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Effect of Passiflora species in the adjuvant treatment of dyslipidemia: A systematic review

Elsa Beatriz Tequín-Ocampo [1], Clara Helena González-Correa [2], William Narváez-Solarte [3]

Abstract

Some research has shown that polyphenols found in certain fruits have hypolipidemic properties when consumed in the diet and therefore this study aimed to present a review of the updated information on the hypolipidemic effect of Passiflora species. Several databases were used in the search for publications from the last 10 years (2013-2023) on advances in the use of Passiflora species for a complementary treatment of dyslipidemia. A total of 670 potential articles were found, of which 654 were excluded, leaving 16 articles for the review. Of the studies included in this analysis, 12 were on *Passiflora edulis*, eight were on the peel, three on the seed and one on the mesocarp. The other articles were on Passiflora species (*P. incarnata, P. ligularis, P. foetida and P. nitida*). Six were in humans, nine in mice and one study was conducted in rabbits. Metabolic syndrome was found to be the most addressed topic in this review, with a total of five studies, followed by the combination of overweight and dyslipidemia. The different parts of the Passiflora species studied showed a hypolipidemic effect and Passiflora edulis (passion fruit) is the most studied, with twelve studies. This effect is probably due to its content of polyphenols, fiber and bioactive compounds that reduce oxidative stress and chronic inflammation underlying various dyslipidemias. However, further studies in humans are needed to confirm these beneficial effects and to establish the doses and time required to obtain a positive result.

Keywords: antioxidant; dyslipidemia; Passiflora; polyphenols.

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[1] M.Sc. Biomedical Sciences Doctoral Program, Universidad de Caldas, Colombia, *Corresponding author: elsa.tequin2132@ucaldas.edu.co, Calle 65 N° 26-10 Central Campus. E-204
orcid.org/0000-0002-6415-2367
[2] Ph.D. Department of Basic Sciences, Universidad de Caldas, Colombia; clara.gonzalez@ucaldas.edu.co
orcid.org/0000-0001-5621-2166
[3] Ph.D. Research Group in Nutrition, Metabolism and Food Safety, Animal Health Department, Universidad de Caldas, Colombia, wnarvaez@ucaldas.edu.co
orcid.org/0000-0003-4698-3818

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Efecto de las *Passifloras* en el tratamiento coadyuvante de la dislipidemia: Una Revisión Sistemática

Resumen

Algunos trabajos de investigación han demostrado que los polifenoles encontrados en ciertas frutas tienen propiedades hipolipemiantes cuando se consumen en la dieta, y por eso este estudio tuvo como objetivo presentar una revisión de la información actualizada sobre el efecto hipolipemiante de las especies de *Passiflora*. Se utilizaron varias bases de datos en la búsqueda de publicaciones de los últimos 10 años (2013-2023) sobre los avances en el uso de especies de *Passiflora* para un tratamiento complementario de la dislipidemia. Se encontraron un total de 670 artículos potenciales, de los cuales 654 fueron excluidos, dejando 16 artículos para la revisión. De los estudios incluidos en el presente análisis, 12 fueron sobre *Passiflora edulis,* ocho sobre la cáscara, tres sobre la semilla y uno sobre el mesocarpio. Los otros artículos fueron sobre especies de *Passiflora (P. incarnata, P. ligularis, P. foetida y P. nitida).* Seis fueron en humanos, nueve en ratones y un estudio se realizó en conejos. El síndrome metabólico fue el tema más tratado en esta revisión, con un total de cinco, seguido por la combinación de sobrepeso y dislipidemia. Las diferentes partes de las especies de *Passiflora* estudiadas mostraron un efecto hipolipemiante, y *Passiflora edulis* (maracuyá) es la más estudiada, con doce estudios. Este efecto probablemente se deba a su contenido de polifenoles, fibra y compuestos bioactivos que reducen el estrés oxidativo y la inflamación crónica subyacentes a diferentes dislipidemias. Sin embargo, se necesitan más estudios en humanos para confirmar estos efectos beneficiosos y para establecer las dosis y el tiempo necesarios para obtener un resultado positivo.

Palabras clave: Antioxidante, dislipidemia; *Passiflora*; Polifenoles.

