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Functional properties of yellow passion fruit bark (*Passiflora edulis*) in metabolic syndrome

Propriedades funcionais da casca do maracujá amarelo (*Passiflora edulis*) na síndrome metabólica

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Abstract

This study aimed to review the literature on the effect of yellow passion fruit bark flour *(Passiflora edulis f. flavicarpa)* on the metabolic disorders that make up the metabolic syndrome. It is a systematic review, carried out through a bibliographic survey of studies published between 2005 and 2017, indexed in the IBECS, PubMed, CisSaúde, Cochrame, MedCarib, Lilacs, Medline and SciELO databases, as well as in Google Scholar, theses and dissertations databases. The selected studies evaluated the effect of yellow passion fruit bark *(P. edulis)* on metabolic syndrome parameters. Experimental studies have demonstrated disagreement regarding the hypoglycemic effect and hypotensive effect. In healthy human studies, supplementation with 30 grams of the *P. edulis* bark flour showed efficiency in glycemic and lipid reduction for LDL and total cholesterol, without toxicity. In studies with people with metabolic syndrome and type 2 diabetes mellitus, hypolipidemic and hypoglycemic effects have also been demonstrated. However, there is still a shortage of publications on the use of *P. edulis* bark for the treatment of metabolic disorders, and a methodological standardization is necessary to enable its recommendation in clinical practice.

Keywords: Passiflora. Flour. Dyslipidemias. Obesity. Diabetes Mellitus. Metabolic Syndrome X.

Resumo

O objetivo deste estudo foi revisar a literatura sobre o efeito da farinha da casca do maracujá amarelo (*Passiflora edulis f. flavicarpa*) nos distúrbios metabólicos que compõem a síndrome metabólica. Trata-se de uma revisão sistemática, realizada por meio do levantamento bibliográfico de estudos publicados entre 2005 e 2017, indexados nas bases de dados IBECS, PubMed, CisSaúde, Cochrame, MedCarib, Lilacs, Medline e SciELO, bem como no Google Scholar, bancos de teses e dissertações. Os estudos selecionados avaliaram o efeito do uso da casca do maracujá amarelo (*P. edulis*) sobre os parâmetros da síndrome metabólica. Os estudos experimentais demonstraram discordâncias quanto ao efeito hipoglicemiante e resultados positivos quanto ao efeito hipotensor. Em pesquisas realizadas com humanos saudáveis, a suplementação com 30 gramas da farinha da casca de *P. edulis* demonstrou eficiência na redução glicêmica e lipidêmica para LDL e colesterol total, sem toxicidade. Em estudos com portadores de síndrome metabólica e diabetes *mellitus* tipo 2, os efeitos hipolipemiantes e hipoglicemiantes também foram demonstrados. Entretanto, ainda há escassez de publicações sobre o uso da casca de *P. edulis* para tratamento de distúrbios metabólicos, sendo necessária padronização metodológica que viabilize sua recomendação na prática clínica.

Palavras-chave: Passiflora. Farinha. Dislipidemias. Obesidade. Diabetes *Mellitus*. Síndrome X Metabólica.

Introduction

Metabolic syndrome (MS) is a complex set of pathologies, covering cardiovascular risk factors related to central fat accumulation, hypertriglyceridemia, dyslipidemia, systemic arterial hypertension and insulin resistance. These elements can vary according to the biological individuality of each human being, considering for their evaluation the parameters referring to ethnicity, gender, eating habits, lifestyles, phenotypes and geographical location.[1,2]

Data from the Ministry of Health show that, in 2012, chronic noncommunicable diseases (NCD) were responsible for 70% of the causes of deaths recorded in Brazil, of which 30% were due to cardiovascular diseases (CVD).[3] These data are reaffirmed by Silva et al.,[4] demonstrating that CVD is the leading cause of death in Brazil, accounting for 29.4% of deaths recorded annually.

