INTERNATIONAL SEVEN JOURNAL
OF MULTIDISCIPLINARY
ISSN: 2764-9547

A viabilidade funcional do uso de fitoterápicos como alternativa ao tratamento farmacológico das dislipidemias: Uma revisão sistemática

The functional viability in the use of herbal medicine as an alternative to the pharmacological treatment of dyslipidemia: Asystematic review

DOI: 10.56238/isevmjv3n2-005
Receipt of originals: 02/16/2024
Publication acceptance: 07/03/2024

Allander Camilo dos Santos Macedo
Medical Course, Alto Vale do Rio do Peixe University – UNIARP
Academic League of Sports Medicine of the University of Alto Vale do Rio do Peixe -LAME

Andréia Felipe de Oliveira Nascente
Medical Course, Alto Vale do Rio do Peixe University – UNIARP
Academic League of Sports Medicine of the University of Alto Vale do Rio do Peixe -LAME

Ariana Centa
Medical Course, Alto Vale do Rio do Peixe University – UNIARP
Translational Health Research Laboratory – UNIARP
E-mail: ariana.aac@hotmail.com

ABSTRACT

Background: Dyslipidemia is caused by an increase in plasma lipoprotein levels and predisposes to the risk of thrombotic events, which highlights the need for early treatment. Traditional therapies have limitations due to the absence of adequate responses and the abandonment of treatment due to its adverse effects. Objective: The present study sought to list alternative treatments for dyslipidemia by means of herbal medicines, which can help traditional methods or replace them. Methods: A systematic review was conducted by searching the databases of the Latin American Caribbean Health Sciences Literature (Lilacs), PubMed and ScienceDirect using the descriptors "phytotherapy" OR "phytotherapeutic drugs" AND "dyslipidemias" OR "cholesterol" OR "atherosclerosis". Results: The databases returned with 80 articles, 9 were excluded because they were duplicates and, after applying the exclusion and inclusion criteria, resulted in a sample of 13 articles. Studies with herbal medicines such as Red Grape Seed Extract (RGSE), Sacha *Inchi Oil*, Green Tea, Eggplant Juice, *Agrimonia eupatoria*, Artichoke and Garlic were evaluated, which showed distinct effects on lipid profiles. Conclusion: The use of herbal medicines in the treatment of dyslipidemia may be a viable alternative, but further studies on this subject are required.

Keywords: Herbal medicines, Phytotherapeutic drugs, Dyslipidemias, Cholesterol, Atterosclerosis.

1 INTRODUCTION

Dyslipidemia occurs due to the increase in the levels of lipoproteins in the plasma, which occurs due to phenotypic and genetic alterations - monogenic or polygenic. This disorder is subdivided into four subtypes, namely isolated hypercholesterolemia, isolated hypertriglyceridemia, mixed hyperlipidemia, and decreased HDL levels1,2.

The occurrence of dyslipidemia leads to greater availability of lipoproteins in the blood, favoring their deposition in the vessels, leading to the occurrence of atheromatous plaques and, consequently, thrombotic events, when these plaques detach, gain circulation and reach different sites, causing ischemic outcomes and tissue death3,4.

In view of the possible complications related to dyslipidemias, there is an urgent need to limit the evolution of this condition through early treatment involving pharmacological and behavioral measures. Considering non-pharmacological therapy, it includes improvements in lifestyle habits, such as improved diet and physical activity. Regarding pharmacological therapy, statins and fibrates, the main drugs used in the treatment of dyslipidemias, are highlighted. These drugs, commonly used in the treatment of dyslipidemias, usually have limitations in their efficacy, even when used in full dosages. In addition, it is common for patients to abandon treatment due to the side effects of drugs. In addition, a process of nutritional transition is taking place in the Brazilian population, in which individuals have ceased to be malnourished and active to become sedentary and obese, reducing the participation of non-pharmacological measures in the treatment of dyslipidemia and relying on drugs alone1,3,4.

Considering the above, it is essential to list alternatives to traditional therapy in order to improve the therapeutic arsenal for dyslipidemias. Thus, this systematic review sought to recognize which herbal medicines, recommended by the medical literature, can be used as an alternative or complementary therapy to fibrates and statins in the treatment of dyslipidemias.

2 METHODOLOGY

2.1 DATA COLLECTION

The present study was a literature review, carried out between August and November 2022, and the search was carried out in the databases of the Latin American Caribbean Health Sciences Literature (Lilacs), PubMed, and ScienceDirect. Articles published in full since 2004 in English, Portuguese and Spanish were included in the search. The descriptors used for the research were "phytotherapy" OR "phytotherapeutic drugs" AND "dyslipidemias" OR "cholesterol" OR "atherosclerosis".

Articles that address drugs already indicated by the 2017 update of the Brazilian guideline

on dyslipidemia and prevention of atherosclerosis, articles with *in vitro* and animal studies, review articles (narrative, integrative, and systematic), book chapters, theses, dissertations, conference proceedings, technical reports, and ministerial documents were excluded from the study.

