CAMU-CAMU (*Myrciaria dubia* (HBK) McVaugh), a small Amazonian fruit rich in vitamin C

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ABSTRACT

The Amazon rainforest is rich in a diversity of species with various bioactive properties that have been widely used to treat a variety of diseases. Many of these diseases the process of infection, an environment of oxidative stress is created that leads to cellular damage causing a decline in the immune system. In this sense, the camu-camu fruit (*Myrciaria dubia* (HBK) McVaugh), native to the Amazon region, has in its nutritional composition several bioactive compounds and the highest level of vitamin C among Brazilian tropical fruits. It is also known for its antioxidant and anti-inflammatory properties. Therefore, the objective of this review is to analyze the evidence collected in the literature on camu-camu and its vitamin C content and other nutrients can be considered a functional food acting among other benefits the strengthening of the immune system, fighting diseases that can caused by oxidative and inflammatory stress.

Keywords: Camu-camu, vitamin C, antioxidant. bioactive compounds.

INTRODUCTION

In the Amazon there are numerous plant species with economic potential, among which stands out the Camu-camu fruit (Camu-camu (HBK) McVaugh). Camu-camu is from the Myrtaceae family and grows on the banks of lakes and rivers in the Amazon Forest [1]. The interest in this fruit has increased because of its impressive quantity of vitamin C, which can reach 6 g/100 g of fresh Pulp and is used as food *in natura* by indigenous and Amazonian riverine populations [2]. Thus, this article aims to increase the visibility of camu-camu (*Myrciaria dubia* (HBK) McVaugh) with regards to the immune system, due its excellent antioxidant activity. This analysis is based on the high content of vitamin C, its nutritional components and bioative compounds when compared with other tropical fruits. It also has other potentially important properties: it is a rich source of fiber, and it contains anthocyanins that are potent antioxidants [3], of minerals, also contains, starch, nitrogen, proteins and vitamins [4]. These properties of the camu-camu fruit have aroused the economic and scientific interests of importers in Japan, Europe and the USA [5,6].

1. CAMU-CAMU (*MYRCIARIA DUBIA* (HBK) MCVAUGH) AND ITS NUTRITIONAL CHARACTERISTICS

A variety of Amazonian plant species, herbs and fruits and their active ingredients are widely used to overall good health but also for the treatment of various diseases. Many fruits, such as cubiu (*Solanum sessiliflorum* Dunal), have been used in hypercholesteromy intervention [7]; tucumã-da-amazônia (*Astrocaryum aculeatum*) for obesity [8]; açaí (Euterpe oleracea) in the prevention of cardiovascular diseases [9]; guarana (Paullina cupana) in the treatment of diabetes [10]; Taperebá (Spondias mombin L.) for the treatment of gastrointestinal diseases [11] ; Murici (*Byrsonima crassifolia* (L.) Kunth in the therapy of human ovarian carcinoma [12] , among others. Recent trials attest to the high content of vitamin C/ascorbic acid in camu-camu [13] and it is considered among researchers to be the greatest natural source of vitamin C among tropical fruits, with concentrations that can vary between 2,000 and 6,500 mg in 100 g of pulp, and is thus superior to acai (*Euterpe oleracea* Mart.), Cajá (*Spondias lutea* L.), umbu (*Spondias tuberosa* Arruda) and even superior to the levels of vitamin C found in acerola **(*Malpighia emarginata*).** which is considered a superior source of ascorbic acid among tropical fruits [14]. In its nutritional composition (**Table 1**) there is a variety of minerals such as sodium, potassium, calcium, zinc, magnesium and manganese; vitamin A, and sugars, such as glucose, fructose, starch, pectin [4]. In its protein constitution, different types of amino acids are present, such as serine, valine, leucine, glutamate, proline, phenylalanine, threonine and alanine and minerals such as sodium, potassium, calcium, zinc, magnesium, and manganese. In addition to phenolic compounds, carotenoids and flavonoids, ellagitanins, anthocyanins, cyanidin-3-glucoside, quercetin, myricetin, catechin, xarinic acid and gallic acid, chlorogenic acid, ellagic acid, syngenic acid, and soluble and insoluble fibers have been described in the fruit [15,16]. The camu-camu is a fruit with a diameter and length of 1, 0 to 3, 2 cm and 1, 2-2, 5 cm respectively. The camu camu plant generally reaches a height of 4-8 m. The fruits are globular with a diameter and length of 1, 0 to 3, 2 cm and 1, 2-2, 5 cm respectively, and their average weight is 11.7g. The ripe fruit is composed, on average, of 65.2% pulp, 19.5% seeds and 15.3% peel. During the ripening process, the color of the peel turns from pink to red, and after the black ripening, the pulp appears pink. In Table 2. general aspects of the fruit of camu-camu (*Myrciaria dubia*).

