Antioxidant, Hypoglycemic and Neuroprotective Activities of Extracts from Fruits Native to the Amazon Region: A Review

Klenicy Kazumy de Lima Yamaguchi¹ and Anderson de Oliveira Souza¹*

¹Federal University of Amazonas, Institute of Health and Biotechnology – Coari/AM, Brazil.

Authors’ contributions

This work was carried out in collaboration between both authors. Both authors equally worked during elaboration of manuscript, as in conceptualization, methodology, formal analysis, data curation, writing (original draft preparation) and writing (review and editing). Also, the authors read and approved the final manuscript.

Article Information

DOI: 10.9734/BJI/2020/v24i630119
Editor(s):
(1) Dr. Anil Kumar, Devi Ahilya University, India.
Reviewers:
(1) Mastewal Birhan Atanaw, University of Gondar, Ethiopia.
(2) Kumari Shubha, ICAR-RCER, India.
Complete Peer review History: http://www.sdiarticle4.com/review-history/61673

Received 28 July 2020
Accepted 03 October 2020
Published 22 October 2020

ABSTRACT

The Amazon forest has the largest biome on the planet, and it is estimated that only 16 to 20% of the identified animal, and plant biodiversity. Considering plant diversity, we will highlight the biological properties of the fruits extracts of Arecaceae, Caryocaraceae, Malvaceae, Myrtaceae, Sapindaceae, and Solanaceae’s families due to their significant biological actions. This review presents the antioxidant, glycemic control, and neuroprotective activities from ten fruit extracts distributed in six botanical families in the Amazon region. We obtained 801 publications (described from 2010 to 2020), of which 64 articles were selected by the benchmark previously chosen. The antioxidant effect was the dominant effect observed in the studies used for this review, followed by glycemic control and protective actions in neurons. This review provides a synopsis of the recent literature exploring the extracts from native fruits to the Amazon region that could efficiently prevent pathologies associated with oxidative stress, and cellular maintenance mechanisms.

Keywords: Amazonian extracts; nutrient-rich food; secondary metabolism; biological activities.

*Corresponding author: E-mail: andersonosouza@uol.com.br;
1. INTRODUCTION

Aging and the constant search for a better and healthier life reinforce the appreciation of natural products use as one of the most effective alternatives for scientific research [1]. Brazil is one of the most endowed countries in biodiversity globally, and the Amazon region stands out for the number of exotic fruits considered rich in bioactive substances associated with health benefits [2].

The diversity in the Amazon rainforest represents not only mineral wealth in soil [3] as well as a food source found in animals [4] and plant species [5]. Over time, the man discovered that plant consumption, mostly fruits, had high nutritional value and medicinal effect, currently among the most significant therapeutic agents obtained from nature [6].

Chemical properties of the substances present in these fruits’ pulps contain different constituents described in scientific literature as biomolecules capable of altering important cellular metabolic aspects. They have aroused the interest of research groups due to the beneficial properties for human organisms associated with prevention and a lower incidence of chronic and degenerative diseases [7,8].

Researchers have been encouraged to detect substances that can protect cells in the central nervous system. Recent studies suggest that phenolic compounds, flavonoids, carotenoids, terpenes, and inorganic molecules have significant therapeutic actions [9,10,11].

Essential compounds of the Amazon fruits with different proven properties, combined with in vitro and in vivo tests, contribute to the development of new treatments that present zero or significantly reduced adverse effects compared to current therapies. In this review, we compiled the results of scientific studies related to the antioxidant and hypoglycemic activities of Amazonian fruit extracts (10 native plants in 6 botanical families) and their possible contributions to commonly unrelated neuroprotective mechanisms. Thus, encouraging studies of synergistic interaction focused on this thematic.

2. NATIVE PLANTS OF THE AMAZON

Recent studies highlighted changes in consumption by claiming a “nutritional transition” occurring around the world. Focusing on the research on such a transition in the Brazilian Amazon, recent studies have explored diet changes in rural and traditional populations. Also, certain native fruits have gained a “cultural marker” status. They are wide consumed regardless of the urbanization rates [12] as some botanical families Areceaceae, Caryocaraceae, Malvaceae, Myrtaceae, Sapindaceae, and Solanaceae.

Palms (Areceaeae) are monocotyledonous flowering plant, often abundant in tropical and sub-tropical ecosystems with commercially and essential therapeutic species such as coconuts, area nuts, and date palms, as well as a large number of indoor and ornamental species [13]. About medicinal use, Areceaceae plants have various therapeutics actions [14]. Traditionally fruits are consumed fresh, boiled, or as juices [15], and some biologically active components included phenolics compounds (catechin, quercetin, gallic acid, rutin, coumaric acid, ferulic acid, chlorogenic acid, quinic acid, caffeic acid, cyanidin-3-O-glucoside, and cyanidin-3-O-rutinoside) [16,17,18,19,20], carotenoids (α-carotene, β-carotene, γ-carotene, lycopene, and xanthophylls) [16,7,21,22,20], flavonoids (anthocyanin, luteolin, apigenin, chrysin, myricetin, and kaempferol) [17,19,23] and fatty acids (palmitic and oleic acid) [24]. Some notable species belonging to this majestic plant family include edible and commercially significant members and forest species as Astrocaryum aculeatum Meyer, Bactris gasipaes Kunth, Euterpe oleracea Mart, and Mauritia flexuosa L. f.

Caryocaraceae is a small botanic family with exclusively neotropical distribution (Central and South America), but it is prevalent in the Amazon rainforest. The Caryocar genus has sixteen species, some of which have therapeutic [25,26] and economic potential [27], with fruits being a source of edible oil. Caryocar species, Caryocar brasiliense A.St.-Hil and Caryocar villosum (Aubl.) Pers are the most studied species because of the extensive use of its fruit as source nutritious (lipids 51.51%, proteins 25.27%, carbohydrates 8.33%, and fibers 2.2%) and therapeutic purposes. In the Amazonian region, only Caryocar villosum (Aubl.) Pers is present, and the local community consumes the pulp fruit for cooking with rice or regional dishes as a substitute for butter and soaps or cosmetic applications [28,27]. Studies have demonstrated the
identification of different compounds, such as phenolic compounds (gallic acid and ellagic acid [28,25] and carotenoids (lutein, antheraxanthin, zeaxanthin, and β-carotene) [6].

Around 1000 species in the world represent the family Malvaceae, distributed widely in tropical and temperature regions. The main spread of these family members, whose majority is widespread, is South America and present almost everywhere except the frigid areas [29]. Compounds from fruits such as flavonoids (flavan-3-ols, procyanidins, flavones, catechin, and epicatechin) [30] and fatty acids: palmitic acid, estearic acid, oleic acid, linoleic acid and α-linoleic acid [31] were characterized. *Theobroma grandiflorum* (Wild. ex Spreng.) Schum. is a Brazilian Amazon rainforest fruit, phylogenetically close to cocoa, with excellent flavor and high agro-economic potential, and the seeds are a product similar to chocolate [31].

The Myrtaceae is a large family of dicotyledonous woody plants containing over 5,650 species organized in 130 to 150 genera. The family is typical in many of the world’s biodiversity hotspots such as Southwestern Australia, and the Cerrado and Atlantic Rainforest in Brazil, where up to 90 species of Myrtaceae per hectare can be found [32]. In the Amazon region, *Eugenia stipitata* MacVaugh and *Myrciaria dubia* (HBK) McVaugh have fruits with a significant use history as edible and as traditional medicines [33,34]. Also, compounds like phenolic compounds (gallic acid) and carotenoid (lutein, α-carotene, β-carotene, cryptoxanthin, zeaxanthin, and zeinoxanthin) [33] have identified.

Sapindaceae is a tropical and subtropical family comprising approximately 2000 species, including many economically important species used for their fruits, e.g., guarana (*Paullinia cupana* Kunth), litchi (*Litchi chinensis* Sonn), longan (*Dimocarpus longan* Lour), and pitomba (*Talisia esculenta* (A. St.-Hil.) Radlk.), wood extraction (*Aesculus* sp) or as ornamentals (*Koelreuteria* sp) [35]. The consumption of *Paullinia cupana* Kunth is commercially exploited mainly by the soft drinks industry. However, it is also highly valued by the cosmetic and pharmaceutical industries [36] primarily by the compounds as phenolic compounds (epicatechin, catechin, and proanthocyanidin) [37,38] and alkaloid (caffeine) [37].

The family Solanaceae has 2,300 species, including many therapeutic (*Solanum sessiliflorum* Dunal) and economically important species, such as tomato, potato, and various peppers. The genus consists of herbs, shrubs, trees, lianas, or rarely epiphytes distributed throughout the world but is most abundant and widely distributed in Latin America’s tropical regions, mainly found in the Amazon forest [39,40]. The Solanaceae family is characteristically ethnobotanical and extensively used by humans as food, spice, and medicine [41]. Probably, the therapeutic effects are related to the compounds known as coumarins (p-coumaric acid, p-hydroxidihydrocumaric acid, vanillic acid, and 5-caffeoylquinic acid) [42,43], flavonoid (naringenin) [42], carotenoids (lycopene, α-carotene, and β-carotene), terpenes (bisabolol, phenylpropene, and apiole), and alkaloid (solasonine) [43].