2.2 ANALYSIS OF THE DATA OBTAINED

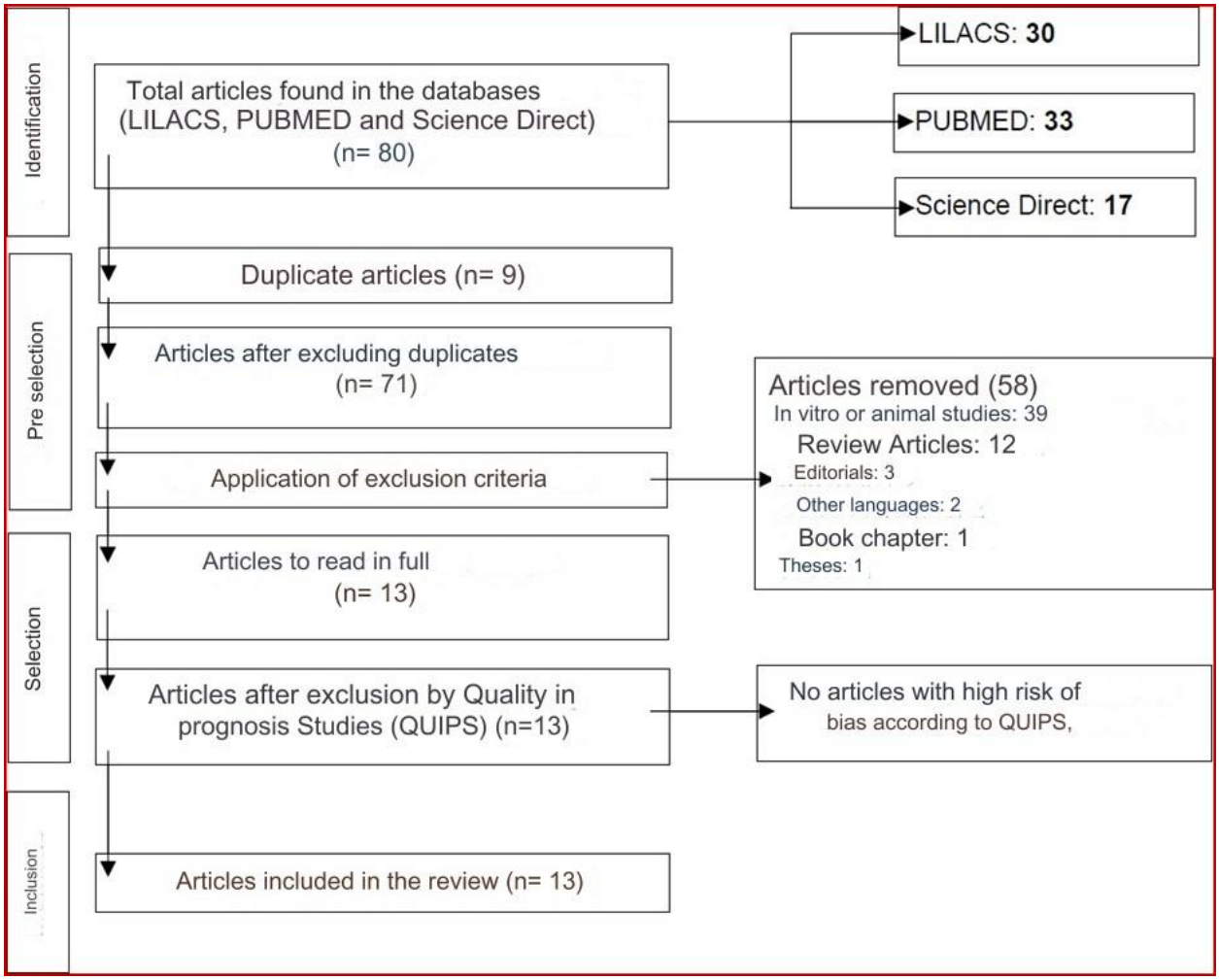
For data analysis, all the bibliographic material collected was evaluated by two researchers, independently, selecting the articles found based on the reading of the title and abstract following the inclusion and exclusion criteria, organizing and compiling the results in a table according to the order of evaluation. Duplicate articles, i.e., articles found in more than one database, were considered only once in this study.

After this initial evaluation, the selected articles were read in full, and those that were not in agreement with the theme or that did not meet the criteria required for the systematic review were discarded. In this same full reading of the articles, they were evaluated for quality and risk of bias, using the *Quality in Prognosis Studies* (QUIPS) tool, which classifies articles as having low, moderate or high risk of bias5.

2.3 SEARCH RESULTS

After searching the articles in the different databases, carried out in August 2022, a total of 80 articles were found in the three databases searched through the descriptors, following the proposed methodology. After the exclusion of nine duplicate articles, a total of 71 articles remained, which were evaluated by title and abstract. After applying the inclusion and exclusion criteria, 58 articles were excluded, leaving 13 articles, which were read in full, all of which were in accordance with the proposed theme, as well as with the established criteria, as shown in Figure 1 and Table 1.

Figure 1 - Diagram of the identification and selection of the studies contained in this systematic review.



Source: The Authors (2022)

Artichoke leaf extract (

Estudo	AUTOR/ANO	Revista	Título
#1	ARGANI et al.[6] (2016)	São Paulo Medical Journal	O efeito do extrato de semente de uva Vermelha na atividade do soro Paraoxonase em doentes com hiperlipidemia leve a moderada
#2	MARQUES Et al.[7] (2020)	Saúde debate	Uso de Práticas Integrativas e Complementares por idosos: PesquisaNacional de Saúde 2013.
#3	GARMEN DIA et al.[8] (2011)	Revista Peruanade medicina experimental e saúde pública	Efeito do óleo de inchi (*plukenetia volúbilis l*) no perfil lipídico em pacientes com hiperlipoproteinemia.
#4	SOUZA etal.[9] (2010)	Revista Mineira de Enfermagem	A enfermagem diante da utilização de plantas medicinais no tratamentocomplementar da hipertensão arterial sistêmica e das dislipidemias.
#5	GARCÍA-LAZO etal.[10] (2015)	Revista Cubana dePlantas Medicinais	Plantas consideradas uteis comohipoglicemiantes, antihipertensivas o hipolipemiantes por pacientes com doenças vasculares periféricas

#6	BATISTA etal.[11] (2009)	Arquivos Brasileiros de Cardiologia	Estudo prospectivo, duplo cego ecruzado da Camellia sinensis (chá verde) nas dislipidemias.
#7	PRAÇA etal.[12] (2004)	Arquivos Brasileiros de Cardiologia	O suco de berinjela (*Solanummelongena*) não modifica os níveis séricos de lípides.
#8	RAHMOU N et al.[13]2020)	Jornal de diabetes E desordensmetabólicas	Efeito do consumo de produtos naturais sobre alguns parâmetros bioquímicosde uma população diabética tipo 2.
#9	ROUHANI etal.[14](2019)	Jornal médico Galen	Eficácia de um remédio herbal persa e eletroacupuntura em perfis metabólicose parâmetros antropométricos em mulheres com síndrome do ováriopolicístico: um estudo controlado randomizado.
#10	PARK etal.[15] (2018)	Jornal Mundial deSaúde Masculina	Eficácia e segurança de um extrato misto de *Trigonella foenum-graecum* Seed e *Lespedeza cuneata* no tratamento da síndrome de deficiência de testosterona: um ensaio clínico randomizado, duplo-cego, controlado por placebo.
#11	DUDA etal.[16] (2008)	Relatórios farmacológicos	Efeitos da suplementação de alho acurto prazo no metabolismo lipídico e estado antioxidante em adultos hipertensos.
#12	IVANOVA etal.[17](2013)	Arquivos de Fisiologia e Bioquímica	Consumo de chá de *Agrimonia eupatoria* em relação a marcadores deinflamação, estado oxidativo e metabolismo lipídico em indivíduos saudáveis.
#13	Study[18](2008)	AUTHOR/ YEAR	Magazine*Cynara scolymus*) reduz o colesterol plasmático em adultos hipercolesterolêmicos saudáveis: um estudo randomizado, duplo-cego controlado por placebo.

