Current Nutrition Reports (2024) 13:611–638
https://doi.org/10.1007/s13668-024-00553-9

REVIEW

Amazonian Fruits for Treatment of Non-Communicable Diseases

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Accepted: 7 June 2024 / Published online: 25 June 2024

Abstract

Purpose of Review The Amazon region has a high biodiversity of flora, with an elevated variety of fruits, such as Camu-Camu (*Myrciaria dúbia*), Açaí (*Euterpe oleracea* Mart.), Tucumã (*Astrocaryum aculeatum* and *Astrocaryum vulgare*), Fruta-do-conde (*Annona squamosa* L.), Cupuaçu (*Theobroma grandiflorum*), Graviola (*Annona muricata* L.), Guarana (*Paullinia cupana* Kunth var. *sorbilis*), and Pitanga (*Eugenia uniflora*), among many others, that are rich in phytochemicals, minerals and vitamins with prominent antioxidant and anti-inflammatory potential.

Recent Findings Studies evaluating the chemical composition of these fruits have observed a high content of nutrients and bioactive compounds. Such components are associated with significant biological effects in treating various non-communicable diseases (NCDs) and related complications.

Summary Regular intake of these fruits from Amazonas emerges as a potential therapeutic approach to preventing and treating NCDs as a nutritional strategy to reduce the incidence or mitigate common complications in these patients, which are the leading global causes of death. As studies remain largely unexplored, this narrative review discusses the possible health-beneficial effects for patients with NCDs.

Keywords Non-communicable diseases · Amazonian fruits · Biodiversity · Inflammation · Oxidative stress

Introduction

The tropical Amazon rainforest in Brazil is renowned for its vast biodiversity, encompassing fauna and flora. It is a crucial terrestrial biome recognized as an essential global flow of carbon and water cycle and a source of plant biodiversity. Indeed, Amazon flora can bring fundamental advances in preparing traditional medicines, providing oils, phytotherapeutic agents, and nutrients with anti-inflammatory properties [1]. It is essential to highlight the ongoing deforestation and degradation of the Amazonian ecosystems by anthropogenic activity, with land and water use changes, pollution, fire, hunting, and logging to produce international commodities such as cattle ranching, sugarcane, and soybean crops. The ongoing conversion of the forest to agriculture or pasture is a significant threat to the Amazon rainforest [2, 3]. Sustainable actions such as exploiting non-timber forest products (nuts, latex, medicinal plants, seeds, fish, oils, vegetables, and fruits) are essential to food security and the local economy, promote less risk to the local population, and can guarantee forest conservation [4].

This region is distinguished by its favorable climate, which is suitable for cultivating various tropical fruits. Many of these fruits (approximately 220 edible varieties) are either harvested from the wild or grown exclusively for local markets, often consumed as pulp or in their natural state. Researchers have explored the chemical composition

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of Amazonian fruits or non-conventional food plants, identifying them as a promising source of health-enhancing bioactive compounds. These fruits exhibit remarkable antioxidant roles since they are rich in phytochemicals, notably carotenoids and phenolic compounds [5]. Thus, the bioactive compounds found in Amazonian fruits must be carefully mapped and studied, and the message of their importance spread. Typical fruits from Amazon, such as Camu-Camu, Açaí, Cupuaçu, Graviola, and Pitanga, are rich in vitamins (C, β-carotene) and polyphenols with high antioxidant and anti-inflammatory potential, anti-obesogenic activity, anticancer and antidiabetic effects [6].

Non-communicable diseases (NCDs) are the leading cause of global deaths and disability in low- and middle-income countries [7]. Due to the salutary effects of bioactive compounds found in these fruits, they can promote health benefits to patients with NCDs; however, studies remain unexplored. In this narrative review, we discuss the composition of Amazonian fruits and their possible health-beneficial effects for patients with NCDs.

Food as Medicine for Patients with Non-Communicable Diseases

NCDs encompass several ranges of conditions, such as cardiovascular disease (hypertension, heart disease, stroke), type 2 diabetes mellitus, cancer, obesity, dementia, and chronic kidney disease. They represent one of the greatest battles against human health and the socioeconomic structure of twenty-first-century countries [8, 9].

Genetic predisposition can be linked to NCDs through polygenic inheritance, inherited genetic mutations, and genome-wide association studies (GWAS). However, it's essential to recognize that genetics rarely determine disease outcomes alone. In general, NCDs are driven by aging and the stress of life (the exposome) that increases allostatic overload and induces a vicious circle of mitochondrial dysfunction [10, 11]. These metabolic derangements could potentially be targeted for prevention and treatment [10, 12, 13]. NCDs lead to disability and death, especially in low- and middle-income countries [7, 14, 15]. Forty-one million deaths per year are caused by NCDs (WHO), with 17 million premature deaths of people before age 70 years. Of all deaths caused by NCDs, 77% occur in low- and middle-income countries [15]. In Brazil, NCDs are a significant cause of mortality and are responsible for over 75% of deaths in the whole population and comprised 15 of the 20 leading causes of premature death in 2015 [16].

Considering the impact of unhealthy eating habits, such as low dietary fiber, high saturated fat and sugar, and ultra-processed food, increasing the occurrence and progression of NCDs, there is a need to change this dietary profile to mitigate the occurrence and complications of these diseases and to reduce the high costs associated with health care caused by these diseases [8, 15, 17, 18]. The battle against NCDs should include the concept of "food as a medicine" (FAM), which consists of a holistic approach using food as a non-pharmacological strategy against metabolic diseases [17]. The beneficial health effects are related to biologically active compounds in the food matrix [17, 19]. Thus, phenolic compounds, carotenoids, sterols, unsaturated fatty acids, vitamins, and trace elements in natural foods like tropical fruits could significantly benefit NCDs patients [19–22].

It is estimated that the Brazilian Amazon biome is the home of more than 220 species of edible fruit plants, representing 44% of the diversity of Brazilian fruits [23]. Table 1 shows the physical characteristics of the most known Amazon fruits. With its rich biodiversity, the Amazon rainforest is an essential source of tropical fruits with many bioactive compounds (Fig. 1). The potential to prevent and treat NCDs with these bioactive nutrients is enormous [24, 25]. Anthocyanins, carotenoids, and betalains are potent bioactive compounds responsible for plant color pigments. Intense colors attract pollinating insects and have anti-inflammatory and anti-oxidizing properties since they activate the cytoprotective transcription factor nuclear erythroid 2-related factor 2 (Nrf2) [26]. However, to confirm this "flower power", sufficiently powered randomized controlled trials as part of the FAM concept are needed [17, 27]. Dietary interventions can potentially treat various NCDs, but generating strong evidence for their integration into clinical medicine will be critical for their success.

Materials and Methods

Search Strategy

The present study included all relevant articles published until October 2023. Articles were searched using the PubMed, Medline, and Scielo platforms. The keywords used and combined in the research were "non-communicable diseases," "Amazonian fruits," "biodiversity," "inflammation," and "oxidative stress." There were no language or type of article restrictions in the research process.

Amazonian Fruits

Açaí

The açaí palm (*Euterpe oleracea* Mart.) belongs to the Euterpe genus and the Arecaceae family. This tree is native to the Amazon and is widely distributed in Central South America. In Brazil, the North (Amapá, Pará, and Tocantins) and Northeast (Maranhão) regions are the

Table 1 Physical characteristics of some Amazonian fruits

Fruit	Shape/color	Taste	Dimensions/weights	Pulp color	Seed
Açaí	Round to oblong and dark purple to black color	Bitter	1–3 cm (Ø) 1–2 g	White	1
Camu-Camu	Round, oval to ovate, and purple-red color	Tart and sour	2–3 cm (Ø) 1–11 g	White, pale to green	1 – 4
Tucumã (*A. aculeatum)*	Oval or spherical shape and yellowish tone	Sweet	3–8 cm (Ø) 30-150 g	Yellow or orange	0 – 2
Tucumã (*A. vulgare)*	Globose or ellipsoid and orange or red	Sweet	3–5 cm (Ø) 20–100 g	Orange	0 – 2
Pitanga	Like mini red pumpkin	Sweet and sour	2–3 cm (Ø) 3–5 g	Reddish	1 – 3
Graviola	Ovoid, cordiforme and irregular	Sweet, mildy sour	15–35 cm 0,5 – 15 kg	White or creamy	≅ 100
Cupuaçu	Oblong and brown	Acid	10–12 cm (Ø) 1–2 kg	Yellow	20–50
Pupunha	Spherical and yellowish to reddish	Sweet	2–5 cm 20–205 g	Yellow to red	1
Guarana	Orange-red with a capsule form, partially covered by white arils	Sweet and sour	2–3 cm 8 g	White	1–3
Fruta-do-conde	Green and rounded or ovoid	Sweet	5–10 cm (Ø) 200–400 g	White	20–60
Bacuri	Yellow to brown and ovoid	Bittersweet	6–10 cm (Ø) 150–1000 g	White	4
Bacaba	Reddish-purple and elliptical to globose	Like avocado	2 cm (Ø) 3 g	White and yellow	> 10
Ingá	Green to brown and pod shape	Sweet	2–3 cm (Ø) 7–30 g	White	4–18
Araçá	Globose or ovoid and yellow or red	Bittersweet	7–12 cm (Ø) 30–800 g	White, yellowish, greenish or reddish	3–20
Buriti	Dark-red and ellipsoid-oblong	Bittersweet	3–5 cm (Ø) 25–75 g	Orange	1

leading exporters of açaí in the world [28]. Among the main commercialized species of this genus, *Euterpe oleracea* stands out due to the characteristics of its cultivation [29]. This species produces the açaí fruit, popularly called "açaí-do-pará" of great economic importance, and which has gained interest as a “superfruit” due to its bioactive