Introduction

Dyslipidemia is, without a doubt, one of the most serious health problems humanity faces. Among the factors that influence this problem are diet and high caloric consumption from foods rich in sugar, and saturated fats. This excessive energy consumption exceeds caloric expenditure which, when combined with a sedentary lifestyle, translates into obesity problems. Finally, another epigenetic factor is a lifestyle related to smoking and excessive alcohol consumption. Likewise, dyslipidemia and diseases such as diabetes and chronic kidney disease, make this metabolic disorder, characterized by abnormal blood lipids levels, a major risk factor for the development of cardiovascular diseases, which are the leading cause of death worldwide (Pineda-Lozano et al., 2021). According to the World Health Organization (WHO), 17.9 million deaths due to cardiovascular diseases were reported in 2017, representing 32% of all deaths worldwide (WHO, 2023). According to this same organization, around 2.8 million people die each year with high cholesterol (≥190 mg/dl), as a risk factor, and its prevalence in the world population in 2020 was 39%. Of these, 54% corresponded to Europe, followed by America (48%), Asia (30%) and Africa (23%) (Mendis et al., 2011) It is estimated that more than 1 billion people worldwide have dyslipidemia, and that the prevalence of this condition has been increasing in recent years (Virani et al., 2020). In America, the prevalence of high cholesterol in men ranges between 31.8% and 56.1%, and in women between 37.5% and 54.3% (WHO, n.d.).

To prevent and treat dyslipidemia, the WHO recommends a series of measures such as following a healthy and balanced diet, exercising regularly, controlling smoking, managing overweight, treating underlying diseases such as diabetes and high blood pressure, and using specific medication when necessary (WHO, 2023). The medication used in the treatment of dyslipidemia entails significant costs and is often associated with unwanted side effects. Therefore, it is essential to conduct research aimed to find more natural alternatives that can address this public health problem. In this context, there is a growing interest in analyzing the impact of some fruits such as Passiflora species, whether the whole fruit or its parts. These fruits are generally rich in phenolic compounds and soluble and insoluble fiber, which have been shown to have anti-inflammatory, antioxidant, and anticancer properties, among others (Leal et al., 2020)2-diphenyl-1-picrylhydrazil (DPPH. This suggests that phenolic compounds could have positive effects on multiple dimensions of dyslipidemias and, by extension, influence other related diseases (Chalé et al., 2014; Foster et al., 2005).

There is evidence of the use of the *Passiflora* species in the treatment of dyslipidemia. The passionflower family includes 12 genera worldwide, with the *Passiflora* being the largest with around 400 species. It is found from Mexico to northern Argentina at altitudes between 1700 and 2600 meters above sea level, with temperatures between 15 and 18ºC and annual rainfall between 2000 and 2500 mm. The most commercially interesting, due to their edible fruits, are the granadilla (*P. ligularis Juss.*), passion fruit (*P. edulis*), badea (*P. quadrangularis*), cholupa (*P. maliformis*), gulupa (*P. edulis Sims.*) and curuba (*P. mollisima*). *Passiflora edulis* has received the most scientific attention in its use for the treatment of chronic diseases such as dyslipidemia and obesity, due to its high polyphenols and fiber content (Angel-Isaza et al., 2021; Nikolova et al., 2024). As a result of this research, it is recommended to include this fruit in the diet due to its favorable response in in vitro and in vivo studies, although the information of its effect in humans is limited.

The objective of this work is to present an analysis of the updated information on the lipid-lowering effect of Passiflora species.

Methods and materials

To develop the systematic review of scientific literature, the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) methodology (Yepes-Nuñez et al.,

2021) was applied. The search was conducted in the Scopus, Science Direct, Web of Science, and Dimensions databases, which in turn include PubMed and Google scholar. The keywords "dyslipidemia" and "*Passiflora*" as well as documents published from 2013 to 2023 were used as search terms. Original articles and reviews of in vitro, in vivo (animal) and human studies that examine the effect of Passiflora species and their bioactive components on dyslipidemia were considered. Duplicate publications, book chapters, and presentations were excluded. Furthermore, given the broadness of the term "polyphenols", it was excluded in the initial search in the databases. The information was limited to English, Spanish and Portuguese.

Finally, for the review of completed documents, those containing the terms hypercholesterolemia, hypertriglyceridemia, Passiflora and dyslipidemia in their title or abstracts were considered. Each selected study had an independent reading by two participating researchers, who had to consider the following criteria: a) inclusion of the publication period; b) originality of the study; c) report of the use of some type of Passiflora species; d) that the study was related to dyslipidemia. A total of 180 publications were identified in the Scopus, Science Direct, and Web of Science databases, and 490 were identified in the Dimensions database for a total of 670 publications. In addition, 654 documents were excluded for the reasons explained in (Figure 1) and 16 articles were considered for this review.