2. CAMU-CAMU (*MYRCIARIA DUBIA* (HBK) MCVAUGH) AND ITS HIGH VITAMIN C CONTENT

Several studies have analyzed the content of vitamin C present in various parts of the fruit (Figure 1). In early stages of maturation, ascorbic acid values of 759.02 mg per 100 g to 1,071.12 mg per 100 g were found in the final stage of maturation the values were between 2,010 ± 65 mg.100 g^{-1} FM [17] to 2,280 ± 65 mg.100 g^{-1} FM. 1,946 per mg/100g [18]. When the fruit was analyzed *in natura*, in the peel of the harvested fruit after 88 days, the concentration was 4752.23 mg of ascorbic acid/100g and in the pulp in the same period 5178.49 mg of ascorbic acid/100g [19]. In the fruit, after freezing and thawing [20,21] obtained 7,355 mg of ascorbic acid 100 g^{-1}, and the values 13,756. 79 mg/100 g for pulp after the freeze-drying process [21]. The vitamin C content found in camu-camu is 20 times higher than that of acerola

(*Malpighia emarginata*) and 100 times higher than found in lemons (*Citrus limon* (L.) Osbeck). Rufino et al. [22] described the antioxidant activity of camu-camu using the DPPH method as IC_{50}= 42. 6 g DM. g^{-1}, which demonstrates a positive synergy between antioxidant activity and vitamin C content. Using the DPPH method, concluded that ascorbic acid has a share of 70% of the antioxidant capacity of camu camu [17]. Studies point out that after the pulp is removed from the fruits, it should be refrigerated or frozen as soon as possible, since the active ingredients, such as ascorbic acid, phenolic compounds and other nutrients, can lose their stability. In addition, the pulp can be fermented at room temperature. Thus, the frozen pulp should be kept in a freezer and protected from direct light. Souza et al. [23] evaluated the effect of freezing on the physico-chemical characteristics of camu-camu pulp stored for 15 months at -18 ºC. The results indicated that there was no significant difference between the quality of the initial pulp of camu-camu and after 15 months of storage at 18 °C. In another study, the pulp of the green, semi-ripe and ripe fruits was frozen at -18 ºC and physico-chemical analyses were conducted monthly, for four months, an aliquote was removed from the pulps and transformed into juices with refrigeration at 4 ºC for 24 h, with analyses performed at 0 h, 2 h, 4h, 6 h and 24 h.

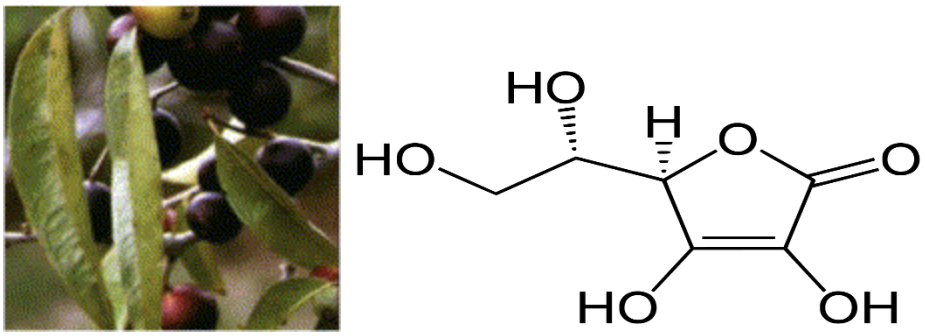

Figure 1. Camu-camu fruit (*Myrciaria dubia* (HBK) McVaugh) and the structure ascorbic acid

Vitamin C concentrations for green, semi-ripe and ripe fruits were 26.84 mg/100 g, 20.21 mg/100 g and 27.46 mg/100 g, respectively. During the storage of frozen pulp and chilled juice, there was a slight variation in the initial and final pH values of soluble solids, while the vitamin C content showed a considerable reduction [24]. For this reason, it is recommended that the fruit in the final stage of ripening or when it has a red color be stored at temperatures of about 10 °C in packages of modified atmosphere [25]. In addition to the form of freezing, it is important to prevent the degradation of the fruit. Salomão-Oliveira et al. [26] observed that freeze-dried camu-camu in gelatin capsule is able to create a light barrier, protecting the fruit against oxidation and moisture absorption. This protection contributes to reduce the degradation of the processed fruit, ensuring the prolongation of the shelf life, as well as the stabilization of the antioxidant components associated with the refrigeration temperature. The storage of the product after analysis of 90 days had an acceptable loss of vitamin C, since ascorbic acid is readily oxidized when exposed to oxygen, light, air temperature, long shelf life and the type of packaging. In addition, it was found that encapsulation and preservation by refrigeration were paramount to ensure the physicochemical and microbiological quality of the freeze-dried camu camu. During the study, two analyses of vitamin C in freeze-dried fruits were performed. At baseline (t = 0) the estimate of vitamin C was 3.04 g/100 g^{-1} and in the third month (T = 3) it was 2.60 g/100 g^{-1}. When camu-camu juice is mixed with other fruits or foods, we have the following results observed the stability of vitamin C in the formulation of camu-camu (*Myrciaria dubia*) and jambolan (*Syzygium cumini*) juice during storage at 25 °C. After analysis, the results indicated a degradation of vitamin C after 10 days of storage. Sarmento et al. [27] evaluated the stability of ascorbic acid in buffalo milk yogurt with different concentrations of camu-camu pulp during the storage period. The physicochemical characteristics of the pulp and buffalo milk yogurt prepared from two