In relation to MS, its prevalence has increased dramatically in the world, both in developed and developing countries. A study carried out in a municipality in the South Region of Brazil showed a prevalence of 53.7% of MS in the population evaluated, with an increase in the occurrence among the elderly, especially females (58%) in relation to males (48.4%).[5]

It should be noted that MS preventive measures include regular physical activity, healthy eating habits and no smoking.[6] Studies comparing sedentary individuals and those performing different levels of physical activity have shown that regular exercise, of moderate to intense intensity, decreases the risk for the development of MS.[7]

In addition, in people diagnosed with MS, healthy lifestyle acts as a complementary therapeutic option, helping pharmacological therapy and potentializing its effects on the body.[8] Currently, the use of soluble and insoluble dietary fibers has aroused the interest of researchers in the beneficial effects on health,[9] related to improved glucose tolerance, decreased serum cholesterol levels and intestinal transit time.[10]

In this sense, as a food source of soluble fibers, the yellow passion fruit bark *(Passiflora edulis f. flavicarpa)* is an important alternative to reduce food waste and to treat MS. Rich in pectin, and abundant in the Northeastern and Southeastern regions of Brazil, usually only the pulp of the passion fruit is used, discarding the bark. However, this can be included as flour in food, representing an alternative or complement to the conventional treatment of MS. It is important to note that the pectin content in yellow passion fruit is high and is related to the attenuation of some symptoms of MS.[11]

In this context, the present article proposes to review the potential of use of yellow passion fruit bark *(P. edulis)* for the treatment of metabolic syndrome.

Material and methods

This systematic review was performed through the search of experimental and clinical studies, published in the period 2005 to 2017, indexed in the IBECS, PubMed, CisSaúde, Cochrame, MedCarib, Lilacs, Medline, and SciELO databases, as well as in Google Scholar, thesis and dissertation databases, which related the use of yellow passion fruit bark *(P. edulis)* and parameters of the metabolic syndrome. For this, we used the descriptors, in Portuguese and English, isolated and combined, obtained from Descriptors in Health Sciences (DeCS: http://decs.bvs.br): cascas (peel), maracujá *(passion fruit), Passiflora,* diabetes, fibra alimentar *(dietary fiber),* farinha *(flour),* pectina *(pectin),* triglicerídios *(triglycerides),* colesterol *(cholesterol),* pressão arterial *(blood pressure),* obesidade *(obesity),* dislipidemias *(dyslipidemias)* and ratos *(rats).*

The selection of the studies was made using previously established eligibility criteria: adequacy to the study problem, clinical trial or experimental design, published in Portuguese, English or Spanish. Publications that did not correspond to the subject matter of the study, as well as review papers and duplicated works, were excluded.

In all databases searched, 34 articles were found, one of which was excluded because it was duplicated, 15 were excluded due to inadequacy to the research problem and 18 articles were selected for reading and qualitative analysis. Two dissertations from original studies were added to these manuscripts, in accordance with the research problem, whose data were not published but which are relevant to this review. All selected studies addressed the nutritional composition of yellow passion fruit bark and its influence on metabolic syndrome parameters, both in humans and in experimental animals. It should be noted that no articles published in 2016 and 2017 were found to investigate this relation.