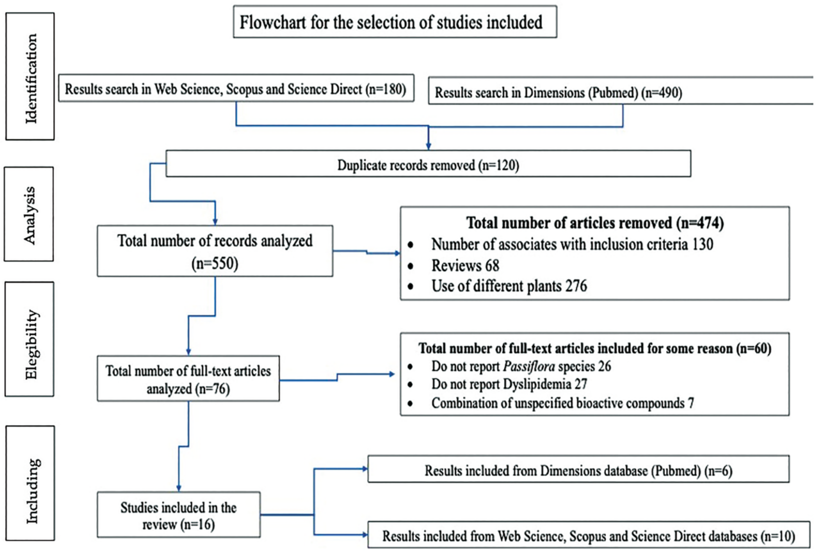

Figura 1. Flowchart for the selection of studies included in the review. A total of 670 records were identified through database searches (180 from Web Science, Scopus, and Science Direct, and 490 from Dimensions/PubMed). After removing 120 duplicate records, 550 records were assessed for relevance. A total of 474 articles were excluded because they did not meet the inclusion criteria, being reviews, or studying different plant species. A full-text analysis of 76 articles was conducted, of which 60 were excluded for various reasons, such as not reporting Passiflora species, not reporting dyslipidemia, or studying combinations of bioactive compounds. Ultimately, 16 studies were included in the review, with 6 from Dimensions/PubMed and 10 from Web Science, Scopus, and Science Direct.

2.1 Data extraction: Critertia

After the collection and selection of articles, data extraction was carried out (Table 1a). The following information was selected:

1. Main author and year of publication,
2. Study population,
3. Number of individuals, gender, and age,
4. Dosage of Passiflora species used and route of administration,
5. Objectives and description of the study,
6. Results.

Table 1a. Studies on the use of *Passiflora* in the adjuvant treatment of dyslipidemia

Article number	Author and date	Title	Study population
1	(Khongrum et al., 2022)	Anti-dyslipidemic, Antioxidant, and Anti-inflammatory Effects of Jelly Drink Containing Polyphenol-Rich Roselle Calyces Extract and Passion Fruit Juice with Pulp in Adults with Dyslipidemia: A Randomized, Double-Blind, Placebo-Controlled Trial	Humans
2	(Sousa et al., 2021)	Cost-Effectiveness of Passion Fruit Albedo versus Turmeric in the Glycemic and Lipaemic Control of People with Type 2 Diabetes: Randomized Clinical Trial». Journal of the American College of Nutrition.	Humans
3	(Kitada et al., 2017)	The Effect of Piceatannol from Passion Fruit (Passiflora edulis) Seeds on Metabolic Health in Humans	Humans
4	(Marques et al., 2016)	passion fruit peel flour (Passiflora edulis fo. flavicarpa) on metabolic changes in HIV patients with lipodystrophy syndrome secondary to antiretroviral therapy	Humans
5	(Adi, 2021)	The effect yellow passion fruit peel juice (Passiflora eduils f.flavicarpa deg) on LDL to HDL cholesterol ratio in type 2 diabetes mellitus patients as predictors of cardiovascular disease	Humans
6	(De Faveri et al., 2020)	Effects of passion fruit peel flour (Passiflora edulis f. flavicarpa O. Deg.) in cafeteria diet-induced metabolic disorders	Mice
7	(da Silva et al., 2014)	Effects of passion fruit (Passiflora edulis) byproduct intake in antioxidant status of Wistar rat tissues	Mice
8	(Panelli et al., 2018)	Bark of Passiflora edulis Treatment Stimulates Antioxidant Capacity, and Reduces Dyslipidemia and Body Fat in db/db Mice	Mice
9	(Ravi Babu Birudu et al., 2015)	Anti-Dyslipidemia Effect of Ethanol Extract of Passiflora foetida on Dextrose Induced Diabetic Rats	Mice
10	(Sarto et al., 2018) we evaluated the effects of dry Passiflora incarnata L. extract over dyslipidemia, left ventricular hypertrophy, and hepatic oxidative stress of LDL receptor knockout mice (LDLr-/-	Dry Extract of Passiflora incarnata L. leaves as a Cardiac and Hepatic Oxidative Stress Protector in LDLr-/- Mice Fed High-Fat Diet	Mice
11	(Teixeira et al., 2014)	Effects of Passiflora nitida Kunth leaf extract on digestive enzymes and high caloric diet in rats	Mice