Source: The Authors (2022)

Quality and risk of bias were determined using the QUIPS tool, as shown in Table 2. According to the analysis, none of the articles presented a high risk of bias, i.e., no article was excluded by this analysis.

+

Title	#1	ARGANI et	São Paulo Medical	The Effect of Red Grape Seed Extract on Serum	#2 Estudo	MARQUES	Health debate
Use of Integrative and Complementary Practices by the elderly: National Health Survey 2013.[6](2016)	#3	GARME N	Peruvian Journal of Experimen tal Medicine and	Effect of inchi oil (	#4	SOUZA et al.	Minas Gerais Journal of Nursing
Nursing in the face of the	#5	GARCÍA	Cuban	Plants	#6	BATISTA	Brazilian

use of medicinal plants in the complementary treatment of systemic arterial hypertension and dyslipidemias.(2020)		-	Journal of Medicinal Plants	considered useful as hypoglycemic agents, antihypertensive drugs or lipid-lowering agents by patients with peripheral vascular diseases		et al.	Archives
Prospective, double-blind study and Camellia sinensis cross (tea green) in dyslipidemias.	#7	PRAÇA et al.	Brazilian Archives of	Eggplant (	#8	RAHMOU	Journal of Diabetes
Effect of the consumption of natural products on some biochemical parameters of a type 2 diabetic population.(2010)	#9	Rouhani	Galen Medical Journal	Efficacy of a Persian herbal remedy and electroacupuncture on metabolic profiles and anthropometric parameters in women with polycystic ovary syndrome: a	#10	PARK et al.	World Journal of Men's Health
Efficacy and Safety of a Mixed Extract of Trigonella foenum-graecum Seed and	#11	DUDA et al.	Pharmacological reports	Effects of Short-Term Garlic Supplementation on Lipid Metabolism and Antioxidant Status in Hypertensive Adults.	#12	IVANOVA etal.	Physiology and Biochemistry
Agrimonia eupatoria tea consumption in relation to markers of inflammation, oxidative state, and lipid metabolism in healthy individuals	#13	BUNDY et al.	Herbal Medicine	Artichoke leaf extract (	+	+	+
PRAÇA et al.[12] (2004)	+	Studies	Participation in the study	Study Friction	Prognostic Factor Measurement	Outcome Measurement	Confounding Bias in the
Statistical Analysis and	Generally	ARGANI	+	+	+	+	+

Reporting[13] 2020)		et al.					
+[14](2019)	+	MARQUES et al.	+	+	?	+/-	+
+/-[15](2018)	+	GARMENDIA et al.	+/-	+	+	+	+
+/-[16](2008)	+	SOUZA et al.	+/-	+	?	+/-	+
+/-[17](2013)	+/-	GARCÍA-LAZO et al.	+	+	?	+/-	+
+/-[18](2008)	+	BATISTA et al.	+	+	+	+	+

(+) High Quality, (+/-) Acceptable, (-) Low Quality, (?) Uncertain
Source: Authors (2022).

2.4 CHARACTERISTICS OF THE ARTICLES STUDIED

Among the thirteen articles that make up the sample of this study, all were published between March 2004 and November 2020, and their main characteristics are summarized in table 3.

The selected articles originate from nine different countries, with two articles originating from Iran (#1 and #9), three from Brazil (#2, #4 and #6), one from Peru , one from Cuba , one from Algeria , one from Korea (#10), one from Poland (#11), one from Bulgaria (#12) and one from England (#13).

Among the articles evaluated, those that presented the direct application of herbal medicines on a population were #1, #3, #6, #7, #9, #10, #11, #12 and #13. They evaluated the application of herbal medicines such as Red Grape Seed Extract (RGSE), Sacha Inchi Oil, Green Tea, Eggplant Juice, Agrimonia Eupatoria, Artichoke and Garlic. One of these studies also evaluated the effects of supplementation of a mix of plants, including fennel, nettle, carrot, red clover and turmeric, and another study evaluated the mixture between Trigonella foenum-graecum and Lespedeza cuneata.

These studies evaluated the impacts of supplementation by performing laboratory tests that contained, for the most part, tests such as glucose, glycated hemoglobin, creatinine, total cholesterol, triglycerides, LDL, HDL, TGO and TGP. It was also common to perform anthropometric evaluations of the patients with waist and hip circumference measurements, as well as BMI. Some studies have also evaluated markers of inflammation such as CRP, TNF-alpha, IL-6.

+	+ **Publica ção**	**PRAÇA et al.**	+	+	+
+	+ 2016	+	+	RAHMOUN et al. 13	+
+	+ 2020	+	+	+	+
ROUHA NI et al.	+ 2011	+	+ (*Plukenetia volubilis linneo oil*)	+	+
+	+ 2010	PARK et al.	+*Artemisia absinthium L.*) Carqueja, capoeira branca, carqueja- branca (*Baccharis crispa Spreng.*) Alcachofra (*Cynara scolymus L.*) Eucalipto-cidrão (*Eucalyptus globulus Labill*) Pixirica (*Leandra australis* (Cham.) Cogn.) Velho-cidrão	+ dislipidemias	+
+	+	+	+*Allium sativum L.*) Noni (*Morinda citrifolia L.*) Abacate (*Persea americana Mill.*) Tanchagem (*Planta- o major L.*) Sálvia (*Salvia officinalis L.*)*Berinjela (Solanum melongena L.)*	DUDA et al.	+
+	+	+	+	+*Camellia sinensis*), que reduziu significativamente, em oito semanas, os níveis de colesterol total e LDL colesterol no grupo de pacientes estudados.	+
IVANOV A et al.	+	+	+	+ alternativo.	+
+	+	BUNDY et al.	+	+	+
+	+	+	1. + 2. U. Dioica: Nome comum: urtiga, nome persa: Gazaneh; 3. D. Carota: Nome comum: cenoura,nome persa: havīj; 4. Trifolium pratense: Nome comum: trevo vermelho, nome persa: Shabdar ghermez; 5. Curcuma longa: Nomecomum: Cúrcuma, nome persa: Zard chobah.	Ocorreu umadiminuição significativa nocolesterol total, nalipoproteína de baixa densidade, triglicerídeos, aspartato aminotransferase e alanina aminotransferase nos grupos eletroacupuntura e fitoterapia + eletroac upuntura.	80
#10	Março 22, 2018	Korea	Extrato misto desementes de Trigonellafoenum-graecum e Lespedeza cuneata (TFGL).	Melhora dos sintomas relacionados a síndrome de deficiência detestosterona.	88
#11	Março 16, 2008	Polônia	Allii sativi bulbusmaceratio oleosa).	Redução do estresse oxidativo relacionadoa hipertensão.	70

Study	Publication Date	Country	Phytotherapeutic(s) studied(s) L. (agrimony, Rosaceae).	Main Results in amação em adultos saudáveis.	Population
#1	May 13,2016 2008	Iran	Red Grape Seed Extract (RGSE)	Potential Beneficial Effects on Prevention of Oxidative Stress and Atherosclerosis	70

Source: The authors (2022).

