

# Assessment of the scientific evidence of the potential use of açai (*Euterpe oleracea*, Mart.) in clinical outcomes: analysis with focus on antioxidant and anti-inflammatory action

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**Palavras-chave:** Frutas, propriedades antioxidantes, propriedades anti-inflamatórias

## ABSTRACT

The açai berry (*Euterpe oleracea*, Mart.), fruit native to the Amazon region and explored mainly in the region of Pará, gained importance in recent years due to potential health benefits, associated with its phytochemical composition and antioxidant capacity, related to its high content of flavonoids. Among these, anthocyanins are responsible for the anti-inflammatory and antioxidant capacity of this fruit. Experimental studies show that due to its composition, the açai berry has antioxidant activity related to its ability to reduce the reactive oxygen species (ROS) and its potential to inhibit cyclooxygenase 2 (COX-2). Another benefit studied is the analysis of their effectiveness in the anti-inflammatory process, being observed inhibition of araquedônico acid-derived mediators, suggesting that the fruit can act in the chronic inflammatory process. Also it was possible to observe that the fruit may have anti-inflammatory effects in healthy patients. Thus, the supplementation of diets with use of açai berry could attenuate inflammation process and oxidative stress, today with more consistent evidence derived primarily from in vitro studies. However, there is still need for further studies to prove the action of this fruit in the mechanisms involved in these processes, isolation of specific compounds and determining their optimal dosage.

**Keywords:** Fruits, Antioxidants, Anti-inflammatories.

## INTRODUCTION

The açai palm (*Euterpe oleracea* Mart.), plant native to the Amazon region, is found mainly in the states of the north region of Brazil. Its fruit has become symbol of the State of Pará in the northern region, this being its main operator, followed by the States of Maranhão, Amapá, Acre and Rondônia (1, 2). Its socioeconomic importance occurs due to the abundance of the fruit in the region, having this full utilization. Its seed is used for crafts and organic fertilizer, its stem provides the palm and its leaves are

used to cover roofs of local residences. In addition, their stems can be intended for the manufacture of cellulose (2).

Despite the açai harvesting occur throughout the year, the best organoleptic, nutritional and antioxidant qualities are obtained when the product is harvested in the months of august to december. The harvest from january to july, due the climatic characteristics, provides nutritional quality product apparently bottom (3).

In Brazil, it's fairly widespread consumption

of the plant, being traditionally the pulp of the fruit of the açai consumed in the form of juice. In addition to this form, there are also several applications in cooking through its use in pies, jams and liqueurs(4).

According to the current legislation, the juice from the açai berry is classified under: açai thick or special (type A) - pulp extracted with the addition of water and features after being filtered more than 14 total solids, with very dense appearance. The açai berry medium or regular (type B) - pulp extracted with the addition of water and after being filtered from 11 to 14 of total solids, having moderately dense appearance and the açai berry slim or popular (type C) - pulp extracted with the addition of water and after being filtered from 8 to 11 of total solids, and thus the appearance little dense(5).

Although the vast majority of consumption is derived from the diluted juices, those possessing low content of açai (4 to 5%), there is a small number, but significant, on the market for the consumption of the juice with high content of açai (40%), designed for dissemination in various media of potential health benefits attributed to fruit(6).

The açai also has been receiving prominence in other producing regions of the country such as Rio de Janeiro, São Paulo, Brasília, Goiás and Northeast region. However, due to its high cost due to additional steps in the production chain and marketing, the most consumed in these regions is the açai berry slim, which is usually mixed with other products, which alters their taste, odor and caloric value. Currently, with the increased consumption in Brazil, an incipient phase of exportation of the product, which reaches North American and European markets (especially Italy), which is sent in the form of frozen pulp(2).

In recent years, the fruit gained importance due to the potential health benefits, associated with its phytochemical composition and antioxidant capacity (4). In addition, the açai berry has been used in dietary supplements, since it contains high energy value and a wide range of nutrients, including proteins, lipids, vitamins and polyphenols(7). The present study has as objective check for evidence that the anti-inflammatory and antioxidant action of açai can mitigate oxidative stress and inflammatory process and analyze the dosages used in in vitro and in vivo studies available in the literature.