formulations with 8.3% (F1) and 12.5% (F2) of camu-camu pulp were evaluated, in addition to the stability of the ascorbic acid in the product stored under refrigeration (5 ± 1 °C) for 28 days. The analyzed pulp and yogurt formulations presented physico-chemical characteristics as seen in the literature and recommended by the legislation in force in Brazil. The results indicate that the ascorbic acid content in the formulations was 242.2 mg/100 g (F1) and 317.73 mg/100 g (F2) at D0 and 171.0 mg/100 g (F1) and 242.2 mg/100 g (F2) on D28 of storage, with a 30% loss in ascorbic acid content during the entire storage period these were not superior to camu-camu.

3. CAMU-CAMU (MYRCIARIA DUBIA (HBK) MCVAUGH) AND ITS ANTIOXIDANT, ANTI-INFLAMMATORY AND IMMUNE FUNCTION.

At the same time, there is a discussion about the action of diet, especially phytochemicals and natural products, in the fight against diseases. Even if there is no concrete evidence of the dose or synergism of these products with the drugs. Therefore, the fruit camu camu could be part of a non-medical offering, since the use of vitamin c and certain phytochemicals have been claimed for a long time [28]. The antioxidant effects of vitamin C have been demonstrated to be beneficial against diseases caused by oxidative damage, such as atherosclerosis and câncer [13] or useful in the form of therapy against Alzheimer's and Parkinson's disease [29,30,31]. Therefore, the different bioactive compounds present in the pulp, juice, and all the residues (peel and seed) present in the fruit have been used in human and animal research, thus subsidizing the potential antigenotoxic, anti-obesity, hypertensive, hepatic protection, and in the prevention of diseases related to the immune system. [3,32-35]. These works, in spite of their initiation, give us information and evidence of the protective action and the antioxidant and anti-inflammatory potential of the fruit. Two studies indicate the activity of camu-camu pulp and seed extract in anti-inflammatory support.Yazawa et al. [36] used camu-camu seed extract, while Da Silva et al. [37] highlighted the action of camu-camu pulp. In the trial of Yazawa et al. [36], the authors analyzed the anti-inflammatory action of methanolic extract of camu-camu seeds in edema lesion after the administration of carrageenan injection in the paw of mice. After 4 hours, the control rats received an oral treatment with dexamethasone (1.0 mg/kg), while the camu-camu groups with lesion demonstrated the following results in calculation of mean and standard deviation in a dose-dependent manner 35.7% ± 6.7% at 2,000 mg/kg, 63.8% ± 7.3% at 1000 mg/kg and 85.1% ± 10.3% at 500 mg/kg. These results were obtained 2 hours after the carrageenan injection. When the extract was tested in vitro, there was inhibition in nitric oxide production from RAW 264.7 cells derived from the in vitromacrophages. After analysis of the extract, triterpenoid betulinic acid was identified, which is a potent anti-inflammatory substance. The research of Da Silva et al. [37] observed the antioxidant, genotoxicand antigenotoxic action of camu-camu pulp on the blood cells of mice. After evaluation of vitamin C per 100 mL of camu-camu, the sampleresult was 52.5 mg. In vitroantioxidant activity evaluated by the DPPH assay in alkaline comet assay was used to analyze genotoxic and antigenotoxic activity. The results indicated that no concentration off camu-camu tested exerted any genotoxic effect and a significant antigenotoxic effect was noted. After the treatments, there was no evidence of toxicity or death in the blood cells. Infections and inflammations in cases of greater severity lead the body to respond to an inflammatory process with an inflammatory cascade characterized by the actions of cytokines, mainly interleukins (IL-1B, IL-2, IL-6) and tumor necrosis factor (TNF). This imbalance between anti-inflammatory and pro-inflammatory cytokines can occur even after the individual has received medical discharge. Trials conducted by Fideles et al. [38] using the atomized