3. ANTIOXIDANT, HYPOGLYCEMIC, AND NEUROPROTECTIVE EFFECT

In this section, we review our findings at species levels. We discuss current scientific evidence that might explain the uses of the extracts of fruits on the Amazon region to antioxidant, hypoglycemic, and neuroprotective actions (Table 1).

Antioxidants are molecules that can control the production of free radicals in living organisms, which may have an endogenous (superoxide dismutase, catalase, glutathione reductase, and other enzymes) or exogenous (through food, like tocopherols, ascorbic acid, polyphenols, selenium, and carotenoids) origins [44,45]. A free radical typically is defined as any species capable of independent existence (hence the term “free”) containing one or more unpaired electrons. Once derived from oxygen or nitrogen metabolism, they are known as reactive oxygen species (ROS) or reactive nitrogen species (RNS) that could attack the essential molecules in the cell, resulting in several cellular damages, such as DNA oxidation or the lysis of biological membranes [46,44].

The antioxidant acts as scavengers or neutralizers of ROS or RNS, making them potential agents to prevent oxidative stress, thereby playing a therapeutic role in various diseases including cancer, diabetes, and neurodegenerative diseases as well as aging [47].
Table 1. Bioactive compounds with antioxidant, hypoglycemic and neuroprotective action (*in vitro* and *in vivo* studies)

| Scientific name (common name) | Botanical family | Part | Chemistry class / Bioactive compound | Antioxidant activity | Hypoglycemic action | Neuroprotective activity |
|-------------------------------|------------------|------|---------------------------------------|----------------------|---------------------|-------------------------|
| Astrocaryum aculeatum Meyer (Tucumã) | Arecaceae | Pulp and peel | Phenolic compound: catechin [7], quercetin, gallic acid, rutin [7, 20], chlorogenic acid [20] and caffeic acid [7]. Carotenoids: β-carotene [7, 20]. Fatty acids: Palmitic and Oleic acid [24]. | *in vitro*: Murine macrophage RAW 264.7 cells culture were protected by ethanolic extracts at 30 μg/mL exposed to PHA [7]. Scavenging ROS in human lymphocytes exposed to H₂O₂ with IC₅₀ 11.24 μg/mL for ethanolic pulp extract and 8.98 μg/mL for ethanolic peel extract [20]. TRAP: 102.38 ± 4.8 μg/mL and 224.57 ± 3.9 ng/mL for ethanolic peel and pulp extracts [20]. | *in vitro*: α-amylase (IC₅₀ 2.9 mg of sample dw/mL of reaction) and α-glucosidase (IC₅₀ 1.7 mg of sample dw/mL of reaction) inhibitory activity of polyamide-purified extracts obtained by solid-phase extraction of native fruits and commercial frozen pulps [60]. | *in vitro*: N/R | *in vivo*: N/R |
| Scientific name (common name) | Botanical family | fruit / part | Chemistry class / Bioactive compound | Antioxidant activity | Hypoglycemic action | Neuroprotective activity |
|-------------------------------|------------------|--------------|--------------------------------------|-----------------------|---------------------|-------------------------|
| *Bactris gasipaes* Kunth (Pupunha) | Arecaceae | Pulp | Carotenoids: α-carotene [22], β-carotene [16, 22], γ-carotene; lycopene, and xanthophylls [22]. | *in vitro*: Scavenging ROS 11.6 ± 0.2 and 9.1 ± 0.3 µg carotenoids/mL for Yurimaguas and Ecuador aqueous extract varieties, respectively [96]. | *in vitro*: N/R | *in vitro*: N/R |
| *Caryocar villosum* (Aubl.) Pers (Piquiá) | Caryocaraceae | Pulp and peel | Phenolic compound: gallic acid and ellagic acid [25, 28]. Carotenoids: lutein, antheraxanthin, zeaxanthin and β-carotene [6]. | *in vitro*: Scavenging ROS (IC<sub>50</sub> 1.7 to 108 µg/mL) and RNS (IC<sub>50</sub> 0.05 to 0.59 µg/mL) at hydroethanolic extract [6]. Scavenging ROS IC<sub>50</sub> 8.52 ± 0.37 µg/mL<sup>−1</sup> at shell hydroethanolic extract and IC<sub>50</sub> 8.48 ± 0.49 µg/mL<sup>−1</sup> at pulp hydroethanolic extract [25]. | *in vitro*: N/R | *in vitro*: N/R |
| *Euterpe oleracea* Mart (Açai) | Arecaceae | Pulp | Phenolic compounds: catechin, gallic acid, chlorogenic acid, caffeic acid, [19], cyanidin-3-O-glucoside and cyanidin-3-O- | *in vitro*: *Caenorhabditis elegans* after exposed at açai aqueous | *in vitro*: Pretreatment of β cell with cyanidin-3-O-glucoside (0.5 µmol/L) | *in vitro*: SH-SY5Y cells culture were protected by açai |
| Scientific name (common name) | Botanical family | fruit / part | Chemistry class / Bioactive compound | Antioxidant activity | Hypoglycemic action | Neuroprotective activity |
|-------------------------------|-----------------|--------------|--------------------------------------|----------------------|---------------------|-------------------------|
| Rutinoside [18]. Flavonoid: anthocyanin, luteolin, apigenin and chrysin [19, 23]. | | | | Extract (100 mg/mL) for 48 hours showed scavenging ROS 79.61 ± 3.33 % inhibition [18]. Scavenging ROS (IC₅₀ 31.25 ± 2.31 ppm) at ethanolic extract [98]. in vivo: Caenorhabditis elegans exposed at açai aqueous extract (100 mg/mL) for 48 hours improved redox status under oxidative stress conditions [18]. Açai pulp intake (200 g/day) in healthy women for 4 weeks reduced the production of ROS [99]. Mice pretreated with açai pulp (200 g/kg) for 14 kg showed ability to control the response to oxidative stress induced by 5-FU [100]. | Prevented cell death induced by H₂O₂ (800 or 1,200 μmol/L) [97]. in vivo: Açai pulp intake (100 g twice daily) in healthy overweight population for 4 weeks reduced in fasting glucose levels and in total cholesterol [64]. Hydroethanolic extract at 5 μg/mL after exposed to rotenone [19]. SH-SY5Y cells culture were protected by açai hydroethanolic extract at 50 μg/mL after exposed to H₂O₂ [77]. PC12 cells culture were protected by açai aqueous extract (0.5 – 50 μg/mL) exposed to β-amyloid protein (0 – 50 μg/mL) for 48 hours [78]. in vivo: Freeze-dried açai poder intake (2 g/kg) in rats for 7 weeks showed neuromodulatory effects in critical brain regions involved in memory, cognition, and overall brain function | |
| Scientific name (common name) | Botanical family | fruit / part | Chemistry class / Bioactive compound | Antioxidant activity | Hypoglycemic action | Neuroprotective activity |
|-------------------------------|-----------------|--------------|--------------------------------------|----------------------|---------------------|-------------------------|
| *Eugenia stipitata* MacVaugh  | Myrtaceae       | Pulp and peel| Phenolic compound: gallic acid [33]. Carotenoid: lutein, α-carotene, β-carotene, cryptoxanthin, zeaxanthin and zeinoxanthin [33]. | in vitro: Scavening ROS (IC<sub>50</sub> 2.65 mg/L) at ethanolic extract [48]. Scavening ROS (IC<sub>50</sub> 0.69 ± 0.23 μg/mL) at ethanolic extract [49]. | in vitro: N/R | in vitro: N/R in vivo: N/R |
| *(Araçá-boi or Araza)*       |                 |              |                                      |                      |                     |                         |
| *Mauritia flexuosa* L. f. (Buriti) | Arecaceae      | Pulp         | Phenolic compound: coumaric acid, ferulic acid, caffeic acid, protocatechuic acid chlorogenic acid and quinic acid [17]. Flavonoids: catechin, epicatechin, apigenin, luteolin, myricetin, kaempferol and quercetin [17]. Carotenoid: α-carotene, β-carotene and lutein [21]. | in vitro: Scavening ROS (IC<sub>50</sub> 704.21 ± 25.14 μg/mL) at methanolic extract [102]. | in vivo: N/R | in vitro: N/R in vivo: N/R |
|                              |                 |              |                                      |                      |                     |                         |

