high-fat diet. Five databases were used: Pubmed, EMBASE, Science Direct, Web of science and Scopus until June 2020 updated December 1, 2022. Research of the articles was carried out by two reviewers, searching and selecting studies after an initial reading of the titles and abstracts. In total, 2,448 papers were found and, after assessing against the inclusion and exclusion criteria, 18 papers were selected for this review. The findings of this review show the beneficial effects of onion and its by-products on inflammatory parameters, obesity, cardiovascular disease, thermogenesis and hepatic alterations generally associated with the consumption of a high-fat diet.

Keywords: high fat diet, onion, onion by-products, *Allium cepa L.*, rats.

Resumo

Os efeitos da cebola e seus subprodutos nas alterações metabólicas induzidas pelo consumo excessivo de uma dieta rica em gordura têm sido foco de muitos estudos. O objetivo deste estudo foi revisar sistematicamente os efeitos da cebola e seus subprodutos antioxidantes, anti-inflamatórios e anti-obesidade em ratos expostos a uma dieta hiperlipídica. Foram utilizadas cinco bases de dados: Pubmed, EMBASE, Science Direct, Web of science e Scopus até junho de 2020, atualizado em 01 de dezembro de 2022. A pesquisa dos artigos foi realizada por dois revisores, buscando e selecionando os estudos após leitura inicial dos títulos e resumos. No total, 2.448 artigos foram encontrados e, após avaliação de acordo com os critérios de inclusão e exclusão, 18 artigos foram selecionados para esta revisão. Os achados desta revisão mostram os efeitos benéficos da cebola e seus subprodutos sobre parâmetros inflamatórios, obesidade, doenças cardiovasculares, termogênese e alterações hepáticas geralmente associadas ao consumo de uma dieta hiperlipídica.

Palavras-chave: dieta hiperlipídica, cebola, subprodutos da cebola, *Allium cepa L.*, ratos.

1. Introduction

Obesity is a multifactorial disease that is growing in the world's population (Popkin et al., 2012; Popkin, 2015). Among the factors associated with this pathology, modern eating habits, characterized mainly by the excessive consumption of ultra-processed foods with a high saturated fat content, have been associated with the appearance of metabolic alterations resulting in the development of diseases (WHO, 2003; Popkin et al., 2012; Popkin, 2015). Obesity induced by the excessive dietary intake of fat is associated with abdominal fat accumulation, adipocyte size expansion, and the triggering of inflammatory processes, and may also predispose the individual to the development of insulin resistance, and non-alcoholic fatty liver disease (NAFLD), among other things (Lam et al., 2012; Dinh et al., 2015; Umekawa et al., 2015; Perez et al., 2015; Lima et al., 2018; Santos, et al., 2022; Macêdo et al., 2021; Cordeiro et al., 2022).

In order to mitigate the effects caused by the excessive consumption of a high-fat diet, studies have investigated the benefits of polyphenols in the health process

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(Pimentel et al., 2013; Zou et al., 2017; Porras et al., 2017; Barroso et al., 2019). These substances, present in vegetables and fruits, are part of a large group of bioactive compounds that are divided into subclasses, flavonoids being the most studied, especially quercetin (Slimestad et al., 2007; Hamauzu et al., 2011; Lee et al., 2012; Moon et al., 2013; Nabavi et al., 2015; Forney et al., 2018; Fraga et al., 2019; Grzelak-Błaszczyk et al., 2020). Among vegetables, the onion (*Allium cepa L.*), a popular consumer product that is rich in quercetin and also in other phenolic compounds such as kampferol, protocatechuic acid, anthocyanin and dietary fiber, has been the focus of some studies due to its effects antioxidant, anti-inflammatory and anti-obesity characteristics (Slimestad et al., 2007; Hamauzu et al., 2011; Lee et al., 2012; Moon et al., 2013; Nabavi et al., 2015; Forney et al., 2018; Fraga et al., 2019; Grzelak-Błaszczyk et al., 2020). Experimental studies have shown the beneficial effects of the consumption of onion peel powder, bulb, or even tea, on NAFLD, inflammation, cardiovascular disease, body weight, and insulin resistance induced by the consumption of an excessive high-fat diet (Hamauzu et al., 2011; Moon et al., 2013; Emamat et al., 2016, 2018).

However, despite the evidence already established with regard to the benefits of using and dose onion or its by-products to reduce the consequences of a high-fat diet intake, no systematic review has been performed to date. Thus, the aim of this study was to systematically review the effects of onion and its by-products antioxidant, anti-inflammatory and anti-obesity in rats subjected to a high-fat diet.

2. Methods

The systematic review was carried out following the recommendations of the *Preferred reporting items for Systematic reviews and MetaAnalysis* (PRISMA) (Moher et al., 2009). Registered the protocol in PROSPERO having as registration number is CDR42020188172. The record can be accessed at https://www.crd.york.ac.uk/PROSPERO.

2.1. Eligibility criteria

The research question was defined according to the PICOS approach (Participants / Population, Interventions / Exposure, Comparison, Outcomes and Study design) Table 1.

Studies that investigated the effect of the high-fat diet and supplementation of the onion or its by-products on any result related to the health of rats or mice were included. The comparison groups were defined as follows: use of a diet rich in fat versus supplemented with onion and its by-products (in any dose or quantity and any duration of consumption / exposure). In addition, to be included, studies needed to report any health-related results. No restrictions for language were applied. Reviews, human studies, and studies with drugs or other substances unrelated to the use of onion or its by-products were excluded. The identified studies were evaluated according to the inclusion criteria: studies with rats or mice that were exposed to a high-fat diet in the early stages or during adulthood.

Table 1. PICOS criteria for inclusion and exclusion of studies.

Criterion	Description
Population	Rat or mouse or mice
Intervention/ exposure	Consumption of a high-fat diet and supplementation of the onion or its by-products
Comparison	The comparison groups were defined as follows: use of a diet rich in fat
Outcome	Any health-related outcome
Study design	Experimental studies in rats, mice, or mouse.

PICOS (Participants / Population, Interventions / Exposure, Comparison, Outcomes and Study design).

2.2. Search strategy and study selection

The evaluation of titles, abstracts, and complete articles was performed between May and June 2020 updated December 1, 2022, following the steps of identification, screening, and eligibility with respect to the inclusion criteria, with no limitation of the year of publication.

The paper research was performed in the electronic databases Pubmed, EMBASE, ScienceDirect, Web of Science and Scopus, using a combination of the terms MeSH (Medical Subject Headings): *high fat diet, high-fat diet, occidental diet, western diet, onion, Allium cepa, rat, mouse, mice*. The boolean operators "AND" and "OR" were used to cross terms: (*high fat diet OR high-fat diet OR occidental diet OR western diet) AND (onion OR Allium cepa) AND (rat OR mouse OR mice*).

Research of the articles was carried out by two reviewers, searching and selecting studies after an initial reading of the titles and abstracts. In cases of disagreement, a third reviewer was used to verify whether the study was eligible.

2.3. Quality and risk-of-bias assessment

The quality of the articles used in this review was evaluated according to the guidelines of ARRIVE - Animals in Research: Reporting In Vivo Experiments (Percie Du Sert et al., 2020). To evaluate the adequacy of the papers according to the guidelines, a scoring system (0 - no; 1 - yes) was used for the 20 items listed in the ARRIVE guidelines. Information about each study analyzed is summarized in Table 2.