In study #1, supplementation of 200 mg/day of Red Grape Seed Extract (RGSE) in dyslipidemic patients increased protein and carbohydrate intake and reduced total cholesterol in a range ranging from 14.8 to 19.7 mg/dl, while placebo-treated patients showed a decrease ranging from 10.1 to 24.9 mg/dl. Triglycerides were reduced between 19.4 and 42.4 mg/dl in RGSE users, while in placebo users it was reduced from 11.3 to 23.7 mg/dl. LDL values in patients supplemented with RGSE decreased between 13.1 and 20.6 mg/dl, while in those supplemented with placebo, levels increased between 13.1 and 42.4 mg/dl6.

Regarding HDL, it was increased between 2.1 and 3.7 with the use of RGSE and decreased between 5.3 and 35.7 mg/dl with the use of placebo. An increase in the levels of apolipoprotein-AI and Paraoxonase (PON) was also noted, which confer antioxidant activity to HDL, contributing to its antiatherogenic activity, in addition to increasing antioxidant enzymes and preventing lipid peroxidation6.

Study #3 aimed to learn about the effect, effective dosage, and side effects of sacha inchi oil (*Plukenetia Volubilis L.*) in the lipid profile of patients with hypercholesterolemia. The subjects were divided into two groups, one being supplemented with 5 ml and the other with 10 ml of olive oil. In the group supplemented with 5 ml of olive oil, there was a reduction in total cholesterol (which reduced between 12.0 and 17.4 mg/dl), LDL (which decreased between 19.6 and 29.4 mg/dl), VLDL (decreased between 8.7 and 22.8 mg/dl), non-HDL cholesterol (decimated between 15.1 and 24.2 mg/dl), triglycerides (reduction from 11.0 to 23.3 mg/dl), Non-esterified fatty acids (decreased between 7.7 and 25.1 mg/dl) and significant increase in HDL (increased between 2.8 and 30.0 mg/dl), without altering glucose, insulin and HOMA index values. On the other hand, in individuals supplemented with 10 ml of olive oil, a reduction in lipid levels (with the exception of a reduction in triglycerides and VLDL) and an increase in HDL was also observed, however, a slight increase in glucose, insulin and the HOMA index was also observed8.

Research number #9 verified the use of traditional Persian medicine plants associated with electroacupuncture in order to alter the metabolic and anthropometric indices of women between 15 and 40 years of age with polycystic ovary syndrome (PCOS), with a BMI greater than or equal to 25. The plants were used by means of a mixture with fennel (*F. vulgare*), nettle (*U. dioica*),

carrot (*D. Carota*), red clover (*Trifolium pratense*) and turmeric (Curcuma longa) and acupuncture was performed in association, as well as the use of 2 tablets of 500 mg of metformin per day14.

After 12 weeks of follow-up, a significant reduction in BMI, body fat, waist-to-hip ratio, fasting insulin and HOMA index was observed in all participants. It can be concluded that the association of herbal medicines, electroacupuncture and metformin promoted a significant reduction in total cholesterol (202.15 to 183.00 mg/dl), LDL (134.35 to 122.80 mg/dl), and a decrease in triglycerides (150.50 to 113.80 mg/dl). HDL levels decreased by about 0.95 to 3.36 mg/dl in all subjects followed. Due to these results, this treatment protocol was suggested by the authors as an alternative to the therapeutic armamentarium of PCOS14.

The tenth study of this review (#10) aimed to evaluate the use of 200 mg of the mixed extract of *Trigonella foenum-graecum* and *Lespedeza cuneata* (TFGL) in the treatment of testosterone deficiency syndrome (TDS), however, the impact of these compounds on the lipid profile of the participants was considerable. It was found that lipid levels decreased globally, with the following reduction values being as follows: total cholesterol (between 9.66±13.70 mg/dL), LDL (13.23±21.66 mg/dL) and triglycerides (65.07±70.63), as well as increased HDL values (5.02±5.72 mg/dL). In the placebo group, on the other hand, there was an increase in the overall lipid profile15.

Study #11 of this review supplemented stage 1 and 2 hypertensive patients with a garlic preparation (270 mg of garlic macerate suspended in rapeseed oil) after meals, three times a day, for 30 days, and this supplementation was associated with the antihypertensive drug previously used by the patient. A statistically significant reduction was found in total cholesterol (5.64 to 5.13 mmol/l) and LDL (3.55 to 3.05 mmol/l) levels. There was also a reduction in lipid peroxidation levels and an increase in vitamin E (12.8 to 15.8 μmol/l). The authors concluded that garlic supplementation seems to reduce oxidative stress related to hypertension as well as decrease lipid oxidation, reducing the risk of atheromatous plaque formation16.

Supplementation with 250 mg of green tea (*Camellia sinensis*) dry extract in hypercholesterolemic patients for 8 weeks was proposed in study number #6 and led to a reduction in weight and BMI by 1.7%, a decrease in total cholesterol of 3.9%, subtraction of LDL by 4.5%, a decrease of 2.1% in HDL and an increase in triglycerides by 7.5% as well as Apolipoprotein-B by 4.4%. The authors did not find great significance in the results and it is believed that this fact is due to the small sample11.

Another tea used in this study was *Agrimonia eupatoria*, presented by research #12 of this review, which evaluated the impact of this consumption on inflammatory markers, oxidative status

and lipid metabolism in healthy individuals. An increase in HDL (from 1.49 to 1.65 mmol/l) and total cholesterol (4.32 to 4.69 mmol/l) was observed, as well as in the levels of total antioxidant capacity. There was a reduction in IL-6, TNF-α and leptin levels in 58% of the patients. The authors concluded that supplementation with *Agrimonia* has the ability to improve oxidative status and reduce inflammation in healthy adults17.

Study #7 evaluated the efficacy of eggplant extract (*Solanum melongena*) associated with orange juice in relation to lovastatin on reducing the lipid profile of dyslipidemic individuals. However, the subjects supplemented with eggplant juice with orange showed no change in the levels of total cholesterol, LDL, HDL and triglycerides throughout the follow-up period. It is also noteworthy that even with values close to statistical significance, the trend observed in this group was an increase rather than a decrease in total cholesterol levels12.

