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An Evidence-Based Systematic Review of Acai (*Euterpe oleracea*) by the Natural Standard Research Collaboration

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ABSTRACT. An evidence-based systematic review of acai (*Euterpe oleracea*) by the Natural Standard Research Collaboration consolidates the safety and efficacy data available in the scientific literature using a validated, reproducible grading rationale. This article includes written and statistical analysis of clinical trials, plus a compilation of expert opinion, folkloric precedent, history, pharmacology, kinetics/dynamics, interactions, adverse effects, toxicology, and dosing.

KEYWORDS. Acai (*Euterpe oleracea*), adverse effects, dosing, evidence-based, interactions, pharmacodynamics, pharmacokinetics, pharmacology, systematic review

SYSTEMATIC AGGREGATION, ANALYSIS, AND REVIEW OF THE LITERATURE

Search Strategy

To prepare this Natural Standard review, electronic searches were conducted in several databases (including AMED, CANCERLIT, CINAHL, CISCOM, the Cochrane Library, EMBASE, HerbMed, International Pharmaceutical Abstracts, Medline, and NAPRALERT) from inception to April 2012. Search terms included the common name(s), scientific name(s), and all listed synonyms. Hand searches were conducted of 20 additional journals (not indexed in common databases), and of bibliographies from 50 selected secondary references. No restrictions were placed on language or quality of publications. Researchers in the field of complementary and alternative medicine (CAM) were consulted for access to additional references or ongoing research.

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Selection Criteria

All literature was collected pertaining to efficacy in humans (regardless of study design, quality, or language), dosing, precautions, adverse effects, use in pregnancy/lactation, interactions, alteration of laboratory assays, and mechanism of action (in vitro, animal research, human data). Standardized inclusion/exclusion criteria were utilized for selection.

Data Analysis

Data extraction and analysis were performed by healthcare professionals conducting clinical work and/or research at academic centers, using standardized instruments that pertained to each review section (defining inclusion/exclusion criteria and analytic techniques, including validated measures of study quality). Data were verified by a second reviewer.

Review Process

A blinded review was conducted by multidisciplinary research-clinical faculty at major academic centers with expertise in epidemiology and biostatistics, pharmacology, toxicology, CAM research, and clinical practice. In cases of editorial disagreement, a three-member panel of the Editorial Board addressed conflicts and consulted experts when applicable. Authors of studies were contacted when clarification was required.

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Synonyms/Common Names/Related Substances

- Açaí, açaí flour, açaí palm, açaí preto (Portuguese), acaí-do-Pará (Portuguese), açaizeiro (Portuguese), Amazonian palm, Amazonian palm berry, anthocyanins, antioxidant, asai, ashaí, assaí, beta-sitosterol, cabbage palm, calcium, cansin, (+)-catechin, chonta, cyanidin, cyanidin 3-diglycoside, cyanidin 3-glucoside, cyanidin 3-rutoside, ellagic acid, ellagitannins, epicatechin, *Euterpe badiocarpa*, *Euterpe oleracea* Mart., fat, fatty acids, ferulic acid, fiber, flavonoids, gallic acid, guasai, hasabis, hausai, heart of palm, homoorientin, huai, isovitexin, iron, jicara, juçara, linoleic acid, manac, manaka, manicole, MonaVie, MonaVie Active, monounsaturated oleic acid, morroke, naidí, oleic acid, omega-6 fatty acids, omega-9 fatty acids, OptiAçai, orientin, palisade pine, palm heart, palmitic acid, palmiteiro, palmito, panan, p-coumaric acid, pelaronidin 3-glucoside phosphorus, phenolic acid, p-hydroxy-benzoic acid, phytonutrients, phytosterols, pina, pinau, pinot, piriá, polyphenols, potassium, prasara, procyanidins, protein, protocatechuic acid, saké, scoparin, taxifolin deoxyhexose, uassi, ungurahua, vanillic acid, vinho de açaí (Portuguese), vitamin A, vitamin B1, vitamin B2, vitamin B3, vitamin C, vitamin E, wasei, wapoe, yisara, yuyu chonta.

CLINICAL BOTTOM LINE/EFFECTIVENESS

Brief Background

- Açaí (acai) is a berry grown on the açaí palm tree (*Euterpe oleracea*), which is native to tropical Central and South America and grows mainly in floodplains and swamps. It produces small flowers that are brown to purple in color.

- Although the soft interior stem may be used as a source for heart of palm, açaí is better known for its fruit, which tastes like a blend of berry and chocolate. The açaí fruit is round, reddish-purple, and 1–2 cm in diameter, with the seeds constituting about 80% of the fruit. The açaí berry is a relative of blueberry, cranberry, and other dark purple fruits. A variety of açaí berry products are available for consumers, including juices, powders, tablets, and capsules.
- In recent times, research on açaí fruit has centered on its potential antioxidant properties (Mertens-Talcott et al., 2008; Rodrigues et al., 2006; Schauss et al., 2006; Udani, Singh, Singh, & Barrett, 2011). In laboratory research, açaí has also displayed anticancer (Pozo-Insfran, Percival, & Talcott, 2006; Stoner et al., 2010) and anti-inflammatory activity (Schauss et al., 2006), possibly related to its antioxidant content. Preliminary in vivo experimentation has also indicated that açaí fruit pulp may be a useful alternative oral contrast agent for magnetic resonance imaging (MRI) (Cordova-Fraga et al., 2004).
- In healthy, overweight subjects, a specific açaí product was found to reduce levels of select markers of metabolic disease risk, and it was used safely for up to one month (Udani et al., 2011). Additional research is warranted.

Scientific Evidence

Antioxidant	B
Metabolic syndrome	C

Natural Standard Evidence-Based Validated Grading Rationale

- Grades reflect the level of available scientific evidence in support of the efficacy of a given therapy for a specific indication.
- Expert opinion and historic/folkloric precedent are not included in this assessment, and are reflected in a separate section of each review ("Expert Opinion and Historic/Folkloric Precedent").
- Evidence of harm is considered separately; the following grades apply only to evidence of benefit.