To assess the risk of bias, the Systematic Review Center for Laboratory animal Research (SYRCLE) (Hooijmans et al., 2014), risk of bias tool was used for the 18 studies selected for this review. The "yes" judgment indicates that the risk of bias is low and the "no" judgment indicates a high degree of risk of bias. If the details of the report are insufficient to assess the appropriate risk of bias, the judgment will be "unclear" Table 3.

3. Results

A total of 2,448 papers were selected from the five databases searched. Of these, 347 were excluded due to duplicated titles and 2,064 after reading the abstracts, as

Table 2. Described variables of the selected articles regarding the analysis of the effects of onion and its by-products in animals submitted to a high-fat diet.

Main author / year	Animal species	Gender/ Age	Composition of the high fat diet	high fat diet exposure period	Onion characteristics and methodology used	Period of exposure to onion or its by-products	Quantity used of onion or its by-products	Main results	Final score of adequacy by ARRIVE
Chang et al. (2022)	Sprague Dawley	Male; 4 weeks	Fat: 43%	12 weeks	*-Allium cepa L.* - The onion pieces were lyophilized at 40°C for 24 hrs and gridded into fine poder. The quercetin was determined using high performance liquid chromatography.	12 weeks	1% e 5% dried onion; 180 mg/kg quercetin	Onion powder Effects: - 1%, 5% and 180mg/kg quercetin: = Energy intake; ↓ Epididymal, Perirenal and Mesenteric Mass; ↓Total cholesterol, TG, LDL, Free fatty acid; ↓TNF-α, IL-6, TBARS; ↓Total cholesterol, TG, TNF-α, IL-6, TBARS in liver; - 1% or 5%: ↓Subcutaneous adipose; adipocyte area epididymal; ↑SOD and Catalase; ↓scores for damage of hepatic; protein expression of ACC-α and Ras; Feces: ↑Acetic and Butyric acid; Total cholesterol and TG; ↓accumulation of lipids in the retina	17/20
Momoh et al. (2022)	Wistar	Male, Age not informed	Fat: 50%	12 weeks	*-Allium cepa L.* - The onion leaves were sliced into tiny pieces and dried at temperature of 22 ± 2 ◦C, and blended into powder.	28 days (4 weeks)	10% and 20%	Onion leaves Effects: - 10% and 20%: = food intake; ↓ Body Weight; Fat mass; ↓ AST; Creatinine, Urea; glucose; =HDL; Uric acid; ↓ Accumulation of lipids in liver; ↓ Kidney inflammation; - 20%: ↓Kidney weight; ALT; ↓Total cholesterol, TG, LDL, and VLDL.	17/20

= no statistically significant effect. ↓ statistically significant decrease. ↑ statistically significant increase. TG: triglyceride; HDL-C: high density lipoproteins; LDL-C: low density lipoproteins; ALT: alanine aminotransferase; AST: aspartate aminotransferase; GGT: geranylgeranyltransferase; TNF-α: Tumor Necrosis Factor alpha; Pgc-1α: gamma peroxisome proliferator-activated receptor-1 alpha coactivator; PPAR-γ: peroxisome proliferator activated receptor; FAS: fatty acid synthase; ACC: acetyl CoA carboxylase; UCP-1: uncoupling protein; SREBP-2: sterol regulatory element binding protein; HMG-CoAR: 3-hydroxy-3-methyl-glutaryl-CoA reductase; Alb: albumin; CPT-1α: carnitine palmitoyltransferase- 1α; (C/EBP)α: CCAAT/enhancer binding protein; IL-6: Interleukin 6; *Cd11b*:Cluster of differentiation 11b; *Cd68*:Cluster of differentiation 68; *Mcp-1*:Monocyte chemoattractant protein 1; PRDM16: PR domaincontaining 16;CIDEA: cell death-inducing DNA fragmentation factor-alpha-like effector A; COX-1: cyclooxygenase; Nad3, Nad4: NADH dehydrogenase: Atp8: adenosine triphosphate; TBARS: thiobarbituric acid-reactive substances; TBX1: T-box transcriptional factor 1.

Table 2. Continued...

Main author / year	Animal species	Gender/ Age	Composition of the high fat diet	high fat diet exposure period	Onion characteristics and methodology used	Period of exposure to onion or its by-products	Quantity used of onion or its by-products	Main results	Final score of adequacy by ARRIVE
Yu et al. (2021)	C57BL/6J	Male, 6-8 weeks	Fat: 34.9% (Soybean Oil and Lard)	8 weeks	-*Allium cepa L.* - Yellow onion peel. The extraction with 5 L distilled water for 5 h at 80 ◦C.	8 weeks	36 mg/kg; 90 mg/kg; 144 mg/kg;	Yellow onion peel extract Effects: - High and medium dose group (144mg/kg and 90mg/kg): ↓ Body Weight; - Low, medium, and High dose group (36mg/kg, 90mg/kg and 144mg/kg): =Liver Mass; ↓Total cholesterol, TG and LDL; =HDL; ↓Total cholesterol, TG in liver; ↓ Accumulation of lipids in liver; ↓ Epididymal adipocytes; ↓ PPARγ, C/EBPα, FAS, ACC, AP2, and SREBP1 expression; ↓ PPARγ protein expression	16/20
Grzelak-Błaszczyk et al. (2020)	Wistar	Male; 4 weeks	Fat: 14% (Palm oil)	4 weeks	- No informed; - Yellow onion residues. The extraction with 50% water solution of ethanol, temperature was 35°C; time was 6 h.	4 weeks	- HF+ Quercetin diglycosides = 0.44%; - HF+ Quercetin monoglycosides = 0.34%; - HF+ protocatechuic acid = 0.25%	HF+ Quercetin diglycosides Effects: ↑ pH of digesta; ↑ β-glucosidase day 7; ↓ β-galactosidase days 3,7,14 and 28; ↓ β-glucuronidase; ↓isovaleric and butyric; ↓ Total SCFA; ↓ Liver Mass; ↓creatinine; HF+ Quercetin monoglycosides Effects: ↓ Diet intake; ↑ β-glucosidase day 3,7,14 and 28; ↑β-glucuronidase day 7,14 and 28; ↓ propionic and isobutyric; ↑Total SCFA; ↓TG and atherogenic index II; HF+ protocatechuic acid Effects: ↑β-glucuronidase day 7 and 28; ↓Total SCFA; ↓Liver Mass; ↓Total cholesterol, TG and atherogenic index I and II; ↑HDL; ↓Uric acid.	16/20

= no statistically significant effect. ↓ statistically significant decrease. ↑ statistically significant increase. TG: triglyceride; HDL-C: high density lipoproteins; LDL-C: low density lipoproteins; ALT: alanine aminotransferase; AST: aspartate aminotransferase; GGT: geranylgeranyltransferase; TNF-α: Tumor Necrosis Factor alpha; Pgc-1α: gamma peroxisome proliferator-activated receptor-1 alpha coactivator; PPAR-γ: peroxisome proliferator activated receptor; FAS: fatty acid synthase; ACC: acetyl CoA carboxylase; UCP-1: uncoupling protein; SREBP-2: sterol regulatory element binding protein; HMG-CoAR: 3-hydroxy-3-methyl-glutaryl-CoA reductase; Alb: albumin; CPT-1α: carnitine palmitoyltransferase- 1α; (C/EBP)α: CCAAT/enhancer binding protein; IL-6: Interleukin 6; *Cd11b*:Cluster of differentiation 11b; *Cd68*:Cluster of differentiation 68; *Mcp-1*:Monocyte chemoattractant protein 1; PRDM16: PR domaincontaining 16;CIDEA:cell death-inducing DNA fragmentation factor-alpha-like effector A; COX-1: cyclooxygenase; Nad3, Nad4: NADH dehydrogenase: Atp8: adenosine triphosphate; TBARS: thiobarbituric acid-reactive substances; TBX1: T-box transcriptional factor 1.

