Cognitive Vitality Reports® are reports written by neuroscientists at the Alzheimer's Drug Discovery Foundation (ADDF). These scientific reports include analysis of drugs, drugs-in-development, drug targets, supplements, nutraceuticals, food/drink, non-pharmacologic interventions, and risk factors. Neuroscientists evaluate the potential benefit (or harm) for brain health, as well as for age-related health concerns that can affect brain health (e.g., cardiovascular diseases, cancers, diabetes/metabolic syndrome). In addition, these reports include evaluation of safety data, from clinical trials if available, and from preclinical models.

Açaí Berries

Evidence Summary

Açaí berries have strong antioxidant effects, but benefits for humans are not as consistent as those in preclinical studies. There are many drug interactions. Also, some açaí supplements may not contain açaí.

Neuroprotective Benefit: Preclinical studies have shown antioxidant, anti-inflammatory, neuroprotective, and precognitive benefits, but no studies have tested açaí berry interventions for brain health in humans.

Aging and related health concerns: Although measures of oxidative stress are decreased with açaí interventions, there are inconsistent reports on whether they improve metabolic disorders, blood pressure, or dyslipidemia.

Safety: Açaí juice is likely safe in moderation given it has been consumed for hundreds of years. However, açaí products interact with many drugs. A study comparing commercially-available açaí supplements found that many products contained little to no açaí.

Availability: available as supplement, puree, powder, or in food products (e.g., sorbet).	**Dose**: Clinical trials have tested different forms and amounts. Examples include 200 mL/day of açaí juice, 200 g/day of açaí pulp, and 2 capsules/day each containing 500 mg of freeze-dried açaí.	**Chemical formula:** varies **MW**: varies Numerous compounds are present in açaí, including anthocyanins (e.g., cyanidin-3-rutinoside, cyanidin-3-glucoside, etc.), flavonoids (e.g., quercetin, luteolin, dihydrokaempferol, orientin, etc.), phytosterols, polyunsaturated essential fatty acids, and vitamins (B1, B2, B3, C, and E).
Half life: varies depending on compound	**BBB**: varies depending on compound	
Clinical trials: The largest randomized controlled trial testing açaí treatment included 37 people with metabolic syndrome.	**Observational studies**: none available	

What is it? Açaí (açaí) is a berry grown on the açaí palm tree (*Euterpe oleracea*), which is native to Central and South America. Açaí berries have recently been referred to as a "superfruit"; however, açaí berries in the form of beverages/juices have been consumed by the natives of the Amazon for hundreds of years. Approximately 10,000 tons of açaí pulp is consumed in Brazil and 1,000 tons are exported to countries such as the US, Japan, Netherlands, and Italy (de Oliveira et al., 2019). The açaí fruit is reddish-purple and 1-2 cm in diameter. The açaí berry contains antioxidants, flavonoids, phytosterols, fatty acids, and other nutrients. Açaí contains high levels of anthocyanins, a group of polyphenols that give açaí berries their deep purple color which have been shown to exert antioxidant effects (Ulbricht et al., 2012; de Oliveira et al., 2019). Cyanidin 3-rutinoside, cyanidin 3-diglycoside, and cyanidin 3-glucoside are the major anthocyanins found in açaí berries. Flavonoids (quercetin, luteolin, dihydrokaempferol, orientin, homoorientin, vitexin) may exert anti-inflammatory properties, while phytosterols may inhibit intestinal absorption of cholesterol. Unlike most fruits and berries, açaí berries contain high levels of polyunsaturated essential fatty acids such as linoleic and linolenic acids. In addition, açaí berries contain proteins, vitamins B1, B2, B3, C, and E, and oleic acid.

Açaí extracts/supplements have been tested in clinical trials, mainly for people with metabolic syndrome and those with hyperlipidemia. In preclinical studies, açaí interventions have been tested for their anti-cancer, anti-diabetic, lipid-lowering, anti-inflammatory, anti-oxidant, anti-microbial, cardioprotective, hepatoprotective, and renoprotective effects (Ulbricht et al., 2012; Soares de Almeida Magalhaes et al., 2020).

Neuroprotective Benefit: Preclinical studies have shown antioxidant, anti-inflammatory, neuroprotective, and precognitive benefits, but no studies have tested açaí berry interventions for brain health in humans.