Level of Evidence Grade	Criteria
A (strong scientific evidence)	Statistically significant evidence of benefit from >2 properly randomized trials (randomized controlled trials [RCTs]), OR evidence from one properly conducted RCT AND one properly conducted meta-analysis, OR evidence from multiple RCTs with a clear majority of the properly conducted trials showing statistically significant evidence of benefit AND with supporting evidence in basic science, animal studies, or theory.
B (good scientific evidence)	Statistically significant evidence of benefit from 1–2 properly randomized trials, OR evidence of benefit from >1 properly conducted meta-analysis OR evidence of benefit from >1 cohort/case-control/ nonrandomized trials AND with supporting evidence in basic science, animal studies, or theory.

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Level of Evidence Grade	Criteria
C (unclear or conflicting scientific evidence)	Evidence of benefit from >1 small RCT(s) without adequate size, power, statistical significance, or quality of design by objective criteria,* OR conflicting evidence from multiple RCTs without a clear majority of the properly conducted trials showing evidence of benefit or ineffectiveness, OR evidence of benefit from >1 cohort/case-control/nonrandomized trials AND without supporting evidence in basic science, animal studies, or theory, OR evidence of efficacy only from basic science, animal studies, or theory.
D (fair negative scientific evidence)	Statistically significant negative evidence (i.e., lack of evidence of benefit) from cohort/case-control/ nonrandomized trials, AND evidence in basic science, animal studies, or theory suggesting a lack of benefit.
F (strong negative scientific evidence)	Statistically significant negative evidence (i.e., lack of evidence of benefit) from >1 properly randomized adequately powered trial(s) of high-quality design by objective criteria.*
Lack of evidence†	Unable to evaluate efficacy due to lack of adequate available human data.

*Objective criteria are derived from validated instruments for evaluating study quality, including the 5-point scale developed by Jadad et al. (1996), in which a score below 4 is considered to indicate lesser quality methodologically.
†Listed separately in the "Historical or Theoretical Uses That Lack Sufficient Evidence" section.

Historical or Theoretical Uses That Lack Sufficient Evidence

- Acne, aging, alcohol abuse, anemia, antibacterial, anti-inflammatory (Noratto, Angel-Morales, Talcott, & Mertens-Talcott, 2011; Schauss et al., 2006), antimutagenic, antiparasitic (Odonne, Berger, Stien, Grenand, & Bourdy, 2011), antiviral (human rotavirus activity, hepatitis), astringent, atherosclerosis, blood cleanser, cancer (Pozo-Insfran et al., 2006; Stoner et al., 2010), contraceptive (birth control), diabetes (Udani et al., 2011), diagnostic procedure (contrast agent) (Cordova-Fraga et al., 2004), diarrhea, digestive aid, energy enhancer, fever, food uses (Sangronis, Teixeira, Otero, Guerra, & Hidalgo, 2006), hair loss, hemorrhage, hypercholesterolemia (Udani et al., 2011), hypertension, immune stimulant (Holderness et al., 2011; Schauss et al., 2006), jaundice, kidney problems, liver disease, malaria, menstrual pain, pain (muscle and joint) (Jensen et al., 2011), sexual dysfunction, skin care (Fowler, Woolery-Lloyd, Waldorf, & Saini, 2010), sun protection, weight loss, and wrinkle prevention.

Expert Opinion and Historic/Folkloric Precedent

- Proponents of alternative medicine have touted the açaí berry as a nonconventional treatment for a number of indications, including aging and acne.
- In Brazilian herbal medicine, the oil of the açaí fruit is used to treat diarrhea; an infusion of the root is used for jaundice; an infusion of the grated fruit rind is used as a topical wash for skin ulcers; and the fruit seeds, crushed and prepared as an infusion, are used for fevers. In the Peruvian Amazon, an infusion of the toasted crushed seeds is used for fever, and a decoction of the root is used for malaria,

diabetes, liver disorders, hair loss, hemorrhage, kidney diseases, and menstrual and muscle pain. In Colombia, where the trees, called *naidí*, grow along the Pacific coastline, the fruit is turned into a popular drink.

- The açaí berry has been shown to contain a number of antioxidants (Mertens-Talcott et al., 2008; Rodrigues et al., 2006; Schauss et al., 2006; Udani et al., 2011), flavonoids, phytosterols, fatty acids, and other nutrients. Anthocyanins, which are the primary constituents of açaí, have been found to have antioxidant effects and protect against oxidative stress. Flavonoids may exert anti-inflammatory properties. Phytosterols reportedly inhibit intestinal absorption of cholesterol. Omega-6 and omega-9 fatty acids have been found to be vital to proper cell contraction and regeneration, and monounsaturated oleic acid may help the body to absorb omega-3 oil through the cell membrane more effectively. Other nutrients, such as potassium, iron, phosphorus, and calcium, offer a variety of health benefits.
- Açaí berry purportedly possesses more proteins than an egg, as well as vitamins B1, B2, B3, C, and E. The oleic acid content of açaí has been reported to be the same as in olive oil.
- Açaí is not listed on the U.S. Food and Drug Administration (FDA) Generally Recognized As Safe (GRAS) list, although it is widely available in a variety of forms, including juices, powders, and capsules.

Brief Safety Summary

- *Likely safe*: When used in food amounts. A lack of adverse effects was seen at acute doses up to 2,000 mg/kg of body weight in laboratory animals (similar to a human consumption of 140 g at one time) (Schauss et al., 2006).
- *Possibly safe*: When used in medicinal amounts, based on a lack of adverse effects noted in a human study evaluating the use of frozen açaí pulp (Sambazon Açaí Smoothie Pack) twice daily for 1 month (Udani et al., 2011).
- *Possibly unsafe*: When the açaí juice is consumed orally. According to a review of research and epidemiologic data from Brazil, açaí juice consumption has been associated with the oral transmission of Chagas' disease, a foodborne illness (Pereira et al., 2009). When used in patients taking antilipemics as, in humans, frozen açaí pulp (Sambazon Açaí Smoothie Pack) twice daily for 1 month reduced total and low-density lipoprotein (LDL) cholesterol, as well as the ratio of total cholesterol to high-density lipoprotein (HDL) cholesterol (Udani et al., 2011). Theoretically, concurrent use with other lipid-lowering agents may have additive effects. When used in patients with diabetes or those using antidiabetic agents as, according to human research, açaí may lower glucose and insulin (Udani et al., 2011). Theoretically, concurrent use with other blood-glucose-lowering agents may increase the risk of hypoglycemia. Caution is also warranted with the use of açaí juice, which may contain added sugars, and may interfere with blood glucose control. When used with caffeine, as some açaí products contain guarana, an herb that contains caffeine. Theoretically, concurrent use with caffeine or other caffeine-containing products may cause additive stimulant effects. When used in patients with autoimmune disorders or those using immunosuppressants as, according to laboratory research, açaí demonstrated immune-stimulating effects (Holderness et al., 2011; Schauss et al., 2006). Theoretically,