Table 2. Continued...

Main author / year	Animal species	Gender/ Age	Composition of the high fat diet	high fat diet exposure period	Onion characteristics and methodology used	Period of exposure to onion or its by-products	Quantity used of onion or its by-products	Main results	Final score of adequacy by ARRIVE
Grzelak-Błaszczyk et al. (2018)	Wistar	Male; 4 weeks	Fat: 14% (Palm oil)	4 weeks	- No informed; - Yellow onion residues. The extraction with 50% water solution of ethanol, temperature was 35°C; time was 6 h.	4 weeks	- HF+ Quercetin= 0.21%; - HF+ Quercetin monoglycosides = 0.36%;	HF+ Quercetin Effects: = Body Weight; ↓mass of colon tissue; ↓Sucrase and Maltase; ↑lactose; ↑β-glucosidase, β-glucuronidase and β-galactosidase;↑SCFA (acetic, propionic and butyric); =TBARS; ↑antioxidant capacity of lipid and of water fraction of serum; = glucose and AST; ↓ALT and atherogenic index II and urea. HF+ Quercetin monoglycosides Effects: = Body Weight; ↓pH of digesta cecum and colon; ↓ mass of colon tissue; ↓Sucrase; ↑lactose; ↑β-glucosidase, β-glucuronidase and β-galactosidase; ↑antioxidant capacity of water fraction of serum; ↓ALT and atherogenic index II.	15/20

= no statistically significant effect. ↓ statistically significant decrease. ↑ statistically significant increase. TG: triglyceride; HDL-C: high density lipoproteins; LDL-C: low density lipoproteins; ALT: alanine aminotransferase; AST: aspartate aminotransferase; GGT: geranylgeranyltransferase; TNF-α: Tumor Necrosis Factor alpha; Pgc-1α: gamma peroxisome proliferator-activated receptor-1 alpha coactivator; PPAR-γ: peroxisome proliferator activated receptor; FAS: fatty acid synthase; ACC: acetyl CoA carboxylase; UCP-1: uncoupling protein; SREBP-2: sterol regulatory element binding protein; HMG-CoAR: 3-hydroxy-3-methyl-glutaryl-CoA reductase; Alb: albumin; CPT-1α: carnitine palmitoyltransferase- 1α; (C/EBP)α: CCAAT/enhancer binding protein; IL-6: Interleukin 6; *Cd11b*:Cluster of differentiation 11b; *Cd68*:Cluster of differentiation 68; *Mcp-1*:Monocyte chemoattractant protein 1; PRDM16: PR domaincontaining 16;CIDEA:cell death-inducing DNA fragmentation factor-alpha-like effector A; COX-1: cyclooxygenase; Nad3, Nad4: NADH dehydrogenase: Atp8: adenosine triphosphate; TBARS: thiobarbituric acid-reactive substances; TBX1: T-box transcriptional factor 1.

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Emamat et al. (2018)	Sprague - Dawley	Male; Age not informed	Fat: 59%; Carbohydrate: 30%; Protein: 11%	7 weeks	- No informed; - Whole yellow onion powder. During powder processing, the leaves were heated to 200 ºC for 15 s and mechanically crushed into fragments of 500–2000µm.	7 weeks	7%	↓ALT, AST, TG, glucose and insulin; = LDL-C e Total cholesterol; ↓TNF-α gene expression in liver; ↓ degree of hepatic steatosis in lobular and portal inflammation; = weight gain; #NOME?	14/20
Forney et al. (2018)	C57BL/6J	Gender not informed; 5 weeks	Fat: 45%;	9 weeks	- No informed; - Red onion extract in 80% ethanol, lyophilized to obtain the powder.	9 weeks	17mg/kg	Red onion extract Effects: ↓weight of inguinal and epididymal adipose tissue; ↓size of inguinal and epididymal adipocytes; ↑density of inguinal and epididymal adipocytes; ↓Cd11b and Cd68, =Mcp-1 and F4/80 (inguinal); ↑Cd11b, ↓Cd68 and Mcp-1 and =F4/80 (epididymal); = leptin and adiponectin; ↓ IL-6; ↑ multilocular adipocytes (inguinal). Quercetin Effects: ↓weight of inguinal and epididymal adipose tissue; ↓size of epididymal adipocytes; ↑ density of epididymal adipocytes; ↓Cd11b and Cd68, =Mcp-1 and F4/80 (inguinal); =Cd11b, ↑Cd68, ↓Mcp-1 and =F4/80 (epididymal); ↑ multilocular adipocytes (inguinal).	15/20

= no statistically significant effect. ↓ statistically significant decrease. ↑ statistically significant increase. TG: triglyceride; HDL-C: high density lipoproteins; LDL-C: low density lipoproteins; ALT: alanine aminotransferase; AST: aspartate aminotransferase; GGT: geranylgeranyltransferase; TNF-α: Tumor Necrosis Factor alpha; Pgc-1α: gamma peroxisome proliferator-activated receptor-1 alpha coactivator; PPAR-γ: peroxisome proliferator activated receptor; FAS: fatty acid synthase; ACC: acetyl CoA carboxylase; UCP-1: uncoupling protein; SREBP-2: sterol regulatory element binding protein; HMG-CoAR: 3-hydroxy-3-methyl-glutaryl-CoA reductase; Alb: albumin; CPT-1α: carnitine palmitoyltransferase- 1α; (C/EBP)α: CCAAT/enhancer binding protein; IL-6: Interleukin 6; *Cd11b*:Cluster of differentiation 11b; *Cd68*:Cluster of differentiation 68; *Mcp-1*:Monocyte chemoattractant protein 1; PRDM16: PR domaincontaining 16;CIDEA:cell death-inducing DNA fragmentation factor-alpha-like effector A; COX-1: cyclooxygenase; Nad3, Nad4: NADH dehydrogenase: Atp8: adenosine triphosphate; TBARS: thiobarbituric acid-reactive substances; TBX1: T-box transcriptional factor 1.