Mice were treated with acai juice (10 μL/g b.w. by gavage once a day) for 4 days significantly protects against convulsion PTZ-induced [81].
| Scientific name (common name) | Botanical family | fruit / part | Chemistry class / Bioactive compound | Antioxidant activity | Hypoglycemic action | Neuroprotective activity |
|--------------------------------|----------------|-------------|------------------------------------|----------------------|---------------------|------------------------|
| *Myrciaria dubia* (HBK) McVaugh (Camu-camu) | Myrtaceae | Pulp | Phenolic compound: ellagic acid [34] [105], catechin, delphinidin 3-glucoside, cyanidin 3-glucoside, rutin [105] and proanthocyanidins [107]. Flavonoids: quercetin, myricetin [105] and catechin [34] [105]. Organic compound: Ascorbic acid [107]. | *in vitro*: The total antioxidant activity of camu-camu was 9.72 of fruit/g of DPPH, with EC$_{50}$ 116.71 μg/mL [106]. | *in vivo*: N/R | *in vitro*: N/R |
| *Paullinia cupana* Kunth (Guarana) | Sapindaceae | fruit | Phenolic compound: epicatechin, catechin [37] and proanthocyanidin [38]. Alkaloid: caffeine [37]. | *in vitro*: Daily intake of 3 g guarana powder containing 90 mg | *in vitro*: N/R | *in vitro*: Exposition of aqueous extract (1 mg/mL) for 24 hours |
| Scientific name (common name) | Botanical family | fruit / part | Chemistry class / Bioactive compound | Antioxidant activity | Hypoglycemic action | Neuroprotective activity |
|-------------------------------|------------------|-------------|----------------------------------------|---------------------|--------------------|------------------------|
|                               |                  |             |                                        | catechin and 60 mg epicatechin was able to reduce H₂O₂ induced DNA damage in lymphocytes, as well as promoting an increase in the activities of catalase and glutathione peroxidase at 1 hour post-dose [109]. TRAP: 0.01 – 10 μg.mL⁻¹ for hydroethanolic guarana extract [110]. Exposition of low-level laser therapy (4 J/cm²) and hydroethanolic guarana extract (5 μg/mL) for 72 hours significantly decreased protein carbonylation, lipoperoxidation and DNA oxidation in human dermal fibroblastos cells culture with guarana [111]. | polyphenol fraction obtention (SPP) of guarana powder showed α-glucosidase inhibition IC₅₀ 1.624 μg GAE/mL (IBPP) and IC₅₀ 9.504 μg GAE/mL (SPP) [38]. | in SH-SY5Y cells culture promoted the protection against protein glycation and aggregation β-amyloid [37]. |
|                               |                  |             |                                        | in vivo: N/R | | |
|                               |                  |             |                                        | in vivo: | Multivitamin and mineral complex with guarana (222.2 mg per tablet) consumed 1 hour prior to moderate-intensity exercise can improve cognitive performance up to 90 min post-exercise in humans [83]. | | |
| Scientific name (common name) | Botanical family | fruit / part | Chemistry class / Bioactive compound | Antioxidant activity | Hypoglycemic action | Neuroprotective activity |
|-------------------------------|-----------------|--------------|--------------------------------------|----------------------|---------------------|-------------------------|
| **Solanum sessiliflorum** Dunal (Cubiu) | Solanaceae | Pulp | Coumarins: $p$-coumaric acid, $p$-hydroxidihydrocumaric acid [42], vanilic acid and $5$-caffeoylquinic acid [43]. Flavonoid: naringenin [42]. Carotenoids: lycopene, $\alpha$-carotene and $\beta$-carotene [43]. Terpene: bisabolol, phenylpropene and apiol [43]. Alkaloid: solasonine [43]. | in vitro: N/R Scavenging ROS ($IC_{50}$ 606.3 ± 3.5 $\mu$g/mL) at hydroethanolic extract [113]. | in vivo: N/R | in vitro: N/R |
| **Theobroma grandiflorum** (Wild. ex Spreng.) Schum. (Cupuaçu) | Malvaceae | Pulp | Flavonoids: flavan-3-ols, procyanidins, flavones, catechin, and epicatechin [30]. Fatty acids: palmitic acid, estearic acid, oleic acid, | Consumption of hydromethanolic cupuaçu extract (7.2 g/kg b.w.) for 40 days reduced lipid | in vitro: N/R | in vivo: N/R |

The study showed a significant association between lower levels of advanced oxidative protein product and habitual guarana consumption by an elderly population residing in the Amazon Riverine region (Brazil) [112].

In vivo: Intake of cubiu (250, 375 and 500 mg/kg b.w. for 14 days) reduced the lipid peroxidation induced by DXR in liver and heart of rats [39].

In vitro: N/R

Hydromethanolic cupuaçu extract (7.2 g/kg b.w.) in STZ-
| Scientific name (common name) | Botanical family | fruit / part | Chemistry class / Bioactive compound | Antioxidant activity | Hypoglycemic action | Neuroprotective activity |
|-------------------------------|-----------------|--------------|--------------------------------------|----------------------|---------------------|-------------------------|
|                               |                 |              | linoleic acid and α-linoleic acid [31]. | peroxidation induced by STZ in rats [31]. Scavenging ROS (DPPH 1913 ± 228 μmol TE/100 g DW) at hydromethanolic extract [31]. | diabetic rats for 40 days demonstrated positive effects on lipid profile [31]. |                                                         |

Legend: 5-FU: 5-Fluorouracil. DPPH: 2,2-Diphenyl-1-picrylhydrazyl. DXR: doxorubicin. DW: dry weight. GAE: gallic acid. NPSH: non-protein sulfhydryl. PHA: phytohemagglutinin. ROS: reactive oxygen species. RNS: reactive nitrogen species. Scavenging ROS or RNS (antioxidant action) by DPPH test. STZ: streptozotocin. TE: Trolox equivalent. TRAP: Total radical-trapping. N/R: not reported
This review shows studies with *in vitro* antioxidant assay based on the reduction of the 2,2-diphenyl-1-picrylhydrazyl (DPPH) free radical in all plant species. Ethanolic *Eugenia stipitata* MacVaug [48,49] and hydroethanolic *Caryocar villosum* (Aubl.) Pers extracts [6,25] showed the most significant capacity to stabilize radicals at a lower concentration, exhibited half-maximal inhibitory concentration (IC50) 0.69 µg/mL for reactive oxygen species (ROS) and 0.05 µg/mL for reactive nitrogen species (RNS), respectively. Exceeding the antioxidant capacity of methanolic *Malpighia umbellata* Rose fruits extract (20.51 µg/mL) [50] or isolated molecules such as chlorogenic acid (2.1 µg/mL) and caffeic acid (1.44 µg/mL) in methanolic solution [51]. *In vivo* assays provide various information regarding the antioxidant ability like the oil extracted from *Astrocaryum aculeatum* Meyer (500, 1000 and 2000 mg/kg b.w.) [52] showed a significant antioxidant effect in mice exposed to doxorubicin (DXR) and the ingestion of *Solanum sessiliflorum* Dunal pulp (250, 375 and 500 mg/kg b.w. for fourteen days) reduced the lipoperoxidation in rats exposed to DXR [39] demonstrated a critical antioxidant effect concerning the study with *Mimosa pudica* L. (400 mg/kg b.w.) [53], *Centella asiatica* (L.) Urb. (500 mg/kg b.w.) [54] and *Taraxacum officinale* (L.) Weber ex F.H. Wigg (500 mg/kg/day) [55] in model animals against oxidative stress damage.

Glycemic control remains a delicate balancing act in animals, mainly in humans. The diabetic patient is responsible for maintaining euglycemic blood glucose levels, a goal requiring education, decision strategies, and the wisdom to avoid hyper- and hypoglycemia that could be lethal [56]. In diabetic patients, the persistent homeostatic glucose mismatch promotes a variety of secondary complications, including cardiovascular diseases [57], retinopathy, and associated blindness, neuropathies that can cause amputations and kidney diseases [58]. Besides, studies showed neurodegeneration and cognitive decline in insulin-resistant patients who do not show hyperglycemia (pre-diabetes), concluding that hyperglycemia as crucial as the loss of insulin action [59].

Recently, α-glucosidase inhibition in the modulation of carbohydrate digestion has been investigated, thereby delaying postprandial glycemia, which is an efficient way to control the early stages of type 2 diabetes. *In vitro* studies were predominant with α-glucosidase inhibitors as *Astrocaryum aculeatum* Meyer native fruits and commercial frozen pulps, which presented IC50 1.7 mg of sample dw/mL of reaction [60], *Myrciaria dubia* (HBK) McVaug pulp exhibited IC50 5.57 µg/mL of reaction [61], and *Paullinia cupana* Kunth demonstrated soluble polyphenol fraction IC50 9.504 µg GAE/mL [38] a stronger inhibitory potency than acarbose IC50 250.49 µg/mL [62] or hydroethanolic *Eugenia uniflora* L. extracts IC50 66.3 µg/mL [63]. *In vivo* tests to verify the hypoglycemic effect, *Euterpe oleracea* Mart pulp intake (100 g twice daily for four weeks) in a healthy overweight population [64] and *Myrciaria dubia* (HBK) McVaug pulp intake (25 mL pulp juice daily for twelve weeks) in obese rats reduced glucose levels demonstrated necessary therapeutic actions [8]. However, lower proportions (dose per period) compared with studies in *Silybum marianum* (L.) Gaertn (140 mg three times daily for forty-five days) [65], *Capparis spinosa* L. fruit extract (1200 mg daily for two months) [66], *Zingiber officinalis* Roscoe powder (3000 mg daily for three months) [67] or *Berberis vulgaris* L. (200 mL juice daily for eight weeks) [68] which improved the glycemic indices in patients with type 2 diabetes. Also, hydroethanolic *Theobroma grandiflorum* (Wild. ex Spreng.) Schum. extract (7.2 g/kg b.w. for forty days) demonstrated positive effects on lipid profile in streptozotocin-diabetic rats [31]. Still, reduced hypoglycemic activity compared to leaves’ extract of *Bauhinia variegata* (L.) Benth (0.2 and 0.4 g/kg for seven days) or metformin (0.5 g/kg for seven days) [69].