açaí may reduce the effects of immunosuppressant agents. When used during pregnancy or lactation, due to a lack of sufficient data. When used in patients with kidney diseases or those using agents that may increase potassium levels, due to its high potassium content (according to secondary sources).
- *Likely unsafe*: When used in patients with a known allergy or hypersensitivity to açaí (*Euterpe oleracea*), its constituents, or members of the Arecaceae family.

DOSING/TOXICOLOGY

General

- Listed doses are based on those most commonly used in available trials, on historical practice, or on manufacturer recommendations. However, with natural products it is often not clear what the optimal doses are to balance efficacy and safety. Preparation of products may vary from manufacturer to manufacturer, and from batch to batch within one manufacturer. Because it is often not clear what the active components of a product are, standardization may not be possible, and the clinical effects of different brands may not be comparable.

Standardization

- A well-known standardization for açaí is lacking.
- A nutrient analysis study using a standardized formulation of freeze-dried açaí fruit pulp and skin powder found 100 g of the powder to contain 533.9 calories, 52.2 g of carbohydrates, 8.1 g of protein, and 32.5 g of total fats (Schauss et al., 2006). The carbohydrate portion included 44.2 g of fiber.
- Reportedly, 100 g of Sambazon Açaí Smoothie Pack (Sambazon Inc., San Clemente, CA) contains 14% dry açaí solids and is diluted with water and sugar (Udani et al., 2011). 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). It 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.

Dosing

Adult (Age ≥ 18)

Oral.

- *General*: According to secondary sources, Brazilians commonly drink up to a liter (34 ounces [oz]) of açaí juice daily. Anecdotal reports suggest that the roots of the açaí palm tree are used medicinally, prepared as a decoction of which 1–2 cups are taken daily. Additional suggested doses from secondary sources include 1 oz of powder mixed with 10–12 oz of water once or twice daily, or freeze-dried açaí in capsules or tablets at 1–2 g daily.
- *Metabolic syndrome*: 100 g of Sambazon Açaí Smoothie Pack (Sambazon Inc.), a frozen product containing açaí pulp, twice daily for 1 month, reduced levels of select markers of metabolic disease risk in overweight adults (Udani et al., 2011).

Children (Age < 18)

- Insufficient available evidence.

Toxicology

- A lack of toxic effects was noted with açaí at acute doses up to 2,000 mg/kg of body weight in laboratory animals (similar to a human consumption of 140 g at one time) (Schauss et al., 2006).

ADVERSE EFFECTS/PRECAUTIONS/CONTRAINDICATIONS

Allergy

- Known allergy or hypersensitivity to açaí (*Euterpe oleracea*), its constituents, or members of the Arecaceae family.

Adverse Effects

- *General*: In healthy, overweight subjects, a specific açaí product used for 1 month reportedly had a lack of adverse effects (Udani et al., 2011).
- *Other*: According to a review of research and epidemiologic data from Brazil, açaí juice consumption has been associated with the oral transmission of Chagas' disease, a foodborne illness (Pereira et al., 2009).

Precautions/Warnings/Contraindications

- Use açaí juice cautiously. According to a review of research and epidemiologic data from Brazil, açaí juice consumption has been associated with the oral transmission of Chagas' disease, a foodborne illness (Pereira et al., 2009).
- Use cautiously in patients taking antilipemics as, in humans, frozen açaí pulp (Sambazon Açaí Smoothie Pack) twice daily for 1 month reduced total and LDL cholesterol, as well as the ratio of total cholesterol to HDL cholesterol (Udani et al., 2011). Theoretically, concurrent use with other lipid-lowering agents may have additive effects.
- Use cautiously in patients with diabetes or those using antidiabetic agents as, according to human research, açaí may lower glucose and insulin (Udani et al., 2011). Theoretically, concurrent use with other blood-glucose-lowering agents may increase the risk of hypoglycemia. Caution is also warranted with the use of açaí juice, which may contain added sugars, and may interfere with blood glucose control.
- Use cautiously with caffeine, as some açaí products may contain guarana, an herb that contains caffeine. Theoretically, concurrent use with caffeine or other caffeine-containing products may cause additive stimulant effects.
- Use cautiously in patients with autoimmune disorders or those using immunosuppressants as, according to laboratory research, açaí demonstrated immune-stimulating effects (Holderness et al., 2011; Schauss et al., 2006). Theoretically, açaí may reduce the effects of immunosuppressant agents.
- Use cautiously in women who are pregnant or breastfeeding, due to a lack of sufficient data.

- Use cautiously in patients with kidney diseases or those using agents that may increase potassium levels (e.g., amiloride, triamterene, azole antifungals, ACE [angiotensin-converting-enzyme] inhibitors, ARBs [angiotensin II receptor blockers], beta-blockers, cyclosporine, heparins, digoxin [high levels], NSAIDs [nonsteroidal anti-inflammatory drugs], penicillin G, potassium, 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), due to açaí's high potassium content, as concurrent use may increase the risk of hyperkalemia (according to secondary sources).
- Avoid use in patients with a known allergy or hypersensitivity to açaí (*Euterpe oleracea*), its constituents, or members of the Arecaceae family.

Pregnancy and Lactation

- Not suggested due to insufficient safety data.
- Information concerning açaí is lacking in the National Library of Medicine's Drugs and Lactation database (LactMed).