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Yang et al. (2018)	Sprague - Dawley	Male; Age not informed	Casein: 20%; Sucrose: 25.3%; Fiber: 4%; Lard: 10%; Custard powder: 5%; Cholesterol: 1.5%	- No informed;	*-Allium cepa L.;* - To obtain the oil, the onion bulbs were minced, soaked in distilled water 1.5 times at 35 °C for 2.5 h.	60 days (8 weeks)	46.3 mg /kg/d and 92.6 mg/kg/ d	Onion Oil Effects: ↓ weight gain; ↓ Lee index; ↓ weight of epididymal and perirenal adipose tissue; - High dose group (92.6mg/ kg/d): ↓TG, Total cholesterol and LDL-C; - High dose group (92.6mg/ kg/d): ↑HDL-C; ↓ atherosclerosis index; ↓ degree of hepatic steatosis; = food intake; ↑ liver and kidney relative weight.	15/20
Devarshi et al. (2017)	C57BL / 6J	Male; 5 weeks	Fat: 45%	9 weeks	- No informed; - Red onion peel extracts	9 weeks	- 17mg/kg	↓ gene expression *Pgc-1α-a;* ↑ gene expression NT-*Pgc-1α;* ↓ gene expression *FL-Pgc-1α.*	out/20
Lee et al. (2017)	C57BL / 6	Male; 4 weeks	Fat:60%	8 weeks	- No informed - Onion peels were washed and air-dried overnight. Onion peel were pulverized for 3 min with 1 L of 60% aqueous ethanol as the extracting solvent.	8 weeks	0.50%	#NOME? = expression PPARγ and FAS (epididymal, retroperitoneal and subcutaneous adipose tissue); = TBX1 and CPT1α (epididymal, retroperitoneal and subcutaneous adipose tissue); ↓ expression ACC (epididymal); ↑ PRDM16, PGC1α and UCP1 (retroperitoneal); ↑ CIDEA (retroperitoneal and subcutaneous)	16/20

= no statistically significant effect. ↓ statistically significant decrease. ↑ statistically significant increase. TG: triglyceride; HDL-C: high density lipoproteins; LDL-C: low density lipoproteins; ALT: alanine aminotransferase; AST: aspartate aminotransferase; GGT: geranylgeranyltransferase; TNF-α: Tumor Necrosis Factor alpha; Pgc-1α: gamma peroxisome proliferator-activated receptor-1 alpha coactivator; PPAR-γ: peroxisome proliferator activated receptor; FAS: fatty acid synthase; ACC: acetyl CoA carboxylase; UCP-1: uncoupling protein; SREBP-2: sterol regulatory element binding protein; HMG-CoAR: 3-hydroxy-3-methyl-glutaryl-CoA reductase; Alb: albumin; CPT-1α: carnitine palmitoyltransferase- 1α; (C/EBP)α: CCAAT/enhancer binding protein; IL-6: Interleukin 6; *Cd11b*:Cluster of differentiation 11b; *Cd68*:Cluster of differentiation 68; *Mcp-1*:Monocyte chemoattractant protein 1; PRDM16: PR domaincontaining 16;CIDEA: cell death-inducing DNA fragmentation factor-alpha-like effector A; COX-1: cyclooxygenase; Nad3, Nad4: NADH dehydrogenase: Atp8: adenosine triphosphate; TBARS: thiobarbituric acid-reactive substances; TBX1: T-box transcriptional factor 1.

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Emamat et al. (2016)	Sprague - Dawley	Male; Age not informed	Fat:59%; Carbohydrate: 30%; Protein: 11%	7 weeks	- No informed; - Whole yellow onion powder. During powder processing, the leaves were heated to 200 ºC for 15 s and mechanically crushed into fragments of 500–2000µm.	4 weeks	7%	↑ weight gain – control group + onion; ↑ food intake – control group + onion; ↓ ALT, TG, glucose and insulin; ↓ TNFα gene expression in liver; #NOME?	13/20
Henagan et al. (2015)	C57BL / 6J	Gender not informed; 5 weeks	Fat:45%	9 weeks	- No informed; - Red onion extract in 80% ethanol, lyophilized to obtain the powder.	9 weeks	17mg	Red onion extract and Quercetin Effects: = food intake; ↓ body weight; ↓percent fat mass; ↑ muscle mass; ↓ insulin test; ↑Energy expenditure; ↓ respiratory exchange ratio; ↑ Mitochondrial number; #NOME? determined by measuring acid soluble metabolites (ASM); ↓ Nd3, Nd4, Cox1 and Atp8 (Only quercetin).	15/20
Matsunaga et al. (2014)	BALB/c	Male; 4 weeks	Fat: 32%	28 days (4 weeks)	- No informed; - lyophilized onion peel tea containing 1.15 mg / g quercetin	28 days (4 weeks)	5%	Effects of onion peel tea: ↓ body weight and weight of epididymal adipose tissue; ↓ total cholesterol on day 14 and glucose and leptin on day 28. ↓ TG on day 14 and 28; ↑alkaline phosphatase on day 28; = ALT, AST, GGT or Alb on days 14 or 28.	11/20

= no statistically significant effect. ↓ statistically significant decrease. ↑ statistically significant increase. TG: triglyceride; HDL-C: high density lipoproteins; LDL-C: low density lipoproteins; ALT: alanine aminotransferase; AST: aspartate aminotransferase; GGT: geranylgeranyltransferase; TNF-α: Tumor Necrosis Factor alpha; Pgc-1α: gamma peroxisome proliferator-activated receptor-1 alpha coactivator; PPAR-γ: peroxisome proliferator activated receptor; FAS: fatty acid synthase; ACC: acetyl CoA carboxylase; UCP-1: uncoupling protein; SREBP-2: sterol regulatory element binding protein; HMG-CoAR: 3-hydroxy-3-methyl-glutaryl-CoA reductase; Alb: albumin; CPT-1α: carnitine palmitoyltransferase- 1α; (C/EBP)α: CCAAT/enhancer binding protein; IL-6: Interleukin 6; *Cd11b*:Cluster of differentiation 11b; *Cd68*:Cluster of differentiation 68; *Mcp-1*:Monocyte chemoattractant protein 1; PRDM16: PR domaincontaining 16;CIDEA:cell death-inducing DNA fragmentation factor-alpha-like effector A; COX-1: cyclooxygenase; Nad3, Nad4: NADH dehydrogenase: Atp8: adenosine triphosphate; TBARS: thiobarbituric acid-reactive substances; TBX1: T-box transcriptional factor 1.

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Moon et al. (2013)	Sprague - Dawley	Male;5 weeks	Fat: 40% Sucrose: 34% Casein: 20%	8 weeks	- No informed; - Onion peel extracts extracted with 60% aqueous ethanol solution (50 ° C, 3 hours).	8 weeks	0.36% e 0.72%	Effects of onion extract (0.36% and 0.72%) on the high fat diet showed: ↓final body weight and weight of mesenteric adipose tissue; = weight of perirenal and epididymal adipose tissuel; ↓feed efficiency ratio; ↓ gene expression PPAR-γ, FAS e ACC; ↑ CPT-1α; Effects of onion extract (0.72%): ↓ retroperitoneal adipose tissue and visceral fat; ↓ C/EBP-α; Effects of onion extract (0.36%): ↑ gene expression UCP-1.	14/20
Benítez et al. (2012)	Wistar	Female; 6 weeks	Glucose: 189g; Casein: 200g; butter: 370g; Cholesterol: 45g	4 weeks	- *Allium cepa L.;* - The onions were milled to obtain a "bagasse" added to the diet.	4 weeks	10%	Effects of onion bagasse on the high fat diet: ↓ body weight and food efficiency; ↑food consumption; = weight of organs such as heart, kidney, intestine and spleen; all animals pallid colored liver and bigger livers; ↓ total cholesterol and TG; ↓ pH cecal content and fecal weight; ↑ HDL-C.	14/20