12	(Takam et al., 2019)the in vivo hypolipidemic effect of west Cameroonian <i>Passiflora edulis</i> variety seed oil (PE	Passiflora edulis seed oil from west Cameroon: Chemical characterization and assessment of its hypolipidemic effect in high-fat diet–induced rats	Mice
13	(Vuolo et al., 2020)	Passion fruit peel intake decreases inflammatory response and reverts lipid peroxidation and adiposity in diet-induced obese rats	Mice
14	(Angel-Isaza et al., 2021)	Polyphenols from Passiflora ligularis Regulate Inflammatory Markers and Weight Gain	Mice
15	(Grosseli et al., 2014)	Uso da polpa e da casca do maracujá (Passiflora edulis f. flavicarpa) sobre o colesterol em coelhos com hipercolesterolemia experimental». Revista de Pesquisa e Inovação Farmacêutica:	Rabbits
16	(Neves Casarotti et al., 2020)supplemented with passion fruit by-product (1%	Probiotic low-fat fermented goat milk with passion fruit by-product: In vitro effect on obese individuals' microbiota and on metabolites production	Human colonic tissue

Table 1b. Studies on the use of *Passiflora* in the adjuvant treatment of dyslipidemia

Article number	Number and gender	Dose	Objective / Type of study
1	40 participants divided into two groups: Group 1: 20 women, and Group 2: 20 men.	Group 1: placebo Group 2: 1 g Passiflora edulis	To evaluate the beneficial effects of consumption of flavonoids present in passion fruit juice, which could have antioxidant and anti-inflammatory properties / Randomized, double-blind, placebo-controlled clinical trial.
2	89 participants divided into three groups: Group 1: 27 women and 6 men, Group 2: 20 women and 8 men and Group 3: 24 women and 4 men.	Group 1: (500mg turmeric + 5mg piperine) Group 2: (500mg of Passiflora edulis peel flour) Group 3: Usual diet	To compare the cost-effectiveness of Passiflora edulis albedo and turmeric in the glycemic and lipid control of people with type 2 diabetes. / Randomized, double-blind, placebo-controlled clinical trial.
3	39 participants, 8 groups of which 20 were men and 19 were women.	20 mg/day piceatannol extract, from the seeds of Passiflora edulis.	To research the effects of Piceatannol from the of Passiflora edulis seeds on dyslipidemia in humans. / Randomized, double-blind, placebo-controlled clinical trial.
4	36 participants, divided into two groups each consisting of 6 women and 12 men.	30 g/day of Passiflora edulis peel flour	To evaluate the effect of Passiflora edulis peel flour consumption on metabolic changes (dyslipidemia) in patients with HIV and lipodystrophy syndrome. / Randomized, double-blind, placebo-controlled clinical trial.

5	40 participants, divided into two groups: Group 1, 11 women and 9 men Group 2, 10 women and 10 men.	40 g/day. Passiflora edulis peel	To research the effect of Passiflora edulis peel juice on the LDL: HDL cholesterol ratio in patients with diabetes mellitus as a predictor of cardiovascular disease. / Quasi-experimental design with non-randomized pretest and posttest, with a control group.
6	30 mice in three different groups	15% Passiflora edulis peel flour	To research the effects of Passiflora edulis peel flour in the treatment of metabolic disorders (dyslipidemia) such as diabetes and obesity. / Experimental design, consisting of three treatments (control: water + standard diet, water + cafeteria diet and cafeteria diet + Passiflora edulis peel.
7	8 male Wistar rats were randomly distributed into two groups, four rats in each group.	Received a diet in which 50% of the cellulose was replaced with Passiflora edulis peel fiber.	To evaluate the effect of Passiflora edulis peel flour consumption on the antioxidant status in Wistar rats. / Experimental design, consisting of two treatments (Control: standard diet without the addition of flour from Passiflora edulis juice extraction byproducts, and standard diet replacing 50% of the fiber with Passiflora juice extraction byproducts).
8	24 mice, of which 14 were obese db/db mice and 10 were lean mice of the same line and age used as a control group.	7 g Passiflora edulis peel	To research the antioxidant capacity of Passiflora edulis peel and its effect on dyslipidemia and body fat. / Experimental design consisting of two treatments (Control: standard diet, and standard diet + Passiflora edulis peel).
9	54 male albino Wistar mice, randomly divided into 9 groups of 6 mice each	Group 1: 100 mg/kg body weight; group; Group 2: 250 mg/kg body weight; Group 3: 500 mg/kg body weight.	To evaluate the effect of Passiflora foetida on dyslipidemia. / Experimental design performed in dextrose-induced diabetic mice, distributed in nine treatments in which three levels of Passiflora foetida extract in ethanol were evaluated (100, 250 and 500 mg/kg body weight).
10	40 male mice homozygous for the LDL receptor (LDLr) gene divided into four groups of ten animals each.	150 mg/kg of dry extract of Passiflora incarnata L.	To evaluate the effects of Passiflora incarnata L. extract on protection against cardiac and hepatic oxidative stress. / Experimental design carried out in LDLr-/- mice consisting of four treatments (Control: standard diet, high-fat diet, high-fat diet + Passiflora incarnata L. extract, and standard diet + Passiflora incarnata L. extract.
11	15 mice were randomly assigned to five groups	Group 1: 100 mg of P. nitida extract per kg body weight; Group 2: 50 mg/kg body weight	To research pancreatic lipase inhibition and metabolic effects of high-calorie diet in mice, using the hydroethanolic leaf extract of Passiflora nitida Kunth (PNE) in in vitro assays or by administering it to mice to study dyslipidemia. Experimental design consisting of five treatments in which two levels of Passiflora nitida extract (100 and 250 mg/kg body weight). were evaluated