Neuroprotection is a widely studied treatment option for central nervous system disorders, as neurodegenerative diseases. The essential pathological mechanisms in brain damage are inflammatory reaction, blood-brain barrier disruption, oxidative stress, and neuronal apoptosis [70,71,72,73]. Studies suggest the therapeutic effects of various natural antioxidants against cerebral damage [74,75,76]. *In vitro* studies with hydroethanolic *Euterpe oleracea* Mart extract at 5 and 50 µg/mL protected SH-SY5Y and PC12 cells culture when verifying the neuroprotective action after exposure to rotenone, H2O2 and β-amylloid aggregation [19,77,78]. Also, aqueous *Paullinia cupana* Kunth extracts at 1 mg/mL promoted SH-SY5Y cells culture protection in front of protein glycation and aggregation β-amyloid [37].
Demonstrating significant therapeutic effect but at higher concentrations compared to Razadyne® (2.873 μg/mL) [79] used mainly in the treatment of Alzheimer’s disease or [6]-gingerol (2.94 μg/mL for 24 hours), a phenol compound found in fresh ginger (Zingiber officinale Roscoe) protected against β-amyloid cytotoxicity, apoptotic cell death and DNA fragmentation in SH-SY5Y cells [80]. Besides in vivo studies, Euterpe oleracea Mart juice (10 μL/g b.w. for four days) significantly protects mice against convulsion pentylenetetrazol-induced [81]. Aqueous Myrciaria dubia (HBK) McVaugh extract (5 mg/mL) for eight hours) reduced β-amyloid aggregation and neurotoxicity in dopaminergic neurons in Caenorhabditis elegans [82]. Ingestion of multivitamin and mineral complex with Paullinia cupana Kunth (222.2 mg per tablet) 1 hour before moderate-intensity exercise can improve cognitive performance in humans [83] in compared to drugs used to treat Alzheimer’s (Rivastigmine, 12 mg three times/day) [84], Parkinson’s (Levodopa, 25 – 100 mg three times/day) [85] or hydroethanolic Caryocar brasiliense A.St.-Hil extract (300 mg/kg b.w.) as cholinesterase inhibitor in rats [26] suggests a better therapeutic effect.

This review showed extracts of native fruits of the Amazon region, which demonstrated important antioxidant, hypoglycemic and neuroprotective actions based on in vitro and in vivo assays. It is possible to associate Amazonian fruits’ consumption with nutritional value and a potential nutraceutical in this context.

4. MATERIALS AND METHODS

Studies related to the presence of compounds with antioxidant, hypoglycemic, and neuroprotective activities of extracts from ten native fruits to the Amazon region (described in the period from 2010 to 2020) were identified by searching electronic databases such as Pubmed, Scielo, ScienceDirect, and Web of Science including publications in English, Spanish, and Portuguese. The studies eligible for this review included trials carried out on humans, animal models, or cell culture submitted to oxidative stress or effects induced by molecules involved in the etiology in metabolic disease, characterized by high blood glucose levels (hyperglycemia) and neurodegeneration.

The terms used as an inclusion criterion were “Amazonian fruits,” “Scientific name of the plant,” as well as the biological effects “antioxidant,” “hypoglycemic,” and “neuroprotective” extracts from Astrocaryum aculeatum Meyer, Bactris gasipaes Kunth, Caryocar villosum (Aubl.) Pers, Euterpe oleracea Mart, Eugenia stipitata MacVaugh, Mauritia flexuosa L. f., Myrciaria dubia (HBK) McVaugh, Paullinia cupana Kunth, Solanum sessiliflorum Dunal, and Theobroma grandiflorum (Wild. ex Spreng.) Schum. However, excluded studies involving leaves, roots, flowers, stem extracts, and documents with preliminary information related to technological processing and functional effects of extracts Amazonian plants missing. In this review, we reached out to 801 publications, of which 64 papers were selected (Fig. 1). After searching on the database, the family Areceaceae which represented by four different plant species (Astrocaryum aculeatum Meyer, Bactris gasipaes Kunth, Euterpe oleracea Mart, and Mauritia flexuosa L. f.), followed by the family Myrtaceae (Eugenia stipitata MacVaugh and Myrciaria dubia (HBK) McVaugh) with two representatives while the families Caryocaraceae (Caryocar villosum (Aubl.) Pers), Sapindaceae (Paullinia cupana Kunth), Solanaceae (Solanum sessiliflorum Dunal) and Malvaceae (Theobroma grandiflorum (Wild. ex Spreng.) Schum.) had one plant species representative each one.

Among the biological effects selected, studies showed antioxidant activity in all plant species. In contrast, the families Areceaceae (Bactris gasipaes Kunth), Caryocaraceae, Myrtaceae (Eugenia stipitata MacVaugh), and Solanaceae were ineffective to glycemic control. No studies with fruit extract and neuroprotective action founded using the families Areceaceae (Astrocaryum aculeatum Meyer, Bactris gasipaes Kunth, and Mauritia flexuosa L. f.), Caryocaraceae, Myrtaceae (Eugenia stipitata MacVaugh), Solanaceae, and Malvaceae. Hence, the families Areceaceae (Euterpe oleracea Mart), Myrtaceae (Myrciaria dubia (HBK) McVaugh), and Sapindaceae (Paullinia cupana Kunth) (Fig. 2) presented significant studies with bioactive antioxidant compounds, hypoglycemic and neuroprotective, as shown in Table 1.
5. CONCLUSION

This review provides an overview of native fruits to the Amazon region usually consumed by the local population or processed and marketed as a functional food. Recent studies with extracts of the species described here have shown significant antioxidants in all plant species. However, in the families, Arecaceae (Astrocaryum aculeatum Meyer, Bactris gasipaes Kunth, and Mauritia flexuosa L. f.), Caryocaraceae, Myrtaceae (Eugenia stipitata MacVaugh), Solanaceae, and Malvaceae showed only neuroprotective activities. However, the families Arecaceae (Euterpe oleracea Mart), Myrtaceae (Myrciaria dubia (HBK) McVaugh), and Sapindaceae (Paullinia cupana Kunth) presented significant studies with bioactive
antioxidant compounds, hypoglycemic and neuroprotective. Therefore, new research should be conducted considering the enormous potential in the mechanisms to protect against oxidative stress, hyperglycemia, or neuronal degeneration or even potentially delay and prevent associated pathologies through the consumption of fruits native to the Amazon region.

ACKNOWLEDGEMENTS

The authors are grateful to the UFAM (Federal University of Amazonas) and also thank two anonymous reviewers for their support through constructive critics and corrections on this manuscript.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Darios F, Stevanin, G. Impairment of lysosome function and autophagy in rare neurodegenerative diseases. J. Mol. Biol. in press; 2020. Available:https://doi.org/10.1016/j.jmb.2020.02.033
2. Costa RS, Santos OV, Lannes SCS, Casazza AA, Aliakbarian B, Perego P, Ribeiro-Costa RM, Conventi A, Silva Júnior JOC. Bioactive compounds and value-added applications of cupuassu (Theobroma grandiflorum Schum.) agroindustrial by-product. Food Sci. Technol. 2020;40:401-407. Available: https://dx.doi.org/10.1590/fst.01119
3. Souza JLLL, Fontes MPF, Gilkes R, Costa LM, Oliveira TS. Geochemical signature of Amazon tropical rainforest soils. Rev. Bras. Ciênc. Solo. 2018;42:e0170192. Available: http://dx.doi.org/10.1590/18069557rbcso20170192
4. Begossi A, Salivonchyk SV, Hallwass G, Hanazaki N, Lopes PFM, Silvano RAM, Dumaresq D, Pittock J. Fish consumption on the Amazon: A review of biodiversity, hydropower and food security issues. Braz. J. Biol. 2019;79:345-357. Available:https://doi.org/10.1590/1519-6984.186572
5. Moraes VH, Müller CH, Souza AGC, Antônio IC. Native fruits species of economic potential from the Brazilian Amazon. J. Appl. Botany. 1994;68:47-52. Available:https://agris.fao.org/agris-search/search.do?recordID=DE95H0092
6. Chisté RC, Freitas M, Mercadante AZ, Fernandes E. The potential of extracts of Caryocar villosum pulp to scavenge reactive oxygen and nitrogen species. Food Chem. 2012;135:1740-1749. Available:https://doi.org/10.1016/j.foodchem.2012.06.027
7. Cabral FL, Bernardes VM, Passos DF, Oliveira JS, Doleski PH, Silveira KL, Horvarth MC, Bremm JM, Barbisian F, Azzolin VF, Teixeira CF, Andrade CM, Cruz iBM, Ribeiro EE, Leal DBR. Astrocaryum aculeatum fruit improves inflammation and redox balance in phytohemagglutinin-stimulated macrophages. J. Ethnopharmacol. 2020;247:112274. Available:https://dx.doi.org/10.1016/j.jep.2019.112274
8. Nascimento OV, Boleti APA, Yuyama LKO, Lima ES. Effects of diet supplementation with camu-camu (Myrciaria dubia HBK McVaugh) fruit in a rat model of diet-induced obesity. An. Acad. Bras. Ciênc. 2013;85:355-363. Available: http://dx.doi.org/10.1590/S0001-37652013000500001
9. Lamarão CV, Gomes MLS, Martins GAS, Rolim CSS, Yamaguchi KKL, Saraiva-Bonatto EC, Silva CC, Veiga Júnior VF. Antioxidantes inorgânicos em frutos amazônicos. Braz. J. Dev. 2020;6:12237-12253. Available:https://doi.org/10.34117/bjdv6n3-184
10. Ayaz M, Sadiq A, Junaid M, Ullah F, Ovais M, Ullah I, Ahmed J, Shahid M. Flavonoids as prospective neuroprotectants and their therapeutic propensity in aging associated neurological disorders. Front. Aging Neurosci. 2019;11:155. Available: https://doi.org/10.3389/fnagi.2019.00155
11. Teles RBA, Diniz TC, Pinto TCC, Júnior RGO, Silva MG, Lavor EM, Fernandes AWC, Oliveira AP, Ribeiro FPRA, Silva AAM, Cavalcante TCF, Quintans Júnior LJ, Almeida JRG. Flavonoids as therapeutic agents in Alzheimer’s and Parkinson’s diseases: A systematic review of preclinical evidences. Oxid. Med. Cell. Longev. 2018;7043213.
12. Lima ACB. Flavors of the city: Acess to regional fruit and fruit consumption in the States of Acre, Brazil. Bol. Mus. Para. Emílio Goeldi. Cienc. Hum. 2014;9:79-92. Available:https://www.scielo.br/pdf/bgoeldi/v9n1/06.pdf