extract of camu-camu seed inhibited induced oxidation and, in vitro,reduced the release of TNF-αand activation of NF-kB in macrophage cell culture. Preclinical studies using knockout Gluo mice show the modulating impacts of vitamin c on cytokine synthesis. These vitamin c deficient animals infected with the influenza virus in the lower respiratory tract [39] had increased synthesis of pro-inflammatory cytokines and decreased synthesis of the inflammatory cytokines TNF-αand IL-1βby isolated neutrophils, respectively. In another trial using septic mice that applied 200 mg/kg of parenteral vitamin C, the mice exhibited reduced synthesis of the inhibitory cytokines TGF-βand IL-10 by Tregs, in addition to moderate elimination of IL-4 and increased sexcretion of IFN-γ, which is an indication of the immunomodulatory action of vitamin c in sepsis [40]. In addition, camu-camucontains the mineral potassium, which increases the in vivo availability of vitamin C. This availability has been proven in the research of Ellinger et al. [41] using a mix of tropical and red fruitswith a mixture of 400 ml of camu-camu juice. This mixture increased the levels of vitamin c in the plasma of 12 participants, when compared to the control group. It has been proven that, depending on the time of harvest, when camu-camu has a red color, the content of total phenolic, anthocyanin and vitamin c increases, thus increasing the antioxidant and anti-inflammatory activity of the fruit. Camu-camu can potentially play a role in integrative therapeutic approaches as a dietary supplement, mainly due to the presence of the high content of vitamin c and its bioactive compounds. Vitamin C is an important enzyme cofactor that influences genes that participate in immunomodulatory function and its effects [41]. Vitamin c encourages neutrophil migration, phagocytic evolution, as well as protection of excessive lesions of infected tissue, increasing neutrophil death, macrophage extraction, as well as proliferation of T and B lymphocytes.. Although more studies are lacking, evidence suggests that camu camu has a potential non-pharmacological strategy against diseases driven by its nutritional composition, i.e., natural source of vitamin c. Thus, camu camu may be part of an alternative non-phytotherapeutic option. Therefore, it is important to be clear in what way and how camu camu can not only be a food supplement, but also possibly add essential values as an antioxidant with viable action against metabolic diseases, restoring inflammatory and immune functions. Although further studies must be done. Knowing that there will be questions from doctors and agencies that regulate the effectiveness of doses and synergism with other drugs. However, the camu camu fruit is surrounded by the literature in evidence that proves its biochemical and nutritional properties, in addition to the recognized high vitamin c content. Finally, the gap and possibilities are open to reinforce what has been reviewed, especially with human studies, thus increasing confidence among consumers, patients, and physicians seeking a drug-free strategy.

Table 1. Nutritional composition of camu camu fruit pulp.

Component per 100 g	Contents
Energy (kcal)[c]	94. 368
Water[c]	93.83± 0.026
Lipidse[e]	0.07±0.006
Proteine[e]	.,51±0.007
Carbohydrate	4.84±0.80

Ash	0.22± 0.03
Fructose[e]	0.3
Glucose[e]	0.2
PHe[c]	2.84±0.31
Total soluble solids (°Brix) [c]	6.18±0.99
Essential amino acids (mg/100 g)	
Valine[c]	242.00±104.65
Leucine[c]	210.50±111.02
Phenylalanine[c]	32.50±14.85
Threonine[c]	32.50±5.66
Essential fatty acids (% of total lipids)	
C18:3ω3 (α-Linolenic)[e]	16.00±0.70
C18:2ω6 (Linoleic) [e]	9.70±0.40
C18:3ω6 (γ-Linolenic) [e]	9.30±0.10
C20:5ω3 (EPA) [e]	7.00±0.10
Minerals (mg/100 g)	
K[c]	87.020±29.322
PO4	18.183±8.122
SO4[c]	14.750±2.192
Ca[c]	14.510±9.346
Cl[c]	9.100±3.536
Mg[c]	7.393±.323
Co[c]	1173.1±0.807
Na[c]	0.934±1.546
Mn[c]	0.820±1.118
Fe[c]	0.255±0.064
Al [c]	0.230±0.138
Zn[c]	0.255±0.064
Cu[c]	0.117±0.072
B[c]	0.050±0.000