INTERACTIONS

Acai/Drug Interactions

- *Antidiabetics*: In humans, frozen açaí pulp (Sambazon Açaí Smoothie Pack) twice daily for 1 month reduced fasting glucose levels (Udani et al., 2011). Theoretically, concurrent use with other blood-glucose-lowering agents may increase the risk of hypoglycemia. Açaí juice products may contain added sugars, however, which may interfere with blood glucose control.
- *Anti-inflammatories*: In vitro, freeze-dried açaí fruit pulp and skin powder (OptiAçai, used in MonaVie products) displayed selective inhibitory activity against COX-1 and COX-2 enzymes (Schauss et al., 2006).
- *Antilipemics*: In humans, frozen açaí pulp (Sambazon Açaí Smoothie Pack) twice daily for 1 month reduced total and LDL cholesterol, as well as the ratio of total cholesterol to HDL cholesterol (Udani et al., 2011). Theoretically, concurrent use with other lipid-lowering agents may have additive effects.
- *Antineoplastics*: In laboratory research, constituents of various formulations of açaí displayed anticancer effects (Pozo-Insfran et al., 2006; Stoner et al., 2010).
- *Caffeine*: Some açaí products contain guarana, an herb that contains caffeine. Theoretically, concurrent use with caffeine may cause additive stimulant effects.
- *Immunosuppressants*: According to laboratory research, açaí demonstrated immune-stimulating effects (Holderness et al., 2011; Schauss et al., 2006). Theoretically, açaí may inhibit the effects of immunosuppressant agents.
- *MRI oral contrast agents*: Açaí has been used as an experimental, clinical oral contrast agent for MRI of the gastrointestinal tract in vivo (Cordova-Fraga et al., 2004).
- *Potassium*: Due to its high potassium content, açaí may be used cautiously with agents that may increase potassium levels (e.g., amiloride, triamterene, azole antifungals, ACE inhibitors, ARBs, beta-blockers, cyclosporine, heparins,

digoxin [high levels], NSAIDs, penicillin G, potassium, 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), as concurrent use may increase the risk of hyperkalemia (according to secondary sources).

Acai/Herb/Supplement Interactions

- *Anti-inflammatories*: In vitro, freeze-dried açaí fruit pulp and skin powder (OptiAçai, used in MonaVie products) displayed selective inhibitory activity against COX-1 and COX-2 enzymes (Schauss et al., 2006).
- *Antilipemics*: In humans, frozen açaí pulp (Sambazon Açaí Smoothie Pack) twice daily for 1 month reduced total and LDL cholesterol, as well as the ratio of total cholesterol to HDL cholesterol (Udani et al., 2011). Theoretically, concurrent use with other lipid-lowering agents may have additive effects.
- *Antineoplastics*: In laboratory research, constituents of various formulations of açaí have displayed anticancer effects (Pozo-Insfran et al., 2006; Stoner et al., 2010).
- *Antioxidants*: In laboratory research, various açaí formulations displayed antioxidant activity (Jensen et al., 2008; Mertens-Talcott et al., 2008; Rodrigues et al., 2006; Schauss et al., 2006; Udani et al., 2011).
- *Caffeine-containing agents*: Some açaí products contain guarana, an herb that contains caffeine. Theoretically, concurrent use with other agents that contain caffeine may cause additive stimulant effects.
- *Hypoglycemics*: In humans, frozen açaí pulp (Sambazon Açaí Smoothie Pack) twice daily for 1 month reduced fasting glucose levels (Udani et al., 2011). Theoretically, concurrent use with other blood-glucose-lowering agents may increase the risk of hypoglycemia. Açaí juice products may contain added sugars, however, which may interfere with blood glucose control.
- *Immunostimulants*: According to laboratory research, açaí demonstrated immune-stimulating effects (Holderness et al., 2011; Schauss et al., 2006). Theoretically, concurrent use with other immune stimulants may have additive effects.
- *Immunosuppressants*: According to laboratory research, açaí demonstrated immune-stimulating effects (Holderness et al., 2011; Schauss et al., 2006). Theoretically, açaí may inhibit the effects of immunosuppressant agents.
- *Potassium*: Due to its high potassium content, açaí may be used cautiously with agents that may increase potassium levels (e.g., amiloride, triamterene, azole antifungals, ACE inhibitors, ARBs, beta-blockers, cyclosporine, heparins, digoxin [high levels], NSAIDs, penicillin G, potassium, potassium supplements, spironolactone, succinylcholine, tacrolimus, trimethoprim, pentamidine, and others), as concurrent use may increase the risk of hyperkalemia (according to secondary sources).

Acai/Food Interactions

- Insufficient available evidence.

Acai/Lab Interactions

- *Glucose levels*: In humans, frozen açaí pulp (Sambazon Açaí Smoothie Pack) twice daily for 1 month reduced fasting glucose by 5.3%, compared with baseline (Udani et al., 2011). Açaí juice may contain added sugars, however, which may interfere with blood glucose control (according to secondary sources).
- *Growth-related oncogene (GRO/KC) levels*: In laboratory research, açaí berries reduced GRO/KC levels (Stoner et al., 2010).
- *Insulin levels*: In humans, frozen açaí pulp (Sambazon Açaí Smoothie Pack) twice daily for 1 month reduced plasma fasting insulin levels (Udani et al., 2011).
- *Interleukins*: In glucose-induced stress and inflammation in human vascular endothelial cells (HUVEC), açaí downregulated interleukin-6 (IL-6) and IL-8 (Noratto et al., 2011). In mouse lung, polysaccharides from açaí induced IL-12 production (Holderness et al., 2011). In laboratory research, açaí berries reduced serum IL-5 (Stoner et al., 2010).
- *Lipid levels*: In humans, frozen açaí pulp (Sambazon Açaí Smoothie Pack) twice daily for 1 month reduced total and LDL cholesterol, as well as the ratio of total cholesterol to HDL cholesterol (Udani et al., 2011). HDL cholesterol, very low density lipoprotein (VLDL) cholesterol, and triglycerides were not affected in a statistically significant manner.
- *Potassium*: Açaí has a relatively high potassium content which may increase potassium levels (according to secondary sources).