13. Eisenerdth WL, Svenning JC, Kissling WD, Balslev H. Geographical ecology of the palms (Arecaceae): Determinants of diversity and distributions across spatial scales. Ann. Bot. 2011;108:1391-1416. Available:https://doi.org/10.1093/aob/mcr146

14. Câmara-Leret R, Paniagua-Zambrana N, Svenning JC, Balslev H, Macía MJ. Geospatial patterns in traditional knowledge serve in assessing intelectual property rights and benefit-sharing in northwest South America. J. Ethnopharmacol. 2014;158:58-65. Available:https://doi.org/10.1016/j.jep.2014.10.009

15. Clement CR, Lleras Pérez E, Van Leeuwen J. O potencial das palmeiras tropicais no Brasil: Acertos e fracassos das últimas décadas. Agrociências. 2005;9:67-71. Available:https://www.embrapa.br/buscade-publicacoes/678989/o-potencial-das-palmeiras-tropicais-no-brasil-acertos-e-fracassos-das-ultimas-dcadas

16. Basto GJ, Carvalho CWP, Soares AG, Costa HTGB, Chávez DWH, Godoy RLO, Pacheco S. Physicochemical and carotenoid content of extruded and non-extruded corn and peach palm (Bactris gasipaes, Kunth). Food Sci. Technol. 2016;69:312-318. Available:https://doi.org/10.1016/j.lwt.2015.12.065

17. Bataglion GA, Silva FMA, Ebertlin MN, Kooen HHF. Simultaneous quantification of phenolic compounds in buriti fruit (Mauritia flexuosa L. f.) by ultra-high performance liquid chromatography coupled to tandem mass spectrometry. Food Res. Int. 2014;66:396-400. Available:https://doi.org/10.1016/j.foodres.2014.09.035

18. Bonomo LF, Silva DN, Boasquivis PF, Paiva FA, Guerra JFC, Martins TAF, Torres AGJ, Paula ITBR, Caneschi WL, Jacolot P, Grossin N, Tessier FJ, Boulanger E, Silva ME, Pedrosa ML, Oliveira RP. Açaí (Euterpe oleracea Mart.) modulates oxidative stress resistance in Caenorhabditis elegans by direct and indirect mechanisms. PLoS One. 2014;9:e89933. Available:https://doi.org/10.1371/journal.pone.0089933

19. Machado AK, Andreazza AC, Da Silva TM, Boligton AA, Do Nascimento V, Scola G, Doung A, Cadoná FC, Ribeiro EE, Cruz IBM. Neuroprotective effects of Açaí (Euterpe oleracea Mart.) against rotenone in vitro exposure. Oxid. Med. Cell. Longev. 2016;8940850. Available:https://doi.org/10.1155/2016/8940850

20. Sagrillo MR, Garcia LFM, Souza Filho OC, Duarte MMMF, Ribeiro EE, Cadoná FC, Cruz IBM. Tucumá fruit extracts (Astrocaryum aculeatum Meyer) decrease cytotoxic effects of hydrogen peroxide on human lymphocytes. Food Chem. 2015;173:741-748. Available:https://doi.org/10.1016/j.foodchem.2014.10.067

21. Cândido TLN, Silva MR, Agostini-Costa TS. Bioactive compounds and antioxidant capacity of Buriti (Mauritia flexuosa L.f.) from the Cerrado and Amazon biomes. Food Chem. 2015;177:313-319. Available:https://doi.org/10.1016/j.foodchem.2015.01.041

22. Jatunov S, Quesada S, Díaz C, Murillo E. Carotenoid composition and nitoxidante activity of the raw and boiled fruit mesocarp of six varieties of Bactris gasipaes. Arch. LatinoAm. Nutr. 2010;60:99-104. Available:https://www.alanrevista.org/ediciones/2010/1/art-15/

23. Yamaguchi KKL, Pereira LFR, Lamarno CV, Lima ES, Veiga-Júnior VF. Amazon Acai: Chemistry and biological activities: A review. Food Chem. 2015;179:137-151. Available:https://doi.org/10.1016/j.foodchem.2015.01.055

24. Santos MFG, Alves RE, Brito ES, Silva SM, Silveira MRS. Quality characteristics of fruits and oils of palms native to the Brazilian Amazon. Rev. Bras. Frutic. 2017;39:e305. Available:https://doi.org/10.1590/0100-29452017305

25. Yamaguchi KKL, Lamarão CV, Aranha ESP, Souza ROS, Oliveira PDA,
25

Vasconcellos MC, Lima ES, Veiga-Júnior VF. HPLC-DAD profile of phenolic compounds, cytotoxicity, antioxidant and anti-inflammatory activities of the Amazon fruit Caryocar villosum. Quim. Nova. 2017; 40:483-490. Available:https://doi.org/10.21577/0100-4042.20170028

26. Oliveira LM, Oliveira TS, Costa RM, Martins JLR, Freitas CS, Gil ES, Costa EA, Passaglia RCAT, Vaz BC, Filgueira FP, Ghedini PC. Caryocar brasiliense induces vasorelaxation through endotelial Ca2+/calmodulin and PI3K/Akt/eNOS-dependent signaling pathways in rats. Rev. Bras. Farmacogn. 2018;28:678-685. Available:http://dx.doi.org/10.1016/j.bjp.2018.07.007

27. Ascarí J, Takahashi JA, Boaventura MAD. The phytochemistry and biological aspects of Caryocaraceae. Rev. Bras. Plantas Med. 2013;15:293-308. Available:http://dx.doi.org/10.1590/S1516-05722013000200019

28. Chisté RC, Mercadante AZ. Identification and quantification, by HPLC-DAD-MS/MS of carotenoids and phenolic compounds from the Amazonian fruits Caryocar villosum. J. Agric. Food Chem. 2012;60:5884-5892. Available:https://doi.org/10.1021/jf301904f

29. Erarslan ZB, Koçyigit M. The important taxonomic characteristics of the family Malvaceae and the herbarium specimens in İSTE. Turk. J. Biosci. Collect. 2019;3:1-7. Available:http://doi.org/10.26650/tjbc.20190001

30. Avila-Sosa R, Montero-Rodríguez AF, Aguilar-Alonso P, Vera-López O, Lazcano-Hernández M, Morales-Medina JC, Navarro-Cruz AR. Antioxidant properties of Amazonian fruits: A mini review of in vivo and in vitro studies. Oxid. Med. Cell. Longev. 2019;8204129. Available:http://doi.org/10.1155/2019/8204129

31. Oliveira TB, Genovese MI. Chemical composition of cupuassu (Theobroma grandiflorum) and cocoa (Theobroma cacao) liquors and their effects on streptozotocin-induced diabetic rats. Food Res. Int. 2013;51:929-935. Available:http://doi.org/10.1016/j.foodres.2013.02.019

32. Grattapaglia D, Vaillancourt RE, Shepherd M, Thumma BR, Foley W, Kühlheim C, Potts BM, Myburg AA. Progress in Myrtaceae genetics and genomics: Eucalyptus as the pivotal genus. Tree Genet. Genomes. 2012;8:463-508. Available:https://doi.org/10.1007/s11295-012-0491-x

