

RELATO DE CASO

Can the consumption of Seeds, Leaves and Fruit Peels avoid the risk factors for Cardiovascular Disorders?

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Não há conflitos de interesse

ABSTRACT

Changes in the feeding pattern of the population have recently led to a greater occurrence of cardiovascular risk factors that contribute to a high rate of morbidity and mortality worldwide. The presence of beneficial bioactive compounds in fruits and processed sub-products have proven to have a negative association with risk factors, such as blood pressure reduction, plasmatic lipoproteins control and increased resistance of LDL-c to oxidation, in addition to glycemic control and antioxidant effects. The aim of this review is to show that several studies have demonstrated many different chemical compounds in seeds, leaves and fruit peels, including their metabolic and physiologic effects on the risk factors of cardiovascular diseases. We reviewed the relevant literature by searching English-language publications in Pubmed, Google Scholar, Scielo and Lilacs, and references from relevant articles published since 2010, especially in the last five years. Eighty-seven relevant articles were included.

Keywords: phytochemicals, antioxidants, fruit, plants

INTRODUCTION

Epidemiological studies have shown that modernity's diseases affect more and more individuals, being responsible for high rates of mortality and morbidity in the population. Among them, cardiovascular diseases are the main cause of mortality worldwide, which can be explained by the occurrence of associated cardiovascular risk factors, such as visceral obesity, insulin resistance, hypercholesterolemia, smoking and hypertension^(1,2,3,4).

Changes in the feeding pattern of the population have visibly contributed to the occurrence of these risk factors, since most of the modifiable

factors are directly associated with the individuals' diet and physical activity. The current feeding pattern is characterized by a high intake of high-calorie, high-fat and sodium-rich foods, and by a limited intake of fibers and antioxidant compounds^(5,6).

In this context, scientific studies have shown that the regular consumption of fruit and vegetables has been associated with the lower incidence of acute myocardial infarction, blood pressure reduction, lipoprotein control and increased resistance of LDL-c (low-density lipoprotein cholesterol) to oxidation, in addition to reduced levels of adhesion molecules and pro-inflammatory markers, both of which are markers of the endothelial function^(7,8,9,10).

In addition to that, studies have widely demonstrated that non-conventional fractions of vegetable raw materials have higher concentrations of phytochemical compounds with beneficial physiological and metabolic properties in experimental models and humans^(11,12). These fractions are composed of seeds, leaves, and peels; they are considered to be domestic or industrial waste and are only sporadically consumed, but present high concentrations of metabolites with beneficial biochemical properties, which may be used to prevent and treat chronic degenerative diseases^(13,14,15).

The aim of this review is to show that several studies have found many different chemical compounds in seeds, leaves and fruit peels, including their metabolic and physiologic effects on the risk factors of cardiovascular diseases.

Methods

We reviewed the relevant literature by searching English-language publications in *Pubmed*, *Google Scholar*, *Scielo* and *Lilacs*, and references from relevant articles published since 2010, especially in the last five years. Eighty-seven relevant articles were included in the study.

Results and Discussion

Seeds: Benefits for Humans and the Environment

The seeds of fruits and some vegetables stand out as some of the most commonly found agro-industrial waste. They are the byproducts of domestic or industrial processes, but they often have significant contents of antioxidant and anti-inflammatory compounds^(15,16,17).

The guava (*Psidium guajava* L.) is one of the most popular tropical fruit, cultivated and consumed throughout the world; the largest part of its production is utilized in pastry, juice, jelly, nectar and the ice-cream industry, which exploit the pulp. The disposal of the seeds and peels corresponds to approximately 30% of the fruit's weight⁽¹⁸⁾. El Anany⁽¹⁹⁾ identified the presence of phenolic and flavonoid compounds in guava (*P. guajava*) seeds, which showed a high

radical-scavenging activity; Farinazzi-Machado et al.⁽²⁰⁾ identified that the seeds of *P. guajava* significantly decreased glycaemia, triacylglyceride and total cholesterol levels, whilst they increased the levels of HDL-c, when administered in experimental models.

Avocado (*Persea americana* Mill.) seeds make up a large portion of the fruit, favoring research on the extraction of biologically active compounds to be used in the food and pharmaceutical industries. In 'Hass' avocado seeds, Daiuto et al.⁽²¹⁾ observed more expressive contents of total phenolic compounds when compared to the fruit pulp; the Trolox equivalent antioxidant capacity and the antioxidant capacity measured by the ABTS+ ([2,2'-azinobis (3-ethylbenz-thiazoline-6-sulfonic acid)] radical capture method were significantly higher in the seed than in the pulp. Studies have also demonstrated the presence of flavanol monomers, proanthocyanidins, hydroxycinnamic acids and flavonol glycosides in avocado seeds⁽²²⁾. Pahua-Ramos et al.⁽²³⁾ identified that the fruit seed flour had hypocholesterolemic effects in experimental models; these results were attributed to the antioxidant phenolic compounds and the considerable nutritional fiber contents.