## METHODOLOGY

It is a systematic review focusing on articles related to the topic *Euterpe oleracea*, Mart. For both, employed the Boolean technique with the words AND, NOT and OR and

the following descriptors of health: Disease prevention, Cardiovascular diseases, açai, *Euterpe oleracea* mart., Atherosclerosis, and their corresponding in Portuguese.

The trace was conducted by means of the manual search with visits to integrated system for libraries and consultations the electronic means of scientific reliability as SCIELO (Scientific Electronic Library Online), LILACS (Latin American literature and Caribbean Center on health sciences) and PUBMED. Selected articles published over the past 13 years and that anticipated the objectives determined in the present research.

## DISCUSSION

### a. Composition and chemical-nutritional aspects

The degree of maturity of the açai berry is important for the biological activity of its pigments. The Green pulp presents fewer phenolic pigments, anthocyanins and antioxidant activity in relation to the ripe pulp, which has the maximum amount of these pigments(8).

The açai berry is considered high-calorie food, this is due to the presence of high amount of fatty acids (oleic, linoleic and Palmitic), with 60% of monounsaturated and polyunsaturated of 13%(1, 2), characterizing a desirable profile of lipids with potential cardiovascular benefit(9). In relation to proteins, their content is higher than milk (3,50%) and egg (12,49%), and the amino acid profile is similar to that found in the egg farm(2).

The pulp is also rich in minerals, including calcium and potassium and vitamins, especially vitamin E, admittedly with antioxidant potential and with action to combat free radicals(10). Although it has not yet been demonstrated in isolation effect in reducing cardiovascular events(11). Contrary to popular belief, the fruit cannot be regarded as significant additional source of iron(1, 2). In relation to fibers, the fruit presents high amount the same, mostly insoluble fibers(12).

The açai berry also contains flavonoids, those responsible for action potential antioxidant and anti-inflammatory properties of fruit(13-15). This is due to the presence of phenolic compounds that desencadeam a reduction in the production of reactive oxygen species (Ros), thus protecting the oxidative damage in vitro cell and providing anti-inflammatory signaling, leading to reduced production of free radicals by polymorphonuclear cells(16). Anthocyanins are natural pigments belonging to this group of flavonoid compounds, having scientific evidence experimental laboratory contribution in reducing cholesterol levels and endothelial inflammatory activity(17-21).

So, in this particular aspect we can conclude that

açai is recognized due to its high chemical compounds content of antioxidant activity, particularly total anthocyanins and phenolics(22). However, the evidence of its beneficial effect are currently derived from laboratory experimentation, there is no unequivocal evidence to date of the potential in clinical patient cohort.

### b. Anthocyanins

The reddish purple color typical of açai is derived from its high anthocyanin content. Anthocyanins and phenolics showed positive and significant correlation with antioxidant activity of açai(23). Its pulp is tested at trial against radical hydroxyl (OH•), Alkoxy (ROO•) and hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) had an impact on attenuation of oxidative stress derived of these compounds(24).

The major anthocyanins found in Acai pulp are represented by cyanidin-3-glucoside, cyanidin-3-rutinoside, pelargonidin-3-glucoside, cyanidin-3-sambubioside, peonidin-3-Glucoside and peonidin-3-rutinoside(4). Through the isolation of anthocyanin cyanidin-3-Glucoside and cyanidin-3-rutinoside in freeze-dried samples of acai berry, it was possible to demonstrate the high degree of presence of these compounds in the fruit(25).

Chemical structure of cyanidin-3-Glucoside(26)

The anti-inflammatory capability of anthocyanins is derived from different mechanisms. Among these, is demonstrated inhibition of nuclear factor Kappa  $\beta$  activation (NF- $\kappa$ B), inflammatory response and inhibition of apoptosis of endothelial cells induced by human CD40 factor. In addition, it was demonstrated even inhibiting the production of nitric oxide (NO), the increase of the expression of the enzyme nitric oxide synthase (iNOS) and induced a reduction in plasma monocyte chemoattractant protein concentration of monocytes 1 (MCP-1)(27), effecting a possible link between effects of açai and beneficial properties in human endothelial function. Was demonstrated positive correlation derived protective polyphenols of açai in human umbilical vascular endothelial cells on inflammatory stress induced by inhibition of gene expression of adhesion molecules and activation of NF- $\kappa$ B(28).