Acai/Nutrient Depletion:

- *Glucose levels*: In humans, frozen açaí pulp (Sambazon Açaí Smoothie Pack) twice daily for 1 month reduced fasting glucose by 5.3%, compared with baseline (Udani et al., 2011). Açaí juice may contain added sugars, however, which may interfere with blood glucose control (according to secondary sources).
- *Lipid levels*: In humans, frozen açaí pulp (Sambazon Açaí Smoothie Pack) twice daily for 1 month reduced total and LDL cholesterol, as well as the ratio of total cholesterol to HDL cholesterol (Udani et al., 2011). HDL cholesterol, VLDL cholesterol, and triglycerides were not affected in a statistically significant manner.

MECHANISM OF ACTION

Pharmacology

- *Constituents*: Açaí contains high amounts of anthocyanins, a group of polyphenols that lend açaí its deep purple color and contribute to its antioxidant activity (Pozo-Insfran et al., 2006). Cyanidin 3-rutoside, cyanidin 3-diglycoside, and cyanidin 3-glucoside are the major anthocyanins found in açaí (Jensen et al., 2008). The antioxidant activity of açaí polyphenols may also be attributed to the conjugate forms: glucuronate, sulfonate, aglycone, and methylate (Pozo-Insfran et al., 2006).
- Proanthocyanidins have also been isolated from açaí extracts (Rodrigues et al., 2006; Schauss et al., 2006). Flavonoid-like compounds, including homoorientin, orientin, taxifolin deoxyhexose, isovitexin, and scoparin, have been identified.

Protocatechuic acid (a phenolic acid) and epicatechin (a polyphenol) have been identified as minor compounds (Rodrigues et al., 2006). Other compounds found in açaí fruit include p-hydroxy-benzoic acid, gallic acid, ellagic acid, (+)-catechin, protocatechuic acid, ellagic acid, p-coumaric acid, ferulic acid, vanillic acid, cyanidin, and pelaronidin 3-glucoside (according to secondary sources). Ellagitannins have been obtained from açaí berries and may contribute to açaí's anticancer effects (Stoner et al., 2010).

- Like other fruits, açaí contains standard vitamins, minerals, and nutrients (Schreckinger, Lotton, Lila, & de Mejia, 2010). According to secondary sources, the açaí berry contains 1%–4% protein, 7%–11% fats, 25% sugar, 0.05% calcium, 0.033% phosphorous, 0.0009% iron, some sulfur, traces of vitamin B1, and some vitamin A and E. It has also been found to contain 88–265 calories per 100 g, depending on the preparation method. Açaí berries contain oleic acid (approximately 60% of total fats), linoleic acid (12% of total fats), palmitic acid (24.1% of total fats), and phytosterols, including beta-sitosterol (78%–91% of total sterols) (Lubrano, Robin, & Khaiat, 1994; Schauss et al., 2006). Açaí flour also has a reportedly high fat content (16%), as well as dietary fiber and iron (Sangronis et al., 2006).
- Reportedly, 100 g of Sambazon Açaí Smoothie Pack (Sambazon Inc.) contains 14% dry açaí solids and is diluted with water and sugar (Udani et al., 2011). 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). It 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.
- Kinghorn, Chai, Sung, and Keller (2011) have also identified bioactive constituents from açaí; additional details, however, are lacking.
- *Anticancer effects*: In human promyelocytic leukemia (HL-60) cells, polyphenolic fractions (at 0.17–10.7 mcM) of frozen açaí pulp (donated by Amazon Energy, LLC) suppressed proliferation, in a dose- and time-dependent manner, through a caspase-3-mediated mechanism (a mechanism of apoptosis) (Pozo-Insfran et al., 2006).
- In rats treated with N-nitrosomethylbenzylamine (NMBA; a carcinogen), a 5% açaí diet administered after carcinogen administration reduced esophageal tumorigenesis (Stoner et al., 2010). The chemopreventive effects were attributed to the ellagitannins in the berries. It was also noted that tumorigenesis was inhibited through the regulation of cytokines. Serum IL-5 and GRO/KC levels were reduced, which correlated to an increase in antioxidant capacity.
- *Antidiabetic effects*: In humans, frozen açaí pulp (Sambazon Açaí Smoothie Pack) twice daily for 1 month reduced fasting glucose by 5.3%, compared with baseline measurements (Udani et al., 2011). Plasma insulin levels were also found to be reduced. The researchers suggested that the antidiabetic effects of açaí may be attributed to the anthocyanin compounds.
- *Anti-inflammatory effects*: In in vitro research, freeze-dried açaí fruit pulp and skin powder (OptiAçai, found in MonaVie products) displayed selective inhibitory activity against COX-1 and COX-2 enzymes (Schauss et al., 2006). The

freeze-dried açaí product (at 250–2,500 mcg/ml) inhibited lipopolysaccharide (LPS)-induced production of nitric oxide in a dose-dependent manner.