= no statistically significant effect. ↓ statistically significant decrease. ↑ statistically significant increase. TG: triglyceride; HDL-C: high density lipoproteins; LDL-C: low density lipoproteins; ALT: alanine aminotransferase; AST: aspartate aminotransferase; GGT: geranylgeranyltransferase; TNF-α: Tumor Necrosis Factor alpha; Pgc-1α: gamma peroxisome proliferator-activated receptor-1 alpha coactivator; PPAR-γ: peroxisome proliferator activated receptor; FAS: fatty acid synthase; ACC: acetyl CoA carboxylase; UCP-1: uncoupling protein; SREBP-2: sterol regulatory element binding protein; HMG-CoAR: 3-hydroxy-3-methyl-glutaryl-CoA reductase; Alb: albumin; CPT-1α: carnitine palmitoyltransferase- 1α; (C/EBP)α: CCAAT/enhancer binding protein; IL-6: Interleukin 6; *Cd11b*:Cluster of differentiation 11b; *Cd68*:Cluster of differentiation 68; *Mcp-1*:Monocyte chemoattractant protein 1; PRDM16: PR domaincontaining 16;CIDEA:cell death-inducing DNA fragmentation factor-alpha-like effector A; COX-1: cyclooxygenase; Nad3, Nad4: NADH dehydrogenase: Atp8: adenosine triphosphate; TBARS: thiobarbituric acid-reactive substances; TBX1: T-box transcriptional factor 1.

Table 2. Continued...

Main author / year	Animal species	Gender/ Age	Composition of the high fat diet	high fat diet exposure period	Onion characteristics and methodology used	Period of exposure to onion or its by-products	Quantity used of onion or its by-products	Main results	Final score of adequacy by ARRIVE
Lee et al. (2012)	Sprague - Dawley	Male; 3 weeks	Fat: 33%;	8 weeks	- No informed;	8 weeks	0.20%	↑ LDLR, SREBP-2, HMG-CoAR and staeroyl - coA desaturase 1 gene expression in liver; ↓ apolipoprotein A1;	out/20
			Sucrose: 10%		- Onion peel extracts extracted with 60% aqueous ethanol solution (50 ° C, 3 hours).			↑ gene expression PPARγ2 and ATP-binding cassette subfamily G member 1 (ABDG1);	
			Casein: 20%					= body weight; = gene expression LXRα;	
								↑ food efficiency; ↓ food consumption;	
Hamauzu et al. (2011)	Wistar	Male; 9 weeks	Fat: 5.1%; Protein: 22.2%	18 weeks	- *Allium cepa L.*; - The powder was prepared from the external layer of the onion.	18 weeks	5%	= body weight; ↓ modulus of elasticity of rat aorta; ↓ atherogenic index; = TG, total cholesterol and HDL-C.	12/20
Kim et al. (2012)	Sprague - Dawley	Male; 3 weeks	Sucrose: 10%;	8 weeks	- No informed;	8 weeks	0.20%	↓ food consumption; ↑ food efficiency index;	dez/20
			Casein: 20%; Cholesterol: 1%		- Onion peel extracts extracted with 60% aqueous ethanol solution.			= body weight; = weight of perirenal and epididymal adipose tissue;	
			Corn oil: 6%					= liver enzymes, blood urea nitrogen and Creatinine; = IL-6 gene expression;	
			Lard: 10%					↑ adiponectin and PPAR2γ gene expression in mesenteric fat; ↓ weight of mesenteric fat;	

= no statistically significant effect. ↓ statistically significant decrease. ↑ statistically significant increase. TG: triglyceride; HDL-C: high density lipoproteins; LDL-C: low density lipoproteins; ALT: alanine aminotransferase; AST: aspartate aminotransferase; GGT: geranylgeranyltransferase; TNF-α: Tumor Necrosis Factor alpha; Pgc-1α: gamma peroxisome proliferator-activated receptor-1 alpha coactivator; PPAR-γ: peroxisome proliferator activated receptor; FAS: fatty acid synthase; ACC: acetyl CoA carboxylase; UCP-1: uncoupling protein; SREBP-2: sterol regulatory element binding protein; HMG-CoAR: 3-hydroxy-3-methyl-glutaryl-CoA reductase; Alb: albumin; CPT-1α: carnitine palmitoyltransferase- 1α; (C/EBP)α: CCAAT/enhancer binding protein; IL-6: Interleukin 6; *Cd11b*:Cluster of differentiation 11b; *Cd68*:Cluster of differentiation 68; *Mcp-1*:Monocyte chemoattractant protein 1; PRDM16: PR domaincontaining 16;CIDEA:cell death-inducing DNA fragmentation factor-alpha-like effector A; COX-1: cyclooxygenase; Nad3, Nad4: NADH dehydrogenase: Atp8: adenosine triphosphate; TBARS: thiobarbituric acid-reactive substances; TBX1: T-box transcriptional factor 1.

Table 3. Risk of bias of the included animal studies, assessed according to the SYRCLE guideline.

Study	Sequence Generation	Baseline Characteristics	Allocation Concealment	Random Housing	Performance Blinding	Random outcome assessment	Blinding of outcome assessment	Incomplete outcome data	Selective outcome reporting	Other sources of bias
Chang et al. (2022)	Y	Y	N	Y	N	U	U	Y	U	Y
Momoh et al. (2022)	Y	Y	N	Y	N	U	U	Y	U	Y
Yu et al. (2021)	Y	Y	N	Y	N	U	U	Y	U	Y
Grzelak-Błaszczyk et al. (2020)	Y	Y	N	Y	N	Y	Y	Y	U	Y
Grzelak-Błaszczyk et al. (2018)	Y	Y	N	U	N	U	U	Y	U	Y
Emamat et al. (2018)	Y	Y	N	Y	N	U	U	Y	U	Y
Forney et al. (2018)	Y	Y	N	Y	N	U	U	Y	U	Y
Yang et al. (2018)	Y	Y	N	Y	N	U	U	Y	U	Y
Devarshi et al. (2017)	Y	Y	N	Y	N	U	U	Y	U	Y
Lee et al. (2017)	Y	Y	N	Y	N	U	U	Y	U	Y
Emamat et al. (2016)	Y	Y	N	Y	N	U	U	Y	U	Y
Henagan et al. (2015)	Y	Y	N	Y	N	U	U	Y	U	Y
Matsunaga et al. (2014)	Y	Y	N	Y	N	U	U	Y	U	Y
Moon et al. (2013)	Y	Y	N	Y	N	U	U	Y	U	Y
Benítez et al. (2012)	Y	Y	N	Y	N	U	U	Y	U	Y
Lee et al. (2012)	Y	Y	N	Y	N	U	U	Y	U	Y
Hamauzu et al. (2011)	Y	Y	N	U	N	U	U	Y	U	Y
Kim et al. (2012)	Y	Y	N	Y	N	U	U	Y	U	Y

Y, yes = low risk of bias; N, no = high risk of bias; U, unclear = unclear risk of bias.

they did not fit the defined inclusion criteria. After the full-text reading, of the 37 remaining articles, 18 studies were considered eligible and were included in the review (Figure 1).