33. Garzón GA, Narváez-Cuenca CE, Kopec RE, Barry AM, Riedl KM, Schwartz SJ. Determination of carotenoids, total phenolic content, and antioxidant activity of Arazá (Eugenia stipitata McVaugh), an Amazonian fruit. J. Agric. Food Chem. 2012;60:4709-4717. Available:https://doi.org/10.1021/jf205347f

34. Chirinos R, Galarza J, Betalleluz-Pallardel I, Pedreschi R, Campos D. Antioxidant compounds and antioxidant capacity of peruvian camu-camu (Myrciaria dubia (H.B.K.) McVaugh) fruit at different maturity stages. Food Chem. 2010;120:1019-1024. Available:https://doi.org/10.1016/j.foodchem.2009.11.041

35. Buerki S, Forest F, Acevedo-Rodríguez P, Callimander MW, Nylander JAA, Harrington M, Sanmartin I, Küpfer P, Alvarez N. Plastic and nuclear DNA markers reveal intricate relationships at subfamilial and tribal levels in the soapberry family (Sapindaceae). Mol. Phylogenet. Evol. 2009;51:238-258. Available:https://doi.org/10.1016/j.ympev.2009.01.012

36. Marques LLM, Ferreira EDF, Paula MN, Klein T, Mello JCP. Paullinia cupana: A multipurpose plant – A review. Braz. J. Pharmacog. 2019;29:77-110. Available:https://doi.org/10.1016/j.bjp.2018.08.007

37. Bittencourt LS, Zeidán-Chuliá F, Yatsu FKJ, Schnorr CE, Morescó KS, Kolling EA, Gelain DP, Bassani VL, Moreira JCF. Guarana (Paullinia cupana Mart.) prevents β-amyloid aggregation, generation of advanced glycation-end products (AGEs), and acrolein-induced cytotoxicity on human neuronal-like cells. Phytother. Res. 2014;28:1615-1624. Available:https://doi.org/10.1002/ptr.5173

38. Pinaffi ACC, Sampaio GR, Soares MJ, Shahidi F, Camargo AC, Torres EAFS. Insoluble-bound polyphenols released from guarana powder: Inhibition of alpha-glucosidase and proanthocyanidin profile. Molecules. 2020;25:679.
Available:https://doi.org/10.3390/molecules20503679
39. Hernandes LC, Aissa AF, Almeida MR, Darin JDC, Rodrigues E, Batista BL, Barbosa Júnior F, Mercadante AZ, Bianchi MLP, Antunes LMG. In vivo assessment of the cytotoxic, genotoxic and antigenotoxic potential of maná-cubiu (Solanum sessiliflorum Dunal) fruit. Food Res. Int. 2014;62:121-127. Available:https://doi.org/10.1016/j.foodres.2014.02.036
40. Coelho CP, Gomes DC, Guilherme FAG, Souza LF. Reproductive biology of endemic Solanum melissarum Bohs (Solanaceae) and updating of its current geographic distribution as the basis for its conservation in the Brazilian Cerrado. Braz. J. Biol. 2017;77:809-819. Available:https://doi.org/10.1590/1519-401520175204159.2006.03907.x
41. Shah VV, Shah ND, Patrekar PV. Medicinal plants from Solanaceae family. Res. J. Pharm. Technol. 2013;6:143-151. Available:https://www.researchgate.net/publication/298170398_Medicinal_plants_from_solanaceae_family
42. Cardona JEC, Cuca LE, Barrera JA. Determination of some secondary metabolites in three ethnovarieties of cocona (Solanum sessiliflorum Dunal). Rev. Colomb. de Química. 2011;40:185-200. Available:http://www.scielo.org.co/scielo.php?script=sci_arttext&pid=S0120-280420110000200004
43. Kaunda JS, Zhang Y-J. The Genus Solanum: An ethnopharmacological, phytochemical and biological properties review. Nat. Products Bioprospect. 2019;9:77-137. Available:https://doi.org/10.1007/s13659-019-0201-6
44. Halliwell B. Oxidative stress and neurodegenerative: where are we now? J. Neurochem. 2006;97:1634-1658. Available:https://doi.org/10.1111/j.1471-4159.2006.03907.x
45. Sousa CMM, Silva HR, Vieira-Jr GM, Ayres MCC, Costa CLS, Araújo DS, Caivalcante LCD, Barros EDS, Araújo PBM, Brandão MS, Chaves MH. Fenóis totais e atividade antioxidante de cinco plantas medicinais. Quim. Nova. 2007;30:351-355.

Available:https://doi.org/10.1590/S0100-40422007000200021
46. Ferreira ALA, Matsubara LS. Radicais livres: Conceitos, doenças relacionadas, sistema de defesa e estresse oxidativo. Rev. Ass. Med. Bras. 1997;43:61-68. Available:https://www.scielo.br/pdf/ramb/v43n1/2075.pdf
47. Apak R, Özyürek M, Güçlü K, Çapanoglu E. Antioxidant activity/capacity measurement. Reactive oxygen and nitrogen species (ROS/RNS) scavenging assays, oxidative stress biomarkers, and chromatographic/chemometric assays. J. Agric. Food Chem. 2016;64:1046-1070. Available:https://doi.org/10.1021/acs.jafc.5b04744
48. Álvarez A, Jiménez A, Méndez J, Murillo E. Chemical and biological study of Eugenia stipitata Mc Vaugh collected in the Colombian Andean Region. Asian J. Pharm. Clin. Res. 2018;11:362-369. Available:https://doi.org/10.22159/ajpcr.2018.v11i12.27253
49. Neri-Numa IA, Carvalho-Silva LB, Morales JP, Malta LG, Muramoto MT, Ferreira JEM, Morales JP, Malta LG, Carvalho-Silva LB, Maróstica Junior MR, Muramoto MT. Evaluation of the antioxidant, antiproliferative and antimutagenic potential of araçá-boi fruit (Eugenia stipitata Mc Vaugh - Myrtaceae) of the Brazilian Amazon forest. Food Res. Int. 2013;50:70-76. Available:https://doi.org/10.1016/j.foodres.2012.09.032
50. Vasavilbazo-Saucedo A, Almaraz-Abarca N, González-Ocampo HA, Ávila-Reyes JA, González-Valdez LS, Luna-González A, Delgado-Alvarado EA, Torres-Ricario R. Phytochemical characterization and antioxidant properties of the wild edible acerola Malpighia umbellata Rose. J. Food. 2018;16:698-706. Available:https://doi.org/10.1080/19476337.2018.1475424
51. Abramovic H, Grobin B, Ulrih NP, Cigic B. Relevance and standardization of in vitro antioxidant assays: ABTS, DPPH, and Folin-Ciocalteu. J. Chem. 2018;4608405. Available:https://doi.org/10.1155/2018/4608405
52. Carneiro ABA, Pinto EJS, Ribeiro IF, Magalhães MRG, Neto MABM. Efeito da Astrocaryum aculeatum (Tucumá) na toxicidade da Doxorubicina: Modelo
experimental in vivo. Acta Paul. Enferm. 2017;30:233-239. Available:https://doi.org/10.1590/1982-0194201700036
53. Patro G, Bhattamisra SK, Mohanty BK, Sahoo HB. In vitro and In vivo antioxidant evaluation and estimation of total phenolic, flavonoidal content of Mimosa pudica L. Pharmacognosy Res. 2016;8:22-28. Available:https://doi.org/10.4103/0974-8490.171099
54. Kumar P, Baraiya S, Gaidhani SN, Gupta MD, Wanjari MM. Antidiabetic activity of stem bark of Bauhinia variegata in alloxan-induced hyperglycemic rats. J. Pharmacol. Pharmacother. 2012;3:64-66. Available:https://doi.org/10.4103/0976-500X.92518
55. Aremu OO, Oyedeji AO, Oyedeji OO, Nkeh-Chungag BN, Rusike CRS. In vitro and In vivo antioxidant properties of Taraxacum officinale in N-Nitro-L-Arginine Methyl Ester (L-NNAME)-induced hypertensive rats. Antioxidants. 2019;8:309. Available:https://doi.org/10.3390/antiox8080309
56. Perlmutter LC, Flanagan BP, Shah PH, Singh SP. Glycemic control and hypoglycemia. Diabetes Care. 2008;10:2072-2076. Available:https://doi.org/10.2337/dc08-1441
57. Kim JH, Bae HY, Kim SY. Clinical marker of platelet hyperreactivity in diabetes mellitus. Diabetes Metab. J. 2013;37:423-428. Available:https://doi.org/10.4093/dmj.2013.37.6.423
58. Pagliuca FW, Melton DA. How to make a functional β-cell. Development. 2013;140:2472-2483. Available:https://doi.org/10.1242/dev.093187
59. Kandimalla R, Thirumala V, Reddy PH. Is Alzheimer’s disease a type 3 Diabetes? A critical appraisal. BBA-Bioenergetics. 2017;1863:1078-1089. Available:https://doi.org/10.1016/j.bbadis.2016.08.018
60. Gonçalves AEDS, Lajolo FM, Genovese MI. Chemical composition and antioxidant/antidiabetic potential of Brazilian native fruits and commercial frozen pulps. J. Agric. Food Chem. 2010;58:4666-4674. Available:https://doi.org/10.1021/jf903875u
61. Fujita A, Sarkar D, Wu S, Kennely E, Shetty K, Genovese MI. Evaluation of phenolic-linked bioactives of camu-camu (Myrciaria dubia McVaugh) for antihyperglycemia, antihypertension, antimicrobial properties and cellular rejuvenation. Food Res. Int. 2015;77:194-203. Available:https://doi.org/10.1016/j.foodres.2015.07.009
62. Yin Z, Zhang W, Feng F, Zhang Y, Kang W. α-Glucosidase inhibitors isolated from medicinal plants. Food Sci. Hum. Wellness. 2014;3:136-174.
63. Vinholes J, Lemos G, Barbieri RL, Franzon RC, Vizzotto M. In vitro assessment of the antihyperglycemic and antioxidant properties of araçá, butiá and pitanga. Food Biosci. 2017;19:92-100. Available:https://doi.org/10.1016/j.foodres.2017.04.004
64. Udani JK, Singh BB, Singh VJ, Barrett ML. Effects of Açai (Euterpe oleracea Mart) berry preparation on metabolic parameters in a healthy overweight population: A pilot study. Nutr. J. 2011;10:45. Available:https://doi.org/10.1186/1475-2891-10-45
65. Ebrahimpour-Koujan S, Gargari BP, Mobasseri M, Valizadeh H, Asghari-Jafarabadi M. Lower glycemic indices and lipid profile among type 2 diabetes mellitus patients who received novel dose of Silybum marianum (L.) Gaertn. (silymarin) extract supplement: A triple-blinded randomized controlled clinical trial. Phytomedicine. 2018;44:39-44. Available:https://doi.org/10.1016/j.phymed.2018.03.050
66. Huseini HF, Hasani-Ranjbar S, Nayebi N, Heshmat R, Siganodi FK, Ahvazi M, Alaei BA, Kianbakht S. Capparis spinosa L. (Caper) fruit extract in treatment of type 2 diabetic patients: A randomized double-blind placebo-controlled clinical trial. Complement. Ther. Med. 2013;21:447-452. Available:https://doi.org/10.1016/j.ctim.2013.07.003
67. Shidfar F, Rajab A, Rahideh T, Khandouzi N, Hosseini S, Shidfar S. The effect of ginger (Zingiber officinale) on glycemic markers in patients with type 2 diabetes. J. Complement. Integr. Med. 2015;12:165-170. Available:https://doi.org/10.1515/jcim-2014-0021
68. Lazavi F, Mirrman P, Sohrab G, Nikpayam O, Angoorani P, Hedayati M. The barberry juice effects on metabolic factors and oxidative stress in patients with type 2 diabetes: A randomized clinical trial. Complement. Ther. Clin. 2018;31:170-174. Available:https://doi.org/10.1016/j.ctcp.2018.01.009