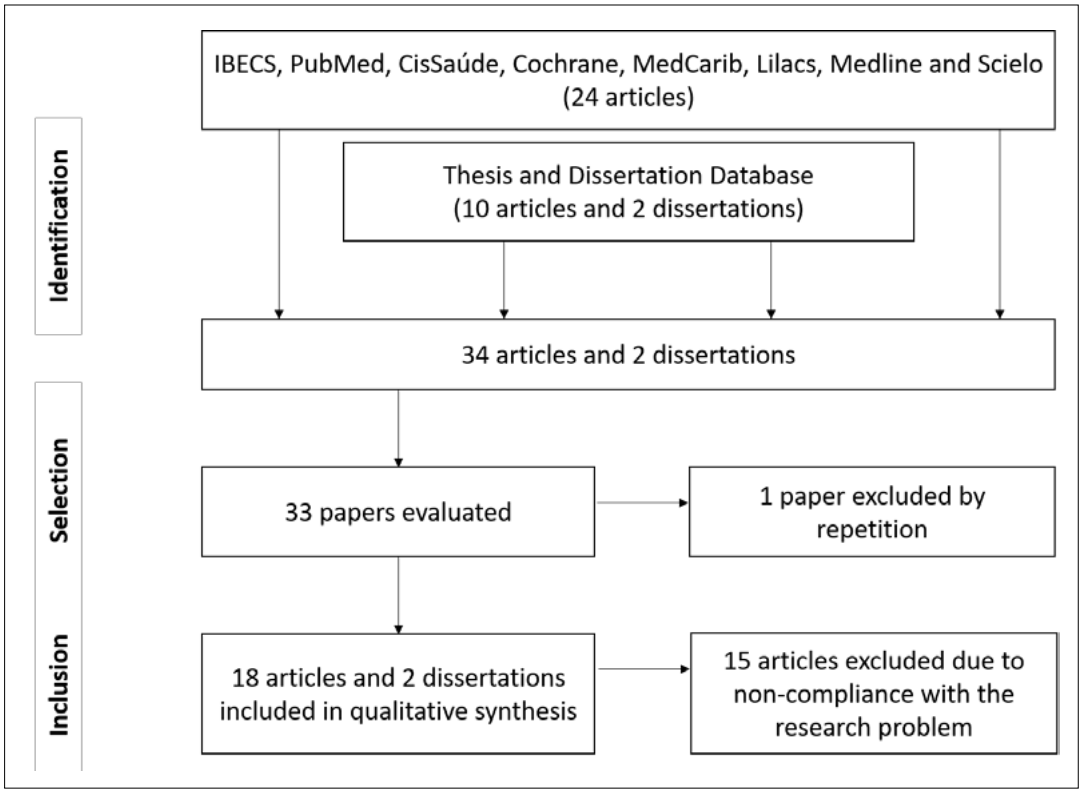

Figure 1. Description of the process of search, selection and inclusion of scientific papers in the systematic review.

Results and discussion

Content of fibers in yellow passion fruit bark

There is more fiber in the yellow passion fruit bark than in the pulp of this fruit.[12] Although it is a residue for the food industry, the high fiber content in the physical-chemical composition of the yellow passion fruit bark allows the flour obtained from it to be considered as a food supplement.[13]

Thus, the use of yellow passion fruit peel flour in human diet is important to increase dietary fiber content, improving the intestinal transit of constipated individuals, and also contributing to the reduction of glycemia and circulating lipids.

The analysis of the centesimal composition and *in vitro* antioxidant activity of the yellow passion fruit bark demonstrates its high amount of fiber (65.2%), varying from 57.3% to 90.3%, depending on the applied methodology.[14] There is predominance of insoluble fiber and high antioxidant activity in methanol / acetone extract.[15] Study carried out by Pinheiro[16] showed a total percentage of dietary fiber in yellow passion fruit bark flour, equivalent to 57.4%, of which 19.2% were soluble and 38.1% were insoluble.

In order to guarantee the use of food waste, reduce expenses and improve consumer acceptability, the food industry produces the yellow passion fruit bark flour. It is important to be aware of the physical, chemical and sensorial characteristics of the product for its application in human nutrition and health benefit.[15]

A comparative analysis of the percentages of fibers found in the different studies is shown in Table 1, where it can be seen that the yellow passion fruit bark is a product with expressive fiber values. However, there is no consensus as to the total content and of each type, which may be related mainly to the different analytical techniques adopted in each work.

Table 1. Percentages of dietary fiber of yellow passion fruit bark (*P. edulis*)

Authors	% Fiber Total	% Fiber Soluble	% Fiber Insoluble	Analytical Techniques
Córdova et al. (2005)	5.81	2.10	5.57	Total dietary fiber: enzymatic-gravimetric method; Soluble and insoluble fiber: methodologies recommendedby AOAC (2000).
Pinheiro (2007)	57.36	19.20	38.05	Soluble and insoluble food fibers: by the AACC method (1999). Soluble fiber: extractionin different concentrationof citric acid, with extraction timesunder reflux inthecondensation system a 97 ºC (solute/solvent = 1:50).
Ferreira and Pena (2010)	9.7	-	-	Total dietary fiber: enzymatic-gravimetric method
Nascimento et al. (2013)	57.32 a 90.32	-	-	-
Cazarin et al. (2014)	65.22	17.11	48.12	Total food fiber and insoluble fiber:gravimetric method; Soluble fiber: difference between total dietary fiber and insoluble fraction.

