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An Amazonian Fruit with a Pespective Action against Obesity: narrative review study

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Abstract

Obesity can contribute to inflammatory processes increasing the prevalence of chronic non-communicable diseases. However, there is a consensus among researchers that fruit and vegetable intake is effective in treating obesity and its comorbidities due to their vast content of phytochemicals and active ingredients. Camu camu, (Myrciaria dubia (HBK) McVaugh) a natural fruit from the Amazon, has attracted the attention of experts due to its high content of vitamin C and polyphenols. Therefore, different bioactive compounds present in camu-camu fruit could be used to delay or prevent various diseases among them obesity.

Keywords: Oxidative stress, camu camu, natural products, Amazon fruits, obesity.

INTRODUCTION

Obesity is one of the most prevalent nutritional disorders among developed and developing countries.

Its incidence affects all age groups, races and genders, with thousands of overweight people worldwide (NCD, 2019). It has been widely demonstrated in scientific literature that obesity is directly associated with numerous diseases, such as systemic arterial hypertension (SAH), coronary heart disease, Type II diabetes, dyslipidemia. Thus, being overweight and obesity have been recognized as public health disorders (Brasil, 2014)

In recent years, knowledge has grown regarding diets and their effect on the reduction of body fat, and the consequent impact on the health of the obese individual.

People with visceral or androgenic type obesity are associated with higher mortality risks (Chooi et al., 2019). This fact is proven because visceral adipose tissue is metabolically more active than subcutaneous adipose tissue. As a consequence, several comorbidities may arise, among them type 2 diabetes mellitus and systemic arterial hypertension (Even et al., 2017). The accumulation of visceral and subcutaneous fat increases cholesterol, triglycerides, LDL and VLDL cholesterol, which can potentiate obesity levels (Bakirova et al., 2016).

Camu camu (*Myrciaria dúbia* HBK [McVaugh]) is a fruit found near rivers and lakes of the Amazon Rainforest, and has a high content of ascorbic acid, phenolic compounds and carotenoids, both in the pulp, seeds and skin as well as great antioxidant potential. It is usually consumed as a juice, jelly, liquor. In industry, it is used as a food additive and is on the list of components present in some cosmetic formulas. Nascimento et al. (2012) used 25ml of camu camu pulp five days a week for 12 weeks in obese rats.

At the end of the experiment there was an alteration in body composition with a reduction of deposits visceral fats and epididymal fat and deposits visceral fats and epididymal fat.

In the protocol of Gonçalves et al. (2019), a group of 17 adults with metabolic syndrome, ingested 50 ml of camu camu juice over a period of 15 consecutive days. After intake of camu camu, there was a reduction in the levels of total cholesterol, LDL cholesterol, triglycerides and body weight in the individuals who drank the juice.

Although there are some gaps still to be filled in studies on the bioactive components present in camu camu, there is the following question. Is camu camu effective for reducing weight and changing body composition in obese or overweight individuals?

The fight against obesity and its proliferation requires the definition of priority action strategies, especially in the prevention of the risks presented by the accumulation of body fat. Therefore, the objective of this narrative review include of the Amazonian fruit camu camu and the evidence of its substantive activity *in vitro*, *in vivo* as a potential antiobesity agent.

2. METHODOLOGY

Several research digital platforms, such as Google Scholar, popular global digital databases, including Science Direct, Springer, PubMed, Web of science, Scielo and Scopus were instruments in the search for relevant data. "Starch and dioscorea and applications" were chosen as the keywords to obtain relevant informations. After careful screening, data related to the current topic were extracted from 67 articles published from 2010 to 2020. The keywords for obtaining the information were also collected from published articles, master's and doctoral theses.

3. THE CAMU CAMU (MYRCIARIA DUBIA (HBK) MCVAUGH)

Individuals with obesity present high levels of mortality due to the development of other metabolic diseases. At this moment there is recognition of new functions of white tissue in obese. Previously seen as a passive deposit of energy today and seen as a secret body of inflammatory substances.