69. Kumari S, Deori M, Elancheran R, Kotoky J, Devi R. In vitro and In vivo antioxidant, anti-hyperlipidemic properties and chemical characterization of Centella asiatica (L.) extract. Front. Pharmacol. 2016;7. Available:https://doi.org/10.3389/fphar.2016.00400

70. Vajda JE. Neuroprotection and neurodegenerative diseases. J. Clin. Neurosci. 2002;9:4-8. Available:https://doi.org/10.1054/jocn.2001.031.201

71. Phaniendra A, Jestadi DB, Periyasamy L. Free radicals: Properties, sources, targets, and their implications in various disease. Indian J. Clin. Biochem. 2015;30:11-26. Available:https://doi.org/10.1007/s12291-014-0446-0

72. Zoerle T, Carbonara M, Zanier ER, Ortolano F, Bertani G, Magnoni S, Stocchetti, N. Rethinking neuroprotection in severe traumatic brain injury: Toward bedside neuroprotection. Front. Neurol. 2017;8:354. Available:https://doi.org/10.3389/fneur.2017.00354

73. Paloczi J, Varga ZV, Hasko G, Pacher P. Neuroprotection in oxidative stress-related neurodegenerative diseases: Role of endocannabinoid system modulation. Antioxid. Redox Signal. 2018;29:75-108. Available:https://doi.org/10.1089/ars.2017.7144

74. Dajas F, Rivera-Megret F, Blasina F, Arredondo F, Abin-Carriquiry JA, Costa G, Echeverry C, Lafon L, Heizen H, Ferreira M, Morquio A. Neuroprotection by flavonoids. Braz. J. Med. Biol. Res. 2003;36:1613-1620. Available:http://dx.doi.org/10.1590/S0100-879X2003001200002

75. Lalkovicová M, Danielisová V. Neuroprotection and antioxidants. Neural Regen. Res. 2016;11:865-874. Available:https://doi.org/10.4103/1673-5374.184447

76. González-Fuentes J, Selva J, Moya C, Castro-Vázquez L, Lozano MV, Marcos P, Plaza-Oliver M, Rodríguez-Robledo V, Santander-Ortega MJ, Villaseca-González N, Arroyo-Jimenez MM. Neuroprotective natural molecules, from food to brain. Front. Neurosci. 2018;12:721. Available:https://doi.org/10.3389/fnins.2018.00721

77. Torma PCMR, Brasil AVS, Carvalho AV, Jablonski A, Rabelo TK, Moreira JCF, Gelain DP, Filóres SH, Augusti PR, Rios AO. Hydroethanolic extracts from different genotypes of açaí (Euterpe oleracea) presented antioxidant potential and protected human neuron-like cells (SH-SY5Y). Food Chem. 2017;222:94-104. Available:https://doi.org/10.1016/j.foodchem.2016.12.006

78. Wong DYS, Musgrave IF, Harvey BS, Smid SD. Açaí (Euterpe oleracea Mart.) berry extract exerts neuroprotective effects against β-amylloid exposure in vitro. Neurosci. Lett. 2013;556:221-226. Available:https://doi.org/10.1016/j.neulet.2013.10.027

79. Castillo WO, Aristizabal-Pachon AF, Montaldi APL, Sakamoto-Hojo ET, Takahashi CS. Galanthamine decreases genotoxicity and cell death induced by β-amyloid peptide in SH-SY5Y cell line. Neurotoxicology. 2016;57:291-297. Available:https://doi.org/10.1016/j.neuro.2016.10.013

80. Lee C, Park GH, Kim CY, Jang JH. [6]-Gingerol attenuates β-amyloid-induced oxidative cell death via fortifying cellular antioxidant defense system. Food Chem. Toxicol. 2011;49:1261-1269. Available:https://doi.org/10.1016/j.fct.2011.03.005

81. Souza-Monteiro JR, Hámoy M, Santana-Coelho D, Arrifano GPF, Parãense RSO, Costa-Malaquias A, Mendonça JR, Silva RF, Monteiro WSC, Rogez H, Oliveira DL, Nascimento JLM, Crespo-López ME. Anticonvulsant properties of Euterpe oleracea in mice. Neurochem. Int. 2015;90:20-27. Available:https://doi.org/10.1016/j.neuint.2015.06.014

82. Azévedo JCS, Borges KC, Genovese MI, Correia RTP, Vattem DA. Neuroprotective effects of dried camu-camu (Myrciaria dubia) HBK McVaugh) residue in C. elegans. Food Res. Int. 2015;73:135-141. Available:https://doi.org/10.1016/j.foodres.2015.02.015
83. Veasey RC, Haskell-Ramsay CF, Kennedy DO, Wishart K, Maggini S, Fuchs CJ, Stevenson EJ. The effects of supplementation with a vitamin and mineral complex with guarana prior to fasted exercise on affect, exertion, cognitive performance, and substrate metabolism: A randomized controlled trial. Nutrients. 2015;7:6109-6127. Available:https://doi.org/10.3390/nu7085272

84. Massoud F, Léger GC. Pharmacological treatment of Alzheimer disease. Can. J. Psychiatry. 2011;56:579-588. Available:https://doi.org/10.1017/jcp.2011.25

85. Connolly BS, Lang AE. Pharmacological treatment of Parkinson disease. A review. JAMA. 2014;311:1670-1683. Available:https://doi.org/10.1001/jama.2014.109569

86. Kahn F. The genus Astrocaryum (Arecales). Rev. Peru. Biol. 2008;15:31-48. Available:http://www.scielo.org.pe/pdf/rpb/v15n1/a04v15s1.pdf

87. Felisberto MHF, Costa MS, Boas FV, Leivas CL, Franco CML, Souza SM, Clerici MTPS, Cordeiro LMC. Characterization and technological properties of peach palm (Bactris gasipaes var. gasipaes) fruit starch. Food Res. Int. in press; 2020. Available:https://doi.org/10.1016/j.foodres.2020.109569

88. Tostes LCL, Lins ALFA, Santos AHO, Guimarães JRS, Ferreira AMSD, Dias MRL. Anatomical aspects and phytochemical potential of Caryocar villosum (Aubl.) Pers. (pequiá). Braz. J. Dev. 2019;5:25807-25829. Available:https://doi.org/10.34117/bjdv5n11-235

89. Oliveira MSP, Schwartz G. Açaí – Euterpe oleracea. Exotic Fruits. 2018;1-5. Available:https://doi.org/10.1016/B978-0-12-803138-4.00002-2

90. Rabelo A. Araçá-Boi (Eugenia stipitata McVaugh). Frutos Nativos da Amazônia comercializados nas feiras de Manaus-AM. INPA, Manaus; 2012.