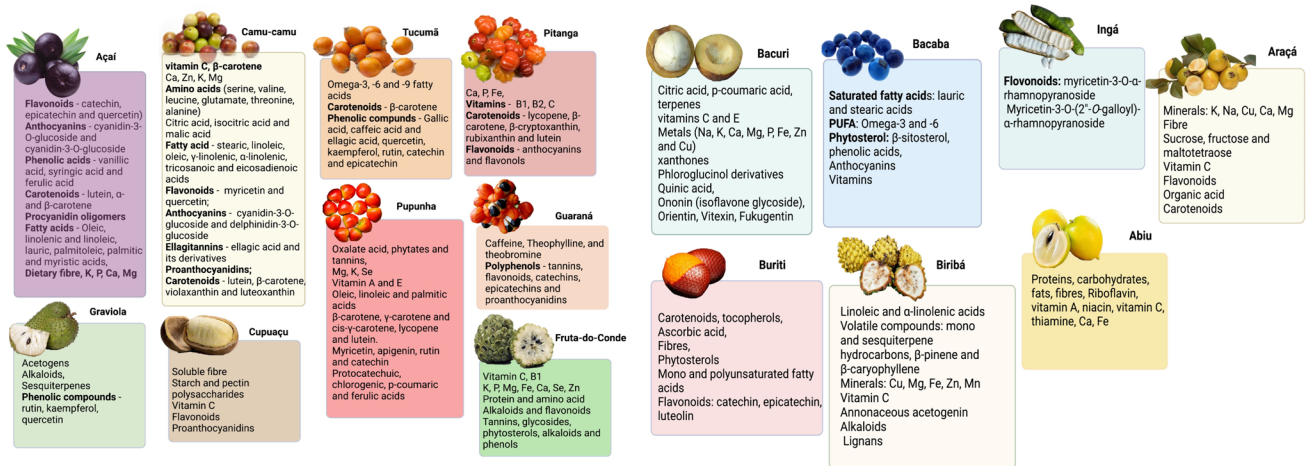

Fig. 1 Nutritional composition of fruits from the Amazon. Created by BioRender

components and potential salutary effects. The demand is growing, and the product is now consumed worldwide. An 89% increase in açaí pulp production in Brazil between 2010 and 2020 generated approximately 1.7 million tons of this fruit [30–38].

The most common form of açaí consumption is a thick, dense juice produced by mechanical pulp extraction. This fruit has always been an essential source of dietary nutrients for people in the Amazon region, representing up to 42% of their diet on a dry weight basis. Among numerous bioactive compounds in the fruit, phenolic compounds, especially anthocyanins and proanthocyanidins, are the most important [32, 39]. Lipids are the primary macronutrient in açaí fruit, including unsaturated and saturated fatty acids, such as oleic acid and palmitic acid, respectively [40, 41]. Dietary fibers and several minerals are also present in açaí [40, 41], which may contribute to their beneficial effects [40, 42].

A potent antioxidant and anti-inflammatory role have been reported [39, 40]. Bioactive compounds from açaí can reduce reactive oxygen species (ROS) production, malondialdehyde (MDA) and, protein carbonyl, and by increasing antioxidant mechanisms, such as catalase (CAT) and glutathione peroxidase (GPx) [43–48]. Studies also report improved inflammatory status, reducing NLRP3 inflammasome protein levels [46, 48–53]. Table 2 shows a compilation of studies investigating the beneficial effects of açaí for health in different models.

Camu-Camu

Camu-camu (*Myrciaria dúbia*) is a popular round-shaped Amazon Forest fruit from the Myrtaceae family. It is well-known as the primary source of vitamin C in Brazilian fruits [55] and for its antioxidant potential. The salutary effects of camu-camu are associated with the high vitamin C content, β-carotene, and phenolic compounds (anthocyanins, ellagitannins, proanthocyanidins), that attenuate oxidative stress (Fig. 1) [56–59]. Camu-camu reduces the production of ROS by increasing the expression of the Nrf2 and the expression of the antioxidant enzyme NAD(P)H: quinone oxidoreductase1 (NQO1) [60]. Moreover, it modulates the expression of mitogen-activated protein kinases (MAPK)/(AP-1) and attenuates nuclear factor kappa-B (NF-κB) and T cell-activated nuclear factor (NFAT) signaling pathways [60, 61]. Camu-camu also has antimicrobial [62], antidiabetic [63–66], antihypertensive [63], and anti-obesity effects [64, 67–70]. Clinical trials need to investigate the potential salutary health-promoting effects of camu-camu (Table 3).

Tucumã

The *Astrocaryum* genus of palm trees belongs to the Arecaceae plant family, which comprises 40 different species geographically distributed in South and Central America [71, 72]. Twenty-two species of tucumã are registered in Brazil [72]. *Astrocaryum aculeatum* G. Meyer and *Astrocaryum vulgare* Mart. are the best-known and appreciated species, and their fruits are popularly called "tucumã-do-Amazonas" and "tucumã-do-Pará," respectively [72]. Tucumã fruits are consumed *in natura*l, stuffing sandwiches or tapioca and processed as pulp that can be used to produce creams and ice creams [72, 73].

Due to its profile of bioactive compounds, tucumã presents an interesting chemical composition from a nutritional point of view. It has a high caloric density, lipid content, predominantly monounsaturated fatty acids, and dietary fibers [74–76]. The fruit contains omega-3, -6, and -9 fatty acids [77]. It has a high content of carotenoids, especially β-carotene (850 RE/100 g), compared to other fruits that are conventional sources, such as acerola (148–283 RE/100 g) and papaya (19–74 RE/100 g) [78]. Tucumã has traditionally been used as a medicinal plant for digestive and respiratory disorders and infections [77, 79]. The rich nutritional composition of tucumã makes it stand out as a functional food, making it a significant research target concerning its salutary effects. Some in vitro and in vivo studies point to antioxidant, anti-inflammatory, hypocholesterolemic, antidiabetic, anticarcinogenic, and neuroprotective effects associated with tucumã edible parts, such as skin and pulp. The antioxidant capacity of tucumã fruits has been linked with β-carotene and bioactive compounds such as quercetin [77].

Tucumã has antioxidant effects by reducing ROS levels and increasing superoxide dismutase and catalase activity. Regarding inflammation, an inhibitory action against macrophage proliferation, cell cycle arrest, and modulation of inflammation-related genes has been reported [77, 80–82]. Inhibition of the expression of inducible nitric oxide synthases (iNOS) and cyclooxygenases 2 (COX-2) resulted in lower production of prostaglandin E2 and NO. Neuroprotective, anti-diabetic, and anti-carcinogenic effects have also been reported (Table 4) [83–86].

Pitanga

Pitanga (*Eugenia uniflora*) also called "Brazilian cherry" is a native fruit from Brazil, produced by the pitangueira (*Eugenia uniflora Linnaeus*) tree. It belongs to the Myrtaceae family, with a wide diversity of plants, comprising approximately 3800—5800 species of shrubs or trees [88,

Table 2 Beneficial effects of açaí for health in vitro, in vivo and human studies