12	72 albino mice of the Wistar strain, divided into six groups of twelve mice each.	Group 2: 1 ml/kg body weight/day of seed oil Group 3 received 2 ml/kg body weight/day of seed oil.	To research the lipid-lowering effect of Passiflora edulis seed oil in mice fed a high-fat diet. Food intake and body weight were measured. Experimental design consisting of three treatments (Control: standard diet, 1 ml/kg body weight/day of seed oil and 2 ml/kg body weight/day of seed oil + standard diet + Passiflora edulis husk).
13	24 male mice distributed into three groups of 8 mice each.	A dose of 5% of Passiflora edulis peel was used in the diet of the mice in the intervention group.	To evaluate the effects Passiflora edulis peel intake on reducing inflammation, lipid peroxidation and adiposity in diet-induced obese mice, the study included three intervention groups: a control group (C), a high-fat diet group (HF) and a high-fat diet with Passiflora edulis peel (HFPF) group.
14	16 overweight adults male Wistar mice were divided into four groups of four rats each, including a control group and three experimental groups.	The concentrations of the polyphenol extracts were 50, 100 and 200 mg/kg body weight.	To evaluate the effects of polyphenol extracts from Colombian Passiflora ligularis on inflammatory markers and weight gain in overweight mice, the study was designed using a 3+1 factorial model, with a control group and three experimental groups that received different concentrations of polyphenol extracts in drinking water.
15	8 male rabbits divided into 3 experimental groups	Group 1: 10 g/kg weight Passiflora edulis Group 2: 8 g/kg weight Passiflora edulis	To research the effectiveness of Passiflora edulis f. flavicarpa “in natura” in reducing cholesterol in rabbits with experimental hypercholesterolemia, the study was carried out in three phases (F1, F2 and F3), each of varying duration. In the first phase, the rabbits received water and commercial feed to record their physiological cholesterol levels. In the second and third phases, the rabbits were divided into three experimental groups (G1, G2 and G3) and received different types of feed and treatments with pulp, seeds, and peel.
16	NA	NA	To evaluate the impact of probiotic fermented food containing low-fat goat milk with Passiflora edulis on the microbiota and metabolite production in obese individuals, the experimental design of the study involved using the SHIME® system (Simulator of the Human Intestinal Microbial Ecosystem) to simulate the human gastrointestinal tract and evaluate the impact of the probiotic fermented food on the gut microbiota and metabolite production .

Abbreviations: n, number of people; TC, Total Cholesterol; LDL, Low-Density Lipoprotein; HDL, High Density Lipoprotein; TG, Triglycerides; NR, does not report; BMI, Body Mass Index.

2.2 Bias analysis

2.1.1. Risk of bias assessment

Risk of bias was assessed using the recommendations of the "Cochrane Handbook of Systematic Reviews of Interventions" (Cumpston et al., 2022)"ISSN":"17413850","PMID":"35352103","abstract":"Aims Decision makers in public health practice and policy rely on access to trustworthy, relevant, synthesized evidence. The second edition of the Cochrane Handbook for Systematic Reviews of Interventions ('the Handbook' as a guide to identify possible problems that may have arisen in the carrying out of the studies (Table 2). The following items were taken into consideration to assess the risk of bias:

Table 2. Risk of bias assessment according to the recommendations of the Cochrane Handbook of Systematic Reviews of Interventions

Article number	Random sequence generation	Allocation concealment	Blinding of personnel	Blinding of results assessment	Complete results data (Positive and negative)	Other biases
1	✓	✓	✓	✓	✓	✓
2	✓	✓	✓	✓	✓	✓
3	✓	✓	✓	✓	✓	✓
4	✓	✓	✓	✓	✓	X
5	X	✓	✓	✓	✓	X
6	✓	✓	✓	✓	✓	✓
7	✓	✓	✓	✓	✓	✓
8	✓	✓	✓	✓	✓	✓
9	✓	✓	✓	✓	✓	✓
10	✓	✓	✓	✓	✓	✓
11	✓	✓	✓	✓	✓	✓
12	✓	✓	✓	✓	✓	✓
13	✓	✓	✓	✓	✓	✓
14	✓	✓	✓	✓	✓	✓
15	✓	✓	✓	✓	✓	
16	N/A	N/A	N/A	N/A	✓	✓

Abbreviations: N/A, not applicable.