The açai berry is also source of phytosterols, showing (78%) sitosterols, stigmasterol (6.5%), campesterol (6%) and avenasterol (6,5%)(29). The concentration of phytosterols found average was in the

fruit in prior analysis was 15 mg for every 100 g of fruit, mainly the  $\beta$ -sitosterol(30).

In experimental study conducted in order to investigate protective action of açai against genotoxicity in vivo induced by doxorubicin (DXR), a powerful group of liposomal anticancer, this demonstrated protective effects of açai pulp observed in acute and subacute both treatments, derived from the fruit pulp before administration of DXR. The result of the chemical analysis confirmed the presence of carotenoids, anthocyanins, phenolic compounds and flavonoids in fruit pulp. In general, subacute treatment (adminstrado more prolonged before toxic damage induction) provided a greater effectiveness in protecting against DNA damage induced by DXR(31). Such evidence may suggest the bases several lines of research.

It is important however to note that features derived from the form of processing can have direct influence on nutritional composition. Progressive damage has been shown to açai fruit after their harvest, favoring the microbial contamination and degradation of anthocyanin(32). Thus, in field analysis, such aspects should be guarded.

### c. Evidence in experimental models

In a study conducted to determine concentrations of total phenolics, total flavonoids and ascorbic acid in comparison using frozen fruit pulps, the antioxidant capacity in the disabling of the alkoxy radical (ROO•), hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) and hydroxyl (OH •), the açai berry was the fruit that showed better ability of reducing the EROs(24). In addition, study aiming to correlate the level of these elements (including total anthocyanins and phenolics of açai pulp) to its potential benefit in reducing oxidative stress, showed significant correlation between the level of these compounds and antioxidant activity of pulps analyzed(23).

The supplementation of diet with açai berry pulp not only acts as an antioxidant, but can also modulate the production of EROs by neutrophils and enhance oxidant balance liver antioxidant for the induction of mRNA expression of antioxidant enzymes in the oxidative stress. The properties of the pulp of açai in vivo and in physiological conditions seem to involve beneficial effects related to antioxidant defense system and partial rollback of the deleterious effects on the liver caused by diabetes in this animal model(33).

In another experiment performed, adding 5 of freeze-dried açai ration provided a reduction in the number of invasive tumours colon ( $p=0,005$ ) and

the reduction of the multiplication of these tumors ( $p=0,001$ ). In addition, it was possible to observe a reduction in the proliferation of tumor cells of Ki-67 ( $p=0,003$ ) and net growth index ( $p=0,001$ ). Therefore, the results of this study indicate that the addition of açai berry can reduce the development of chemically induced colon carcinogenesis in rats(34).

Due to its high content of polyphenols, freeze dried açai pulp was exploited by its protective effect in rat microglial cells. The fractions extracted with methanol (MeOH) ethanol (EtOH) and were particularly rich in anthocyanins, whereas the fraction extracted using acetone (ACE) was rich in other phenolic compounds. The açai berry resulted in significant decrease in production of nitrite ( $p<0,05$ ), accompanied by reduction of expression of inducible nitric oxide synthase (iNOS), besides significant reduction dependent on the concentration of cyclo-oxygenase-2 (COX-2), enabled by p38mitogen-activated protein kinase (p38 MAPK), tumor necrosis factor  $\alpha$  (TNF $\alpha$ ), and NF- $\kappa\beta$ . The present study suggests that ultimately the açai berry can potentially interfere favorably in motor and cognitive functions(35).

Diverse study conducted in experimental model also suggests oil of Euterpe oleracea on inflammatory response, due to inhibition of arachidonic acid-derived mediators. With this, the açai berry can potentially have a beneficial role in chronic inflammatory processes (36).