The results tabulated in the present study were: identification of the work (main author and year); species of animal that served as the study model; age and gender; high-fat diet composition; period of exposure to the diet; onion type and experimental methodology used; exposure period of onion, bulb, oil or tea or peel powder; dosage used of onion, bulb, oil or tea or peel powder; and main results (Table 2).

In 83% of the articles, male animals were used, 1 study used female animals and 2 studies did not report the gender of the animal. In 66.6% of the studies Wistar or Sprague-Dawley rats were used and in 33.3% C57BL/6 and Balb/c mice, aged three to nine weeks, were considered young animals. The percentage of fat in the high-fat diets varied between 5.1% and 60% and the period of exposure to this diet varied between 4 and 18 weeks. The period of exposure to onion or its by-products varied between 4 and 12 weeks.

The main benefits of onion and its by-products, found in this review, lipid profile and cardiovascular risk with decreased total cholesterol, low-density lipoprotein cholesterol (LDL-C), triglycerides (TG), atherosclerosis index and aorta elastic modulus, and increased high-density lipoprotein cholesterol (HDL-C) (Hamauzu et al., 2011; Benítez et al., 2012; Matsunaga et al., 2014; Emamat et al., 2018; Yang et al., 2018; Grzelak-Błaszczyk et al., 2020; Yu et al., 2021; Momoh et al., 2022; Chang et al., 2022).

Decreased or non-altered mesenteric, epididymal, perirenal, retroperitoneal, inguinal, and weight gain adiposity were also observed (Lee et al., 2012; Benítez et al., 2012; Kim et al., 2012; Moon et al., 2013; Matsunaga et al., 2014; Henagan et al., 2015; Emamat et al., 2016, 2018; Lee et al., 2017; Forney et al., 2018; Yang et al., 2018; Grzelak-Błaszczyk et al., 2018; Yu et al., 2021; Chang et al., 2022).

Liver abnormalities were also attenuated, with decreases observed in liver enzymes alanine aminotransferase (ALT) and aspartate aminotransferase (AST), the degree of steatosis and lobular and portal inflammation (Emamat et al., 2016, 2018; Yang et al., 2018; Grzelak-Błaszczyk et al., 2018; Momoh et al., 2022; Chang et al., 2022).

Inflammatory and metabolic parameters were reduced by the addition of onion or its by-products, as seen in the expression of pro-inflammatory cytokine Tumor Necrosis Factor alpha (TNFα), Interleukin 6 (IL-6), Cluster of differentiation 11b (*Cd11b*), Cluster of differentiation 68 (*Cd68*), respectively, Monocyte chemoattractant protein 1 (*Mcp-1*), and factors such as peroxisome proliferator-activated receptor-gamma (PPARγ), fatty acid synthase (FAS), and acetyl CoA carboxylase (ACC), as well as a decrease in leptin, insulin, and glucose, with increased expression of the uncoupling protein (UCP-1), PR domain containing 16 (PRDM16), and cell death-inducing DNA fragmentation factor-alpha-like effector A (CIDEA), followed by an increase in mitochondria, and multilocular adipocytes in white adipose tissue (Lee et al., 2012; Kim et al., 2012; Moon et al., 2013; Matsunaga et al., 2014; Henagan et al., 2015; Emamat et al., 2016, 2018; Forney et al., 2018).

Of the studies selected for this review, 13% showed an increase in the total concentration of short chain fatty acids (SCFA), of intestinal enzymes such as β-glucosidase and β-glucuronidase and of propionic and butyric acid in groups supplemented with onion or its by-products (Grzelak-Błaszczyk et al., 2018, 2020).

In addition, it should be noted that the papers that composed this review reached 50% to 85% of the items recommended by the ARRIVE protocol (Table 2). In assessing the risk of bias, it was observed that 50% of the questions in the SYRCLE protocol, were positively filled by all selected

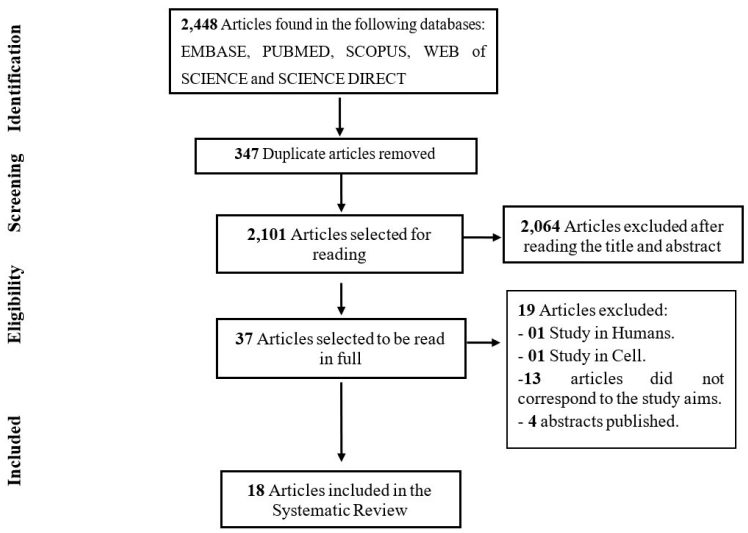

Figure 1. Flowchart of the search result in the information sources, the selection and inclusion of the original articles in the systematic review (Moher et al., 2009).

articles, considering a low risk of bias. However, all studies showed inadequacies in 20% of the questions related to Allocation Concealment and Performance Blinding, presenting a high risk of bias. It was also observed that 30% of the questions related to Random outcome assessment, Blinding of outcome assessment and Selective outcome reporting, were unclear in all studies in this review (Table 3).

4. Discussion

Excessive consumption of high saturated fat diets is associated with obesity, predisposing the individual to the appearance of metabolic and inflammatory changes. One way to mitigate the negative effects caused by the consumption of a high-fat diet is the addition of onion or its by-products in the diet, as onion contains elements such as quercetin, a well-studied flavonoid that may contribute to the prevention or treatment of diseases. The most studied forms of quercetin are aglycone (free form), quercetin monoglycosides, and quercetin diglycosides. The onion peel has a higher concentration of quercetin aglycone compared to the whole onion, which may be related to the hydrolysis of quercetin glycosides during the formation of the peel (Grzelak-Błaszczyk et al., 2018; Xu et al., 2019). This vegetable and its by-products are rich in fiber and also contain other flavonoids, such as kampferol and protocatechuic acid, both of which exert their own health benefits (Slimestad et al., 2007; Hamauzu et al., 2011; Benítez et al., 2012; Lee et al., 2012; Moon et al., 2013; Matsunaga et al., 2014; Emamat et al., 2016, 2018; Grzelak-Błaszczyk et al., 2018; Yang et al., 2018). This systematic review evaluated a number of studies that investigated the effects of onion or its by-products singly or in combination with garlic oil, either at different doses or exposure periods, but always added to a high-fat diet. Studies have also shown that onion or its by-products, reduced the deleterious health effects of high-fat diet (Figure 2).