Research #13 used 320 mg of the aqueous extract of the artichoke leaf (*Cynara Scolymus*) - ALE, which was administered daily for 12 weeks in adults with mild and moderate hypercholesterolemia. There was a reduction in total cholesterol of about 4.2% in the group supplemented with ALE, while there was an increase of 1.9% in the values of the team that received placebo. The other lipid parameters did not present statistical significance to the point of being considered18.

Another profile of studies found was those that sought to know if Rouhani sought to know which plants were related, through popular knowledge, to the reduction of biological lipids. In this review, these studies covered #2, #4, #5 and #8.

Survey number #2 estimated the prevalence of integrative and complementary practices (ICP) by the elderly, and these PICs included activities such as acupuncture, homeopathy, medicinal plants and phytotherapy. Among the PICs used, medicinal plants and phytotherapy were mentioned in 62.6% of the cases, followed by acupuncture (22.2%) and homeopathy (11.2%), and only 6.7% of these practices were performed through the Unified Health System. In all PICs, women led the use when compared to men. Patients with high cholesterol, arthritis or rheumatism, chronic back problems, and depression also made greater use of PICs7.

Studies #4 and #5 aimed to assess participants' knowledge regarding the use of herbal medicines in the treatment of comorbidities. In study number #4, farmers and their families listed 196 plants that they used in the treatment of diseases, 6 of these were related to the reduction of cholesterol levels, such as: *Arthemísia absinthium* (wormwood), *baccharis crispa* (Gorse), *Cynara scolymus L.* (artichoke), *Eucalyptus globulus labill* (eucalyptus citron), *Leandra australis* (pixirica)[9].

Study #5 interviewed patients with peripheral vascular diseases in order to find out which plants were assimilated as having hypoglycemic, antihypertensive or hypolipidemic properties. As a result, more than 80% of the participants reported making occasional use of medicinal plants and in relation to hypercholesterolemia, 215 plants were mentioned, among which are: *allium sativum L.* (Alho), *Morinda citrifolia L* (noni), *Persea Americana Mill* (Abacate), *Plantago major L* (banana da terra), *Salvia officinalis L* (Salvia de Castilla), *Solanum melongena L* (beringela)[10].

Finally, research #8 in order to discover the impact of the use of herbal medicines on the biochemical parameters of type 2 diabetic patients divided the participants into individuals who reported using herbal medicines or not, evaluating whether this practice impacted the control of the treatment, through laboratory parameters. It was observed that men who did not use herbal medicines had poor glycemic control, with higher levels of glycated hemoglobin and a greater number of comorbidities, when compared to individuals of the same age group who use them. On the other hand, in the population that used medicinal plants, blood glucose was about 16 mg/dl lower, but they also had a high level of triglycerides. The plants consumed, alone or in combination, by the studied population were olive leaves, cinnamon, mint, lavender, white mugwort, fenugreek, common juniper. The authors concluded that the use of herbal medicines did not present benefits in the treatment of diabetes or associated diseases, such as dyslipidemias.

3 DISCUSSION

Dyslipidemia occurs when lipids or lipoproteins become unbalanced and accumulate in the blood, which is influenced by genetic dysfunctions and lifestyle habits. These disorders have been affecting individuals in increasingly early stages of life, including childhood19. The treatment of these disorders includes improvement of lifestyle habits and the use of lipid-lowering drugs such as statins and fibrates, which have limitations depending on the level of uncontrolled lipids or treatment abandonment due to the adverse effects of these drugs1,3,4.

Brazil is a country of great natural wealth and, associated with this, there is a growing tendency in the population of this country to inquire about the risks arising from the unbridled use of medicines, as well as the impact of the adverse effect of allopathic drugs on health. In addition, there are questions about the costs related to the use of polypharmacy. Considering these factors and also the limitations of the treatment of dyslipidemias, the use of herbal medicines gains great prominence and importance, as well as requires further research for its development and establishment20. Thus, studies that highlight the potential of herbal medicines and support their use are of great importance for the composition of therapeutic arsenals of the various

comorbidities.

The use of plants in the treatment of comorbidities is a long-standing exercise, with reports dating back to the Neanderthals. Phytotherapy in Brazil is also a traditional practice and has a strong cultural component21,22. Considering this custom, Marques et al.[7] (2020) estimated the prevalence of integrative practices among the elderly, among which phytotherapy was included, and corroborated the trend previously evidenced, since medicinal plants and phytotherapy were mentioned 62.6% of the time as a therapeutic measure. It is important to highlight that women led the use of herbal medicines when compared to men.

Brazilians' familiarity with the use of plants in the treatment of comorbidities was also evidenced in the study by Souza et al.[9] (2010) in which farmers and their families living in the southern region of Rio Grande do Sul – Brazil highlighted 196 medicinal plants that they use in the treatment and/or control of diseases, including dyslipidemias. The individuals surveyed highlighted that the preferred method of preparation of the teas of these plants was infusion, using mainly the leaves of the plants, followed by the bark and flower9.

In 2006, the Brazilian Ministry of Health established the National Policy for Integrative and Complementary Practices (PNPIC) where it highlights phytotherapy as an ancient practice that has great potential to adapt to the Brazilian reality, since the country has great variety in its flora, being the largest diversity in the world. This federal document indicated that in 2004 the use of herbal medicines was a practice that occurred in 22 of the country's 27 federative units21. Because phytotherapy is a widely worshipped exercise in Brazil, it is essential that health professionals know how to indicate it with mastery, however, it was found that they feel unprepared to guide the use of phytotherapics, which indicates the need for educational actions for this public7.

Popular knowledge highlights *Arthemísia absinthium* (wormwood), *Baccharis crispa* (gorse), *Cynara scolymus L.* (artichoke), *Eucalyptus globulus labill* (eucalyptus citron) and *Leandra australis* (pixirica)[9]. Studies have shown that black gorse can be used to reduce high cholesterol22,23. Artichoke is also related to the reduction of cholesterol levels, since it inhibits the hepatic synthesis of cholesterol and prevents the oxidation of low-density lipoproteins (LDL), and its antioxidant power (due to the concentration of vitamin E) is also highlighted, reducing the oxidation of lipids, proteins and DNA24. In a study conducted at the Royal Berkshire Hospital, in the United Kingdom, supplementation with 320 mg of the aqueous extract of the artichoke leaf promoted a reduction in total cholesterol by about 4.2% in the supplemented individuals18.