The residue obtained in the wine sector in the grape pressing process corresponds to almost 40%, and it is characterized by its high polluting potential, formed by the stalks of bunches, peels, and seeds. The latter are considerable sources of tocopherols, unsaturated fatty acids, linoleic acid and phenolic compounds⁽²⁴⁾. Ngamukote et al.⁽²⁵⁾ found taurocholic acid, taurodeoxycholic acid, and glycodeoxycholic acid at levels ranging from 38.6% to 28.2% in grape seeds, in addition to gallic acid, catechin, and epicatechin – these are compounds to which inhibitory effects of the pancreatic cholesterol esterase and decreased absorption of intestinal cholesterol are attributed. Another study revealed the antioxidant activity of grape (*Vitis vinifera* L.) seeds through the reduction of lipid oxidation and the inhibition of the production of free radicals induced by ethanol in experimental models⁽²⁶⁾.

Proanthocyanidins extracted from grape seeds have shown several beneficial effects: reduction of food ingestion and body weight of animals;

significant reduction of the levels of triglycerides, total cholesterol, low density lipoproteins and advanced glycation end products (AGEs); increase of high-density lipoproteins; activity of antioxidant enzymes such as superoxide dismutase, glutathione peroxidase and catalase^(27,28,29).

Hippophae rhamnoides L. (sea buckthorn) has been used in traditional medicine for a long time due to its multiple biological properties (anticancer, antimicrobial, and cardioprotective)⁽³⁰⁾. Its fruits are rich in vitamin C (average content of 695mg/100g), vitamin A, vitamin E, amino acids, minerals, β -sitosterol and polyphenolic acids. The administration of sea buckthorn seed waste reduced the body weight as well as the total cholesterol and hepatic triglycerides in experimental models⁽³¹⁾.

The passion fruit's peels and seeds (which represent around 40% of the fruit's total weight) resulting from the fruit cutting and extraction process for the extraction of the juice are still mostly discarded. Studies have shown that the seeds are rich in linoleic acid, tocopherols, vitamin E, fiber, and total phenolic content, like gallic acid and quercetin^(32,33).

Piceatannol is a polyphenolic antioxidant found in passion fruit (*Passiflora edulis*) seeds and others plants. In fact, piceatannol has been shown to have various cardioprotective effects, such as inhibition of platelet aggregation, inhibition of LDL-c oxidation, vasorelaxant effects in endothelium-intact aortas and reduction of myocardial tissue damage during ischemic events^(34,35). In studies with experimental models, piceatannol reduced fasting blood glucose levels and enhanced the secretion of insulin^(36,37).

The seeds of the Amazonian fruit *Byrsonima crassifolia*, popularly known as muruci, were used in diabetic rats, which revealed the seeds' potential effect in: reducing glucose levels and blood lipids; increasing insulin sensitivity; protecting against the activity of AGEs (advanced glycation end products); they are considered a potential, safe, anti-diabetic agent^(38,39).

Other seeds have demonstrated hypoglycemic and lipid-lowering effects in experimental models. The tamarind (*Tamarindus indica*) seed proved to be effective in the control of blood glucose

levels and fasting insulin levels, in addition to total cholesterol, triglyceride, and LDL-c levels, when administered to Wistar rats^(40,41). In a study developed by Sharma et al.⁽⁴²⁾, the seeds of the *Eugenia jambolana* demonstrated an anti-hyperglycemic and hypolipidemic effect in rabbits with severe diabetes induced by alloxan.

Peels: Does their use bring benefits?

Many phenolic compounds present in plants extracts are known for their cardiovascular regulatory properties and many are amply available in fruit and vegetable's peels, including flavones (luteolin, apigenin), flavonols (rutin, quercetin, kaempferol), phenolic acids, catechin, and others^(11,43).

Citrus fruit peels have high concentrations of bioactive compounds with antioxidant and anti-inflammatory effects. Loizzo et al.⁽⁴⁴⁾ identified the presence of apigenin, rutin, quercetin, kaempferol, and nobiletin in the peel extract of *Citrus aurantifolia*, and Boshtam et al.⁽⁴⁵⁾ observed an LDL-c oxidation prevention effect using the peel extract of the same plant.