Wine consumption of açai in experimental model mitigated atherosclerosis through effects involving reduction of synthesis and absorption of sterols, reduction of oxidative modification of lipoproteins and improves endothelial function(30). Costa et al. (2012) revealed that chronic treatment with açai seed extract prevents the development of arterial hypertension and endothelial dysfunction. These effects are associated with the synthesis, antioxidant action, and the inhibitory effect on the levels of matrix metalloproteinase-2 (MMP-2). In this way, the açai berry works in reducing oxidative stress and levels of MMP-2(37).

#### **d. Research in humans**

In a study conducted in vitro and in vivo, in order to investigate the anti-inflammatory and antioxidant properties of a patented juice containing açai as the predominant ingredient, along with smaller amounts of other fruits. Ingestion of this demonstrated substantial juice antioxidant capacity to protect cells from oxidative damage in vitro. In addition, resulted in significant reduction in plasma lipid peroxidation in the 2 hours

period, in vivo, being possible to observe an increase in plasma antioxidant capacity. About anti-inflammatory capability, it was possible to observe significant statistic reduction of three pro-inflammatory article-chemotactic formyl-metionyl-leucyl-phenylalanine (FMLP), Leukotriene B<sub>4</sub>, interleukin 8. However, it is speculated whether the fruit may or may not have anti-inflammatory effects for healthy patients(38).

In randomized were observed healthy subjects aged 18-50 years and no smoking. The subjects were divided into 2 groups, was offered 400 ml of fruit juice. Ingestion of juice containing açai and cranberry compound, rich in ascorbic acid and anthocyanins increased the concentration of ascorbic acid in plasma, stabilized pró-oxidante balance in healthy nonsmokers, but did not reduce the oxidative stress markers(39).

In another protocol developed in humans, the plasma antioxidant capacity was significantly increased after the 7mlkg consumption of the juice and pulp of açai. Individual increases in plasma antioxidant capacity of 2,3 to 3 times were observed for the consumption of juice and pulp of açai, respectively. The antioxidant capacity in the urine, the generation of ROS and uric acid concentrations in plasma were not significantly altered by the treatments. The results demonstrate the absorption and effects of antioxidant anthocyanins in plasma due to the consumption of açai in humans(26).

Pilot study noted 10 adults with overweight (IMC  $\geq 25$  kg/m<sup>2</sup> e  $\leq 30$  kg/m<sup>2</sup>), who consumed 100g of pulp of açai twice a day for 1 month. Proved to be reduction in fasting glucose and insulin levels after treatment of 30 days (both  $p<0,02$ ). It was possible to observe significant statistical reduction in total cholesterol levels, as well as a reduction in LDL-c and the relationship between total cholesterol and HDL-c, as well as moderate their postprandial plasma glucose reduction after standard meal consumption. The consumption of açai pulp demonstrated so reduction in levels of disease risk metabolic markers in overweight adults(40).

Pilot study with humans with chronic joint disease which participants ingested 120 ml of fruit juice containing predominantly patented the pulp of açai (Euterpe oleracea Mart.) and other fruit concentrates during 12 weeks. Was associated with a significant reduction of pain, improved range of motion and realisation of physical activity daily. Plasma antioxidants were monitored, being possible to see improvement within 2 weeks and who remained increased throughout the 12 weeks. The inflammatory marker C-reactive protein (CRP) was reduced by 12 weeks, but this change

did not reach statistical significance. Lipid peroxidation reduced slightly until the end of the experiment. With this, it was possible to observe the significant association between increased antioxidant capacity, improves range of motion and reduction of chronic pain(41).

## CONCLUSION

Currently the açai berry has been receiving prominence due to its high content of flavonoids. Among these, anthocyanins are responsible for the anti-inflammatory and antioxidant capacity of this fruit. Studies are being conducted in order to assess whether the consumption of açai can mitigate oxidative stress and inflammatory process.

The available evidence show that supplementation in diets with the use of açai can mitigate oxidative stress and inflammatory processes, mainly in in vitro studies. However, there is a need for more studies with larger population showing the action of this fruit and its mechanisms involved in these processes and the determination of its optimal dosage. In addition, the changes demonstrated in the initial models of cardiac remodeling and its antioxidant action can raise the hypothesis that their dietary supplementation has potential benefit also in this condition.

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**Figura 1:** Chemical structures of cyanidin-3-O-glucoside (A) and cyanidin-3-O-rutinoside (B)