1. Random sequence generation and allocation concealment: The use of a tool that allows the random assignment of the individuals subject to the experiment was identified (random location of the individuals, unrestrictedly random design, and block design, among others).
2. Blinding of personnel and blinding of the assessment results: It is specified that the personnel were unaware of the treatments administered to the groups or the origin of the samples at the time of testing and obtaining the results. Effective blinding can also ensure that the groups compared receive a similar amount of care, secondary treatment, and diagnostic research.
3. Complete results data: all results obtained are described, whether positive or not, or statistically significant.
4. Other biases: special individual considerations for each article when applicable.

All experimental studies met the requirements for "random sequence generation," "allocation concealment," and "complete outcome data. Regarding the "other biases" section, possible biases were found in two studies with humans (Khongrum et al., 2022; Sousa et al., 2021).

A different number of participants was used for each intervention group due to the withdrawal of some of the participants which affected the homogeneity of the groups in the initial stage for some independent variables. This could be a source of bias considering that more homogeneous groups should ideally be used.

3. Results

The study findings suggest that *Passiflora* species may have beneficial effects on lowering blood lipids. Of the 16 studies included in this analysis (Figure 2), 12 focused on *Passiflora edulis*, eight on the peel, three on the seed and one on the mesocarp. Other articles focused on *Passiflora* species, such as *P. incarnata* (Angel-Isaza et al., 2021), *P. ligularis* (Sousa et al., 2021), *P. foetida* [9] and *P. nítida* (Yepes-Nuñez et al., 2021).

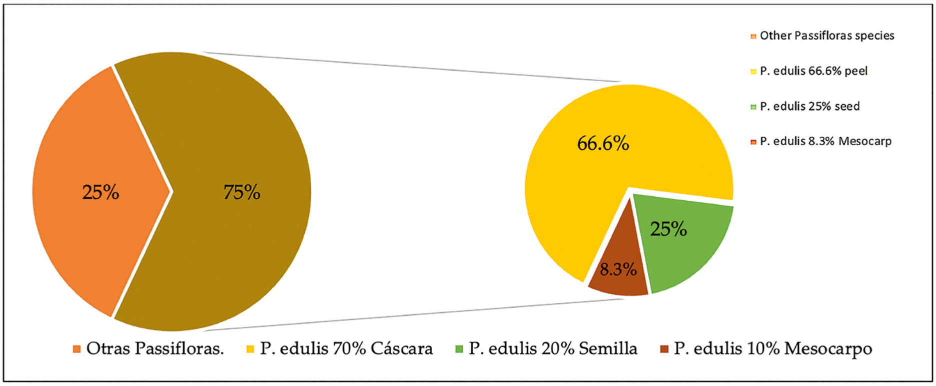

Figura 2. Distribution of studies on Passiflora species and their parts. The larger pie chart shows that 75 % of the studies focus on Passiflora edulis, while 25 % focus on other Passiflora species. The smaller pie chart zooms in on the studies related to P. edulis, with 66.6 % examining the peel, 25 % focusing on the seed, and 8.3 % on the mesocarp.

Table 3. Studies on the use of *Passiflora* in the adjuvant treatment of dyslipidemia.

Article number	Population	Evaluated variables (%)					Intervention time/ weeks	Findings in humans
		n	TC	LDL	HDL	TG		
1	Human	40	↓	↓ 16	↑ 4.75	↓ 17	8	The findings indicated an improvement in the lipid profile, with the highest content of Passiflora edulis.
2	Human	99	↓ 4.8	↓ 11.7	↑ 10.8		16	Both Passiflora edulis albedo and turmeric with piperine were effective in reducing serum triglycerides and improving glycemic and lipid profiles.
3	Human	39	↓	NR	NR	NR	8	Supplementation with piceatannol from Passiflora edulis did not affect blood glucose levels, lipids, blood pressure, BMI, or mood levels. A trend towards decreased total cholesterol and LDL cholesterol levels was observed in the Piceatannol. supplemented group
4	Human	36	↓ 12	NR	NR	NR	12	Passiflora edulis peel flour decreased cholesterol, triglyceride, and body mass index levels.