Br[c]	0.021±0.005
Cr[c]	0.015±0.004
Mo[c]	0.004±0.002
Se (µg)	0.429±0.089
Vitamins (mg/100 g)	
Vitamin C [c]	2210.00 ± 650.00
Niacin[c]	0.48 ± 0.28
Riboflavin[c]	0.03 ± 0.02
Thiamine[c]	0.01 ± 0.00
Bioactive compounds	
Polyphenols(mg/100g) a	1120
Anthocyanins (µg/g) [d]	0.739
Flavonoids (mg/100g) [d]	16.93
Total Phenols (mg GAE.100 g^{-1}) b	1.492.88±0.6
Total Flavonoids (mg EQ.100 g^{-1}) b	23.66±0.11
Total Carotenoids (mg Eq. ß-caroteno.100 g^{-1}) b	545.92±28.06
DPPH (IC50 µg/ml) [b]	26,70±0,76
ABTS (µmol/g) [b]	1.127.99±4.2
β- carotene (mg.100 g^{-1}) [b]	71.81±3.25
Chromium (µg^{-1}) [b]	7.60±1.72

GAE: galic acid equivalente; QE: quercetin equivalente; Eq: equivalent. Aguiar et al. [18][a] Salomão-Oliveira et al. [26][b]; Castro Gómez et al. [43][c]; Ribeiro et al. [44] [d]; Aguiar et al. [46] [e]

Table 2. General aspects of the fruit of camu-camu (*Myrciaria dubia*)

Botanical nomenclature	*Myrciaria dubia* (HBK) McVaugh Botanical Family: Myrtaceae	Balisteiro et al. [46]
Synonyms	*Myrciaria divaricata* (Bentham) O. *Berg Myrciaria paraensis* O. *Berg Myrciaria spruceana* O. *Berg Psidium dubium* (HBK)	Camones et al. [47]
Common names	Camu-camu, camu-camu negro, caçari, araça, azedinha, algracia, guayabillo blanco, guayabito, limoncillo (Venezuela)	Campos et al. [48]
Geographical Distribution	Brazilian, Bolivian, Colombian, Ecuadorian, Peruvian and Guyanese Amazon	Castro Gómez et al. [43]
Plant Material	Studies using leaves, fruits (pulp, peels and seeds); - Bush of 3 m to 8 m in height; - Edible fruit, sour taste, pink pulp, spherical fruit with a diameter of 1-3 cm, ripe with reddish-brown to black-purple coloring; - Seeds 8-5 mm long and 5.5-11 mm wide, one to three units, noticeably flattened and covered by a network of fibrils.	Do Nascimento [49]
Pharmaceutical formulation: lyophilized or atomized Pulp	Vitamin C capsules or tablets, collagen inducer.	Nascimento et al. [32]
Pulp food industry	Drinks: liquor, beers. Foods: cereal bars, flours, animal feed, yogurt, blends, cheese, milk, candied fruit, jelly/jam, popsicles, candy, cookies	Nascimento et al. [32]
Health promoting properties	Anti-anemic activity, anti-inflammatory activity, healing activity, antiplasmodic activity, antigenotoxic activity, anti-obesity activity, neuroprotective activity, antidiabetic activity, antimicrobial activity, cell antiregeneration activity and hepatoprotective activity	De Azevêdo et al. [50]
Micronutrients and macronutrients with pharmacologic activity identified in seed pulp and peel	Ca, Mn K, Mg), Fe, Zn, Al, B, Br, Cr, Mo, Se, Cu, Na, P, K, S, B, Fe, Na, Se, Co, Cl. Vitamin C, niacin, riboflavin, thiamine,	Nascimento et al. [32]
Amino acids with pharmacologic activity identified in seed pulp and peel	Valine, leucine, threonine, serine, glutamate, proline, phenylalanine, threonine, alanine, aminobutanoate	Sarmento et al. [27]
Bioactive substances identified in seed pulp and peel	Anthocyanins (delphinidine 3-glycoside and cyanidine 3-glycoside), translutein, lutein, beta-carotene, zeaxanthin and neoxanthin, morin, rutin, kaempferol, quercetin, myricetin, catechin, epicatechin, xarinic acid and gallic acid, chlorogenic acid, ellagic acid, syngic acid, caffeic acid, ferulic acid,	Ellinger et al. [46]
Fatty acids with pharmacologic activity identified in seed pulp and peel	C18: 3ω3 (α-linolenic); C18:2ω6 (linoleic); 5Ω3 (EPA); tridecanoic acid; palmitic acid; stearic acid; oleic acid; eicosadienoic acid; tricosanoic acid.	Fidelis et al. [38]
Traditional Use	Asthma, arteriosclerosis, cataracts, depression, flu, gingivitis, glaucoma, hepatitis, infertility, migraine, osteoporosis and Parkinson's disease.	Balisteiro et al. [46]
Adverse effects	There are no known adverse effects and/or contraindications from ingestion of the fruit or camu-camu residues.	Nascimento et al. [32]

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REFERÊNCIAS

1.Yuyama K, Aguiar JPL, Yuyama LKO. 2002. Camucamu: um fruto fantástico como fonte de vitamina c. Acta Amaz.2002;32: 169-174

2. Akter, MS, Oh S, Eun, JB, Ahmed, M. Nutritional compositions and health promoting phytochemicals of camu-camu (Myrciaria dubia) fruit: A review. *Food Research International*.2011; *44*(7), 1728-1732.