Extracts of the unripe *Citrus sunki* peels had an anti-obesity effect through the increase in β -oxidation and lipolysis in the adipose tissue, without any observed liver damage, by reducing serum levels of glutamic pyruvic transaminase, glutamic oxaloacetic transaminase and lactate dehydrogenase, hepatic mediators⁽⁴⁶⁾. Thirteen flavonoids were quantified in grapefruit peel extracts by HPLC; the main flavonoids occurring in fresh, oven-dried, and freeze-dried grapefruit (*Citrus paradisi Macf.*) peels are naringin and isonaringin⁽⁴⁷⁾.

Ajila et al.⁽⁴⁸⁾ identified varying concentrations of gallic acid, syringic acid, mangiferin, ellagic acid, gentisyl-protocatechuic acid and quercetin in raw peels of ripe mango (*Mangifera indica* L.). According to the literature, compounds such as quercetin, gallic acid, and ellagic acid regulate hepatic and enterocyte cholesterol metabolism by controlling the key enzymes, including the activity of hepatic 3-hydroxy-3-metil-glutaril-CoA (HMG-CoA) reductase and enzyme acyl-CoA cholesterol acyltransferase (ACAT-2)^(49,50). Studies have also shown that the quercetin

metabolites, which have an expressive presence in the extracts of apple peels, were responsible for the oxidation inhibition of LDL-c molecules *in vitro*⁽⁵¹⁾.

Anthocyanins are bioactive compounds responsible for the blue and purple coloring of fruits, flowers, and peels. The jaboticaba (*Myrciaria cauliflora*) peel has high concentrations of anthocyanins, such as cyanidin-3-O-glucoside and delphinidin-3-O-glucoside. The consumption of jaboticaba peels was shown to increase HDL-cholesterol and improve insulin resistance in experimental animals; the tested doses of jaboticaba peels did not present cytotoxic properties in the animals of the study^(52,53). According to Suttirak and Manurakchinakorn⁽⁵⁴⁾, the anthocyanin contents increase during the ripening of the fruits, since the peel of ripe mangosteen (*Garcinia mangostana*), which has an intense purple coloration, shows an expressive concentration of this phytochemical and a high antioxidant activity.

Rai et al.⁽⁵⁵⁾, using raw *Psidium guajava* fruit peels, demonstrated their hypolipidemic and hepatoprotective effects, since their use in rats induced to severe diabetes, significantly reducing the plasma levels of triglycerides, total cholesterol, and LDL-c.

The yellow passion fruit (*Passiflora edulis*) peel has been studied for many years because of its hypoglycemic and anti-inflammatory properties, being currently consumed in the form of flour and food additive. Studies have demonstrated the presence of a high concentration of soluble fibers, especially pectin, phenolic compounds, such as isoorientin, coumarin, cyanidin-3-the-glycoside, quercetin-3-O-glycoside and edulic acid, among other yellow flavonoids. The treatment of experimental models and humans with the flour or yellow passion fruit peel extract revealed antihypertensive, antioxidant and antihyperglycaemic effects, in addition to decreased insulin resistance and hypolipidemic activity^(56,57,58,59,60,61).

The pitaya is a rustic fruit belonging to the Cactaceae family, known worldwide as “dragon fruit”. Among the species, the white pulp red pitaya (*Hylocereus undatus*) stands out; its peel is considered a residue from the fruit consumption or processing. However, this fruit peel has variable concentrations

of phenolic compounds (40.68mg GAE.100g-1 to 116.14mg GAE.100g-1 – the equivalent of gallic acid), in addition to vitamin C and betalains of the betacyanin type – substances derived from betalamic acid, with significant antioxidant activity^(62,63,64). Song et al.⁽⁶⁵⁾ observed that the betacyanins present in the peel of the white pulp red pitaya caused a reduction in body weight and an improvement in adipose tissue hypertrophy, in addition to controlling glycemia and insulin resistance in rats treated with a hyperlipidemic diet.

In a study conducted by Jung⁽⁶⁶⁾, the peels of pomegranates contained four monoterpenes: beta-thujene; o-cymene; beta-phellandrene; and gamma-terpinene; in addition to various volatile compounds, such as hydrocarbons, alcohols, aldehydes and ketones. Administration of the peel extracts of this fruit, in a study by Sadeghipour et al.⁽⁶⁷⁾, significantly decreased total serum cholesterol, triglycerides and LDL-c levels in rats fed on a high-lipid diet, and maintained normal levels of the TGO and TGP enzymes.

Leaves: better than the pulp?

Recent studies have revealed that the leaves of fruit and vegetables have higher nutrient and phytochemical values when compared with their respective edible parts, possibly because they are more exposed to oxidative stress⁽⁶⁸⁾.