5	Human	40	NR	NR	NR	NR	2	A decrease in the LDL: HDL cholesterol ratio was observed in the group that consumed Passiflora edulis peel flour, with an average of 0.56 versus 0.25 in the control group.
6	Mice	30	↓ 25	NR	NR	↓ 30	16	Passiflora edulis peel flour improved insulin production and elimination in mice and showed high antioxidant capacity and a chemical composition rich in phenolic compounds and flavonoids.
7	Mice	8	↓	NR	NR	NR	2	The consumption of Passiflora edulis peel flour modulates the antioxidant capacity of tissues in different ways, possibly thanks to its content of thermogenic/ ergogenic compounds.
8	Mice	24	↓ 25	NR	NR	↓ 10	16	Passiflora edulis peel flour reduced cholesterol levels, triglycerides, and body weight.
9	Mice	54	↓ 25	↓ 30	↑ 12	↓ 3	6	Passiflora Foetida extract decreased blood lipid levels and improved hyperlipidemia associated with diabetes.
10	Mice	40	↓	NR	↑	↓	4	Passiflora incarnata L. extract has an antioxidant effect, helping to prevent heart and liver diseases related to oxidative stress.
11	Mice	15	NR	NR	NR	↓ 15	4	Passiflora nitida inhibited pancreatic lipases activity and partially reduced cafeteria diet induced dyslipidemia.
12	Mice	72	↓ 5	↓ 13	NR	↓ 12	4	Passiflora edulis seed oil reduced triglycerides, total and LDL cholesterol, and increased HDL cholesterol levels.
13	Mice	24	↓	NR	NR	NR	10	Bioactive compounds of Passiflora edulis peel reduced the adverse effects of oxidative stress in high-fat diets.
14	Mice	16	↓	NR	NR	NR	6	Polyphenol extracts of Passiflora ligularis can reduce weight gain in obese mice having beneficial effects in inhibiting inflammation and weight management.

15	Rabbit	8	↓ 75	NR	NR	NR	15	Passiflora edulis fo. “flavicarpa” pulp reduced cholesterol in hypercholesterolemic rabbits.
16	Human (tissue)	NR	NR	NR	NR	NR	2	The addition of Passiflora edulis byproducts in low-fat fermented goat milk with probiotics helped modulate the intestinal microbiota in the colon.

Abbreviations: n, number of people; TC, Total Cholesterol; LDL, Low-Density Lipoprotein; HDL, High Density Lipoprotein; TG, Triglycerides; NR, does not report; BMI, Body Mass Index.

To more precisely identify the results of the research consulted, the following categories were designed: a) effect in different matrices; b) type and part of the *Passiflora* species used; and c) disease studied. Of the 16 studies analyzed, six were conducted in humans (1,2,3,4,5 and 16), nine in mice (6, 7, 8, 9, 10, 11, 12, 13 and 14), and one study (15) was conducted in rabbits (Table 1a).

The researchers focused on examining three specific parts of *Passiflora* species: eight studies were conducted on the peel (1, 2, 4, 5, 6, 7, 8 and 13), two on the seed (3 and 12) and six on the pulp (9, 10, 11,14, 15, 16] (Figure 3). metabolic syndrome was found to be the most addressed topic in this review, with a total of five (3, 6, 8, 13 and 14) of the 16 articles, followed by the combination of overweight and dyslipidemia (1, 7, 10, 11 and 15).

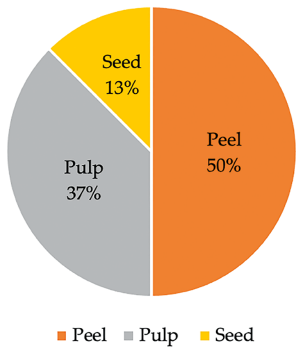

Figura 3. Distribution of studies focusing on different parts of Passiflora species. Half of the studies (50 %) focus on the peel, 37 % on the pulp, and 13 % on the seed.

4. Discussion

Research on *Passiflora* species in humans has been conducted under different conditions and circumstances. *Passiflora edulis* is the species used in the largest number of studies, highlighting that all of them show favorable results for the control of dyslipidemia, reducing the concentration in 8%, 12% and 8% for the total cholesterol level, low-density lipoprotein (LDL), triglycerides (TG) respectively, and showing an approximate 8 % increase in high-density lipoprotein (HDL) (Khongrum et al., 2022; Kitada et al., 2017), (Table 1b). Together, these studies provide evidence of the potential benefits of the various parts of the fruit in improving lipid and glycemic profiles in humans. In addition, the authors agree that further research is needed to fully understand its impact and mechanisms of action.