Types of evidence:

- Several laboratory studies

Human research to suggest prevention of dementia, prevention of decline, or improved cognitive function:
None available.

Human research to suggest benefits to patients with dementia:
None available.

Mechanisms of action for neuroprotection identified from laboratory and clinical research:
While no studies have tested açaí berry interventions for neuroprotection in humans, there are several potential mechanisms of action for neuroprotection. Açaí berries contain high levels of anthocyanins (cyanidin 3-rutinoside, cyanidin 3-diglycoside, and cyanidin 3-glucoside), a group of polyphenols that have been shown to exert antioxidant effects (Ulbricht et al., 2012). Açaí berries also contain flavonoids (quercetin, luteolin, dihydrokaempferol, orientin, etc.), which exert anti-inflammatory properties.

In old rats, freeze-dried açaí powder (*Euterpe oleracea*) added to rodent chow (20 g/kg diet, 2%, w/w) for 7 weeks significantly reduced the proinflammatory transcription factor NF-κB in the hippocampus, while increasing the antioxidant transcription factor Nrf2 in both the hippocampus and frontal cortex (Poulose et al., 2017). The endogenous antioxidant enzyme, SOD, and an autophagy marker, beclin 1, were also increased with açaí-supplemented diet. Ubiquitinated p62/SQSTM1 (indication of dysfunctional autophagy) was decreased in the frontal cortex but unchanged in the hippocampus with açaí-supplemented diet. In a related study, the same açaí-supplemented diet for 8 weeks resulted in improved working memory (as measured by the Morris water maze) and reference memory in 19-month-old rats compared to control-diet fed old rats (Carey et al., 2017). BV-2 microglial cells treated with blood serum collected from açaí-fed rats produced less nitric oxide (NO) and TNF-α than control-fed rats. Also, endotoxin (LPS)-induced expression of iNOS was significantly attenuated when cells were pretreated with blood serum from açaí-fed rats.

In mice, treatment with clarified açaí juice (*Euterpe oleracea*; at 10 µL/g body weight, daily) for 4 days prior to endotoxin (LPS) exposure prevented despair-like behavior to a magnitude similar to that of the antidepressant imipramine treatment (Souza-Monteiro et al., 2019). The açaí juice pretreatment exerted antioxidant effects (preventing lipid peroxidation) as well as anti-aging effects (increasing telomerase reverse transcriptase mRNA expression) in the hippocampus, striatum, and prefrontal cortex. The açaí treatment also protected hippocampal cells, preventing neuronal loss.

In vitro studies have also shown neuroprotective potential of açaí. In PC12 cells exposed to Aβ42, pretreatment with açaí extract significantly improved cell viability (Wong et al., 2013). Açaí extract exposure also disrupted Aβ42 fibril and aggregate morphology. In rat primary neurons and in HT22 hippocampal neurons, açaí pulp extract protected against dopamine-induced calcium influx (Poulose et al., 2014). At an açaí concentration of 5 µg/mL, recovery was equivalent to neurons unexposed to dopamine. Also, pretreatment with açaí extracts up to 1 mg/mL prior to exposure to an autophagy inhibitor significantly attenuated the dendritic truncation and accumulation of polyubiquitinated proteins. Açaí extracts activated the phosphorylation of mammalian target of rapamycin, increased the turnover of autophagosomes and MAP1 B LC3-II, and decreased accumulation of LC3-ubiquitin binding P62/SQSTM1. In mouse brain BV-2 microglial cells exposed to LPS, freeze-dried açaí pulp administration resulted in significant decreases in nitrite production, accompanied by a reduction in inducible nitric oxide synthase (iNOS) expression (Poulose et al., 2012). This was also accompanied by a significant concentration-dependent reduction in COX-2, p38-MAPK, TNFα, and NF-κB.

APOE4 interactions: Unknown.

Aging and related health concerns: Although measures of oxidative stress are decreased with açaí interventions, there are inconsistent reports on whether they improve metabolic disorders, blood pressure, or dyslipidemia.