91. Oliveira AIT, Cabral JB, Mahmoud TS, Nascimento GNL, Silva JFM, Pimenta RS, Morais PB. In vitro antimicrobial activity and fatty acid composition through gas chromatography-mass spectrometry (GC-MS) of ethanol extracts of Mauritia flexuosa (Buriti) fruits. J. Med. Plants Res. 2017;11:635-641. Available:https://doi.org/10.5897/JMPR2017.6460

92. Aguiar JPL, Souza FCA. Camu-camu super fruit (Myrciaria dubia (H.B.K) Mc Vaugh) at different maturity stages. Afr. J. Agric. Res. 2016;11:2519-2523. Available:https://doi.org/10.5897/AJR2016.111167

93. Martins M, Kluczkovski AM, Santos ACS, Fernandes OCC, Scussel VM. Evaluation of ochratoxin A and fungi in powdered guaraná (Paullinia cupana Kunth), a caffeine rich product from Amazon forest. Afr. J. Microbiol. Res. 2014;8:545-550. Available:https://doi.org/10.5897/AJMR2014.36579

94. Jimenez MM. Neuroprotective natural molecules, from food to brain. Front. Neurosci. 2018;12:721. Available:https://doi.org/10.3389/fnins.2018.00721

95. Martini MH, Lenci CG, Figueira A, Tavares DO. Localization of the cotyledon reserves of Theobroma grandiflorum (Willd. ex Spreng.) K. Schum., T. subincanum Mart., T. bicolor Bonpl. and their analogies with T. cacao L. Rev. Bras. Bot. 2008;31:147-154. Available:https://doi.org/10.1590/S0100-84042008000100013

96. Quesada S, Azofeifa G, Jatunov S, Jiménez G, Navarro L, Gómez G. Carotenoids composition, antioxidant activity and glycemic index of two varieties of Bactris gasipaes. Emir. J. Food Agr. 2011;23:482-489. Available:http://ejfa.me/index.php/journal/article/view/1272

97. Sun CD, Zhang B, Zhang JK, Xu CJ, Wu YL, Li X, Chen KS. Cyanidin-3-glucoside-rich extract from Chinese bayberry fruit protects pancreatic β cells and ameliorates hyperglycemia in streptozotocin-induced diabetic mice. J. Med. Food. 2012;15:288-298. Available:https://doi.org/10.1089/jmf.2011.1806

98. Silva HR, Assis DC, Prada AL, Silva Junior JOC, Sousa MB, Ferreira AM, Amado JRR, Carvalho HO, Santos AVTLT, Carvalho JCT. Obtaining and characterization of anthocyanins from Euterpe oleracea (açaí) dry extract for nutraceutical and food preparations. Rev. Bras. Farmacogn, 2019; 29:677-685.
99. Barbosa PO, Pala D, Silva CT, Souza MO, Amaral JF, Vieira RAL, Folly GAF, Volp ACP, Freitas RN. Açaí (Euterpe oleracea Mart.) pulp dietary intake improves cellular antioxidant enzymes and biomarkers of serum in healthy women. Nutr. 2016;32:674-680. Available:https://doi.org/10.1016/j.nut.2015.12.030

100. Magalhães TAFM, Souza MOS, Gomes SVG, Silva RM, Martins FS, Freitas RN, Amaral JF. Açaí (Euterpe oleracea Martius) promotes jejunal tissue regeneration by enhancing antioxidant response in 5-Fluorouracil-induced mucositis. Nutr. Cancer. 2020;5:1-11. Available:https://doi.org/10.1080/01635581.2020.1759659

101. Poulse SM, Bielinski DF, Carey A, Schauss AG, Shukitt-Hale B. Modulation of oxidative stress, inflammation, autophagy and expression of Nrf2 in hippocampus and frontal cortex of rats fed with açai-enriched diets. Nutr. Neurosci. 2017;20:305-315. Available:https://doi.org/10.1080/1028415X.2015.1125654

102. Nobre CB, Sousa EO, Camilo CJ, Machado JF, Silva JMFL, Filho JR, Coutinho HDM, Costa JGM. Antioxidative effect and phytochemical profile of natural products from the fruits of “babaçu” (Orbignia speciose) and “buriti” (Mauritia flexuosa). Food Chem. Toxicol. 2018;121:423-429. Available:https://doi.org/10.1016/j.fct.2018.08.068

103. Scacco G, Vari R, Flessi C, Del Gaudio I, D’Archivio M, Santangelo C, Iacovelli A, Galvano F, Pluchinotta FR, Giovanni C, Masella R. Protocatechuic acid activates key components of insulin signaling pathway mimicking insulin activity. Mol. Nutr. Food Res. 2015;59:1472-1481. Available:https://doi.org/10.1002/mnfr.201400816

104. Romero ABR, Carvalho-Martins MC, Nunes PHM, Ferreira NRT, Brito AKS, Cunha PFM, Lima A, Assis RC, Araújo EM. In vitro and in vivo antioxidant activity of Buriti fruit (Mauritia flexuosa L.f.). Nutr. Hosp. 2015;32:2153-2161.

105. Azevêdo JCS, Fujita A, Oliveira EL, Genovese MI, Correia RTP. Dried camu-camu (Myrciaria dubia H.B.K. Mc Vaugh) industrial residue: A bioactive-rich Amazonian powder with functional attributes. Food Res. Int. 2014;62:934-940. Available:https://doi.org/10.1016/j.foodres.2014.05.018

106. Silva FC, Arruda A, Ledel A, Dauth C, Romão NF, Viana RN, Ferraz ABF, Picada JN, Pereira P. Antigenotoxic effect of acute, subacute and chronic treatments with Amazonian camu-camu (Myrciaria dubia) juice on mice blood cells. Food Chem. Toxicol. 2012;50:2275-2281. Available:https://doi.org/10.1016/j.fct.2012.04.021

107. Fujita A, Borges K, Correia R, Franco BDGM, Genovese MI. Impact of spouted bed drying on bioactive compounds, antimicrobial and antioxidant activities of commercial frozen pulp of camu-camu (Myrciaria dubia Mc. Vaugh). Food Res. Int. 2013;54:495-500. Available:https://doi.org/10.1016/j.foodres.2013.07.025

108. Gonçalves ANSS, Lelis-Santos C, Curi R, Lajolo FM, Genovese MI. Frozen pulp extracts of camu-camu (Myrciaria dubia McVaugh) attenuate the hyperlipidemia and lipid peroxidation of type 1 diabetic rats. Food Res. Int. 2014;64:1-8. Available:https://doi.org/10.1016/j.foodres.2014.05.074

109. Yonekura L, Martins CA, Sampaio GR, Monteiro MP, Cesar LAM, Mioto BM, Mori CS, Mendes TMN, Ribeiro ML, Arçari DP, Torres EAFS. Bioavailability of catechins from guarana (Paullinia cupana) and its effect on antioxidant enzymes and other oxidative stress markers in healthy human subjects. Food Funct. 2016;7:2970-2978. Available:https://doi.org/10.1039/c6fo00513f

110. Portella RL, Barcelos RP, Rosa EJF, Ribeiros EE, Cruz IBM, Suleiman L, Soares FAA. Guarana (Paullinia cupana Kunth) effects on LDL oxidation in elderly people: An in vitro and in vivo study. Lipids Health Dis. 2013;12:1-9. Available:https://doi.org/10.1186/1476-511X-12-12

111. Maldaner DR, Pellenz NL, Barbsan F, Azzolin VF, Mastella MH, Teixeira CF,
Duarte T, Maia-Ribeiro EA, Cruz IBM, Duarte MMMF. Interaction between low-level laser therapy and Guarana (Paullinia cupana) extract induces antioxidant, anti-inflammatory, and anti-apoptotic effects and promotes proliferation in dermal fibroblasts. J. Cosmet. Dermatol. 2020;19: 629-637.
Available:https://doi.org/10.1111/jocd.13055

112. Krewer CC, Ribeiro EE, Ribeiro EAM, Moresco RN, Rocha MIUM, Montagner GFFS, Machado MM, Viegas K, Brito E, Cruz I. Habitual intake of Guarana and metabolic morbidities: An epidemiological study of an elderly Amazonian population. Phytother. Res. 2011;25:1367-1374.
Available:https://doi.org/10.1002/ptr.3437

113. Mascato DRLH, Monteiro JB, Passarinho MM, Galeno DML, Cruz RJ, Ortiz C, Morales L, Lima ES, Carvalho RP. Evaluation of antioxidant capacity of Solanum sessiliflorum (Cubiu) extract: An in vitro assay. Nut. Metab. 2015;364185.
Available:https://doi.org/10.1155/2015/364185

© 2020 Yamaguchi and Souza; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sdiarticle4.com/review-history/61673