3. Zanatta CF, Cuevas E, Bobbio FO, Winterhalter P, Mercadante AZ. Determination of Anthocyanins from Camu-camu (Myrciariadubia) by HPLC − PDA, HPLC− MS, and NMR. J Agric Food Chem. 2005; 53: 9531-9535

4. Akachi T, Yasuyuki S, Kawaguchi T, Tatsuya MT, Sugiyama K. 1-methylmalate from Camu-camu (Myrciaria dubia) suppressed D-galactosamine-induced liver injury in rats. Biosci Biotechnol Biochem,2010; 74: 573-578.

5. Castañeda CB, Ramos QF, Ibáñez VL. Evaluation of the antioxidant capacity of seven Peruvian medicinal plants. J Med Hor. 2008 8: 56-78.

6. Genovese MI, Pinto MS, Gonçalvez AES, Lajolo FM. Bioactive compounds and antioxidant capacity of exotic fruits and Commercial Frozen Pulps from Brazil. Food Sci Technol Int.2008; 14: 201-208

7. Maia JRP, Schewertz MC, Sousa RF, Aguiar JPL, Lima ES. Efeito hipolipemiante da suplementação dietética com a farinha do cubiu (Solanum sessiliflorum Dunal) em ratos hipercolesterolêmicos. 2015; *17, Pags. 112-119.*

8. Leal C, Junior MM, Lima,V. Avaliação da resposta glicêmica ao consumo de casca de tucumã-da-amazônia (astrocaryum aculeatum) em modelo experimental de obesidade. *Revista dos Trabalhos de Iniciação Científica da UNICAMP*.2019; (27), 1-1.

9. De Liz, S, Cardoso AL, Copetti CLK, De Fragas Hinnig P, Vieira FGK, Da Silva EL, Di Pietro, P. F. Açaí (Euterpe oleracea Mart.) and juçara (Euterpe edulis Mart.) juices improved HDL-c levels and antioxidant defense of healthy adults in a 4-week randomized cross-over study. *Clinical Nutrition*. 2020; *39*(12), 3629-3636.

10. Abboud RDS., Ribeiro ICDA, Da Silva VAP, Corrêa LBNS, Boaventura GT, Chagas MA. El consumo de guaraná (Paullinia cupana) mejora los parámetros hepáticos y renales en ratas diabéticas inducidas por aloxano. *Nutrición Hospitalaria*. 2020; *37*(2), 343-348.

11. Brito SA, Barbosa IS, De Almeida C, De Medeiros JW, Silva Neto JC, Rolim LA, Wanderley AG. Evaluation of gastroprotective and ulcer healing activities of yellow mombin juice from Spondias mombin L. *PloS one*. 2028; *13*(11), e0201561.

12. De Souza VR, Brum MCM, Guimarães IDS, Dos Santos PDF, Do Amaral TO, Abreu JP, Teodoro AJ. Amazon fruits inhibit growth and promote pro-apoptotic effects on human ovarian carcinoma cell lines. *Biomolecules*. 2019; *9*(11), 707.

13. Grigio ML, Chagas EA, Rathinasabapathi B, Chagas PC, Da Silva ARV, Sobral S. TM,De Oliveira RR. Qualitative evaluation and biocompounds present in different parts of camu-camu (Myrciaria dubia) fruit. *African Journal of Food Science*.2017; *11*(5), 124-129.

14. Vidigal MC, Minim VP, Carvalho NB, Milagres MP, Gonçalves AC. Effect of a health claim on consumer acceptance of exotic Brazilian fruit juices: Açaí (Euterpe oleracea Mart.), Camu-camu (Myrciaria dubia), Cajá (Spondias lutea L.) and Umbu (Spondias tuberosa Arruda). *Food Research International4 2011;4*(7), 1988-1996.

15. De Azevêdo JCS, Fujita A, De Oliveira EL, Genovese MI Correia RTP. Dried camu-camu (Myrciaria dubia HBK McVaugh) industrial residue: A bioactive-rich Amazonian powder with functional attributes. *Food Research International*. 2014; *62*, 934-940.

16. Ferreira FB. Extração e purificação de compostos bioativos de cubiu (" Solanum sessiliflorum'), camu-camu (" Myciaria dubia") e araçá-roxo (" Psidium myrtoides") utilizando filtração por membranas com e sem promotores de turbulência. 2020.