References	Sample	Intervention	Results
Anti-inflammatory effects			
Silva et al. 2022 [49]	Raw 264.7 macrophages (ATCC® TIB-71™) transfected with the NF-κBpLUC gene	Hydroethanolic açaí meal extract (pulp) at 1, 10 or 100 µg/mL for 30 min and 24 h	↓ ABTS radical cation and peroxyl radical; ↓ NF-κB activation; ↓ TNF levels
Fernandes et al. 2021 [46]	Macrophage cell line 264.7	Cells were concomitantly exposed to a proinflammatory concentration of olanzapine with different concentrations of açaí extract (0.01 – 10 µg/mL; from skin and pulp fractions) for 24 and 72 h	Açaí treatment at 5 µg/mL: ↓ ROS, NO, IL-1β, IL-6, TNF and IFN-γ levels; Casp-1, -3 and -8 expression; ↑IL-10 Açaí treatment prevented an increase in cellular proliferation induced by olanzapine
Machado et al. 2019 [48]	Macrophage cell line RAW 264.7	# doses of freeze-dried hydroalcoholic açaí extract (0.001–1000 µg/mL; extract from pulp and peel) for 24 h	↓ ROS levels (except at 500 µg/mL); NO (at all doses); 1 µg/mL of açaí extract in PHA-activated macrophages: ↓ IL-1β; IL-6; TNF; casp1, casp3 and casp8, and NLRP3 inflammasome protein levels; ↑ IL-10 ↑ cell cycle arresting (↓S phase and ↑G2/M phases) ↓ macrophage proliferation
Kim et al. 2018 [50]	37 participants with metabolic syndrome	Placebo or açaí group to consume 325 mL 2x/d of açaí-beverage (equivalent to 163 g of açaí pulp/d) for 12 wks	↓ IFN-µ and 8-isoprostane levels
Ajit et al. 2016 [51]	Immortalized rat astrocyte (DI TNC1) cell line expressing a luciferase reporter driven by the NF-κB or the Nrf2/ARE	# doses of açaí berry extract (6.25–50 µg/mL) for 1 h	↓ LPS-induced NF-κB activity (at ≥ 12.5 µg/mL), ↑ antioxidant Nrf2/ARE response ↑ HO-1 expression
Anti-oxidant effects			
Dias et al. 2015 [52]	Human colon myofibroblast CCD-18Co cells	Polyphenolic extract (from 1 to 5 mg GAE/L) for 24 h and 48 h	↓ TNF-α, COX-2, TLR-4; TRAF-6; NF-κB; VCAM-1; ICAM-1 ↓ ROS and prevented LPS-induced ROS production in the cells
Barbosa et al. 2020 [54]	Primipara female *Fischer* rats (90 days old; w/ approximately 200 g) and their offspring (six male pups per dam)	**Female rats were assigned into 4 groups**: Control; HF: HFD (60% total calories as fat); CA: control diet w/ 2% of açaí pulp; HFA: HFD w/ 2% of açaí pulp **6 male pups per dam**. The offspring (P21) were allocated in the respective group (C-P21, CA-P21, HF-P21 and HFA-P21) according to the dam treatment	Açaí supplementation in dams: ↓ steatosis, ↓ liver weight in HFA *vs*. HF group; ↓ MDA, protein carbonyl, ↓CAT, GPx and SOD activity in the liver; Açaí supplementation in offspring, in HFA-P21 diet: ↓Liver weight; ↑mRNA expression of *Gpx1*, *Gpx4* and *Sod1* in the liver tissue
De Liz et al. 2020 [45]	30 healthy adults	100 mL of açaí fruit juice (*E. oleracea*) or juçara fruit juice (*E. edulis*) twice daily for 4 weeks	Both treatments: ↑ HDL-c; TAC; GPx; OSI (TOS/TAC)
Pala et al. 2018 [44]	40 healthy young volunteers	200 g of açai pulp/day for 4 wk	↑ apo A-I, paraoxonase 1 activity, TAC, CE; ↓ ROS, ox-LDL and MDA
Barbosa et al. 2016 [43]	35 young women	200 g of açaí pulp/day for 4 wk	↓ ROS production by PMN cells; serum protein carbonyl levels; ↑ TAC of PMN cells; CAT activity; serum sulfhydryl groups

Table 2 (continued)

References	Sample	Intervention	Results
Cardioprotective effects			
Figueiredo et al. 2022 [47]	Male Wistar rats (200–250 g)	The rats were submitted to myocardial infarction (MI) or sham surgery, and then were allocated into six groups: sham or infarcted animals fed with standard chow alone or enriched with açaí pulp (2% or 5% of the açaí pulp) for 90 days	Açaí supplementation after MI: ↑ energy metabolism (↑β-OHADH, PDH, CS and complex I activity; ↓LDH activity); ↓ OS (↓MDA and SOD activity; ↑GPx); ↓ deposition of collagen (↓TIMP-1 and ICF percentage)
e Souza et al. 2017 [33]	Male Wistar rats (210 ± 20 g)	5 groups and treated orally with: (1st) OFEO (1226 mg/kg) alone or (2nd) with GSC (2 mL/day) daily for 40 days; 3rd group: distilled water (40 days) and GSC (from the 20th to the 40th day); the fourth group: simvastatin (40 days) and GSC (from the 20th to the 40th day; and the fifth group: only distilled water daily (40 days)	OFEO treatment alone vs. GSC group: ↓ BW and caloric intake; LDL-c OFEO + GSC group vs. GSC-induced dyslipidemia group: ↓TC; LDL-c; ↑ HDL-c OFEO and OFEO + GSC groups exhibited no atheroma in the vascular endothelium, which reflects OFEO antiatherogenic properties
Neuroprotective effects			
Cadoná et al. 2021 [34]	Microglia cells (EOC 13.31 cell line)	# doses of freeze-dried hydroalcoholic açaí extract (0.001–1000 µg/mL) for 24, 48 and 72 h	Açaí extract (0,1 µg/mL): Reverted LPS-induced increased in cellular proliferation, NO production and ROS levels ↓ NLRP3 protein levels; Casp1 and IL-1β expression
Poulose et al. 2012 [35]	BV-2 murine microglial cells	# doses of açaí extract (10–1000 µg/mL) or control media for 4 h and then stimulated with LPS (100 ng/mL) overnight	Açaí pulp fractions: ↓ NO and iNOS; ↓ p38-MAPK, TNF, NF-κB and COX-2 (MEOH, ETOH and ACE fractions promoted a concentration-dependent reduction)
Hepatoprotective effects			
Carvalho et al. 2019 [53]	In vitro: HepG2 human liver carcinoma cells In vivo: 32 Male Swiss mice, approximately 30 days old, weighing 25 g	In vitro: treatment w/ different concentrations of aqueous açai extract (0 – 400 µg/mL) for 24, 48 and 72 h In vivo: 2 groups: control group; HF—group that received HFD (32% lard, 1% cholesterol) After 6 weeks these groups were subdivided into groups C and A, and HF and HFA, respectively. The A and HFA were treated with aqueous açai extract (3 g/kg/d) for 6 wks	In vitro, açaí treatment: ↓ peroxyl radicals, with considerable total ORAC; ↓ ROS levels (at 100 mg/mL) in TBHP-treated cells; In vivo*:* ↓ ALT levels, ↓TNF-α serum levels and inflammatory cells in the liver; ↓ TBARS and carbonylation of proteins, and trough modulation of GR, SOD and CAT

Table 2 (continued)

References	Sample	Intervention	Results
Zhou et al. 2018 [30]	Wistar rats, 7-week-old, weighting 220–240 g	Alcohol group (alcohol intake); EO group (alcohol + EO puree intake) and control group (distilled water intake) In the 1st week, animals in the 'alcohol' and EO groups received alcohol (56%; 0.8 mL/100 g) per day by oral gavage. The quantity of alcohol was increased by 0.1 mL once every two weeks until 8th week (1.5 m/100 g) EO group received EO puree (1 mL/100 g) and control group received the same volume of distilled water by oral gavage for 8 wks	EO treatment in alcohol-treated rats: ↓ALT, aspartate aminotransferase, alkaline phosphatase, TG and COL levels in the serum; ↓MDA, TG, TNF, TGF-β and IL-8 levels, and mRNA expression levels of NF-κB and CD-68 in the liver; ↑Hepatic index (hepatic index = liver weight/animal weight × 100); ↑SOD activity and GSH levels in liver tissues EO treatment alleviated alcohol-induced histopathological liver damage, such as severe steatosis and abundant infiltrated inflammatory cells
Anti-diabetic effects			
dos Santos et al. 2023 [31]	Fifty-two 4-weeks old male Swiss mice	4 groups: N group: normal fat diet (AIN-93 M); NA group: normal-fat diet w/ 2% AP; H group: HFD (60% total calories from fat); HA group: HFD containing 2% AP for 10 wks	NA group presented lower BW gain vs. control group; HA-fed group: better insulin sensitivity in ITT, and lower fasting glucose and fasting adiponectin vs. H group; Improved phosphorylation of AKT/GSK3-β in mice hippocampi; Improved CAT activity and higher GSH content in the hippocampus vs. H group; Presented a prevention of cognitive impairment induced by HFD analyzed in the NOR test
Nephroprotective effects			
El Morsy et al. 2015 [36]	Male adult Wistar rats (185–200 g)	Sham-operated control group (received oral corn oil); animals of the other groups received oral corn oil alone or açaí extract (500 and 1000 mg/kg) dissolved in corn oil before bilateral renal I/R induction for 15 days	Açaí fruit extract at both concentrations: ↓BUN, serum creatinine level; renal MDA and collagen -IV content; Açaí extract at 1000 mg/kg: ↓serum LDH activity, renal KIM-1, MPO, INF-γ, ET-1 and casp3 contents; ↑renal IL-10 content
Unis 2014 [37]	Wistar albino rats (150–200 g)	Oral açaí berry extract (100 and 200 mg/kg/day) for 7 days before or 7 days after induction of acute kidney injury	↓urea and creatinine, and BUN, ↑ CAT and GSH Renal histopathological changes

Table 2 (continued)

References	Sample	Intervention	Results
Microbiota protective effects			
Song et al. 2021 [38]	Male C57BL/6 J mice (4 wk old)	Mice were randomly assigned in one of the three groups: mice fed with LFD, HFD, and anthocyanin-rich extract of açai group (150 mg/kg/d) for 14 wk	Açaí treatment: ↓HFD-induced elevation in BW; TG; TC; NEFA, LDL-c, serum ALT and aspartate aminotransferase levels; ↓lipid accumulation and alleviated the formation of steatosis vs. HFD group ↓fasting serum glucose and insulin levels Supplementation altered hepatic gene expression profile (↓*Fas*, *Scd1* and *Elov6*, and *Pparα* and *Srebf1*; ↑*HL, Cpt1b* and *Acox1*) Açaí treatment changed the structure of the gut microbiota (↓proportions of Firmicutes and Proteobacteria, and ↑abundance of Verrucomicrobia and *Akkermansia muciniphila*)