AOAC: Association of Official Analytical Chemists; AACC: American Association of Cereal Chemists

Experimental studies performed with laboratory animals

In this systematic review, we found seven studies performed with animal models. Of these, one was conducted with mice *(Mus musculus),* one with rabbits *(Oryctolagus cuniculus)* and five with rats *(Rattus norvegicus),* of which four were of the Wistar lineage and one of unspecified lineage. The results were positive for the effect of yellow passion fruit bark flour on the parameters of MS in all the experiments.

Araújo, Braga & Medeiros[17] induced diabetes *mellitus* by alloxan in 27 male Wistar rats, equally distributed in three groups. Yellow passion fruit bark flour supplementation was performed for 24 hours after oral induction at concentrations of 20, 30 and 160 mg / kg weight. Glycemia was measured before and after supplementation, with glycemic values being verified at the intervals of 0, 1, 2, 4 and 6 hours. The results demonstrated a dose-dependent hypoglycemic effect, more expressive after four hours of oral administration of *P. edulis* bark flour, with a dosage of 160 mg / kg weight.

With similar experimental design, Silva et al.[18] verified the action of pectin present in the yellow passion fruit bark in male Wistar rats that had alloxan-induced diabetes. However, in this study, the animals were distributed in only two groups: (1) diabetic control and (2) diabetic treated with pectin for five days, with doses of 0.5 to 25 mg/kg weight/day being administered orally. At the end of the experiment, the reduction of the glycemic and triglyceridemic levels of the animals of the group treated with pectin was demonstrated, suggesting that the bioactive compound can be used as an alternative treatment for type 2 diabetes *mellitus*.

The metabolic effects of *P. edulis* bark flour were also evaluated in an experimental study conducted with 18 male and albino mice, divided equally into three groups. The animals were induced to dyslipidemias by fructose and by hypercholesterolemic ration, as well as diabetes *mellitus*, by alloxan. Supplementation was performed in all groups by means of an aqueous suspension of *P. edulis,* in the dosages of 1% and 2%. The results demonstrated a reduction in total cholesterol and triglyceride levels in the different types of dyslipidemia inductions, with greater or lesser impact depending on the inducing substance. There was no significant reduction in the glycemia of mice induced to diabetes by alloxan, even with the use of different doses.[19]

The effect of yellow passion fruit bark flour on hypercholesterolemia was also evaluated in male rabbits, subdivided into three groups: (1) control, (2) treated with pulp and seed and (3) treated with the fruit bark. At the end, a 75% reduction in plasma total cholesterol was demonstrated in the last twogroups.[20]

The hypolipidemic effect observed in the afore mentioned studies was attributed by the authors to the presence of pectin. However, disagreements regarding the hypoglycemic effect may arise from differences between animal models, concentrations of *P. edulis,* period of supplementation and interval of time after supplementation to perform the biochemical analyzes. Despite this, the relevance in the hypolipidemic results observed, even in different species, should be considered.

Another parameter of MS, evaluated in relation to the use of *P. edulis*, is systemic arterial hypertension. Ichimura et al.[21] evaluated blood pressure levels of naturally hypertensive rats after supplementation with methanolic extract of the yellow passion fruit bark, demonstrating antihypertensive effect. In this specific study, the action was attributed to γ-Aminobutyric acid (GABA) and, to a lesser extent, to the vasodilator effect of polyphenols, especially luteolin.

In recent years, the prevalence and incidence of systemic arterial hypertension has increased among young individuals,[22] as well as in individuals with MS in all age groups, which reinforces the need to carry out studies and tests with yellow passion fruit bark flour with hypertensive individuals.