Similar to the effect of *Passiflora* species consumption in humans, in studies conducted in a murine model, beneficial effects are observed on the lipid profile of animals treated with these plant species, either through the pulp or through the by-products of fruit juice extraction. The main effects include the average decrease of 18 %, 9 % and 5 % in the level of total cholesterol, LDL and TG respectively, and an approximate 8 % increase in HDL (De Faveri et al., 2020; Ravi Babu Birudu et al., 2015). Although, Vuolo and Angel-Isaza (Angel-Isaza et al., 2021; Vuolo et al., 2020), do not report an effect on lipid concentration, they did observe a decrease in the body weight of the animals. According to studies and medical recommendations, it is suggested that a 1% reduction in LDL cholesterol can translate into a 1-2 % reduction in the risk of cardiovascular disease. Therefore, any significant reduction in cholesterol through diet can have a positive medical impact.

Da Silva (2014) and Panelli (2018) (Da Silva et al., 2014; Panelli et al., 2018), highlight the antioxidant capacity of *Passiflora edulis* peel in different animal tissues, showing a reduction in lipid peroxidation and improved antioxidant defense, even under high-fat diet conditions. The importance of the soluble and insoluble fibers of *Passiflora* species in reducing the absorption of dietary lipids in the gastrointestinal tract is also highlighted in synergy with the content of phenolic compounds, giving prominence to flavonoids, as the substances with high antioxidant capacity present in the different parts of Passiflora species. Polyphenols act as antioxidants, neutralizing free radicals and reducing oxidative stress, which in turn reduces the formation of atherosclerotic plaques in the arteries. Furthermore, research emphasizes the therapeutic potential of chemical compounds present in these plants, such as turmeric and piperine, in the management of glycemia and lipemia due to their anti-inflammatory, antioxidant and hypoglycemic properties (Table 1b).

It is important to note the little-explored Passiflora species such as *Passiflora incarnata, Passiflora foétida* and *Passiflora ligularis* in which the authors Sarto (2018), Ravi Babu

(2015), and Angel-Isaza (2021) (Angel-Isaza et al., 2021; Ravi Babu Birudu et al., 2015; Sarto et al., 2018)biguanides, metformin HCl, DPP-4 inhibitors etc. The folk medicine is practiced by local people. The people use herbal medicine to control and treat the various types of diseases. In India, tribal people used different types of medicinal plants to control the diabetes. In present study ethanol extracts of Passiflora foetida leaves were evaluated for anti-dyslipidemia activity in dextrose induced diabetic rats. The ethanol extracts of P. foetida were administered at the doses of 100 mg/kg body weight, 250 mg/kg body weight and 500 mg/kg body weight to the dextrose induced diabetic rats. The silver nanoparticles were prepared by the reaction of 1 mM silver nitrate and 5% leaf extract of P. foetida. The antidyslipidemia activity of ethanol extracts was compared with standard drugs Glipizide, Sitagliptin and Vildagliptin. The standard drugs normally decreased the lipid parameters in diabetic rats. The ethanol extract at the dose of 500 mg/kg body weight showed significant lowering effect on dextrose induced diabetic rats. The total cholesterol, triglycerides, low-density lipoprotein (LDL, in addition to observe an improvement in blood lipid levels and a reduction in the size of adipocytes in adipose tissue, showed effects in the reduction of pancreatic lipase and a decrease in postprandial triglyceride levels.

The need to understand the key aspects of studies with *Passiflora* species is highlighted, including the parts of the plant used, the amounts of polyphenols, toxicity, the absorption mechanisms, and their impact on specific tissues of the organism. These factors are essential to assess the potential health benefits of *Passiflora* species and their application in future treatments.

Accumulating evidence consistently supports the potential benefit of various *Passiflora* species in improving metabolic health, lipid regulation, antioxidant capacity, and weight management. The variety of studies provides insight into the potential positive effects of these compounds on different aspects of health from diabetes to inflammation and obesity. The consistency in the results suggests that these plants could be considered in dietary and therapeutic interventions to improve metabolic health and prevent associated diseases. However, more research is needed to fully understand the underlying mechanisms and long-term efficacy in clinical settings.

Future research is crucial to fully understand the underlying mechanisms and optimal duration of these interventions. The variability in results highlights the complexity of the effects of these compounds on cardiovascular and metabolic health.

5. Conclusions

The different parts of the Passiflora species studied showed a lipid-lowering effect. This effect is probably due to their content of polyphenols, fiber and bioactive compounds that reduce oxidative stress and chronic inflammation underlying different dyslipidemias. However, more studies in humans are needed to confirm these beneficial effects and to establish the doses and time required for a positive result. It is essential to understand the toxicity and absorption capacity of polyphenols and bioactive compounds to avoid adverse effects in humans. Likewise, it is crucial to understand the biochemical mechanisms involved in lipid absorption to focus studies on specific tissues such as adipose tissue.

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Data Availability Statement: The raw data supporting the conclusions of this article will be made available upon request from authors.

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