All selected papers in this review used male or female rats or mice, aged three to nine weeks, being considered young animals. These animals were exposed to a high-fat diet with onion peel powder, bulb, oil, leaves or tea added at different periods, ranging from 4 to 18 weeks. The amount of onion peel and leaves powder also varied between the authors studied, from 0.2% to 20%, onion extract varying in mg (17mg) and percentage (0.21% to 0.44%) and the onion peel tea varied from 46.3 mg/kg to 92 mg/kg animal weight. Independent of the amount of onion or its by-products used, the introduction of this vegetable brought benefits to the supplemented animals.

To analyze the quality of the papers, we used the ARRIVE protocol, specific for experimental studies (Percie Du Sert et al., 2020). Most articles in this review were found to meet more than 50% of the ARRIVE checklist with most of the criteria not met being related to the absence of facilities description, animal veterinary conditions, and the description of scientific implications such as study limitations.

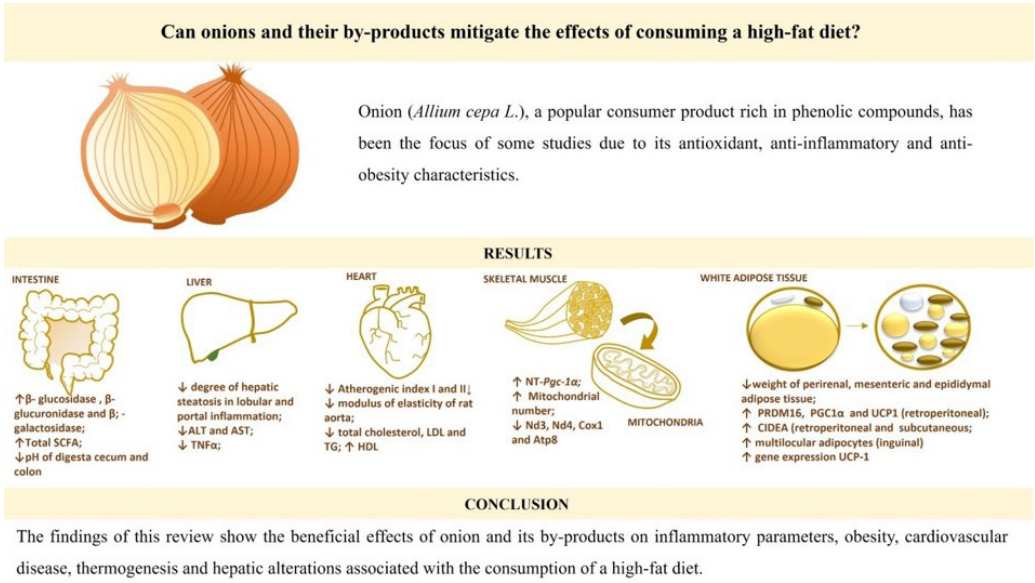

Figure 2. Graphical Abstract. Onions and their by-products mitigated the effects of consuming a high-fat diet in different organs, tissues, and cells. In the intestine, there was an increase in intestinal enzymes, short-chain fatty acids, and a decrease in digestive pH. In the liver, the degree of steatosis was reduced, as well as liver enzymes and the expression of TNF-α, a pro-inflammatory cytokine. In the heart, there was a reduction in the rates of atherosclerosis I and II, in the modulation and elasticity of the aorta, and an improvement in the lipid profile. At the mitochondrial level, there was an increase in Pgc-1 and a decrease in mitochondrial genes with quercetin supplementation but not with onion extract. There was an increase in genes specific for brown adipose tissue in white adipose tissues, genes such as UCP-1, PRDM16, and CIDEA. Thus, the use of these products may have additional implications for the prevention of pathologies related to obesity.

There was a risk of bias in the selected studies when related to Allocation Concealment and Performance Blinding. Some studies were evaluated with unclear risk for evaluation Random outcome assessment, Blinding of outcome assessment and Selective outcome reporting. However, most articles had a low risk of bias in 50% of the questions in the SYRCLE assessment.

Onion is known for its antioxidant, anti-obesity, anti-inflammatory, and prebiotic powers. These attributes are mainly due to the presence of quercetin, a highly studied flavonoid with important functional characteristics (Moon et al., 2013; Nabavi et al., 2015; Forney et al., 2018; Fraga et al., 2019). This flavonoid is capable of eliminating free radicals due to its effect on the potentiation of antioxidant enzymes such as glutathione (GSH) and superoxide dismutase (SOD) (Hayek et al., 1997; Erden Inal and Kahraman, 2000; Kobori et al., 2015). In this process, the donation of electrons contributes to stabilizing these free radicals, thus reducing the oxidative stress and consequent associated diseases (Hayek et al., 1997; Erden Inal and Kahraman, 2000; Kobori et al., 2015). Quercetin, for example, can reduce the oxidation of LDL molecules due to the elimination of free radicals, thus preventing diseases such as atherosclerosis (Ji et al., 2019).

In this review, 22% of the selected articles showed an improvement in the lipid profile, especially in LDL levels, of animals supplemented with onion oil compared to the group that was submitted only to a high-fat diet, confirming the protective effect of onion (Yang et al., 2018). Also, studies have demonstrated improvements in all lipid profiles, with a decreased serum determination of total cholesterol and TG, and an increase in HDL-C, confirming that animals benefited from the powder, tea, oil or extracts of onion concentrated of protocatechuic acid (Benítez et al., 2012; Matsunaga et al., 2014; Emamat et al., 2018; Yang et al., 2018; Grzelak-Błaszczyk et al., 2020; Yu et al., 2021; Chang et al., 2022; Momoh et al.,2022).

Cardiovascular protection associated with the consumption of powder, oil or extracts of onion concentrated with protocatechuic acid and quercetin monoglycosides was also observed in the heart structure of rats, which showed benefits in the atherosclerosis index, as well as decreasing the elasticity of the aorta of these animals, even when combined with a high-fat diet (Hamauzu et al., 2011; Yang et al., 2018; Grzelak-Błaszczyk et al., 2018, 2020).

Another important characteristic of onion is its anti-inflammatory effect. Inflammation may occur due to various stimuli, one of which may be the excessive consumption of a high saturated fat diet. This eating habit may predispose the individual to intestinal dysbiosis, with an increase in gram-negative bacteria, which has in its outermost layer the endotoxin called lipopolysaccharide (LPS). LPS binds to toll-like 4 membrane receptors (TLR4), increasing intestinal permeability, triggering inflammatory processes, and releasing pro-inflammatory cytokines such as TNFα and IL-6, as well as elevating nuclear factor kappa B (NF-Kb) levels (Poggi et al., 2007; Manco et al., 2010; Guo et al., 2013; Ma et al., 2017). Quercetin, present in onion, significantly inhibits these inflammatory effects. This was confirmed in this review, with 20% of the studies showing that the onion, rich in this flavonoid, reduces the excretion of inflammatory cytokines, mainly TNFα and IL-6 (Emamat et al., 2016, 2018; Forney et al., 2018).