There are suggestions that this inflammatory state (local or systemic) is cause or consequence of disorders such as insulin resistance, diabetes mellitus 2, hyperlipidemia, hypertension, atherogenesis, leading to metabolic syndrome (Even et al., 2017; Bakirova et al., 2019; Gonçalves et al., 2019)

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 (Langley et al., 2015) The camu camu (*Myrciaria dubia (HBK) McVaugh*) is a native fruit found on the banks of the Rio Negro in the Amazon Rainforest. With its remarkable, content of ascorbic acid (between 1,600 and 6,112 mg/100 g of pulp), it is one of the richest known fruits in terms of vitamin C. Camu camu has a high vitamin C content when compared with other fruits, and is 20 times higher than acerola (Malpighia emarginata) and 100 times higher than lemon (*Citrus limon* (L.) (Vidigal et al., 2011)

The antioxidant effects of vitamin C have been demonstrated to be beneficial against diseases caused by oxidative damage, such as atherosclerosis and cancer (Grigio et al., 2017) or useful in the form of therapy against Alzheimer's and Parkinson's disease (Monacelli et al., 2017; Kocot et al., 2017; Contreras-Duarte et al., 2018).

In addition, its nutritional composition includes several phenolic compounds, carotenoids and flavonoids (Villanueva-Tiburcio et al., 2010; de Azevêdo et al., 2014).

Ferreira, (2020) evaluated the bioactive compounds present in cubiu (*Solanum sessiliflorum*), camu camu and araçá roxo (*Psidium myrtoides* O. Berg) fruits. Camu camu showed values from fresh fruit –

much higher than cubiu and 12% higher than araçá roxo, dietary fibers and amino acids.

Therefore, the different bioactive compounds present in the *Myrciaria* could be used to prevent inflammatory and chronic diseases such as obesity, dyslipidemia, hypertension and diabetes (Zanatta et al., 2015).

Furthermore, the fruit has a high food and pharmaceutical potential and is marketed in the United States, France, Japan and the European Union (Nascimento et al., 2013).

The fruit presents a versatility of its residues (figure 1), the pulp, peel, seed, in lyophilized form, in extract or in capsules were used in vivo and in vitro (Carmo et al., 2019; Nascimento et al., 2013: Schwertz et al., 2012; Vargas, 2012). 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.



Figure 1. pulp, seed and peel of camu camu

3.1. Characterization and nutritional compositions of camucamu fruits

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. The nutritional composition of the fruit demonstrates the presence of minerals such as sodium, potassium, calcium, zinc, magnesium, and manganese (Araújo, 2019). Camu camu also contains significant levels

of vitamin A, glucose, fructose, starch, pectin, phosphorus, nitrogen (Akachi et al., 2012).

The fruits of camu camu still preserve different types of amino acids such as serine, valine, leucine, glutamate, proline, phenylalanine, threonine, and alanine. In addition, its nutritional composition includes several phenolic compounds, carotenoids and flavonoids, anthocyanins, cyanidin-3-glucoside, quercetin, myricetin, catechin, xarinic acid e gallic acid, chlorogenic acid and ellagic acid were found in the fruit (De Azevêdo et al., 2014; Ferreira, 2020).

3.2. The camu camu (Myrciaria dubia (HBK) McVaugh) and vitamin C

The antioxidant effects of vitamin C have been demonstrated to be beneficial against diseases caused by oxidative damage (Monacelli et al., 2017) or useful in the form of therapy against Alzheimer's and Parkinson's disease (Kocot et al., 2017; Contreras-Duarte et al., 2018).Several analyses of the ascorbic acid content of camu camu have been performed.

Pinto et al. (2013) reported that the values of ascorbic acid varied from 759.02 mg per 100 g (in the green phase) to 1,071.12 mg per 100 g (in the violet phase).

Similarly, Chirinos et al. (2010). and Aguiar et al. (2018), respectively $2,010 \pm 65 \text{ mg}.100 \text{ g}^{-1} \text{ FM}$, $2,280 \pm 65 \text{ mg}.100 \text{ g}^{-1} \text{ FM}$. 1.946 mg/100g Vitamin c in the maturation phase: Yuyma et al. (2011) and Grigio et al. (2016), obtained 7,355 mg of ascorbic acid 100 g⁻¹ in the pulp. Neves et al. (2015) measured 13,756.79 mg/100 g for lyophilized pulps.

Camu camu has a high vitamin c content when compared with other fruits, and is 20 times higher than acerola (Malpighia emarginata) and 100 times higher than lemon (*Citrus limon* (L.) Osbeck) Vidigal et al. (2011) and Rufino et al. (2011) described the antioxidant activity of the camu camu in the PPHD test as being IC_{50} = 42.6 g DM.g⁻¹, demonstrating a positive synergism between antioxidant activity and vitamin c content; Chirinos et al. (2010) using the DPPH method, concluded that ascorbic acid has a 70% share of the antioxidant capacity of camu camu.