ABTS 2,2'-azinobis-3-ethylbenzothiazoline-6-sulfonic acid, *Acox1* acyl-coenzyme A oxidase 1, *AKT* protein kinase B, *ALT* alanine aminotransferase, *AP* açaí powder, *Apo A-I*, apolipoprotein A-I, *ARE* Antioxidant response element, *β-OHADH* β-hydroxyacyl coenzyme-A dehydrogenase, *BUN* blood urea nitrogen, *BW* body weight, *CAT* catalase, *Casp1* Caspase 1, *Casp3* Caspase 3, *Casp8* Caspase 8, *CD68* cluster of differentiation 68, *CE* cholesteryl esters, *COL* cholesterol, *COX-2* cyclooxygenase 2, *Cpt1b* carnitine palmitoyltransferase 1b, *CS* citrate synthase, *EO* Euterpe oleracea, *Elov6* ELOVL fatty acid elongase 6, *ET-1* endothelin-1, *ETAC* ethyl acetate, *ETOH* ethanol, *Fas* fatty acid synthase, *GAE* gallic acid equivalents, *GSH* reduced glutathione, *GPx* glutathione peroxidase, *Gpx1* glutathione peroxidase 1, *Gpx4* glutathione peroxidase 4, *GR* glutathione reductase, *GSK3-β* glycogen synthase kinase 3-β, *HDL-c* high density lipoprotein-cholesterol, *HFD* high fat diet, *HL* hepatic lipase, *HO-1* Heme oxygenase 1, *HFA* HFD supplemented with açaí, *HFA-P21* Offspring from HFA group, *HOMA-IR* homeostatic model assessment for insulin resistance, *HOMA-IS* homeostatic model assessment for insulin sensitivity, *ICAM-1* intercellular adhesion molecule 1, *ICF* interstitial collagen fraction, *IFN-γ* interferon gamma, *IL-1β* interleukin 1 beta, *IL-10* interleukin 10, *IL-6* interleukin 6, *IL-8* interleukin 8, *I/R* ischemia/reperfusion, *ITT* insulin tolerance test, *KIM-1* kidney injury molecule-1, *LDH* lactate dehydrogenase, *LFD* low-fat-diet, *LPS* lipopolysaccharide, *MDA* malondialdehyde, *MEOH* methanol, *MPO* myeloperoxidase, *NEFA* non-esterified fatty acid, *NF-κB* nuclear factor kappa B, *NLRP3* nod-like receptor pyrin containing 3, *NO* nitric oxide, *NOR* novel object recognition test, *OFEO* oil from the fruits of Euterpe oleracea, *OS* oxidative stress, *OSI* oxidative stress index, *Pparα* peroxisome proliferator-activated receptor alpha, *P38-MAPK* p38 mitogen-activated protein kinase, *PDH* pyruvate dehydrogenase complex, *PHA* phytohemagglutinin, *PMN* polymorphonuclear cells, *Scd1* stearoyl-CoA desaturase 1, *SEM* scanning electron microscopy, *SOD* superoxide dismutase, *Sod1* superoxide dismutase 1, *Srebf* sterol regulatory element binding transcription factor 1, *TAC* total antioxidant capacity, *TC* total cholesterol, *TG* triglyceride, *TGF-β* transforming growth factor-β, *TAC* total antioxidant capacity, *TBARS* thiobarbituric acid-reactive substances, *TBHP* tert-butyl hydroperoxide, *TIMP-1* tissue inhibitor of metalloproteinase-1, *TLR-4* toll-like receptor 4, *TNF* tumor necrosis factor, *TOS* total oxidant status, *TRAF-6* TNF receptor-associated factor 6, *VCAM-1* vascular cell adhesion molecule 1

Table 3 Beneficial effects of Camu-camu (*Myrciaria dúbia*) for health (in vitro and in vivo studies)

References	Sample	Intervention	Results
Anti-inflammatory and Antioxidant effects			
Fidelis et al (2020) [61]	In vitro: Lung adenocarcinoma epithelial cell (A549), human colon carcinoma (HCT8) and noncancerous human lung fibroblast (IMR90) In vivo: Male Wistar rats (4 weeks old, ~ 400 g)	In vitro: 24 h of incubation with optimized lyophilized camu-camu seed extract (LOCSE) at dosages of 1, 3, 10, 30, 100, 300 and 1000 µg/mL In vivo: LOCSE at dosage 30 µg/mL	In vitro: ↓ TNF-α cytokine release; ↓ NF-κB activation In vivo: ↓ lipid peroxidation; ↓ DPPH radical elimination ↑ Antioxidant capacity; ↓ Oxidation of human LDL to conjugated dienes
Do et al. (2021) [60]	Immortal human keratinocyte HaCaT cells	Incubation with camu-camu extract (different doses) for 1 h before being stimulated with 15 mM D-glucose for 6 h	↓ ROS overproduction (at dosages of 1 µg/mL and 10 µg/mL) ↓ Phosphorylation of MAP kinase signaling in a dose-dependent manner 1 µg/mL -↓ inhibited p-IkBα and NF-κB induced by high glucose 10 µg/mL -↑ phosphorylated NFATc1 ↓ Activation of COX-2 expression ↑ Nrf2 protein expression and NQO1 expression
Antidiabetic activity			
Balisteiro et al. (2017)[65]	23 healthy subjects	300 mL of camu-camu juice administered after 10–12 h of fasting	↓ Serum glucose concentrations ↑ Plasma iron reducing capacity
Peña et al. (2022) [66]	Female mice 4 to 5 weeks old weighing 18 to 22 g	50 g of camu camu pulp were diluted in 500 mL of distillates and homogenized 4 groups of 6 mice were formed, a volume of 100, 500 or 1000 mg/kg of the aqueous extracts and control group	The extract showed antidiabetic effect from the glycemic control At dosages of 100 and 500 mg/kg of the extract, glycemic control similar to glibenclamide control was observed 1000 mg/kg- glycemic control similar to the negative or healthy control group
Antiobesity effects			
Anhê et al. (2018) [69]	8-week-old male C57Bl/6 J mice randomly into four groups (n = 12) and fed chow or a high-fat high-sucrose diet (HFHS)	Treatment was HFHS diet and daily oral doses (200 mg/kg) of resuspended crude camu camu extract, vitamin C (6.6 mg/kg) or drinking water over 8 weeks	Prevented weight gain, ↓ fat accumulation, inflammation and endotoxemia Improved glucose tolerance and insulin sensitivity ↑ Energy expenditure and upregulation of uncoupling protein 1 mRNA expression in brown adipose tissue
do Nascimento et al. (2018) [70]	Neonate male Wistar rats receiving monosodium glutamate	Four groups: sedentary group S (no treatment), exercise group E (continuous swimming training), Camu-camu group C (25 mL of pulp of Camu-camu/day) and exercise and Camu-camu group EC (25 mL of pulp of Camu-camu/day, continuous swimming); for 12 weeks	↓ cholesterol, triglycerides, glucose, HDL, LDL and in all groups, except for the control group
Others effects			
Gonçalves et al. (2014) [59]	Male Wistar rats with diabetes induced	2 main groups: control or non-diabetic and diabetic treatment I (1 g/kg of aqueous extract of frozen camu-camu pulp) or II (3 g/kg of aqueous extract of frozen camu-camu pulp) for 30 days	At both doses: ↑ Plasma antioxidant activity ↓ Triacylglycerol and total cholesterol and plasma lipid peroxidation

TNF tumor necrosis factor, *NF-κB* nuclear factor kappa B, *DPPH* 2,2-difenil-1-picrilhidrazil, *HDL* High Density Lipoprotein, *LDL* Low Density Lipoprotein, *ROS* reactive oxygen species, *NAFTc1* nuclear factor of activated T cells 1, *COX-2* Cyclooxygenase-2, *Nrf2* factor 2 related to erythroid nuclear factor 2, *NQO1* NAD(P)H quinone dehydrogenase 1

89]. Pitanga is a rich source of bioactive compounds, such as carotenoids and phenolic compounds [32, 90–94]. In addition to maturation, climate, soil type, growth conditions, geographic production area, harvesting, processing, and storage influence fruit composition [93]. Due to its antipyretic, antirheumatic, anti-inflammatory, and hypocholesterolemic effects, pitanga leaves have been part of Brazilian traditional medicine [95]. However, only a few studies have investigated the effects of the edible part of pitanga. Studies conducted in vivo have reported antioxidant effects, such as reduced levels of ROS, protein carbonyl content, and TBARS [96, 97]. In addition, anti-inflammatory, anti-diabetic, hepatoprotective, and neuroprotective effects related to the use of pitanga have been reported (Table 5) [98–103].

Graviola

Graviola (*Annona muricata* L.) is known as soursop, guanabana, paw-paw, or sirsak. It is a natural fruit tree from the Annonaceae family of plants used in various food recipes, such as ice cream, syrups, nectars, jams, jellies, sweets, and drinks [105, 106]. Previous studies report that all parts of graviola have been used as a natural remedy to treat headaches, diarrhea, skin illness, fever, rheumatism, skin illnesses, and infections [106–111].

The main bioactive compounds of this fruit are acetogenins, alkaloids, phenolic compounds, and sesquiterpenes (Fig. 1) [105, 112], which confer antioxidant, anticancer, antidiabetic, antihypertensive, hypolipidemic, gastroprotective, and hepatoprotective activities [105, 113–115]. Graviola leaf extract seems to decrease ROS formation by positively regulating the expression of antioxidant genes, such as superoxide dismutase 1 (SOD1) and Nrf2, which may be an ally in the prevention of diseases related to ROS formation [115].