- In LPS-induced inflammatory stress in HUVEC, açaí was found to inhibit vascular endothelial adhesion molecules-1 (VCAM-1) through nuclear factor-kappaB (NF-kappaB) inhibition (Noratto et al., 2011). In glucose-induced stress and inflammation in HUVEC, açaí downregulated the inflammatory markers IL-6 and IL-8, which correlated to downregulation of microRNA-126.
- *Antioxidant effects*: Açaí contains high amounts of anthocyanins, a group of polyphenols that lend açaí its deep purple color and contribute to its antioxidant activity (Pozo-Insfran et al., 2006). Cyanidin 3-rutoside, cyanidin 3-diglycoside, and cyanidin 3-glucoside are the major anthocyanins found in açaí (Jensen et al., 2008). The antioxidant activity of açaí polyphenols may also be attributed to its conjugate forms: glucuronate, sulfonate, aglycone, and methylate (Pozo-Insfran et al., 2006).
- In vitro, the methanol and ethanol seed extracts from açaí also displayed good antioxidant capacity against peroxyl radicals (Rodrigues et al., 2006).
- In freshly purified human neutrophils, pretreatment with the freeze-dried açaí extracts (OptiAçai) before hydrogen peroxide (H_2O_2)-induced oxidative stress reduced the formation of reactive oxygen species (ROS), even at low doses (0.1 parts per trillion) (Schauss et al., 2006). This formulation also scavenged peroxyl radicals, with a reported total oxygen radical-absorbing capacity (ORAC) value of 1,026.9 mcM of TE/g, which the researchers noted as being higher than other fruits and vegetables.
- The antioxidant capacity of Sambazon Açaí Smoothie Pack (Sambazon Inc.) was reported to be 46 mcM of TE/ml (Udani et al., 2011).
- In a pharmacokinetic analysis in healthy volunteers, the plasma antioxidant capacity was increased up to threefold by açaí juice and pulp (Mertens-Talcott et al., 2008). The plasma antioxidant capacity was found to be significantly higher compared with the control product (applesauce).
- In an in vitro cell-based antioxidant protection of erythrocytes (CAP-e) assay, the containing-containing proprietary fruit and juice blend MonaVie Active displayed antioxidant-protecting effects, even at low doses (0.016 g/l) (Jensen et al., 2008). The ORAC value of the fruit and juice blend was 22.8 mcM of TE/ml. The antioxidants in this juice were able to penetrate the plasma cell membrane and protect against intracellular oxidative damage. Additionally, pretreatment of polymorphonuclear (PMN) cells with the juice blend was found to inhibit ROS formation in a dose-dependent manner. In vivo, the açaí juice blend was found to inhibit lipid peroxidation within 2 hours of consumption.
- *Immune effects*: In in vitro research, freeze-dried açaí fruit pulp and skin powder (OptiAçai, used in MonaVie, obtained from K2A LLC in Provo, UT) increased macrophage activity (Schauss et al., 2006). However, the effect was not produced in a dose-dependent manner, and low concentrations of the formulation appeared to exert higher immunostimulatory action than higher concentrations. The freeze-dried açaí (at 250–2,500 mcg/ml) also inhibited LPS-induced production of nitric oxide in a dose-dependent manner.
- In human peripheral blood mononuclear cells (PBMCs), the polysaccharide fraction of açaí was found to exert immunomodulatory activity and stimulate

gamma-delta T cells and myeloid cells (Holderness et al., 2011). In mouse lung, these polysaccharides induced IL-12 production by promoting Th1 (interferon [IFN]-gamma-producing) response.

- *Lipid effects*: In human study, frozen açaí pulp (Sambazon Açaí Smoothie Pack) twice daily for 1 month reduced total and LDL cholesterol, as well as the ratio of total cholesterol to HDL cholesterol (Udani et al., 2011). HDL cholesterol, VLDL cholesterol, and triglycerides were not affected in a statistically significant manner.
- *MRI oral contrast agent effects*: Açaí fruit pulp has been used as an experimental, clinical oral contrast agent for MRI of the gastrointestinal tract in vivo (Cordova-Fraga et al., 2004). Açaí pulp presented an increase in T(1)-weighted MRI signal, equivalent to that of gadolinium-diethyltriamin pentaacetic acid, and a decrease in T(2)-weighted images. Paramagnetic Fe, Mn, and Cu ions in açaí may contribute to the T(1) signal enhancement and T(2) opacification.

Pharmacodynamics/Kinetics

- *Absorption*: Using a noncompartmental pharmacokinetic analysis of total anthocyanins (quantified as cyanidin 3-O-glucoside), the C_{max} values were 2,321 and 1,138 ng/l, the T_{max} values were 2.2 and 2.0 hr, and the area under the curve (AUC) last values were 8,568 and 3,314 ng/h/l for pulp and juice, respectively (Mertens-Talcott et al., 2008).

HISTORY

- The word "açaí" is borrowed from the indigenous peoples of South America and means "fruit that cries." Açaí has been a traditional food of the natives of the Amazon for hundreds of years. Açaí beverages are prepared by extracting juice from the fruit pulp and skin. The fruit is used as a natural ink or dye, and the wood is used in house construction (palm-thatched roofs). Ethnobotanists have recorded no fewer than 22 different uses for all parts of the tree. In the Brazilian Amazon, the Indian tribes of the forest cut down the tree and eat the palm heart, turn the fruit into a juice drink, and use the mature palm fronds for the roof of their houses. They then urinate on the rest of the tree to attract a species of palm beetle to lay its eggs inside the tree. Several weeks later, they return to harvest 3–4 pounds of beetle grub larvae, which are an important source of protein (62%) and fat (4.5%) in their diet.
- In the Amazon, the liquid of the açaí berry is often combined with a starchy root vegetable called manioc (which has been dried and ground into a flour) and eaten as a purple porridge. Açaí is a staple food for many economically disadvantaged inhabitants of the lower Amazon region area. The manioc-manioc porridge is quite poor in nutrition but is very filling, containing a large amount of starch and sugar.
- In Belém, a major port and gateway into the Brazilian Amazon, an enormous açaí fruit market called Feira do Açaí houses 70–120 vendors selling over 200,000 kg of açaí fruit daily during the dry season.

- According to secondary sources, due to what has been called the "açaí craze" in the United States, one proposed project in Brazil has called for the planting of five billion açaí trees in the next 10 years.

EVIDENCE TABLE

Condition Treated (Primary or Secondary Outcome)	Evidence/ Study Type	Author, Year	*N*	Statistically Significant Results?	Quality of Study: 0–2 = poor 3-4 = good 5 = excellent	Magnitude of Benefit (How Strong is the effect)	Absolute Risk Reduction	Number of Patients Needed to Treat for One Outcome	Comments
Metabolic syndrome	Open-label pilot study	Udani et al., 2011	10	Yes (glucose; cholesterol; insulin); borderline (LDL)	0	Small (glucose); medium (cholesterol); small (LDL)	NA	NA	100 g Sambazon Açaí Smoothie Pack was consumed twice daily, in the morning and evening, for 1 month

Explanation of columns in Natural Standard Evidence Table

1	2	3	4	5	6	7	8	9	10
Condition	Study design	Author, year	*N*	Statistically significant?	Quality of study 0–2 = poor 3–4 = good 5 = excellent	Magnitude of benefit	Absolute risk reduction	Number needed to treat	Comments

Condition

- Refers to the medical condition or disease targeted by a therapy.