17. Chirinos R, Galarza J, Betalleluz-Pallardel I, Pedreschi R, Campos, D. Antioxidant compounds and antioxidant capacity of Peruvian camu camu (Myrciaria dubia (HBK) McVaugh) fruit at different maturity stages. Food chemistry. 2010; 120(4), 1019- 1024.

18. Aguiar JPL, Amaral Souza FCA. Antioxidant capacidant and bioactive compounds and health benefits of camu-camu puree (Myrciaria dubia (HBK) Mc Vaugh). International Journal of Development Research. 2018; 8(6), 20742-20745.

19. Arellano-Acuña, E., Rojas-Zavaleta, I., & Paucar-Menacho, L. M. (2016). Camu-camu (Myrciaria dubia): Fruta tropical de excelentes propiedades funcionales que ayudan a mejorar la calidad de vida. *Scientia Agropecuaria*, *7*(4), 433-443

20. Yuyama, K. (2011). The camu-camu culture in Brazil. Fruticultura, 33, pp. 1–11

21.Neves LC, Da Silva VX, Chagas EA, Lima CGB, Roberto SR. Determining the harvest time of camu-camu [Myrciaria dubia (HBK) McVaugh] using measured pre-harvest attributes. Scientia Horticulturae. 2015; 186, 15-23.

22. Rufino MS, Alves RE, Fernandes FA, Brito ES. Free radical scavenging behavior of ten exotic tropical fruits extracts. Food Research International. 2011;44(7), 2072-2075.

23. Souza ALR, Pagani MM, Gomes FS, Cabral LMC. (2011). Effect of frozen storage on the quality of camu camu (Myrciaria dubia (HBK) McVaugh,) pulp. In *Embrapa Agroindústria de Alimentos-Artigo em anais de congresso (ALICE)*. In: International congress on engineering and food, 11., 2011, Athens. Food process engineering in: National Technical University of Athens, 2011.

24. Silva MR, Júnior RTDOS, Da Conceição Ferreira CC. Stability of vitamin c in fresh cagaita and during pulp and juice storage. *Pesquisa Agropecuária Tropical*.2008; *38*(1), 53.

25. Hernández M S, Carrillo M, Barrera J, Fernández-Trujillo JP. Camu-camu (Myrciaria dubia Kunth McVaugh). In *Postharvest biology and technology of tropical and subtropical fruits.2011;*352-37. Woodhead Publishing.

26. Salomão-Oliveira A, Costa SS, Dos Santos KSCR, De Souza TP, Marinho HA. Ascorbic acid from lyophilized camu-camu fruit: stability and quality control of hard capsules. *Revista de Ciências Farmacêuticas Básica e Aplicada*. 2016; *37*(1).

27. Sarmento RC, Machado Pinto MR, Silva Craveiro R, De Freitas EPB, Modesto Junior EN,Mota, R. V. (2019). Stability of ascorbic acid in buffalo milk yogurt with camu-camu (Myrciaria dubia) in different concentrations. *Revista do Instituto de Laticínios Cândido Tostes*.2019; *74*(3), 149-158.

28. Langley PC, Pergolizzi Jr JV, Taylor Jr R, Midway, C. Antioxidant and associated capacities of Camu camu (Myrciaria dubia): a systematic review. The journal of alternative and complementary medicine. 2015. 21(1), 8-14.

29. Monacelli F, Acquarone E, Giannotti C, Borghi R, Nencioni A. Vitamin C, aging and Alzheimer's disease. Nutrients. 2017; 9(7), 670.

30. Kocot J, Luchowska-Kocot D, Kiełczykowska M, Musik I,Kurzepa, J. Does vitamin C influence neurodegenerative diseases and psychiatric disorders?. Nutrients.2017; 9(7), 659. 13.

31. Contreras-Duarte S, Chen P, Andía M, Uribe S, Irarrázaval P, Kopp S, Rigotti, A. Attenuation of atherogenic apo B-48-dependent hyperlipidemia and high density lipoprotein remodeling induced by vitamin C and E combination and their beneficial effect on lethal ischemic heart disease in mice. Biological research. 2018.

32. Nascimento OV, Boleti A, Yuyama LK, Lima ES. Effects of diet supplementation with Camu-camu (Myrciaria dubia HBK McVaugh) fruit in a rat model of diet-induced obesity. *Anais da Academia Brasileira de Ciências.* 2013; *85*, 355-363.

33.Carmo HMOD, Souza FMA, Soares ACL, Munhoz JAM, Santos FGA, De Siqueira NG, Silva RPM. Dietary supplementation with CamuCamu versus sleeve gastrectomy in Wistar rats weight control. Revista do Colegio Brasileiro de Cirurgioes. 2019. 46(4), e2238-e2238.