Types of evidence:

- 2 systematic reviews
- 9 randomized controlled clinical trials
- 4 open-label studies
- Numerous laboratory studies

Blood pressure, Cardiovascular health: LITTLE/NO CHANGES IN BP.
In a double-blind randomized controlled cross-over trial of 33 healthy overweight men, the effects of a single dose of an açaí-based smoothie (frozen açaí pulp, donated by Sublime Foods Company Ltd; contained 694 mg total polyphenol/phenolic acids; 493 mg of anthocyanins) versus a macronutrient-matched control smoothie (polyphenol content below detection levels, <10 mg) were compared against a high-fat breakfast meal challenge (Alqurashi et al., 2016). The açaí smoothie treatment improved vascular function, with postprandial increases in flow-mediated dilation (by 1.4 ± 0.6 %) when compared with the control smoothie (by 0.4 ± 0.6 %). There was also a significantly lower incremental area under the curve (iAUC) for total peroxide oxidative status after açaí consumption relative to the control. No significant changes were observed in systolic or diastolic blood pressure, heart rate, or postprandial glucose response.

In a double-blind randomized controlled trial of 18 healthy volunteers, single dosing of açaí (2 capsules, 500 mg each; Nature's Bounty, Inc., Bohemia, NY) did not significantly alter ECG or hemodynamic endpoints (Gale et al., 2014). The only exception was a significantly lower standing systolic blood pressure seen at 6 hours with açaí treatment vs. placebo (− 4.6 ± 9.3 mmHg versus 2.2 ± 8.5 mmHg). ECG endpoints included QTc, QT, RR, PR, and QRS intervals.

In an open-label study of 35 healthy women, supplementation with açaí pulp (200 g/day; pasteurized frozen açaí pulp; IceFruit, Auckland, New Zealand) for 4 weeks did not change systolic or diastolic blood pressure (Barbosa et al., 2016).

In an open-label pilot study in 10 overweight adults, açaí pulp intervention (100 g açaí pulp; Sambazon® Açai Smoothie Pack, Sambazon Inc, San Clemente, CA) twice daily for 1 month had no effect on blood pressure or nitric oxide metabolites (Udani et al., 2011).

In rodents, açaí interventions induced endothelium-dependent vasodilation, likely due to the activation of the NO-cGMP pathway combined with the antioxidant effects due to procyanidins and catechins that promote production of endothelial nitric oxide (reviewed in: Soares de Almeida Magalhaes et al., 2020).

***Dyslipidemia*:** MIXED/UNCHANGED.
In a double-blind randomized controlled trial of 69 overweight dyslipidemic people, a hypoenergetic diet supplemented with açaí pulp (200 g/day; frozen açaí pulp from Belém, Pará, Brazil, obtained from a commercial establishment in Rio de Janeiro) for 60 days did not significantly alter lipid profile measures

(total cholesterol, LDL, HDL, VLDL, triglycerides) compared to placebo treatment (200 g/day; water with carboxymethylcellulose, sucralose, açaí flavoring, and soybean oil)(Aranha et al., 2020).

In a randomized cross-over single-blind clinical trial of 30 healthy adults (ages 19-48), intake of açaí juice (*E. oleracea*; harvested in Pará State, Northern Brazil; 200 mL/day) for 4 weeks increased concentrations of HDL cholesterol by 7.7% (from 62.5 ± 3.5 mg/dL to 67.3 ± 3.5 mg/dL)(de Liz et al., 2020). There were no significant changes in total cholesterol, LDL cholesterol, small dense LDL-cholesterol, or triglyceride levels. The comparator was juçara juice (*E. edulis*; harvested in Santa Catarina, Southern Brazil; 200 mL/day) for 4 weeks and this treatment increased HDL cholesterol by 11.4%. The açaí and juçara juices were produced by a specialized company (Duas Rodas, Garuva, SC, Southern Brazil).

In an open-label study of 35 healthy women, supplementation with açaí pulp (200 g/day; pasteurized frozen açaí pulp; IceFruit, Auckland, New Zealand) for 4 weeks did not result in significant changes in total cholesterol, LDL, HDL, or triacylglycerols (Barbosa et al., 2016).

In an open-label pilot study in 10 overweight adults, açaí pulp intervention (100 g açaí pulp; Sambazon® Açai Smoothie Pack, Sambazon Inc, San Clemente, CA) twice daily for 1 month significantly reduced total cholesterol (from 159 ± 37 mg/dl to 142 ± 28 mg/dl; p=0.03), and a trend for a reduction in LDL cholesterol (p=0.051)(Udani et al., 2011). There were no significant changes in levels of VLDL cholesterol, HDL cholesterol or triglycerides.