Study Design

Common types include the following:

- *Randomized controlled trial (RCT)*: An experimental trial in which participants are assigned randomly to receive either an intervention being tested or placebo. Note that Natural Standard defines RCTs as being placebo-controlled, while studies using active controls are classified as equivalence trials (see below). In RCTs, participants and researchers are often blinded (i.e., unaware of group assignments), although unblinded and quasi-blinded RCTs are also often performed. True random allocation to trial arms, proper blinding, and sufficient sample size are the basis for an adequate RCT.
- *Equivalence trial*: An RCT which compares two active agents. Equivalence trials often compare new treatments to usual (standard) care, and may not include a placebo arm.
- *Before and after comparison*: A study that reports only the change in outcome in each group of a study, and does not report between-group comparisons. This is a common error in studies that claim to be RCTs.
- *Case series*: A description of a group of patients with a condition, treatment, or outcome (e.g., 20 patients with migraine headache underwent acupuncture and

17 reported feeling better afterwards). Case series are considered weak evidence of efficacy.
- *Case-control study*: A study in which patients with a certain outcome are selected and compared to similar patients (without the outcome) to see whether certain risk factors/predictors are more common in patients with that outcome. This study design is not common in the complementary & alternative medicine literature.
- *Cohort study*: A study which assembles a group of patients with certain baseline characteristics (for example, use of a drug), and follows them forward in time for outcomes. This study design is not common in the complementary and alternative medicine literature.
- *Meta-analysis*: A pooling of multiple trials to increase statistical power (often used to pool data from a number of RCTs with small sample sizes, none which demonstrates significance alone but in aggregate can achieve significance). Multiple difficulties are encountered when designing/reviewing these analyses; in particular, outcomes measures or therapies may differ from study to study, hindering direct comparison.
- *Review*: An author's description of his or her opinion based on personal, nonsystematic review of the evidence.
- *Systematic review*: A review conducted according to prespecified criteria in an attempt to limit bias from the investigators. Systematic reviews often include a meta-analysis of data from the included studies.

Author, Year

- Identifies the study being described in a row of the table.

N

- The total number of subjects included in a study (treatment group plus placebo group). Some studies recruit a larger number of subjects initially, but do not use them all because they do not meet the study's entry criteria. In this case, it is the second, smaller number that qualifies as *N*. *N* includes all subjects that are part of a study at the start date, even if they drop out, are lost to follow-up, or are deemed unsuitable for analysis by the authors. Trials with a large number of dropouts that are not included in the analysis are considered to be weaker evidence for efficacy. For systematic reviews, the number of studies included is reported. For meta-analyses, the number of total subjects included in the analysis or the number of studies may be reported.

Statistically Significant?

- Results are noted as being statistically significant if a study's authors report statistical significance, or if quantitative evidence of significance is present (such as *p* values). P = pending verification.

Quality of Study

- A numerical score between 0 and 5 is assigned as a rough measure of study design/reporting quality (0 being weakest and 5 being strongest). This number is

based on a well-established, validated scale developed by Jadad et al. (1996). This calculation does not account for all study elements that may be used to assess quality (other aspects of study design/reporting are addressed in the "Evidence Discussion" section of reviews).

- A Jadad score is calculated using the seven items in the following table. The first five items are indications of good quality, and each counts as one point toward an overall quality score. The final two items indicate poor quality, and a point is subtracted for each if its criteria are met. The range of possible scores is 0–5.

Jadad score calculation

Item	Score
Was the study described as randomized (this includes words such as randomly, random, and randomization)?	0/1
Was the method used to generate the sequence of randomization described and appropriate (table of random numbers, computer-generated, etc.)?	0/1
Was the study described as double blind?	0/1
Was the method of double blinding described and appropriate (identical placebo, active placebo, dummy, etc.)?	0/1
Was there a description of withdrawals and dropouts?	0/1
Deduct one point if the method used to generate the sequence of randomization was described and it was inappropriate (patients were allocated alternately, or according to date of birth, hospital number, etc.).	0/−1
Deduct one point if the study was described as double blind but the method of blinding was inappropriate (e.g., comparison of tablet versus injection with no double dummy).	0/−1

Magnitude of Benefit

- This summarizes how strong a benefit is: small, medium, large, or none. If results are not statistically significant, "NA" for "not applicable" is entered. In order to be consistent in defining small, medium, and large benefits across different studies and reviews, Natural Standard defines the magnitude of benefit in terms of the standard deviation (*SD*) of the outcome measure. Specifically, the benefit is considered:
  - Large: if > 1 *SD*
  - Medium: if 0.5 to 0.9 *SD*
  - Small: if 0.2 to 0.4 *SD*
- In many cases, studies do not report the *SD* of change of the outcome measure. However, the change in the *SD* of the outcome measure (also known as effect size) can be calculated, and is derived by subtracting the mean (or mean difference) in the placebo/control group from the mean (or mean difference) in the treatment group, and dividing that quantity by the pooled *SD* (Effect size = [Mean Treatment − Mean Placebo]/*SD*p).

Absolute Risk Reduction

- This describes the difference between the percent of people in the control/placebo group experiencing a specific outcome (control event rate), and the percent of people in the experimental/therapy group experiencing that same

outcome (experimental event rate). Mathematically, absolute risk reduction (ARR) equals experimental event rate minus control event rate. ARR is better able to discriminate between large and small treatment effects than relative risk reduction (RRR), a calculation that is often cited in studies ([control event rate − experimental event rate]/control event rate). Many studies do not include adequate data to calculate the ARR, in such cases "NA" is entered into this column. P = pending verification.

Number Needed to Treat

- This is the number of patients who would need to use the therapy under investigation, for the period of time described in the study, in order for one person to experience the specified benefit. It is calculated by dividing the ARR into 1 (1/ARR). P = pending verification.

Comments

- When appropriate, this brief section may comment on design flaws (inadequately described subjects, lack of blinding, brief follow-up, not intention-to treat, etc.), notable study design elements (crossover, etc.), dosing, and/or specifics of study group/sub-groups (age, gender, etc.). More detailed description of studies is found in the "Evidence Discussion" section that follows the "Evidence Table" in Natural Standard reviews.