34. Schwertz MC, Maia JRP, Sousa RFSD, Aguiar JPL, Yuyama LKO, Lima ES. Hypolipidemic effect of camu-camu juice in rats. Revista de Nutrição. 2012; 25(1), 35-44.

35. Vargas B. L. Ação do camu-camu [Myrciaria dubia (Kunth) McVaugh] liofilizado sobre a glicemia e o perfil lipídico de adultos jovens. 2012.

36. Yazawa K, Suga K, Honma A, Shirosaki M, Koyama, T. Anti-inflammatory effects of seeds of the tropical fruit camu-camu (Myrciaria dubia).Journal of nutritional science and vitaminology. 2011;57(1), 104-107.

37. Da Silva FC, Arruda A, Ledel A, Dauth C, Romão NF, Viana RN, Pereira P. Antigenotoxic effect of acute, subacute and chronic treatments with Amazonian camu–camu (Myrciaria dubia) juice on mice blood cells. *Food and chemical toxicology*. 2012; *50*(7), 2275-2281.

38. Fidelis M, de Moura C, Kabbas Junior T, Pap N, Mattila P, Mäkinen, S, Granato, D. Fruit seeds as sources of bioactive compounds: Sustainable production of high value-added ingredients from by-products within circular economy. *Molecules*.2019; *24*(21), 3854.

39. Kim Y, Kim H, Bae S, Choi J, Lim SY, Lee N, Lee WJ. Vitamin C is an essential factor on the anti-viral immune responses through the production of interferon-α/βat the initial stage of influenza A virus (H3N2) infection Immune network. 2013;13(2), 70.

40. Gao YL, Lu B, Zhai JH, Liu YC, Qi H. X, Yao Y, Shou ST. The parenteral vitamin C improves sepsis and sepsis-induced multiple organ dysfunction syndrome via preventing cellular immunosuppression.Mediators of Inflammation,2017
.
41. Ellinger S, Gordon A, Kürten M, Jungfer E, Zimmermann BF, Zur B, Stehle, P. Bolus consumption of a specifically designed fruit juice rich in anthocyanins and ascorbic acid did not influence markers of antioxidative defense in healthy humans. *Journal of agricultural and food chemistry*.2012; *60*(45), 11292-11300.

42.Young JI, Züchner S, Wang G. Regulation of the epigenome by vitamin C. Annual review of nutrition. 2015;35, 545-564

43. Castro Gómez JC, Maddox JD, Cobos Ruiz M, Imán Correa SA. Myrciaria dubia "Camu Camu" Fruit: Health-Promoting Phytochemicals and Functional Genomic Characteristics. *Breeding and Health Benefits of Fruit and Nut Crops, 2018, chapter 5, pp. 85-116*.

44. Ribeiro PFDA., Stringheta PC, Oliveira EBD, Mendonça AC, Sant'Ana HMP. Teor de vitamina C, β-caroteno e minerais em camu-camu cultivado em diferentes ambientes. *Ciência Rural*. 2016;*46*, 567-572.
45. Aguiar JPL, Do Amaral Souza FDC. Antioxidants, chemical composition and minerals in freeze-dried camu-camu (Myrciaria dubia (HBK) Mc Vaugh) pulp. *Food and Nutrition Sciences*. 2015; *6*(10), 869.

46. Balisteiro DM, de Araujo RL, Giacaglia LR, Genovese MI. Effect of clarified Brazilian native fruit juices on postprandial glycemia in healthy subjects. *Food Res Int.2017; 100*: 196-203.

47. Camones MÁI, Guerra EMT, Castañeda, BC. Efecto irritante in vitro de formulaciones cosméticas con extracto de camu camu, mediante el método Het Cam. *Horizonte Médico.* 2013; *13*(2), 12-18.

48. Campos APR, Chisté RC, Pena RDS. Camu-camu (Myrciaria dubia) and jambolan (Syzygium cumini) juice blend: sensory analysis and bioactive compounds stability. *Food Science and Technology*, (AHEAD). 2020.

49. Do Nascimento OV,Silva EL. CAMU-CAMU (Myrciaria dubia (HBK) McVaugh), a small Amazonian fruit rich in vitamin C and a supplement for immunity. *Research, Society and Development*. 2021 *10*(6), e27810615877-e27810615877.

50. De Azevêdo JCS, Fujita A, De Oliveira EL, Genovese MI, Correia, RTP. Dried camu-camu (Myrciaria dubia HBK McVaugh) industrial residue: A bioactive-rich Amazonian powder with functional attributes. *Food Research International*. 2014; *62*, 934-940.