Cancer: INCONCLUSIVE, BUT PROMISING BASED ON PRECLINICAL STUDIES
In an open-label phase 2 single-arm study in 21 biochemically recurrent prostate cancer patients (asymptomatic with a rising PSA of at least 0.2 ng/mL), açaí treatment (2 oz daily of Açaí Juice Product) for up to 30 weeks lengthened PSA doubling time in 71% of patients (Kessler et al., 2018). However, the study did not meet its primary endpoint of 50% or greater reduction in PSA. Only 1 out of 21 patients achieved greater than 50% reduction in PSA, and 15 patients had a PSA decline from baseline. The Açaí Juice Product (Eurobotanicals Inc, Fort Worth, TX) was a mixture of tea extracts and fruit juices, with 80% of the juice coming from the açaí berry. The juice product contained: *Euterpe oleracea* (açaí) extract, white grape juice concentrate, cranberry apple syrup, concord grape juice concentrate, pear juice concentrate, passion fruit juice concentrate, cranberry juice concentrate, dark sweet cherry juice concentrate, *Euterpe oleracea* (açaí) extract (from freeze dried powder), *Coffea arabica* (coffee) berry extract, and concentrated fruit extracts/powders of the following: wild blueberries, grapes, grape seeds, raspberries, raspberry seeds, cranberries, prunes, cherries, strawberries, and wild bilberries (VitaBerry Plus high-ORAC fruit blend); *Camellia sinensis* (green tea) leaf extract, *Camellia sinensis* (white tea) leaf

extract, *Aloe barbadensis* leaf extract; *Punica granatum* (pomegranate) extract, ascorbic acid, and potassium.

A systematic review of preclinical literature on the anticancer potential of açaí extract interventions identified and discussed 6 articles of which all studies showed anticarcinogenic and chemopreventive activities in experimental models of cancer (Alessandra-Perini et al., 2018). Açaí interventions reduced cancer incidence, tumor cell proliferation, and size of the tumors, and these effects were attributed to the anti-inflammatory, antiproliferative, and proapoptotic properties of açaí. For example, açaí selectively inhibited cancer cells (but had no toxicity to non-malignant cells) by protecting against reactive oxygen species, downregulating proinflammatory factors (NF-kB, TNF-α, IL-1β, IL-6, VCAM-1, ICAM-1, and others), and activating the mitochondrial proapoptotic pathway (by activation of caspase-3) (reviewed in: Soares de Almeida Magalhaes et al., 2020). However, clinical studies of açaí interventions are necessary to validate these preclinical findings.

***Inflammation*:** MIXED/INCONCLUSIVE
In a double-blind randomized controlled trial of 69 overweight dyslipidemic people, a hypoenergetic diet supplemented with açaí pulp (200 g/day; frozen açaí pulp from Belém, Pará, Brazil, obtained from a commercial establishment in Rio de Janeiro) for 60 days decreased inflammation as measured by IL-6 levels compared to placebo (200 g/day; water with carboxymethylcellulose, sucralose, açaí flavoring, and soybean oil)(Aranha et al., 2020).

In a prospective open-label study of 40 healthy women, açaí pulp (200 g/day; IceFruit® Lot 04/13; purchased from a local supermarket) for 4 weeks decreased a cell adhesion molecule (p-selectin) and a few adipokines (leptin and visfatin), but no changes were seen with other adhesion molecules (ICAM-1, IVAM-1, MCP-1), interleukins (IL-10, IL-17, IL-1β, IL-6, IL-8), or other adipockines (adipotectin, adipsin)(de Souza et al., 2021). No corrections for multiple comparisons were performed, so significant findings could be due to type I error.

In an open-label pilot study in 10 overweight adults, açaí pulp intervention (100 g açaí pulp; Sambazon® Açai Smoothie Pack, Sambazon Inc, San Clemente, CA) twice daily for 1 month did not significantly change high sensitivity C-reactive protein (Udani et al., 2011).

In an open-label clinical pilot study involving 14 people with joint/arthritic pain, treatment with açaí pulp fruit juice (120 mL/day; MonaVie Active® fruit juice, predominantly containing açai pulp) for 12 weeks resulted in significant pain reduction, improvement in range of motion measures, and improvement in

activities of daily living (Jensen et al., 2011). Serum antioxidant status was improved within 2 weeks and continued to improve throughout the 12 weeks of study participation. The inflammatory marker C-reactive protein was decreased at 12 weeks, but this was not statistically significant. Lipid peroxidation was also decreased mildly at 12 weeks.