EVIDENCE DISCUSSION

Antioxidant

- *Summary*: Açaí contains high amounts of anthocyanins, a group of polyphenols that lend açaí its deep purple color and contribute to its antioxidant activity (Pozo-Insfran et al., 2006). Cyanidin 3-rutoside, cyanidin 3-diglycoside, and cyanidin 3-glucoside are the major anthocyanins found in açaí (Jensen et al., 2008). The antioxidant activity of açaí polyphenols may also be attributed to the conjugate forms: glucuronate, sulfonate, aglycone, and methylate (Pozo-Insfran et al., 2006).
- *Pharmacokinetic analysis (not included in the Evidence Table)*: In a pharmacokinetic analysis in healthy volunteers, the plasma antioxidant capacity was increased up to threefold by açaí juice and pulp (Mertens-Talcott et al., 2008).
- *In vitro studies (not included in the Evidence Table)*: In vitro, the methanol and ethanol seed extracts from açaí also displayed antioxidant capacity against peroxyl radicals (Rodrigues et al., 2006).
- In freshly purified human neutrophils, pretreatment with the freeze-dried açaí extracts (OptiAçai) before H_2O_2-induced oxidative stress reduced the formation of ROS, even at low doses (0.1 parts per trillion) (Schauss et al., 2006). This formulation also scavenged peroxyl radicals, with a reported total ORAC value of 1,026.9 mcM of TE/g, which the researchers noted as being higher than other fruits and vegetables.
- In vitro, the antioxidant capacity of Sambazon Açaí Smoothie Pack (Sambazon Inc.) was reported to be 46 mcM of TE/ml (Udani et al., 2011). The plasma

antioxidant capacity was found to be significantly higher compared with the control product (applesauce).

- In an in vitro CAP-e assay, the containing-containing proprietary fruit and juice blend MonaVie Active displayed antioxidant-protecting effects, even at low doses (0.016 g/l) (Jensen et al., 2008). The ORAC value of the fruit and juice blend was 22.8 mcM of TE/ml. The antioxidants in this juice were able to penetrate the plasma cell membrane and protect against intracellular oxidative damage. Additionally, pretreatment of PMN cells with the juice blend was found to inhibit ROS formation in a dose-dependent manner. In vivo, the açaí juice blend was found to inhibit lipid peroxidation within 2 hr of consumption.

Metabolic Syndrome

- *Summary*: Research suggests that reducing ROS production and increasing antioxidant activity may be important in preventing the development of metabolic syndrome. In preliminary study, the effects of açaí pulp were evaluated in overweight subjects at risk for these disorders (Udani et al., 2011). While some favorable effects were found on select metabolic disorder markers, well-designed clinical trials are needed before firm conclusions may be drawn.
- *Evidence*: Udani et al. (2011) conducted an open-label pilot study to deduce the effects of açaí (*Euterpe oleracea*) on metabolic parameters in healthy, overweight subjects ($N = 10$). The inclusion criteria were being an overweight (body mass index [BMI] of 25–30 kg/m^2) adult between 18 and 65 years of age. Exclusion criteria were alcohol or drug abuse, cigarette use, diabetic medication use 4 weeks or less preceding the study, immunosuppressant use in the previous 5 years, infection, insulin use in the previous 3 years, major systemic inflammatory or chronic diseases, or symptomatic hypoglycemia in the preceding month. Pregnant or lactating females, and subjects with a baseline exhaled (breath) nitric oxide (eNO) measurement >35 ppb were also excluded. Females of childbearing age used birth control. However, the use of anti-inflammatories, antioxidants, multivitamins, or steroids was not permitted during the study. Subjects were instructed to take Sambazon Açaí Smoothie Pack (Sambazon Inc.), a frozen product containing açaí pulp, as a smoothie. The contents were to be added into a Blender Bottle, along with water and sugar (equivalent to 4 g or one sugar packet). The 100 g Sambazon Açaí Smoothie Pack was consumed twice daily, in the morning and evening, for 1 month. The product was pasteurized and manufactured in a good manufacturing practice (GMP) facility in Brazil. The pulp contained 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 contained 3.5 mg/ml of total phenolics (gallic acid) and 0.77 mg/ml of total anthocyanins (cyanidin 3-glucoside). The pulp had 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. The in vitro antioxidant capacity of the contents was 46 mcM of TE/ml. Outcome measures included blood glucose (capillary), insulin, cholesterol (total cholesterol, HDL cholesterol, LDL cholesterol, and triglycerides), eNO metabolites, and high sensitivity C-reactive protein (hs-CRP). Treatment with açaí reduced fasting glucose (98.0 ± 10.1 mg/dl to 92.8 ± 10.9 mg/dl, $p = .018$) and insulin levels (baseline: 8.92 ± 5.4 mcU/ml; end of

treatment: 6.68 ± 3.3 mcU/ml, $p = .017$) from baseline. An improved postprandial rise in plasma glucose was also noted (AUC at baseline: 205.6 ± 18.6, and after 30 days of açaí: 189.7 ± 26.3, $p = .047$). Total cholesterol (159.2 ± 37.4 mg/dl to 141.8 ± 28.3 mg/dl, $p = .03$), LDL cholesterol (90.1 ± 29.1 mg/dl to 78.1 ± 25.3 mg/dl, $p = .051$), and the total cholesterol:HDL cholesterol ratio (3.79 ± 1.0 to 3.42 ± 0.9, $p = .051$) were reduced. A lack of statistically significant changes was noted for blood pressure, eNO, HDL cholesterol, hs-CRP, triglycerides, and VLDL cholesterol. There was a lack of adverse events. Limitations of the study include a lack of randomization and blinding, as well as a small sample size.

BRANDS USED IN CLINICAL TRIALS/THIRD-PARTY TESTING

- OptiAçai, a patented freeze-dried açaí fruit pulp/skin powder found in MonaVie products (K2A LLC) (Schauss et al., 2006).
- Sambazon Açaí Smoothie Pack (Sambazon Inc.) (Udani et al., 2011).

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