Simultaneously considered a disease and risk factor for chronic diseases, obesity is also a parameter of the metabolic syndrome that can be influenced by the consumption of *P. edulis* bark flour, as verified by Figueiredo et al.[23] In the study, Wistar rats were subdivided into two groups for one month: the first group was fed with albedo flour from passion fruit, and the second group received the flour from the whole passion fruit bark (albedo + flavedo). In both groups, body weight reduction was observed, with no change in dietary intake.

Similar result was found by Lage, Guerra & Pelogia[24] in a study conducted with Wistar rats distributed into groups with different dietary offers, for 21 days: (1) water and ration, (2) ration with *P. edulis* bark flour, (3) hypercaloric ration and (4) hypercaloric ration with *P. edulis bark flour.* The results of the intervention demonstrated that the flour of the yellow passion fruit bark promoted the reduction of body weight, even in hypercaloric diets.

These results on excess weight and other parameters of the metabolic syndrome can be attributed to the pectin and / or the anti-inflammatory components contained in the yellow passion fruit bark flour, which suggest the use of this food residue as nutraceutical.

Experimental studies performed with healthy humans

Despite the importance of animal studies, they do not allow fully safe inferences for humans. Their results lead to the realization of clinical trials that seek the confirmation of the experimental findings and enable their applicability to human health. From the total of selected studies, three clinical trials evaluated the effect of yellow passion fruit bark flour supplementation on human health; two of which were conducted with healthy individuals and one with people prone to develop disorders in lipoprotein metabolism.

Thus, in two clinical trials conducted with healthy volunteers of both genders and older than 30 years of age, 10g of yellow passion fruit bark flour was supplemented, three times a day, for two months. The results showed no toxic or adverse effects, but favored the reduction of 2% of body weight. In addition, blood glucose, total cholesterol, LDL cholesterol and triglycerides levels were reduced, while HDL cholesterol values remained unchanged, and the hypoglycemic and hypolipidemic potential of the yellow passion fruit bark flour was confirmed.[25,26]

With similar goal, Miranda et al.[27] conducted a clinical trial with 28 healthy volunteers, sedentary and susceptible to the development of dyslipidemias, of both genders and between 30 and 60 years of age. Two types of food supplements were offered (rolled oats and yellow passion

fruit bark flour) in the same amount (30 g / day), for two months. Biochemical analyzes of glucose, total cholesterol, HDL cholesterol and triglycerides were performed in fasting, before and after 30 and 60 days of supplementation. The results demonstrated an increase in HDL concentrations and a reduction in serum glucose concentrations among individuals supplemented with oats, as well as a reduction in glycemia and total cholesterol in individuals supplemented with yellow passion fruit bark flour. However, a more expressive hypocholesterolemic effect was observed in the use of *P. edulis* flour than in the use of rolled oats.

The comparison proposed by the authors in the aforementioned study is relevant because it allows evidencing the therapeutic potential of the yellow passion fruit bark flour, comparing it to oats, food whose functional properties and health claim are consolidated in the scientific literature.

Experimental studies performed with humans with metabolic disorders

The effect of yellow passion fruit bark flour supplementation on MS parameters should also be evaluated in people diagnosed with this syndrome, to evaluate its efficacy under pathophysiological conditions. Of the total of seven human studies included in this review, four were conducted with people with MS or some of the pathologies that comprise it.

Two clinical trials tested the effect of yellow passion fruit bark flour supplementation of 30 g / day for two months on 43 volunteers of both genders, aged over 60 years, with MS and DM2. Body weight and body mass index remained unchanged, but a reduction in blood pressure was demonstrated. In women, a reduction in central obesity was observed, not enough to adjust the values of waist circumference to those of reference. The levels of total cholesterol and LDL cholesterol did not change with supplementation, but the levels of triglycerides, fasting glycemia, basal glycemia and glycated hemoglobin were significantly reduced, in addition to an increase in HDL cholesterol levels.[28,29]

In both studies, it was emphasized that the hypoglycemic and hypolipidemic effect were significant for people with MS and DM2.[28,29] These results confirm the therapeutic effects of yellow passion fruit bark flour supplementation for the control of metabolic disorders, and suggest that this easily obtainable and low cost food product can be used as an alternative or complementary therapy for MS.