In *in vitro* research, açaí treatments inhibit inflammation by inhibiting COX-1, COX-2, VCAM-1, IL-6, IL-8, and NF-kB (reviewed in: Ulbricht et al., 2012; Soares de Almeida Magalhaes et al., 2020).

Lifespan: POTENTIAL EXTENSION IN FLIES
In normal flies and fly models of oxidative stress (p38MAPK mutants), açaí extract treatment conferred protection from oxidative stress (Vrailas-Mortimer et al., 2012). Supplementation with açaí was sufficient to rescue the lifespan deficit observed in p38MAPK mutants as well as in wild type animals treated with the oxidizing agents (hydrogen peroxide or the herbicide paraquat). In wild-type flies (*Drosophila melanogaster*), açaí supplementation at 2% in food increased the lifespan of female flies fed a high fat diet compared to non-supplemented controls (Sun et al., 2010). Açaí supplementation increased the transcript level of a small heat-shock-related protein (l2efl) and two detoxification genes (GstD1 and MtnA), while decreasing the transcript level of a key gene involved in gluconeogenesis (Pepck). Açaí supplementation also increased the lifespan of female flies exposed to oxidative stress (sod1 RNAi).

In SH-SY5Y cells exposed to rotenone, açaí extract increased the protein levels and enzyme activity of mitochondrial complex I (Machado et al., 2016). This may not be ideal as a longitudinal transcriptome analysis in a short-lived killifish identified complex I as a hub for an inverse correlation with lifespan (Baumgart et al., 2016).

Metabolic disorders: MIXED/INCONSISTENT
Metabolic syndrome is associated with proinflammatory cytokines (e.g., CRP, TNF-α, and IL-6). In a double-blind randomized controlled trial of 37 people with metabolic syndrome, treatment with açaí beverage (25% açaí, 70% water, 5% sucrose, and citric acid; 325 mL twice daily; 162.6 g açaí pulp/day) for 12 weeks failed to show any changes in plasma biomarkers for lipid and glucose metabolism (total cholesterol, triglycerides, leptin, blood glucose, insulin, HOMA-IR, GHbA1c, GIP, C-Peptide, PAI-1, resistin) (Kim et al., 2018). There were significant reductions in an inflammation biomarker (IFN-γ by 76.2%) and an oxidative stress marker (8-isoprostane by 31.2%) following 12 weeks of açaí beverage consumption but not for the placebo control group. No changes were seen in other proinflammatory markers (hs-CRP, TNF-α, and IL-6), particularly CRP which was the prespecified primary outcome. No

corrections for multiple comparisons were performed, so significant findings could be due to type I error.

In a double-blind randomized controlled trial of 69 overweight dyslipidemic people, a hypoenergetic diet supplemented with açaí pulp (200 g/day; frozen açaí pulp from Belém, Pará, Brazil, obtained from a commercial establishment in Rio de Janeiro) for 60 days decreased oxidative stress (as measured by plasma 8-isoprostane) and inflammation (as measured by IL-6 and IFN-γ levels)(Aranha et al., 2020). However, the difference compared to placebo (200 g/day; water with carboxymethylcellulose, sucralose, açaí flavoring, and soybean oil) was only significant for plasma 8-isoprostane. Body mass and BMI decreased with açaí pulp treatment, but these metrics decreased in the placebo group too. No changes in blood glucose levels or lipid profile measures were found with açaí treatment.

In a randomized cross-over single-blind clinical trial of 30 healthy adults (ages 19-48), intake of açaí juice (*E. oleracea*; harvested in Pará State, Northern Brazil; 200 mL/day) for 4 weeks resulted in a significant decrease in carbohydrate intake (by 12.6%; $p<0.05$), but no significant changes were seen in weight, BMI, energy intake, or protein intake (de Liz et al., 2020).

In an open-label study of 35 healthy women, supplementation with açaí pulp (200 g/day; pasteurized frozen açaí pulp; IceFruit, Auckland, New Zealand) for 4 weeks did not significantly change body weight, BMI, waist circumference, body fat, glucose, insulin, or HOMA-IR (Barbosa et al., 2016).