In order to recognize plants related to the treatment of dyslipidemias, according to popular knowledge, García-Lazo et al.10 (2015) highlighted references to Allium sativum L. (Garlic),

Morinda citrifolia L (noni), Persea Americana Mill (Avocado), Plantago major L (plantain), Salvia officinalis L (Salvia de Castilla), Solanum melongena L (eggplant) and according to the research, preclinical studies corroborated the efficacy of these plants however, No conclusive data were presented in clinical trials.

Regarding these compounds, recent studies cite that garlic reduces cardiovascular risk by inhibiting the enzyme cyclooxygenase (COX), responsible for the release of thromboxane (TXA2), which causes platelet aggregation, vasoconstriction and increased blood viscosity. Garlic also inhibits the hepatic synthesis of cholesterol and LDL, reducing their levels by 5% and 6%, respectively (when total cholesterol is above 200 mg/dL)[25].

A garlic preparation was also used in a supplementation (270 mg of garlic macerate suspended in rapeseed oil, which contained 0.27 mg of allicin derivatives) performed after meals, being prescribed to patients with primary hypertension in stages 1 and 2 in association with antihypertensive drugs. There was a reduction in the levels of total cholesterol, triglycerides, LDL and an increase in HDL, and the changes were statistically significant for total cholesterol and LDL. A reduction in lipid peroxidation levels was also found, as well as an increase in vitamins A, C, E, and carotenes, however, the statistical significance was positive only for vitamin E. Garlic supplementation seems to reduce oxidative stress related to hypertension as well as decrease lipid oxidation, reducing the risk of atheromatous plaques16.

The use of avocado as a lipid-lowering potential was also evidenced by a study with mice that highlighted that the freeze-dried flour of the avocado seed is full of essential fatty acids (such as omega-6 and omega-3), responsible for reducing cellular inflammation (inhibiting cytokines such as IL-6 and TNF-alpha) and the deposition of atheromatous plaques26. Avocado also has high concentrations of vitamin E and has the ability to inhibit the intestinal absorption of cholesterol, as well as reduce its synthesis in the liver27.

Regarding noni, a study carried out in Indonesia highlights that the flavonoids rich in this fruit are responsible for inhibiting HMG-CoA, as well as increasing the activity of lecithin cholesterol acetyltransferase (LCAT), which increases HDL levels. This study also highlights that the reduction of cholesterol increases the expression of LDL receptors in the liver and extrahepatic tissues, reducing the levels of total and LDL cholesterol in the plasma28.

As for eggplant, Praça et al.12 (2004) investigated its use associated with orange juice, comparing the efficacy of this association with the lipid-lowering potential of lovastatin. Individuals using eggplant juice did not show changes in total or LDL cholesterol levels and that the trend observed in this group was an increase rather than a decrease in total cholesterol levels.

Thus, considering the available studies, there is still no scientific robustness capable of indicating eggplant as a treatment for dyslipidemias27.

A plant of very common use in Brazil is green tea, which was brought to the country 100 years ago by Chinese immigrants and became popular in the country when its consumption was related to weight loss, however, it has several properties, being anticarcinogenic, antioxidant, anti-inflammatory and glycemia-reducing29. In a study conducted by Rahmoun et al.13 (2020), supplementation with green tea (Camellia sinensis) dry extract allowed results such as a reduction in weight and BMI by 1.7%, a reduction in total cholesterol by 3.9%, LDL by 4.5%, a decrease of 2.1% in HDL and an increase in triglycerides by 7.5%, as well as APO-B by 4.4%, However, these data did not show great statistical significance, which may have been influenced by the small sample size, as well as the short follow-up period.

The effects of green tea are due to its rich concentration of catechins and lead to a decrease in food consumption, a reduction in lipid absorption, as well as the suppression of cholesterol, LDL and triglyceride concentrations. Also noteworthy are the antioxidant, anti-inflammatory (inhibiting TNF-alpha and IL-6), hypoglycemic (by increasing insulin sensitivity and increasing GLUT4 activity) and anticarcinogenic (inducing apoptosis in tumor cells and protecting cells from the action of free radicals). In relation to weight loss, the action of green tea is defined as the increase in thermogenesis and fat oxidation, exerted by the stimulation of the sympathetic nervous system. All these benefits highlight green tea as a functional food that can be used in the treatment of comorbidities30.

Another tea capable of reducing inflammation and altering the lipid profile was Agrimonia eupatoria, where the supplementation of this promoted an increase in HDL and total cholesterol. In addition, there was a reduction in IL-6 and TNF-α as well as a reduction in leptin levels in 58% of the patients. It is recognized by the authors as being able to improve lipid markers, oxidative status and reduce inflammation in healthy adults. Thus, such supplementation has a preventive role in metabolic, cardiovascular and diabetes disorders17.

Sacha inchi oil (Plukenetia Volubilis L.), a plant native to Peru, contains too much omega-3 and omega-6 polyunsaturated acids. Supplementation with this oil led to a reduction in total cholesterol, LDL, VLDL, non-HDL cholesterol, triglycerides, non-esterified fatty acids (NEFA) and a significant increase in HDL, without altering glucose, insulin and HOMA index values8. These findings are corroborated by a study also carried out in Peru, where the author compared a group that used the oil associated with atorvastatin with another group that used only atorvastatin. It was observed that patients supplemented with Sacha achieved lower levels of total and LDL

cholesterol and increased HDL levels, as well as did not alter hepatic and renal markers and hemoglobin, demonstrating the safety of supplementation31.

Another supplementation to be highlighted is red grape seed extract (RGSE), which reduced the levels of LDL, total cholesterol, triglycerides and promoted a slight increase in HDL, as well as an increase in the levels of apolipoprotein-AI and paraoxonase (PON), which confer antioxidant activity to HDL, contributing to its anti-atherogenic activity. It also led to an increase in antioxidant enzymes, preventing lipid peroxidation6.

Supplementation with 200 mg of mixed extract of Trigonella foenum-graecume Lespedeza cuneata (TFGL) in individuals with testosterone deficiency syndrome (TSS) had a direct impact on the lipid profile of these patients, with a decrease in the levels of total cholesterol (9.66±13.70 mg/dL), LDL (13.23±21.66 mg/dL) and triglycerides (65.07±70.63), as well as increased HDL (5.02±5.72 mg/dL)15.

Other herbal medicines that had their actions tested by studies were the combination of fennel (F. vulgare), nettle (U. dioica), carrot (D. Carota), red clover (Trifolium pratense) and turmeric (Curcuma longa) that were associated with electroacupuncture and 500 mg of metformin. In 12 weeks of intervention, a significant reduction was observed in the variables BMI, body fat, waist-to-hip ratio, reduction in triglycerides, AST and ALT, and the results were more effective when electroacupuncture was associated with phytotherapy14. Turmeric also had its efficacy proven when associated with the Artemisia iwayomogi plant, after use for 10 weeks, where it promoted a reduction in hepatic steatosis and atherosclerosis. Curcumin, present in turmeric, is a lipophilic polyphenol that helps in lipid control, reducing the formation of triglycerides and increasing the oxidation of fatty acids32.