Acetogenin (Fig. 2) is a long hydrocarbon chain (32 or 34 carbons) with a terminal α, β-unsaturated γ-lactone ring. The hydrocarbon chain often contains one or more tetrahydrofuran (THF) or tetrahydropyran (THP) rings, as well as other functional groups like hydroxyl (-OH) and ketone (C = O) groups. Acetogenin is produced via the polyketide pathway [116].

The acetogenins include a variety of substances [117] that inhibit the formation of mitochondrial ATP, which may slow the growth of cancer cells [118]. Acetogenin can also induce apoptosis by decreasing the expression of anti-apoptotic proteins, leading to increased expression of pro-apoptotic proteins and also the expression of caspases [114, 119]. Graviola leaf extract reduces ROS formation by positively regulating the expression of antioxidant genes, such as superoxide dismutase-1 and Nrf2, which may be used to prevent NCDs related to oxidative stress and cancer [114, 120–124]. It also presents health benefits, such as anti-inflammatory and antidiabetic effects (Table 6) [115, 125–131]. Moghadamtousi et al. (2014) showed that ethyl acetate extract from graviola leaves has a cytotoxic effect on colon cancer cells, arresting the cancer cells in the G1 phase of the cell cycle and leading to the induction of apoptosis [114]. Regarding anti-diabetic effects, a study showed that alloxan-induced diabetic rats treated with aqueous extract of A. muricata peel presented lower fasting blood glucose and high insulin plasma levels. Also, they observed a reduction in inflammation markers [127].

Cupuaçu

Cupuaçu (*Theobroma grandiflorum*) belongs to the *Theobroma* genus. The cacao tree (*Theobroma cacao* L.) belongs to the same family [132, 133]. The Brazilian North region has the most extensive distribution of the cupuaçu market, followed by the northeast and central west regions [133]. The pulp's acidic taste makes it usable in juices, liquors, creams, ice creams, jellies, and candies [134, 135].

As the cupuaçu pulp is rich in fiber, especially the soluble type, it is a valid source of starch and pectin polysaccharides. Fresh cupuaçu pulps are rich in ascorbic acid, which is lost during processing to obtain frozen pulps [134]. Analysis of the cupuaçu pulp has reported efficient antioxidant activities, and it possesses bioactive compounds, such as phenolic compounds, flavonoids, and proanthocyanidins. These phytochemical components are found in smaller amounts in commercial frozen pulps, which may reflect degradation due to the processing/storage steps [134, 136, 137].

To this date, only a few in vitro and in vivo studies have investigated cupuaçu effects on risk factors of NCDs [132, 134]. Results exhibit a potential impact of cupuaçu extract in controlling nitrosative stress and downregulating kidney inflammatory factors [138]. A study investigated the protective effect of different types of tropical fruit, including cupuaçu, in a model of intestinal inflammation. Cupuaçu seems to increase the colonic mucin and promote myeloperoxidase reduction and alkaline phosphatase activity. It also leads to a smaller colonic diameter, wall thickness, and more conserved villus [139]. In mice subjected to endotoxemia induced by LPS, the unfermented cupuaçu juice promoted anti-inflammatory effects and reduced the number of leukocytes [140].

Pupunha

Popularly known as “pupunha”, *Bactris gasipaes* Kunth belongs to the *Arecaceae* palm family [141] and comes in two varieties [142], including the peach palm (fruit) and heart of palm [143]. Palm trees are characterized by long, smooth-textured trunks filled with thorn-covered internodes. The heart of the palm can be cooked and used in salads

Table 4 Beneficial effects of tucumã for health (in vitro, in vivo, and human studies)

References	Sample	Intervention	Results
Antioxidant and anti-inflammatory effects			
Cabral et al. 2020 [80]	Murine macrophage RAW 264.7 cell line stimulated w/ PHA	Different doses of *A. aculeatum* fruit extract (1–300 µg/mL) for 72 h	↓ROS (30–100 µg/mL); NO production (10 µg/mL); macrophage proliferation in all concentrations; Arrested the cell cycle in G0/G1 phase in all concentrations 30 µg/mL of fruit extract: ↓DNA denaturation; TBARS levels; protein carbonylation; mRNA expression of IL-1β and IL-6 ↑SOD and CAT activity (30 µg/mL), T-SH and NPSH levels; mRNA expression of IL-10
Dos Santos et al. 2015 [81]	Methanolic extract from mesocarp and epicarp from tucumã	β-Carotene/Linolenic Acid (immediately and in 15-min intervals for 120 min) and ORAC (1 h) methods	92% oxidation inhibition of β-Carotene/Linolenic Acid 64 µM Trolox·g^{-1} by ORAC
Sagrillo et al. 2015 [77]	Human lymphocyte cell cultures exposed to H_2O_2	Different doses from ethanolic extracts isolated from the pulp and peel extracts of *A. aculeatum*	↑Cells viability (300 – 900 µg/mL) ↓Caspase-1, -3 and -8; DNA denaturation (peel partially reverted at 300–1200 µg/mL; pulp completely reverted at 900–1500 µg/mL)
Bony et al. 2012 [87]	J774 macrophage cell line activated by LPS and IFN γ and 6 week-old male Balb/c mice	In vitro: # concentrations of ethanolic unsaponifiable fraction of *A. vulgare* M pulp (5–40 µg/mL), 6, 24 and 48 h *In* vivo (8 mice/group): Control (IP injected w/ saline); LPS 1.5 h and LPS 6 h groups (IP injected w/ LPS at 20 µg/mL); EUF 1.5 h and 6 h groups (pre-treated by IP w/ 25 mg/kg EUF 2 h before LPS injection), 1.5 h and 6 h after LPS injection	↓NO production (40 µg/mL) and COX-1 and -2 expression (250 µg/mL); Activated J774 macrophages: ↓NO production, iNOS (40 µg/mL), PGE_2 (40 µg/mL), COX-2 (40 µg/mL); TNF (20 and 40 µg/mL), IL-6 (40 µg/mL) and -10 (10–40 µg/mL) production In vivo: ↓TNF, IL-6 and -10 serum concentration, and antioxidant capacity
Neuroprotective effects			
Jantsch et al. 2020 [85]	Wistar rats, 130–150 days age	Control; Control + Tucumã extract; Hyperlipidemic; Hyperlipidemic + Tucumã	Tucumã extract prevented memory loss and oxidative damage of proteins and lipids molecules, and improved antioxidant response (↓ROS levels and ↑T-SH) in the cerebral cortex of hyperlipidemic rats
Baldissera et al. 2017a [83]	Heterogenic adult female Swiss mice (70 days old; 28 ± 1.5 g)	Four groups: non-diabetic/water; non-diabetic/tucumã oil (5.0 mL/kg); diabetic/water, and diabetic/tucumã oil for 14 days	Tucumã prevented diabetes-induced memory impairment, TBARS and PC increased levels, AChE increased activity, and the reduction of CAT, SOD and Na+, K+-ATPase activities
Anti-diabetic effects			
Baldissera et al. 2017b [84]	Heterogenic adult female Swiss mice (70 days old; 28 ± 1.5 g), alloxan induced DM	Four groups: non-diabetic/water; non-diabetic/tucumã oil (5.0 mL/kg); diabetic/water, and diabetic/tucumã oil for 14 days	↓ insulin levels, blood glucose and redox status (TBARS levels, CAT and SOD activities), -protective effect in opposite of pancreatic damage due diabetic-induced oxidative stress, DNA damage ↓ cell viability

Table 4 (continued)

References	Sample	Intervention	Results
Anti-carcinogenic effects			
Copetti et al. 2019 [86]	Human APL derived NB4 cells	Ethanolic tucumã (*A. aculeatum*) pulp and peel extracts (100 – 1500 µg/mL) or tucumã + all-trans retinoic acid	↓cell proliferation ↓ promyelocytic leukemia/retinoic acid receptor-α gene expression ↑ dsDNA levels ↑ casp -1, -3, and -8 levels
Nascimento et al. 2021 [82]	Human PBMCs and MCF-7 breast cancer cells	Nanocapsule Tucumã oil (*A. vulgare*): PBMCs: 100 – 1000 µg/mL, 24 h; MCF-7: 1 – 200 µg/mL, 72 h	PBMCs: ↓cell viability (TN: 100, 200 and 500 µg/mL); ↑ROS (FT: 200 µg/mL); ↑NO (TN: all concentrations and FT: 200 µg/mL) MCF-7: ↓cell viability (TN: 5–200 µg/mL; FT: 50, 70 and 130–200 µg/mL); IC_{50}: 50 µg/mL (TN) and 130 µg/mL (FT)

APL acute promyelocytic leukemia, *casp* caspase, *COX* cyclooxygenases, *dsDNA* double-strand DNA, *FT* free Tucumã oil, *IC50* inhibition proliferative concentrations, *IFN* interferon, *IL* interleukin, *PBMC* peripheral blood mononuclear cells, PGE_2 prostaglandin E_2, *ROS* reactive oxygen species, *LPS* lipopolysaccharide, *MCF-7* breast adenocarcinoma cells, *NO* nitric oxide, *TN* tucumã oil nanocapsules, *TNF* tumor necrosis factor

[144]. As the fruit has high levels of oxalate acid, phytates, and tannins, it is marketed in processed form, such as flour, oil, and cooked fruit [145, 146]. The peach palm has been applied in beer industries and is used for amylase extraction in microbial strains, in the development of functional food products, and for animal feed [147]. This fruit is a good source of minerals, vitamins A and E, and fatty acids and is rich in carotenoid dietary fiber (Fig. 1) [6].