In an open-label pilot study in 10 overweight adults, açaí pulp intervention (100 g açaí pulp; Sambazon® Açai Smoothie Pack, Sambazon Inc, San Clemente, CA) twice daily for 1 month resulted in significant reductions in fasting glucose (98.0 ± 10.1 mg/dL to 92.8 ± 10.9 mg/dL; $p = 0.018$) and insulin levels (8.9 ± 54 µU/ml at baseline, to 6.7 ± 33 µU/ml; $p = 0.017$)(Udani et al., 2011). Consumption of açai pulp for 30 days also significantly reduced the post-prandial increases in glucose levels following a standardized meal.

***Oxidative stress*:** DECREASED

In a randomized cross-over single-blind clinical trial of 30 healthy adults (ages 19-48), intake of açaí juice (*E. oleracea*; harvested in Pará State, Northern Brazil; 200 mL/day) for 4 weeks significantly increased total antioxidant capacity (by 66.7%; from 0.3 ± 0.0 to 0.5 ± 0.0 mM Trolox equivalent/L), catalase activity (by 275.1%), glutathione peroxidase activity (by 15.3%), and a decrease in oxidative stress index (by 55.7%) compared to baseline ($p<0.05$ for all) (de Liz et al., 2020). The açaí juice was produced by a specialized company (Duas Rodas, Garuva, SC, Southern Brazil).

In a double-blind randomized controlled trial of 69 overweight dyslipidemic people, a hypoenergetic diet supplemented with açaí pulp (200 g/day; frozen açaí pulp from Belém, Pará, Brazil, obtained from a commercial establishment in Rio de Janeiro) for 60 days decreased oxidative stress levels as measured by plasma 8-isoprostane) compared to placebo (Aranha et al., 2020).

In a double-blind randomized controlled cross-over trial of 33 healthy overweight men, the effects of a single dose of an açaí-based smoothie (frozen açaí pulp, donated by Sublime Foods Company Ltd; contained 694 mg total polyphenol/phenolic acids; 493 mg of anthocyanins) versus a macronutrient-matched control smoothie (polyphenol content below detection levels, <10 mg) were compared against a high-fat breakfast meal challenge (Alqurashi et al., 2016). The açaí smoothie treatment significantly lowered plasma total oxidant capacity compared to the control smoothie.

In a randomized controlled crossover trial of 12 healthy adults, a single serving of a blended juice of açaí, camu-camu, and blackberries (400 mL; 44% açaí, 12% camu-camu, and 44% blackberry juice) increased plasma ascorbic acid (by 117%) and maintained total oxidant scavenging capacity compared to the control solution (sugar solution)(Ellinger et al., 2012). However, parameters of plasma antioxidative capacity (Trolox equivalent antioxidant capacity and Folin-Ciocalteu reducing capacity) were not affected by intake of the blended juice.

In a double-blind randomized controlled trial of 12 healthy subjects, a single serving of a juice blend (MonaVie Active, containing a mixture of fruits and berries including açaí, as the predominant ingredient) resulted in an increase in serum antioxidants (at 1 and 2 hours post-consumption) as well as inhibition of lipid peroxidation (at 2 hours post-consumption)(Jensen et al., 2008). In polymorphonuclear cells, reduced formation of reactive oxygen species ($p < 0.003$) and reduced migration toward pro-inflammatory chemoattractants (fmlp, leukotriene B4, and IL-8) were seen.

In an acute four-way crossover clinical trial of 12 healthy volunteers, açaí pulp (7 mL/kg; Bossa Nova Beverage Group, Los Angeles, CA), clarified açaí juice (7 mL/kg; manufactured from the açaí pulp by centrifugal separation), applesauce (7 mL/kg; from a nationally distributed US brand), and a non-antioxidant beverage (control; 7 mL/kg; sweetened and artificially colored) were compared (Mertens-Talcott et al., 2008). Plasma antioxidant capacity was significantly increased by the açaí pulp and applesauce. Plasma antioxidant capacity was increased by 2.3- and 3-fold for açaí juice and açaí pulp, respectively.

In an open-label study of 35 healthy women, supplementation with açaí pulp (200 g/day; pasteurized frozen açaí pulp; IceFruit, Auckland, New Zealand) for 4 weeks reduced serum concentration of protein carbonyl and increased total serum sulfhydryl groups (Barbosa et al., 2016). Activities of other antioxidants (SOD and glutathione peroxidase) were unchanged.