The use of plants in food supplementation has had its efficacy tested through several studies, and effective results are not always found. An example is the study by Rahmoun et al.13 (2020) who sought to discover the impact of the use of herbal medicines on the biochemical parameters of type 2 diabetic patients, finding that in the population that uses medicinal plants, associated with traditional medication, blood glucose was about 16 mg/dl lower, when compared to individuals who did not use them. However, this study highlighted that when participants who used plants as a single therapy, they obtained less control of blood glucose, presenting alterations in 84% of cases. The authors concluded that the use of herbal medicines did not present benefits in the treatment of diabetes or associated diseases, such as dyslipidemias. They also reported that some plants used by the population may have toxic dosages, so indiscriminate use should not be encouraged.

Another example of toxicity caused by herbal medicines is evidenced in the use of Red Yeast Rice (AVF) - a traditional Chinese food, with reports dating back to 1368. For the formation of this compound, the rice is fermented by a yeast called Monascus purpureus, which generates a product with lipid-lowering capacity, which occurs due to the high concentration of monacolins. When used in the traditional way, rice goes through a fermentation process that, depending on the way it is done, can result in the formation of citrinin, a toxin that is related to fetal malformations, teratogenicity, carcinogenesis, as well as liver and kidney toxicity. The allopathic drug lovastatin was derived from the AVF33. Such cases indicate the need for professional training in the prescription of herbal medicines in order to indicate only substances that have a proven effect and that do not produce toxic effects.

Encouraging the use of herbal medicines and conducting research in this area allows the physician, a prescribing professional, to increase clinical possibilities, which directly affects the quality of care that is offered to the patient. In addition, it expands an immense field of new discoveries, considering that the Brazilian flora contains great diversity. For these benefits to happen, it is essential that more research be carried out on this topic in order to highlight the benefits of the use of herbal medicines as well as to identify the risks in their use, aiming to avoid them during clinical practice.

4 CONCLUSION

The present systematic review showed that the use of herbal medicines in the treatment of dyslipidemia can be a viable alternative, as long as it is guided by trained professionals. It was observed that the use of herbal medicines as a complementary measure to allopathic treatments can lead to enhanced results. However, as it is an expanding area, it is noted that most of the studies brought incipient data or with possible biases, in addition to the fact that the occurrence of small samples as well as short follow-up periods was common. Therefore, it is essential that research be carried out that shows the potential of herbal medicines in the treatment of dyslipidemias, researching new plants or even evaluating the results of those brought to light by popular knowledge.

CONFLICTS OF INTEREST

The authors express no conflicts of interest related to the publication of this work.

REFERENCES

Faludi A, Izar M, Saraiva J, Chacra A, Bianco H, Afiune Neto A, et al. ATUALIZAÇÃO DA DIRETRIZ BRASILEIRA DE DISLIPIDEMIAS E PREVENÇÃO DA ATEROSCLEROSE - 2017. Arquivos Brasileiros de Cardiologia [Internet]. 2017[citado 12 de maio de 2022];109(1). Disponível em: http://www.gnresearch.org/doi/10.5935/abc.20170121

Valença SEO, Brito ADM, Silva DCG da, Ferreira FG, Novaes JF, Longo GZ. Prevalência de dislipidemias e consumo alimentar: um estudo de base populacional. Ciênc saúde coletiva. novembro de 2021;26(11):5765–76.

Schulz I. Tratamento das dislipidemias: como e quando indicar a combinaçãode medicamentos hipolipemiantes. Arq Bras Endocrinol Metab. abril de 2006;50(2):344–59.

Souza NA de, Vieira SA, Fonsêca PC de A, Andreoli CS, Priore SE, Franceschini S do C de C. Dislipidemia familiar e fatores associados a alterações noperfil lipídico em crianças. Ciência saúde coletiva. janeiro de 2019;24(1):323–32.

Hayden JA, van der Windt DA, Cartwright JL, Côté P, Bombardier C. Assessing Bias in Studies of Prognostic Factors. Ann Intern Med. 19 de fevereiro de2013;158(4):280.

Argani H, Ghorbanihaghjo A, Vatankhahan H, Rashtchizadeh N, Raeisi S, Ilghami H. O efeito do extrato de semente de uva vermelha na atividade do soro paraoxonase em doentes com hiperlipidemia leve a moderada. Sao Paulo Med J. 13de maio de 2016;134:234–9.

Marques P de P, Francisco PMSB, Bacurau AG de M, Rodrigues PS, Malta DC, Barros NF de. Uso de Práticas Integrativas e Complementares por idosos: Pesquisa Nacional de Saúde 2013. Saúde debate. 16 de novembro de 2020;44:845–56.

Garmendia F, Pando R, Ronceros G. Efecto del aceite de sacha inchi (plukenetia volúbilis l) sobre el perfil lipídico en pacientes con hiperlipoproteinemia. Rev Peru Med Exp Salud Publica. dezembro de 2011;28:628–32.

Souza ADZ de, Vargas NRC, Ceolin T, Heck RM, Haeffner R, Viegas CR da S. A enfermagem diante da utilização de plantas medicinais no tratamento complementar da hipertensão arterial sistêmica e das dislipidemias. Revista Mineirade Enfermagem. 1º de dezembro de 2010;14:473–8.

García-Lazo G, Lauzant-Diaz E, Díaz Batista A, Garcia-Mesa M. Plantas consideradas útiles como hipoglicemiantes, antihipertensivas o hipolipemiantes porpacientes con enfermedades vasculares periféricas. Revista Cubana de Plantas Medicinales. março de 2015;20(1):38–47.

Batista G de AP, Cunha CLP da, Scartezini M, von der Heyde R, BitencourtMG, Melo SF de. Estudo prospectivo, duplo cego e cruzado da Camellia sinensis (chá verde) nas dislipidemias. Arq Bras Cardiol. agosto de 2009;93:128–34.

Praça JM, Thomaz A, Caramelli B. O suco de berinjela (Solanum melongena)não modifica os níveis séricos de lípides. Arq Bras Cardiol. março de 2004;82(3):269–72.

Rahmoun NM, Boukli-Hacene G, Bettioui RA, Ghembaza CE, Ghembaza ME. Effect of the

consumption of natural products on some biochemical parameters of a type 2 diabetic population. J Diabetes Metab Disord. junho de 2020;19(1):233–41.