Camu Camu	Aguiar et al., 2016	Castro et al., 2018	Freitas et al., 2016	Aguiar et al., 2018	Siicex,2016	Castro Gómez et al.,2018	Fernandez et al., 2020
Water (g)	91.83	93.83 ± 0.51	87.42 ± 0.08	92.8	93.20	94.1-94.4	8.21 ± 0.03
Energetic Value (cal)	91.2	19.48 ± 3.68	50.64	89.2	16.00	17 - 20.9	369.08 ± 0.02
Ash (g)	0.258	0.22 ± 0.03	0.32 ± 0.02	0.213	0.20	0.2-0.3	-
Carbohydrates (g/100 g)	8.6	4.84 ± 0.80	11.68 ± 6.37	5.9	5.90	3.5 ± 4.7	84.41±0.03
Fiber (g/100 g)	2.50	0.56 ± 0.40	-	1.69	0.50	0.1 ± 0.6	-
Protein (g/100 g)	0.53	0.51 ± 0.07	$0.44 \pm t \ 0.12$	0.99	0.50	0.4 ± 0.5	5.97±0.08
Lipids (g/100g)	0.032	0.17 ± 0.10	0.79 40 ± 10.24	0.024	-	0.2 ± 0.3	40.2
Niacin (g/100 g)	0040	0.48 ± 0.28	_	0.039	0.61	0.16.	45,4
Riboflavin (g/100 g)	0.015	0.03 ± 0.02	-	0.013	0.04	09.7	15.57
Ferro (mg/100 g)	0.247	0.424 ± 0.152	39.40 ± 1.36	0.232	0.50	180 ± 665	0.79 ± 0.07
Calcium(mg/100 g)	12.1	14.510 ± 9.346	163.80 ± 18.70	8.64	15.73	6.2 ± 15.7	18.8±0.07
Vitamin C (mg/100 g)	1230	2210.00	2260.57	1946	1410	2031 ± 0.04	-

Table 1. Camu camu nutritional composition

3.3. The camu camu (Myrciaria dubia (HBK) McVaugh) and phenolicos compound

Different types of phenolic compounds present in the camu camu such as flavonols, flavanones, anthocyanins, when quantified and important to verify the state of ripeness and the method of extraction (table 4). Bataglion et al. (2015) after analyzing the camu camu *in natura*, found 40 mg quercetin equivalent/100 g), and in the dry pulp found 1.176 \pm 14.8 mg GAE.100 g⁻¹ FM; Langley et al. (2015) cite five Brazilian fruits and seven commercial pulps in their review, among them the camu camu with high contents of chlorogenic acid and ellagic acid.

Fideles et al. (2019) submitted camu camu to drying at 60 °C and obtained 17.93-27.20 mg quercetin equivalent/100 g). Myoda et al. (2010), after analysis of the flavanoid content of camu camu peel and seeds, observed that these values are higher than the sum of the peel and the acerola seed. Fracassetti et al. (2013) compared the values of flavanoids between camu camu flour and pulp powder respectively (4,007.95 mg/100 g versus 48.54 mg/100 g).

During the ripening stage of the fruit (38.98 - 60.75 quercetin equivalent/100 g) Neves et al. (2015), 1120 polyphenols (mg/100 g) Yuyama, (2011), and the unripe fruit accumulated phenolic compound contents of 1,420 mg GAE.100g-1 FM Chirinos et al. (2010). The total

phenolic content of dried camu camu is $10,100 \pm 25$ mg GAE.100 g⁻¹. Neves et al. (2015) and 1161 mg GAE/100 g DM Aketer et al. (2011); and anthocyanins in ripe fruit present 21.95 mg/g. Villanueva-Tiburcio et al. (2010). Ferreira, (2020) evaluated the bioactive compounds present in cubiu (*Solanum sessiliflorum*), camu camu and araçá roxo (*Psidium myrtoides* O. Berg) fruits.

Camu camu showed values of 732 mg GAE/100 g ff from fresh fruit – much higher than cubiu and 12% higher than araçá roxo (Kerimi et al. 2019). Kaneshima et al. (2013) state that C-glycosidic elastin together with the ascorbic acid, anthocyanins, cyanidin-3-glucoside, ascorbic acid, total polyphenols, flavonoids quercetin, myricetin, catechin, xarinic acid and the present gallic acid of the camu camu fruit seeds may be responsible for the antioxidant activity of the fruit.

Kerimi et al. (2019). after analyzing and comparing the antioxidant capacity of other Brazilian fruits such as acerola, jabuticaba (*Plinia cauliflora*), cagaita (Stenocalyx dysentericus), açaí (*Euterpe oleracea*), java plum (*Syzygium cumini*), with camu camu, there was a positive correlation between ascorbic acid and total polyphenols in the oxygen radical absorbance capacity (ORAC) assay (r = 0.795; p < 0.001) and DPPH (r = 0.989; p < 0.001). The camu-camu fruit rich in bioactive components could strategically be used to slow down or prevent metabolic diseases and their comorbidities as and demonstrated in in vivo and in vitro research.