Due to its phytochemical composition and lipid fraction, peach palms have been used in traditional medicine to treat hepatitis, malaria, worms, parasites, and stomach pain. The antioxidant potential of peach palms occurs through the conjugated dienes present in β-carotene, which can eliminate ROS and incite mechanisms of enzymatic and non-enzymatic, promoting protection against mitochondrial stress and apoptosis [148]. β-carotene contributes to its anti-inflammatory action by modulating the expression of cyclooxygenase-2, nitric oxide synthase 2, and attenuating the synthesis of inducible nitric oxide synthase [149]. Antimicrobial effects against *Staphylococcus aureus* [150] and anti-obesogenic activity [151] have also been studied. Thus, peach palms can be a promising therapeutic strategy against NCDs.

Guaraná

The best-known Amazonian fruit, guarana, is famous for being a caffeine-rich energy fruit. *Paullinia cupana* Kunth var. *sorbillis* or just "Guaraná", has been widely cultivated by indigenous tribes in the interfluves of the Amazon and carried with it due to the appearance of the fruit when ripe—the famous story of having been born from the eye of a murdered boy [152]. Guarana contains caffeine, theophylline, theobromine, and polyphenols (Fig. 1) [153–156]. Initially, guarana was used in the colonial period to treat headaches, fever, and diarrhea. Overconsumption of guarana causes dizziness, insomnia, and impotence [152, 157]. Previous studies have investigated the effects of guarana in improving fatigue, but the results are contradictory [158], and others have observed cognitive improvement effects [159]. It has been observed that guarana presents antioxidant and protective action in intestinal tissue [160], beneficial effects on hepatic and renal parameters [161], anti-obesogenic action [162], exhibited anti-inflammatory, cardioprotective, and beneficial effects in the context of hyperlipidemia [163], and antitumor action [164].

Like other Amazonian fruits, Portella et al. analyzed in vitro and in vivo the effects of guarana (doses from 1 to 5 ug/kg) on LDL oxidation in older adults. They observed that guarana had antioxidant activity by minimizing the production of diene conjugates and acid-reactive substances thiobarbiturate [165]. Likewise, Yonekura et al. (2016), when evaluating the effects of guarana seed powder (3 g dose)

Table 5 Beneficial effects of pitanga for health (in vitro, in vivo, and human studies)

References	Sample	Intervention	Results
Antioxidant effects			
Tambara et al. 2018 [97]	Different strains from *Caenorhabditis elegans* (N2 [WT]; CF1553 muIs84; CF1553 muIs84; CL2070 dvIs70; TK22; TJ356; and CF1038)	# doses of ethanolic extract of purple pitanga (PEE) (*Eugenia uniflora* L.), for 30 min	PPE improved the survival, reproduction and lifespan of the worms in pre- and post-exposure to H_2O_2 and juglone, and also improved the lifespan of the OS hypertensive strain *mev-1* PPE: ↓ROS, protein carbonyl content in H_2O_2 -induced OS ↑SOD-3 expression (50 – 500 µg CAE/mL); nuclear localization of DAF-16 (higher concentrations of PPE)
Oliveira et al. 2017 [96]	Male wistar rats aged 21 days	standard chow; standard chow + *E. uniflora*; highly palatable diet (HPD); highly palatable diet + *E. uniflora* (200 mg/Kg/day) for 150 days	*E. uniflora* extract treatment in animals in HPD: Prevented the increase of visceral fat mass, weight gain, blood glucose levels, TC, LDL-c and TAG levels, and the rise of AChE activity in the prefrontal cortex ↓TBARS in the hippocampus Prevented the reduction of SOD and CAT activities in the prefrontal cortex, hippocampus and striatum Antidepressant-like effect
Anti-inflammatory effects			
Soares et al. 2014 [103]	6 healthy young female volunteers In vitro: HGF-1	100 ml of pitanga juice or control drink in their mouths for a total of 10 min. The total juice volume was slipt into two aliquots of 30 mL for 3 min each and one aliquot of 40 mL for 4 min Gum epithelial cells were harvested and incubated with or without 10 µg/mL *PG*-LPS for 6 h In vitro: 10 µg/mL *PG*-LPS and 119 µg/mL C3G or 30 µg/mL OxS for 6 h	↓ IL-8 in non-stimulated cells ↓ IL-8 release in cells stimulated *PG*-LPS In vitro assay: ↓LPS-stimulated *CXCL8* mRNA expression and IL-8 release
Anti-diabetic effects			
Cardoso et al. 2018 [101]	Adults male Wistar rats	Control; *E. uniflora* (200 mg/kg/day); *P. cattleianum*; dexamethasone; dexamethasone + *E. uniflora*; dexamethasone + *P. cattleianum for* 21 days	*E. uniflora* prevented: Impaired glucose tolerance, increase in glucose and TAG levels, and in TBARS values and ROS production
Hepatoprotective effects			
Denardin et al. 2017 [104]	GRX cell line (from the livers of C3H/HeN mice)	Treatment with crescent concentrations of purple pitanga fruit extract (5, 50 and 100 µg/mL) for 72 h	↑ATG7 expression; number of mature autophagosome (50 and 100 µg/mL); number of autophagosomes and autolysosomes (5 and 100 µg/mL); autophagy and mitophagy Mitochondrial translocation into lysosomes in cells (50 and 100 µg/mL)

Table 5 (continued)

References	Sample	Intervention	Results
Denardin et al. 2014 [102]	HSC cell line (GRX—from livers of C3H/HeN mice)	GRX cells were treated w/ 5, 50 and 100 µg CAE/mL, for 24, 48 and 72 h. The routinely cultured cells were used as controls	↓cell viability (50 µg/mL for 72 h and 100 µg/mL for 48 and 72 h); cell proliferation (dose dependent); mitochondrial content (50 and 100 µg/mL at all time points); mitochondrial membrane potential (50 µg/mL for 72 h and 100 µg/mL for 48 and 72 h); ↑percentage of dead cell-stained w/ 7-AAD (50 µg/mL for 48 and 72 h and 100 µg/mL in all time points); Treatment w/ pitanga extract promoted alterations on cell cycle progression
Neuroprotective effects			
Flores et al. 2020 [99]	44 male Swiss mice, 8 weeks old, weighing 35–40 g	6 groups: control/Vehicle; control/fluoxetine; control/extract; CUS/vehicle; CUS/fluoxetine; CUS/extract. Animals in CUS groups underwent a series of stressors for 21 days	*E. uniflora* extract: Prevented the depressant-like effects of CUS; Impaired the CUS-induced increase in TBARS and ROS production in prefrontal cortex and hippocampus; Prevented the reduction of GPx in the hippocampus; Prevented the CUS-induced increase in AChE activity

7-AAD 7-amino-actinomycin D, *AChE* acetylcholinesterase, *ATG7* autophagy-related protein 7, *C3G* cyanidin-3-glucoside, *CAE* chlorogenic acid, *CAT* catalase, *CUS* chronic unpredictable stress, *GPx* Glutathione peroxidase, *HGF-1* human gingival fibroblasts, *HSC* hepatic stellate cells, *i.p.* intraperitoneally, *LDL-c* cholesterol-LDL, *PG-LPS* Porphyromonas gingivalis, *OxS* oxidoselina-1,3,7(11)-trien-8-one, *ROS* reactive oxygen species, *SOD* superoxide dismutase, *SOD-3* superoxide dismutase-3, *TAG* triacylglycerol, *TBARS* thiobarbituric acid reactive substances, *TC* total cholesterol, *WT* wild type

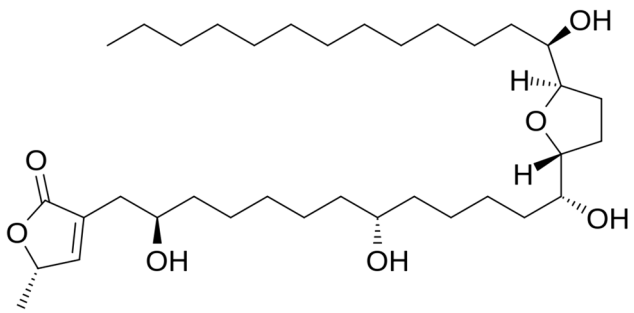

Fig. 2 Chemical structure of annonacin (type of acetogenin)

containing 90 mg of (+)-catechin and 60 mg of (-)-epicatechin on antioxidant enzymes and markers of oxidative stress in overweight individuals, they observed that the supplementation implied an increase in the plasmatic absorption capacity of oxygen radicals, attenuated LDL oxidation and DNA damage. Also, the antioxidant enzymes catalase, glutathione peroxidase, and catechins activities were increased [156]. Other studies reported similar results; this reinforces the antioxidant potential of guarana [166–168].

Anti-inflammatory activity was also observed in guarana, as elucidated by Maldaner et al. (2020); administering guarana extract (doses of 1,3,5,10 or 30 ug/kg) in the HFF-1 cell model noticed negative regulation of the expression of pro-inflammatory proteins and positive regulation of the expression of interleukin-10 [169]. Similarly, Machado et al. (2021) observed a reduction in the inflammatory marker tumor necrosis factor-alpha (TNF-α) when administering 90ug/mL of guarana extract free of methylxanthine and rich in tannin in THP-1 cells [167]. Guarana also has anti-inflammatory effects, so clinical trials with this powerful Amazonian fruit are needed to study its biological mechanisms and health effects.