The antioxidant effects of açaí berries are generally attributed to the high amounts of anthocyanins (cyanidin 3-rutoside, cyanidin 3-diglycoside, and cyanidin 3-glucoside) and their conjugate forms (glucuronate, sulfonate, aglycone, and methylate)(reviewed in: Ulbricht et al., 2012).

***Physical endurance*:** POTENTIAL IMPROVEMENT
In a small randomized controlled trial of 14 athletes, a single dose of açaí beverage (*Euterpe oleracea*; containing 27.6 mg of anthocyanins) increased time to exhaustion during short-term high-intensity exercise, decreased the metabolic stress induced by the exercise, reduced perceived exertion, and enhanced cardiorespiratory responses (Carvalho-Peixoto et al., 2015). The full text of this study was inaccessible, and therefore, details of this study could not be evaluated.

Safety: Açaí juice is likely safe in moderation given it has been consumed for hundreds of years. However, açaí products interact with many drugs. A study comparing commercially-available açaí supplements found that many products contained little to no açaí.

Types of evidence:

- 1 systematic review of safety and efficacy data
- 2 randomized controlled clinical trials
- 1 open-label clinical trial
- 1 systematic review of preclinical studies
- 1 acute and subchronic oral toxicity study in rats
- Numerous laboratory studies

Açaí berries (*Euterpe oleracea*) are likely safe for consumption given that Brazilians commonly drink up to a liter of açaí berry juice daily (Ulbricht et al., 2012). However, açaí juice consumption has been associated with the oral transmission of Chagas' disease, a foodborne illness caused by a tropical parasite (Pereira et al., 2009).

Clinical trials have reported that adverse events are rare with açaí interventions, though all clinical studies have been small and short-term. A randomized controlled cross-over trial of 30 healthy adults reported that the only clinical effect possibly related to the intake of açaí juices (200 mL/day) for 4 weeks was dark stools (seen in 10/30 subjects)(de Liz et al., 2020). In an open-label pilot study in 10 overweight adults, açaí pulp intervention (100 g açaí pulp; Sambazon® Açai Smoothie Pack) twice daily for 1 month did not result in any adverse events or changes in vital signs (body temperature, pulse, or respiratory rate)(Udani et al., 2011). A double-blind randomized controlled trial of 18 healthy volunteers reported that there were no adverse events throughout the duration of a study that tested single doses of açaí (2 capsules; Nature's Bounty, Inc., Bohemia, NY)(Gale et al., 2014).

A systematic review of preclinical literature on açaí extract interventions reported no genotoxic effects (Alessandra-Perini et al., 2018). Six studies showed an absence of toxicity of açaí, and 4 studies reported no significant differences in animal body weight or food consumption after treatment.

An oral toxicity study in rats reported that a 90-day treatment of açaí-fortified fruit and berry functional juice beverage (10, 20, and 40 g/kg body weight; MonaVie Active®) did not show significant effects on body weight, food and water consumption, ophthalmology, organ weights, urinanalysis, hematological and clinical chemistry, or gross pathology compared to control rats (Schauss et al., 2010). Three animals died during the treatment study (male, 20 g/kg bw/day; male 40 g/kg bw/day; and, female, 10 g/kg bw/day), but the animals died without preceding clinical symptoms, histopathological lesions, or evidence of injury to tissue or organs except for signs of suffocation/aspiration congestion, which was concluded to be due to problems with the gavage administration of the fluid preparation, and not due to the açaí intervention itself. The no-observed-adverse-effect level (NOAEL) was determined to be 40 g/kg/day for male and female rats, which was the highest dose tested. The single dose LD50 based on a 14-day acute oral toxicity study was greater than 20,000 mg/kg, the highest dose tested. This açaí-fortified beverage was not mutagenic, clastogenic, cytotoxic, or genotoxic, as determined by the bacterial reverse mutation assay, chromosomal aberration assay, mouse micronucleus assay, and mammalian cell gene mutation (L5178Y) assay.