Rouhani M, Motavasselian M, Taghipoor A, Layegh P, Asili J, Hamedi SS, et al. Efficacy of a Persian Herbal Remedy and Electroacupuncture on Metabolic Profiles and Anthropometric Parameters in Women with Polycystic Ovary Syndrome:A Randomized Controlled Trial. Galen Med J. 2019;8:e1389.

Park HJ, Lee KS, Lee EK, Park NC. Efficacy and Safety of a Mixed Extract ofTrigonella foenum-graecum Seed and Lespedeza cuneata in the Treatment of Testosterone Deficiency Syndrome: A Randomized, Double-Blind, Placebo- Controlled Clinical Trial. World J Mens Health. setembro de 2018;36(3):230–8.

Duda G, Sulibursk a J, Pupek-Musialik D. Effects of short-term garlic supplementation on lipid metabolism and antioxidant status in hypertensive adults.Pharmacol Rep. abril de 2008;60(2):163–70.

Ivanova D, Vankova D, Nashar M. Agrimonia eupatoria tea consumption in relation to markers of inflammation, oxidative status and lipid metabolism in healthysubjects. Arch Physiol Biochem. 2013;119(1):32–7.

Bundy R, Walker AF, Middleton RW, Wallis C, Simpson HCR. Artichoke leafextract (Cynara scolymus) reduces plasma cholesterol in otherwise healthy hypercholesterolemic adults: A randomized, double blind placebo controlled trial. Phytomedicine. 3 de setembro de 2008;15(9):668–75.

Guedes MR, Moura AM de, Barros Silveira M, Oliveira ACCP de, Caldeira DM,Bernardes V. Dislipidemia em crianças e adolescentes de diferentes faixas etárias residentes no município de Goiânia. RSD. 6 de janeiro de 2022;11(1):e25711124671.

Klein T, Longhini R, Bruschi ML, Mello JCP. Fitoterápicos: um mercado promissor. Revista de Ciências Farmacêuticas Básica e Aplicada [Internet]. 1º desetembro de 2009 [citado 18º de novembro de 2022];30(3). Disponível em: https://rcfba.fcfar.unesp.br/index.php/ojs/article/view/421

Brasil M da S. Política nacional de práticas integrativas e complementares no SUS: atitude de ampliação de acesso [Internet]. 1a. ed. Sampaio LFR, organizador. Brasília, DF: Ministério da Saúde, Secretaria de Atenção à Saúde, Departamento de Atenção Básica; 2006 [citado 22 de novembro de 2022]. 91 p. Disponível em: https://bvsms.saude.gov.br/bvs/publicacoes/politica_nacional_atencao_basica_2006. pdf

Oliveira FA de. Plantas medicinais: uma opção no cuidado em saúde [Internet]. [Niterói]: Universidade Federal Fluminense; 2014 [citado 22 de novembro de 2022]. Disponível em: http://app.uff.br/riuff/handle/1/2889

Siqueira JB de V, Ceolin T, Ceolin S, Minuto J do C, Oliveira SG, Oliveira ADLde. Uso de plantas medicinais por hipertensos e diabéticos de uma estratégia saúdeda família rural. Revista Contexto & Saúde. 2 de junho de 2017;17(32):33–45.

Reolon-Costa A da, Grando MF, Cravero VP. Alcachofra (Cynara Cardunculus[var. Scolymus (l) Fiori]): Alimento funcional e fonte de compostos promotores da saúde. Revista Fitos [Internet]. 2017 [citado 22 de novembro de 2022];10(4). Disponível em: http://www.gnresearch.org/doi/10.5935/2446-4775.20160038

Silva RMJ da, Reis CC dos, Cardoso ML, Matos J de A, Madeira ERS, Ferreira VEP, et al. Uso de fitoterápicos no tratamento da dislipidemia: Um estudo derevisão. RSD. 19 de fevereiro de 2022;11(3):e22311326395.

Marques AR. Efeitos da farinha liofilizada da semente de abacate (persea americana) em camundongos alimentados com dieta hiperlipídica [Internet] [Dissertação]. [Brasil]: Fundação Universidade Federal de Mato Grosso do Sul; 2022[citado 22 de novembro de 2022]. Disponível em: https://repositorio.ufms.br/handle/123456789/4389

Santos HV, Pereira JM, Freitas RF, Royo V de A. Caracterização laboratorialdas dislipidemias e o uso de fitoterápicos. Revista Multitexto. 2015;3(1):21–8.

Forcepta C, Nisa K, Anggraini DI. The effect of noni (Morinda citrifolia) fruit giving against dyslipidemia | medical profession journal of lampung. 2021;11(3):253–8.

Urzedo NDR. O chá verde e suas propriedades: uma breve revisão bibliográfica abrangendo os anos 2000 a 2020 [Internet] [Trabalho de Conclusão deCurso]. [Brasil]: Universidade Federal de Uberlândia; 2020 [citado 22 de novembro de 2022]. Disponível em: https://repositorio.ufu.br/handle/123456789/30879

Moraes A da SM, Souza VRS. Chá verde e suas propriedades funcionais nasdoenças crônicas não transmissíveis. REINPEC. 18 de outubro de 2016;2(1):216– 77.

Laguna Marcos L, Tadeo Chavez RL. Influência de aceite de Sacha Inchi (plukenetia volubilis), como coadyuvante del tratamiento farmacológico hipolipemiante, en pacientes dislipidémicos del C.S. Aparicio Pomares, Huánuco 2017 [Internet]. [Huánuco-PERÚ]: Universidad Nacional Hermilio Valdizán Medrano; 2019 [citado 22 de novembro de 2022]. Disponível em: http://repositorio.unheval.edu.pe/handle/20.500.13080/4284

Sousa DF de. Custo-efetividade incremental da farinha do albedo do maracujáamarelo versus cúrcuma no controle glicêmico e lipídico de pessoas com diabetes mellitus tipo 2 [Internet]. [Redenção -CE]: Universidade Integração Internacional de Lusofonia Afro-Brasileira; 2019 [citado 18 de maio de 2022]. Disponível em: https://repositorio.unilab.edu.br/jspui/handle/123456789/repositorio.unilab.edu.br/jspui/handle/123456789/1994

Bunnoy A, Saenphet K, Lumyong S, Saenphet S, Chomdej S. Monascus purpureus-fermented Thai glutinous rice reduces blood and hepatic cholesterol andhepatic steatosis concentrations in diet-induced hypercholesterolemic rats. BMC Complement Altern Med. dezembro de 2015;15(1):88.