Fruta-do-conde

Fruta-do-conde (*Annona squamosa L*), called custard apple, is cultivated worldwide in tropical and subtropical regions [170]. Commercially, bark, roots, leaves, stems, and seeds are used for pharmacological purposes and have been applied in treating dysentery, epilepsy, bleeding, and fever [171]. The seed powder was traditionally used to treat lice infestations, the leaf extract was applied to boils and ulcers, and the fruit was used to reverse vomiting and treat tumors [172]. Furthermore, its oil has a potent antiparasitic and antimalarial action [173]. Fruta-do-conde contains more than 18 phenolic compounds, mainly alkaloids or flavonoids [174], and is rich in bioactive compounds [172, 174, 175]. Due to its high protein and oleic and linoleic acid content, the seed has the best nutritional value [176]. Studies suggest custard apples can be a potent antioxidant, antimicrobial, antidiabetic, antiviral, anticancer, and hepatoprotective agent [172, 177].

Seyfried et al.[178] reported the beneficial effects of fruta-do-conde on breast cancer cells, including inhibition of migration and antiproliferative activity [178]. Fadholly et al. corroborated these results when studying the ethanolic extract of fruta-do-conde in human colon cancer cell lines [179]. The antidiabetic activity of the leaves of the fruit can be mediated by quercetin [180]. Davis et al. concluded that its antidiabetic activity occurred through increased glucose uptake, modulation of insulin signaling through inhibition of protein tyrosine phosphatase 1B, and stimulation of phosphorylation of insulin receptor-β and insulin receptor-1 substrate beyond the upregulation of GLUT4 [181]. Compounds from this fruit may have inhibitor effects of α-glucosidase and α-amylase [182].

Quercetin-3-O-glycoside in the leaves increases the antioxidant capacity associated with increased expression of superoxide dismutase and catalase [180]. Fruta-do-conde also has antimicrobial and antifungal capacity due to an active compound of acetogenin and certain flavonoid compounds [183, 184]. Recently, it was observed that it may prevent or treat neurodegenerative diseases since the extract of the seeds and pulp has inhibitory activity for acetylcholinesterase [185]. Limited but consistent data suggest that clinical trials using fruta-do-conde should be carried out in NCDs.

Bacuri

Bacuri (*Platonia insignis Mart*) is a native Brazilian Amazon species commonly used in South America in several food products, such as beverages, ice cream, and candies. Only the fruit pulp is used, and the peels and seeds are considered a waste product. Because of the sensory qualities of the fruit pulp, it is widely used in the production of beverages like juices and ice creams. It can also be eaten fresh, aligning with various culinary applications [186]. It is common in Brazil to use seed butter from bacuri to treat skin diseases since it can be used in a topical formulation with anti-inflammatory properties [187].

Bacuri has documented antioxidant activity and high α-glycosidase inhibitory capacity [188, 189]. Shells and seeds of bacuri can be used as phenolic-rich bioproducts obtained by a simple extraction method, increasing the value chain of this fruit. They observed the beneficial effects of the treatment with bacuri seed butter on body weight, growth, body mass index, lipid profile, atherosclerotic indices, and liver function in dyslipidemic hamsters [190, 191]. Moreover, bacuri positively affects glycemic control and reduces liver damage [186]. Ononin, an

Table 6 In vitro and in vivo studies regarding the effects of Graviola (*Annona muricata* L.)

References	Sample	Intervention	Results
Anti-inflammatory and Anti-oxidant effects			
Saraiva et al. 2022 [120]	Murine phagocytic immune cells and experimental LPS-induced acute lung injury (ALI)	Ethyl acetate fraction (EtOAc.f), n-butanol fraction (BuOH.f) from *A. muricata* L. leaves	In immune cells: both EtOAc.f and BuOH.f ↓ ROS, IL-6 In LPS-induced ALI: oral administration of EtOAc.f ↓ MPO activity in lung tissue
Han et al. 2023 [121]	Cisplatin-induced toxicity in macrophages	0–1,000 µg/ml *Annona muricata* leaf polysaccharides for 2 h and then incubated with cisplatin (0, 10, 15, and 20 µM) for 24 h	↓ Upregulation of BAX, cytosolic cytochrome c and caspases-3, − 8 and − 9 ↓ Bcl-2 levels ↓ ROS, mitochondrial apoptotic pathways
Anticancer effects			
Moghadamtousi et al. (2014) [114]	HCT-116 and HT-29 cancer cells	Treated with EEAM (10 µg /ml) for 24, 48 and 72 h	Cell cycle arrest at G_1 phase
Salsabila et al. 2021 [122]	4T1 breast cancer cells	*Annona muricata L.* extract (25 µg/mL) and doxorubicin	↓ ROS G2/M arrest AME decreased dox-induced senescence
Naik et al. 2021 [123]	Ascites carcinoma bearing mice	Leaf methanol extracts of *A. muricata* (100, 200 or 500 mg/kg b.wt.) for 10 days	↓ Solid tumor volume development by 58.11% and 65.70%, respectively
Rojas-Armas et al. 2022 [124]	Murine Model of Breast Cancer	Essential oil from *Annona muricata* leaves at doses of doses of 50, 100, and 200 mg/kg/day for 13 weeks	Doses of 100 and 200 mg/kg: ↓ in tumour frequency and tumour volume ↑ reduced glutathione (GSH) ↓ MDA
Antidiabetic effects			
Alsenosy et al. 2019 [125]	Streptozotocin-induced diabetic rats	Graviola (100 mg/kg/d) for four weeks	Restored testicular GSH levels and Total SOD activities ↓ testicular *Bax* and *IL-1β* expressions ↑ *CYP17A1* expression ↑ testicular testosterone and estradiol levels
Son et al. 2021 [126]	C57BL/6 male mice diabetes induced with high-fat diet + two-times streptozotocin (STZ) injection	*Annona muricata extract* (50 or 100 mg/kg) by gavage for 9 weeks	↓ glucose plasma levels, HbA1c ↓4-HNE in 100 mg/kg group 50 mg/kg group improved hepatic morphology
Ojo et al. 2022 [127]	Diabetic rats (alloxan induced)	Aqueous extract of *Annona muricata* peels (6.76, 13.53, 27.06 mg/kg) for 21 days	All doses: ↓ Fasting blood glucose ↑ Serum insulin and HOMA-β levels ↓Homa- IR, TG, VLDL-c, LDL-c, and total cholesterol,↑HDL-c ↓IL-6, TNF, and NF-κB levels
Others effects			
Oridupa et al. 2021 [128]	Experimentally-induced hypertensive male Wistar rats	*A. muricata* extract at 100, 200 or 400 mg/kg for 42 days	↓ Blood pressure, leukocyturia, proteinuria and ketonuria

Table 6 (continued)

References	Sample	Intervention	Results
Abdul Wahab et al. 2023 [129]	Male Wistar rats	*Annona muricata* leaf extract (100, 200 and 400 mg/kg), daily for 14 days	↓ neutrophil migration, ROS production, phagocytic activity and expression of CD11b/CD18 integrin ↓ ceruloplasmin, MPO and lysozyme expressions ↓ T and B lymphocytes proliferation, Th1 and Th2 cytokine production, CD4 + and CD8 + co-expression, immunoglobulins (IgM and IgG) expression
Helal and Abd Elhameed et al. 2021 [130]	Acetic acid (AA)-induced ulcerative colitis (UC) in rats	Graviola (100 mg/kg/day) for 7 days	↓ colonic damage ↓ nitric oxide, MDA levels MPO activity ↑ reduced glutathione (GSH) content ↓ expression of Bax and caspase-3 ↓ mRNA expression of Wnt1
Shukry et al. 2020 [131]	Mono Sodium Glutamate-Induced Hepatic Injury in rats	Graviola (200 mg/kg) for 4 weeks	↓ MDA, ROS, nitric oxide, hydrogen peroxide (H_2O_2), IL-6 level, P53, hepatic cellular damage, caspase-3, and B-cell lymphoma 2 (BCL-2)-like protein 4 (Bax), iNOS ↑ SIRT1

MPO myeloperoxidase, *HbA1c* hemoglobin A1c, *4-HNE 4-Hydroxynonenal*, *EEAM* ethyl acetate extract of Annona muricata leaves, *MDA* malondialdehyde, *Wnt1* Wnt family member1, *SOD* total superoxide dismutase, *GSH* glutathione, *TNF* tumor necrosis factor

isoflavone glycoside from bacuri, has antifungal activity against several *Candida* species [192].

Bacaba

Bacaba (*Oenocarpus bacaba Mart.*) is a palm native to the Amazon rainforest in northern Brazil, such as Tocantins, Pará, and Amazonas, also known as "bacabas verdadeiras", "red bacaba", "bacaba-açu", "bacaba-de-azeite", and "bacabão" [193]. The fruit pulp is consumed in nature, frozen, as jam, ice cream, energy drinks, edible oils, and fermented drinks. Bacaba is rich in bioactive compounds [81, 194]. Although it can be an excellent source of phenolic compounds with potential health benefits, they have yet to be much explored. Bacaba may control inflammatory processes in cardiovascular processes [195, 196]. It has been observed that a rich-phenolic extract from *Oenocarpus bacaba* induced apoptosis in a breast cancer cell line through a mitochondria-dependent pathway [197].