Drug interactions: Açaí berries may interact with many classes of drugs (Ulbricht et al., 2012). Açaí products should be used cautiously with lipid lowering drugs as concurrent use may have additive lipid-lowering effects (Udani et al., 2011). Açaí products should be used cautiously in patients with diabetes or those using anti-diabetes agents as açaí may lower glucose and insulin. Theoretically, concurrent use of açaí with blood-glucose-lowering agents may increase the risk of hypoglycemia. People with autoimmune disorders or those using immunosuppressants also need to be careful with açaí products as

they may reduce the effects of immunosuppressant agents (Ulbricht et al., 2012). Açaí products may also interact with anti-inflammatory agents based on an *in vitro* study showing freeze-dried açaí pulp inhibited COX-1 and COX-2 enzymes. People with kidney disease or those using agents that may increase potassium levels may also need to be cautious with açaí products as açaí has high potassium content and concurrent use may increase the risk of hyperkalemia. Agents that may increase potassium levels include amiloride, triamterene, azole antifungals, angiotensin-converting-enzyme inhibitors, angiotensin II receptor blockers, beta-blockers, cyclosporine, heparins, digoxin, NSAIDs, penicillin G, potassium supplements, spironolactone, succinylcholine, tacrolimus, trimethoprim, pentamidine, and others, as well as herbs and supplements such as potassium, digitalis, noni juice, dandelion, horsetail, and nettle. Açaí products should also be used cautiously with caffeine as some açaí products contain guarana, a herb that contains caffeine; concurrent use with caffeine or other caffeine-containing products may cause additive stimulant effects.

Due to açaí's anti-neoplastic and antioxidant effects in preclinical studies, açaí berry products may interact with antineoplastic medications and antioxidant herbs/supplements (Ulbricht et al., 2012).

Sources and dosing: Açaí berry products are available in the forms of puree, juices, powder, tablets, and capsules. However, based on a research study that compared 19 commercially-available açaí berry supplements, significant differences were seen in the total anthocyanin concentrations, phenolic contents, and antioxidant capacities, and over half of the supplements contained little or no açaí fruit or had sufficient amounts of water to substantially lower the concentration of açaí chemical components (Earling et al., 2019). Generally, freeze-dried açaí products had the highest anthocyanin and orientin/isoorientin concentrations while water-containing liquid supplements and frozen pulp had lower amounts. But a freeze-dried product does not guarantee high concentrations of anthocyanins as one of the tested products contained no anthocyanins or orientin/isoorientin. Only 3 products out of the 20 contained high concentrations of açaí anthocyanins and flavonoids. Two supplements (1 liquid form and 1 capsule form) contained little or no açaí berry, while including unlisted ingredients that altered the products' chemical composition and antioxidant properties. Brand/product names of these supplements were not disclosed.

A systematic review of the safety and efficacy of açaí (*Euterpe oleracea*) noted that Brazilians commonly drink up to a liter of açaí berry juice daily (Ulbricht et al., 2012). Other suggested doses included 1 oz of powder mixed with 10-12 oz of water once or twice daily. For freeze-dried açaí, 1-2 g daily of capsules or tablets were suggested.

The Sambazon Açaí Smoothie Pack (100 g açaí pulp; Sambazon® Açai Smoothie Pack, Sambazon Inc, San Clemente, CA) used in a pilot study of overweight individuals contains 14% dry açaí solids and is diluted with water and sugar (Udani et al., 2011). The açaí pulp was pasteurized and manufactured in a GMP facility in Brazil. The pulp contains 6.42 g of fatty acids per 100 g: 61.4% octadecanoic acids (18:1 oleic acid), 20.8% hexadecanoic acids (16:0 palmitic), and 11.2% octadecadienoic acids (18:2 linoleic acid). The pulp also contains 3.5 mg/ml of total phenolics (gallic acid) and 0.77 mg/ml of total anthocyanins (cyanidin 3-glucoside). Each serving of 100 g has 71.8 calories, 5.8 g of total carbohydrates (<0.25 g of sugars), 4.9 g of total fats (1.1 g of saturated fat), 5.33 g of fiber, and 1 g of protein.

Research underway: Two clinical studies are testing açaí interventions in clinical trials. One is testing açaí berry extract as a treatment for adult patients with COVID-19 (NCT04404218). The other is testing whether an açaí pulp treatment has effects on endothelial function and arterial stiffness in overweight and obese individuals (NCT04434534).

Search terms:

Pubmed, Google: açaí, *Euterpe oleracea*

- + cognitive, + ApoE4, + clinical trial, + lifespan, + meta-analysis, + systematic review

Websites visited for acai:

- Clinicaltrials.gov (2)
- NIH RePORTER (0)
- Examine.com (0)
- DrugAge (0)
- Drugs.com
- WebMD.com
- Labdoor.com (0)
- ConsumerLab.com

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