The hypolipidemic effect of the *P. edulis* bark flour was also demonstrated in a study with supplementation of 30 g / day for two months, in 19 women with hypercholesterolemia, in the age group of 30 to 60 years. The results showed a significant reduction of total cholesterol and LDL cholesterol.[30]

Queiroz et al.[31] evaluated the effect of yellow passion fruit bark flour on insulin sensitivity in 43 volunteers with DM2 of both genders. Dietary supplementation was performed with 30 g / day of flour, for two months, with biochemical tests before and after consumption. The results showed that the *P. edulis* bark flour had an effect on glycemic control, with an expressive reduction of fasting glycemia, glycated hemoglobin and an increase in the HOMA IR index.

In this way, it was verified that the intervention work evaluated showed positive action of the yellow passion fruit bark flour on glycemic and lipidemic parameters, confirming the potential of this product as a complementary therapeutic method for MS.

It should be noted that no adverse effects were reported with the dosages evaluated and that, despite the promising results, it is necessary to carry out new studies with representative sample size of the evaluated populations and standardization of the supplemented daily dosage. Thus, it will be possible to establish a recommendation of yellow passion fruit bark flour as a functional food, for complementary treatment of metabolic dysfunctions.

Final considerations

Although there are few studies evaluating the use of yellow passion fruit bark *(Passiflora edulis)* in the treatment of metabolic syndrome (MS), results available in the literature are promising as a clinical alternative for its use as an adjuvant in the control of metabolic disorders associated with this pathology.

Through this review, it was concluded that the supplementation of yellow passion fruit bark flour, even in different dosages, exerts an effect on reducing body mass in animal models, as well as on reduction in glycemic, triglyceride, total and LDL cholesterol levels, increased HDL, and reduced blood pressure levels, both in animal models and in clinical trials. These specific physiological responses qualify the yellow passion fruit as functional food, because they are attributed to a naturally occurring component in its chemical structure - pectin - whose therapeutic action occurs due to the soluble nature of this fiber. Its gelling activity decreases the absorption of carbohydrates and lipids, reduces the glycemic peak, and promotes prolonged satiety by increasing the volume of the food bolus and its viscosity in the gastrointestinal tract.

Yellow passion fruit flour is obtained by grinding the fruit bark, which guarantees high pectin concentrations. However, the bark and the immature fruit of *P. edulis* also contain cyanogenic glycosides (prunasin, sambunigrin and amygdalin) in its composition, which can cause adverse effects, if consumed in high quantity, such as respiratory disorders, dizziness, nausea, vomiting, diarrhea and weakness.

In this context, it is emphasized that the studies cited in this review, which assessed the fruit's toxicity potential, did not demonstrate toxic effects by the consumption of yellow passion fruit flour at the dosages and administration periods evaluated. Thus, the prescription of 30g / day of yellow passion fruit bark flour, as a food enriching the diets of patients with metabolic syndrome or with a tendency to develop metabolic disorders, can generate health benefits without the occurrence of adverse effects.

However, its use should be carried out with caution, under the guidance and follow-up of a nutritionist, explaining to the patient with metabolic syndrome that the functional food does not eliminate the need for pharmacological treatment. In addition, another important aspect to be emphasized is the recommendation for the use of yellow passion fruit bark flour from organic agriculture, since in traditional cultivation there is a high concentration of agrochemicals with cumulative potential to generate adverse effects on the health of individuals.

It is recommended that further experimental and clinical studies should be conducted to assess the potential toxicity of yellow passion fruit flour, at different dosages, administration forms and treatment period, so that a quantity representing the safety limit for food consumption without occurrence of undesirable health effects can be established.

Contributors

Claro ML worked at all stages, from the design of the study to the revision of the final version of the article; Teixeira SA participated in the design of the study and its final version; Rodrigues GP worked at all stages, from the design of the study, the writing of the article and to the revision its final version.

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