In a study developed by Wang et al.⁽⁶⁹⁾, apple (*Morus alba*) leaves were shown to have higher concentrations of polyphenolic and flavonoid compounds when compared to the levels found in the fruit pulp. Other studies have shown the presence of such phenolic compounds as mulberrofuran, chalcone, kuwanon, isobavachalcone, flavones norartocarpetin, kuwanon and 6-geranylapiogenin in leaves of the apple tree^(70,71). Lee et al.⁽⁷²⁾ used different concentrations of an aqueous extract of *Morus alba* L. in experimental models and observed protective effects against atherogenic diet-induced hypertension, hyperlipidemia and vascular dysfunction. In addition to the anti-atherogenic effect of the apple leaves, Sharma et al.⁽⁷³⁾ identified a reduction of fasting glycemia in diabetic rats.

By studying the leaves and seeds of the avocado (*Persea americana* Mill) of the Hass and Shepard varieties, Kosińska et al.⁽²²⁾ identified that the total phenolic content and antioxidant activity of these plants was considerably higher in the leaves than in the fruit seeds. Another study identified the presence of catechins, procyanidins and hydroxycinnamic acids in the leaves of the avocado *Persea americana* Mill of the Hass and Fuerte varieties⁽⁷⁴⁾.

In the raspberry (*Rubus idaeus* L.) leaves, different phytochemical compounds were identified, including flavonoids, quercetin derivatives, luteolin derivatives, kaempferol derivatives and isorhamnetin derivatives⁽⁷⁵⁾. Another study revealed that the leaves of this plant showed antioxidant activity through its polyphenol contents, in addition to cytotoxic activity against colon adenocarcinoma⁽⁷⁶⁾.

Barbalho et al.⁽⁷⁷⁾ evaluated the effects of the pulp and leaves of the mountain soursop (*Annona montana*) in the biochemical profile of Wistar rats. They identified that the leaves produced better effects in the reduction of blood glucose and lipid variables in animals when compared to the fruit pulp, and that they didn't provoke an elevation of hepatic mediators in the animals of the experiment.

Liberal et al.⁽⁷⁸⁾ found polyphenols, namely ellagitannins, proanthocyanidins, and quercetin and kaempferol glucuronide derivatives in *Fragaria vesca* leaves extracts. These authors observed that the aqueous extract of strawberry leaves had an anti-inflammatory potential through the inhibition of nitric oxide production and the increased expression of several pro-inflammatory proteins in lipopolysaccharide-triggered macrophages.

The pomegranate (*Punica granatum* L.) leaves also revealed anti-diabetic and antihyperlipidemic effects in Wistar rats induced to diabetes, in concentrations of 500 mg/kg of the plant's leave extract⁽⁷⁹⁾. Balwani et al.⁽⁸⁰⁾ isolated the compound 2-methyl-pyran-4-one-3-O-β-d-glucopyranoside from pomegranate leaves, identifying that it inhibits the expression of cell adhesion molecules, suggesting possible anti-inflammatory effects. Bekir et al.⁽⁸¹⁾ also observed the presence of expressive concentrations of total phenols, flavonoids, tannins and anthocyanins in different extracts of *P. granatum* leaves.

Studies performed with Fig (*Ficus carica* Linn) leaves demonstrated an antioxidant and anti-inflammatory activity based on the identification of steroid compounds, flavonoids such as quercetin and luteolin, and phenolic compounds^(82,83).

Fagbohun & Odufuwa⁽⁸⁴⁾ observed that the leaves of the cashew tree (*Anacardium occidentale* L.) demonstrated hypoglycemic activity in rats induced to diabetes by streptozotocin. And the leaves of the sapodilla (*Manilkara zapota*) also demonstrated cardioprotective effects by reducing the levels of glucose, insulin, leptin, cholesterol and triglycerides in Wistar rats⁽⁸⁵⁾.

Omar et al.⁽⁸⁶⁾ demonstrated that the administration of leave extracts from the jackfruit tree (*Artocarpus heterophyllus*) reduced lipid peroxidation, the levels of total cholesterol, LDL-c and triglycerides, in addition to reducing fasting glycemia and glycated hemoglobin values and increasing the HDL-c levels in diabetic rats by 37%. In a similar study, Chackrewarthy et al.⁽⁸⁷⁾ observed a reduction in the glucose levels (39%), total cholesterol (23%) and triglycerides (40%) in animals fed with jackfruit leaves.

Conclusion

Considering that there is a high prevalence of cardiovascular disorders in the population, which results in high morbidity and mortality rates, and that their risk factors can be prevented by the regular consumption of vegetable raw materials, studying the ingestion of non-conventional vegetable fractions becomes relevant, since these fractions have numerous bioactive compounds that protect vascular health. It is also relevant to consider that the use of seeds and peels, described as by-products of plant raw materials processing, not only has beneficial effects but could also contribute to less environmental waste.

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