Increased intestinal permeability, induced by the consumption of a high fat-diet, may be associated with the development of NAFLD, due to the increase of gram-negative bacteria that release lipopolysaccharides LPS (Poggi et al., 2007; Manco et al., 2010; Guo et al., 2013). Increased LPS levels in the liver inhibit the fasting-induced adipose factor (Fiaf) that regulates lipoprotein lipase, whose function is to store fat in organs such as the liver and adipose tissue (Poggi et al., 2007; Aguirre and Venema, 2015; Larsen et al., 2019). Studies using powder, oil or extracts of onion concentrated with quercetin monoglycosides showed an improvement in the activity scores of NAFLD, improving the degree of steatosis, decreasing hepatic ALT and AST enzymes and lobular and portal inflammation (Emamat et al., 2016, 2018; Yang et al., 2018; Grzelak-Błaszczyk et al., 2018; Yu et al., 2021; Chang et al., 2022; Momoh et al.,2022).

In addition to the benefits of quercetin, pectin, a soluble dietary fiber, is another important component present in onions, which may contribute to the balance of intestinal microbiota and the reduction of cardiovascular risks (Hamauzu et al., 2011; Benítez et al., 2012). This is because pectin is easily degraded by commensal bacteria in the gut, generating energy from the fermentation process and producing SCFA, primarily butyrate, which serve as an energy source for epithelial cells (Habinowski and Witters, 2001; Hamauzu et al., 2011; Guo et al., 2013). The formation of SCFA can inhibit the development of pathogenic bacteria and assist in intestinal immunity, improving their integrity and favoring adhesion of probiotic strains in the intestinal epithelium (Habinowski and Witters, 2001).

Fiber intake can provide benefits, such as reduced energy intake, increased satiety due to its viscosity, and gel formation, which may favor decreased intestinal absorption of food components such as fat, thereby reducing serum lipids and total cholesterol (Habinowski and Witters, 2001; Hamauzu et al., 2011; Benítez et al., 2012). In addition, the consumption of fiber-rich foods may benefit intestinal transit time with a decreased caecal pH due to fermentation by commensal bacteria producing SCFA, and thus improving constipation (Benítez et al., 2012; Grzelak-Błaszczyk et al., 2018). In this review, an increase in SCFA was observed in animals supplemented with onion extract concentrated in quercetin and quercetin monoglycosides, with an increase in the concentrations of propionic and butyric acid (Grzelak-Błaszczyk et al., 2018, 2020). There was also an increase in intestinal enzymes such as β-glucosidase and β-glucuronidase, which can be associated with bacterial adaptation to higher levels of quercetin glycosides present in the diet (Grzelak-Błaszczyk et al., 2018, 2020).

The anti-obesity effect is another functional characteristic of quercetin, present in onion, and some authors claim that this flavonoid has an antiadipogenic effect due to the activation of *adenosine monophosphate*-activated protein kinase (AMPK) (Berg et al., 2001; Devarshi et al., 2017). Quercetin can reduce adipocyte hyperplasia which is an important process for the development of metabolic syndrome (Berg et al., 2001; Devarshi et al., 2017).

In this review, than 38.8% of the studies found benefits from the addition of onion powder, tea, oil, or extract concentrated in quercetin and monoglycoside quercetin to the diet, including reduced body weight and weight of epididymal, perirenal, mesenteric, inguinal, and retroperitoneal adipose tissues (Lee et al., 2012; Benítez et al., 2012; Kim et al., 2012; Moon et al., 2013; Matsunaga et al., 2014; Henagan et al., 2015; Forney et al., 2018; Yang et al., 2018; Yu et al., 2021; Chang et al., 2022). With regard to food intake, the animals that were exposed to onion presented an increased food efficiency index and decreased consumption, possibly related to the satiety provided by the dietary fiber intake, which may contribute to a reduction in weight (Benítez et al., 2012; Kim et al., 2012). Also observed was an increased expression of adiponectin (in mesenteric adipose tissue), an adipokine secreted by adipocytes that exerts some protective effects which are anti-atherogenic and anti-inflammatory (Berg et al., 2001; Kim et al., 2012). The decreased expression of inflammatory genes such as *Cd11b* and *Cd68* in inguinal adipose tissue and of *McP-1* and IL-6 genes in epididymal adipose tissue in groups supplemented with onion extract attenuated the inflammatory effect of the high-fat diet (Forney et al., 2018).

The positive effects of onion can also be observed with the increased expression of the uncoupling protein 1 (UCP-1), important in the thermogenesis process, suggesting that this vegetable can stimulate lipid catabolism, promoting fat burning (Moon et al., 2013; Lee et al., 2017). This process can occur by the action of quercetin on white and brown adipose tissue, in which this flavonoid activates AMPK which in turn activates PPARγ (Lee et al., 2012; Kim et al., 2012; Moon et al., 2013). This subsequently interacts with the gamma 1 peroxisome proliferator-activated receptor (Pgc-1α), its coactivator increases UCP-1 transcription, contributing to the browning of white adipose tissue and the activation of brown adipose tissue (Moon et al., 2013; Devarshi et al., 2017; Lee et al., 2017; Choi et al., 2018). This browning can be observed by the presence of multilocular adipocytes in white adipose tissue presenting morphology and functions similar to those found in brown adipose tissue (Forney et al., 2018).

Other genes specific to brown adipose tissue showed greater expression in retroperitoneal and epididymal white adipose tissue, genes such as PRDM16 transcriptional co-regulator necessary for the development of brown and beige adipocytes, and CIDEA an important protein in the formation of lipid droplets brown and beige adipose tissue (Harms et al., 2014; Barneda et al., 2015; Lee et al., 2017).

The onion extract was also able to increase the number of mitochondria in skeletal muscle, improving fat metabolism, insulin sensitivity, and increasing energy expenditure (Henagan et al., 2015; Emamat et al., 2016, 2018). There was also a reduction in mitochondrial genes *Nd3, Nd4* (subunits of complex I), *Cox1* (a subunit of complex IV) and *Atp8* (a subunit of ATPsintase) in groups supplemented with quercetin, but not in those supplemented with onion extract, than can indicate changes in the oxidative phosphorylation system (OXPHOS) which is located in the inner mitochondrial membrane (Henagan et al., 2015; Bouchez and Devin, 2019).

The anti-obesity effect of onion and its by-products may be justified by the reduction of adipogenesis through pathways involved in lipid metabolism (Moon et al., 2013). Authors have shown in their experimental studies that the addition of onion peel extract reduced PPARγ expression as an adipogenesis transcription factor, thus contributing to decreased adipocyte proliferation (Moon et al., 2013). Also, PPARγ regulates the enzymes fatty acid synthase (FAS) and acetyl CoA carboxylase (ACC), consequently reducing the expression of these genes (Moon et al., 2013; Lee et al., 2017).

The studies that make up this review show methodological differences, such as the use of different by-products, dosages, and administration periods, which made it impossible to carry out a meta-analysis due to the heterogeneity of the data. This review, demonstrated the importance of consuming onion and its by-products. Benefits related to the inflammatory parameters, obesity, cardiovascular disease, thermogenesis, and liver disorders were observed, associated with the consumption of a high-fat diet.

In conclusion, was observed the beneficial effects of onion or its by-products on inflammatory parameters, obesity, cardiovascular diseases, thermogenesis and hepatic alterations associated with the consumption of a high-fat diet. Thus, the use of these products may have further implications in preventing obesity-related pathologies. Despite these beneficial effects, the minimum amount sufficient to bring benefits or the limit amount /excessive that were able of causing damage to health were not shown in the studies. Therefore, further studies are needed to determine these issues.

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