Ingá

Ingá (*Inga vera* and *Inga laurina*) belongs to the Fabaceae family and comprises about 300 species, whose name derives from the indigenous terminology "Angá" or "ingá" which means "seed is involved." Inga species are rich in myricetin, which has shown potent antioxidant properties and antitumor activity [191]. Amazonian indigenous communities use several species of the Inga genus to treat injuries, pain, and inflammations; they also use it as antipyretic and antirheumatic agents, which is directly related to the presence of phenolic compounds in these species [198]. Studies have been performed to evaluate the cytotoxicity, genotoxicity, antigenotoxicity and chemoprevention effects of flavonoids myricetin-3-O-(2″-O-galloyl)-α-rhamnopyranoside and myricetin-3-rhamnoside from Inga laurina leave extract. Researchers have observed the induction of the enzyme quinone reductase and demonstrated a protective effect against damage induced by hydrogen peroxide in the antigenotoxicity test [199, 200]. Lima et al. explored the effects of the ethanolic extract from I. laurina seeds against cancer cell lines (HepG2, HT-29, and T98G). They observed eliminating ROS, DNA repair, tumor protein expression, and apoptosis, suggesting potential effect antitumor [191].

Araçá

Araçá (*Eugenia stipitata* McVaugh) is an evergreen fruit tree native to the Western Amazon. It comprises more than 500 species, of which 400 are found in Brazil [133, 201, 202]. Araçá-boi, or arazá, is an edible fruit with a sour taste; because of this, industrial processing has emerged

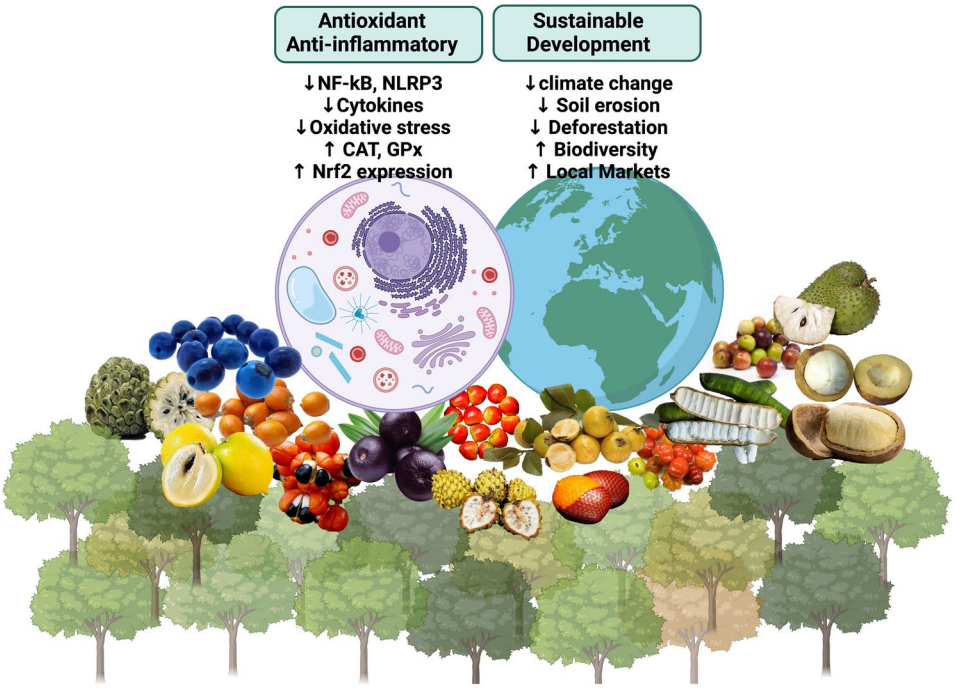

Fig. 3 Fruits from the Amazon Rainforest are rich in phenolic compounds and have antioxidant and anti-inflammatory properties, also, exploring these fruits may be a powerful tool for forest conservation. Created by BioRender

as an approach to improve its commercial market through the production of juice, nectars, syrup, ice creams, and jams [203–205]. Few studies have investigated the phytochemical composition of edible parts of araçá fruits [206, 207]. Although Neri-Numa et al.[207] observed that araçá extract did not exhibit antiproliferative effects against tumor cell lines of different human tissues, they found antimutagenic activity and antigenotoxic effect of araçá in Swiss albino mice [207]. Essential oil from the fruit may have antibacterial and antiprotozoal effects [208].

Buriti

The pulp and seeds of buriti (*Mauritia flexuosa* L.f.) can be used for several purposes that can benefit health [209]. It is rich in bioactive compounds and has antimicrobial, prebiotic, antidiabetic, and anticancer properties [210–212]. In general, the quantification of bioactive compounds varies in the different parts of buriti and its juice, oil, and flour [209]. β-carotene represents the main fraction of carotenoids, and buriti oil has plenty of α-tocopherol [213, 214]. Ascorbic acid is another antioxidant present in the pulp in high concentrations [215]. The fruit is also rich in fibers and minerals [209, 210, 213, 216, 217].

Given the nutraceutical properties of buriti, its potential health effects need studies [211]. It was reported that those that received buriti oil had lower low-density lipoprotein and hemoglobin, increased monocytes, serum superoxide dismutase activity, and liver glutathione peroxidase, demonstrating systemic antioxidant protection in this animal model with iron overload [218]. Another study in rats evaluated the consumption of cookies made with 15% refined buriti oil and found that rats fed with cookies showed increased serum and liver levels of retinol and lower total and LDL cholesterol [219].

Bicalho et al. developed a dairy by-product nutritional supplement with buriti fruit to improve malnutrition in mice and older women in a long-term care facility. They found an improvement in anthropometric parameters with higher serum albumin and better lipid profile. In older women, buriti increased hemoglobin [220]. Finally, buriti reduces MPO and ALP and significantly increases intestinal short-chain fatty acid (SCFA) levels [139].

Biribá

Biribá (*Annona mucosa*) is a rich source of bioactive compounds [6, 221–223] that have antioxidant [223], antimicrobial activities [224], and anticancer [225, 226], which is attributed to the anticancer effects. Although biribá reduces ATP production in the tumor cells [227], no animal experiments or published clinical trials have yet studied the use of biribá.

Abiu

Abiu (*Pouteria caimito*) has anti-inflammatory and ROS-scavenging properties [228, 229]. However, only one study evaluated the effects of abiu pulp on physiological parameters in rats and found a reduction in total leukocytes compared to the control group [230]. Meira et al. reported that administering ethanolic extract of abiu leaves in rats effectively against inflammatory pain and anti-hypersensitive action [231].

Final Remarks

The present review gathers information about the composition and beneficial effects of different fruits from the Amazon. Some limitations of the present study include the need for more information regarding the composition and utilization of the fruits. Additionally, during the research process, disease names such as cardiovascular diseases, diabetes, obesity, and chronic kidney disease were not used in isolation.

According to the concept of FAM, several Amazonian fruits can be used as nutritional strategies for preventing and treating NCDs. Camu-camu, açaí, tucumã, graviola, pitanga, fruta-do-conde, guaraná, and cupuaçu are rich in phenolic compounds and have antioxidant and anti-inflammatory properties. These super fruits can prevent NCDs, conserve forests, promote sustainable development, and strengthen indigenous communities and local food markets (Fig. 3). Studies on how regular consumption of Amazonian fruits can modify an intermediate inflammatory phenotype can potentially reduce the global burden of NCDs. Deforestation of Amazonas to create more land for industrial cattle farming and red meat production is a significant threat to sensitive Amazon ecosystems and the overall planetary health. As an alternative to these destructive behaviors, the Brazilian government should stimulate the indigenous population to organize harvesting and use the powerful Amazonian fruits loaded with bioactive nutrients. Such a paradigm shift may be an unprecedented "win–win" opportunity for improving our health and the environment [232]. Studies of the Amazon fruits may be "lowing hanging fruits to pick."

Acknowledgements This work was supported, in part, by the Conselho Nacional de Pesquisa (CNPq), Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), and Fundação de Amparo à Pesquisa do Estado do Rio de Janeiro (FAPERJ).

Author Contributions Ligia S Lima and Denise Mafra performed conceptualization and design. Material preparation, data collection, writing, and analysis were performed by Ligia S Lima, Márcia Ribeiro, Ludmila FMF Cardozo, Nara X Moreira, Peter Stenvinkel, and Denise Mafra. Writing—review and editing were performed by all authors. Denise Mafra performed supervision. L.S.L.: Design Research, Conducted Research, Analyzed Data, and Wrote Paper. M.R.; L.F.M.F.C.; N.X.M.; P.S.: Design Research, Conducted Research, and Wrote Paper. A.J.T.: Analyzed Data. D.M.: Design Research, Conducted Research, Analyzed Data, Wrote Paper, and Had Primary Responsibility for Final Content. All authors read and approved the final version of the manuscript.

Funding Conselho Nacional de Pesquisa (CNPq), Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), and Fundação de Amparo à Pesquisa do Estado do Rio de Janeiro (FAPERJ) support Denise Mafra research.

Compliance with Ethical Standards

Conflict of Interest The authors declare no conflict interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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