4. STUDIES CAMU CAMU (MYRCIARIA DUBIA (HBK) MCVAUGH) ANTI-OBESITY ACTIVITY

Castro et al. (2018) report in an ethnopharmacological survey, involving medicinal plants from the Amazon region, that the fruit of the camu camu *(Myrciaria dubia (HBK) McVaugh)* was used in medicinal mixtures to treat several diseases including diabetes, hypercholesterolemia and inflammation.

These findings have attracted the attention of several researchers regarding the pharmacological effect of this *Myrciaria* species. Ellinger et al. (2012) elaborated a mixture containing various fruits that were added to camu camu juice in an attempt to reduce oxidative stress in obese smokers. Gonçalves, (2012) supplemented a

group of 17 normocholesterolemic adults with 50 ml of camu camu juice during a period of 15 consecutive days.

The intake of camu caused a reduction in the levels of total cholesterol, LDL-cholesterol, triglycerides.

Vargas, (2012) divided 18 volunteers into two groups: 1) supplemented group, which received capsules of freeze-dried camu camu daily for 15 days; 2) control group, which received a capsule containing 320 mg synthetic vitamin c. At the end of the trial, the supplemented group significantly reduced fasting blood glucose and insulin levels in laboratory tests,

Carmo et al. (2019) studied Wistar rats that were submitted to hyperlipidic diet lasting four weeks, three groups participated in the experiment: Control Group (CG); Camu Camu Group (CCG), which was submitted to the gavage procedure for administration of camu camu hydroalcoholic extract, 1g/kg/day for four weeks, and the Bariatric Surgery Group (BSG), which was submitted to a vertical gastrectomy procedure. The CG's weight increased, the BSG showed a significant reduction in weight and BMI (p <0.05), while the CCG reduced only in BMI (p <0.05).

In addition, Nascimento et al. (2013) supplemented 25 mL of camu camu fruit pulp daily for 12 weeks in rats with experimental obesity and, at the end of the experiment, there was a significant reduction in the weight of fat in white fat tissues. Schwertz et al. (2012) used an induced hyperlipidic diet in Wistar rats, which then received camu camu juice (0.4-10 mL /kg) for 2 weeks.

Treated animals showed a reduction in triacylglycerols, total cholesterol and hepatic and fecal cholesterol.

The fruit presents the reduction of body weight, visceral fat and the elimination of lipids in the feces and liver showing, in other words, hypolipidemic by the camu camu. In table 1 and 2 demonstrates the action of the camu camu in metabolic diseases.

The studies presented so far suggest that camu camu could be a viable anti-inflammatory option and a powerful antioxidant, established in disease prevention and health promotion by several studies, in vivo and in vitro (Nascimento et al., 2013; Schwertz et al., 2012; Akachi et al., 2010; Myoda et al., 2010).

Other important information on the fruit and versatility of residues. Not only the pulp is studied, but the skin and the seed have

already proven their antioxidant and anti-inflammatory action (Carmo et al., 2019).

Thus, the camu camu presents potential for new research that can support the antioxidant potential. Although these investigations using the camu camu are preliminary, there is an indication of its antiobesity potential applied in tests with rat Wister after 12 weeks of supplementation of 25ml of the camu camu pulp. At the end of 12 weeks of LDL.VLDL, the level of insulin, cholesterol, triglycerides were reduced in addition to reducing the weight of the animals and visceral fat deposits (Nascimento et al., 2013).

The first hypothesis is the antioxidant and anti-inflammatory action due to the high content of ascorbic acid and phenolic compounds, anthocyanins, carotenoids, among others (Grigio et al., 2017). These compounds act on the reactive species of oxygen and nitrogen, increasing immunity, regulating cellular synthesis and degradation and modulating the levels of certain catabolic hormones (Babu et al., 2013).

Moreover, the camu camu contains the mineral potassium (Araujo, 2019) that increases the in vivo availability of vitamin c. Affirmed in the experiment of Ellinger et al. (2012) using a 400ml mixture of camu camu juice with açaí and Andean blackberries. This mixture increased the levels of vitamin c in the plasma of 12 participants when compared to the control group.

Depending on the time of harvest, the red camu camu increases the content of total phenolic and anthocyanin increasing the antioxidant and anti-inflammatory activity of the fruit (Zilo et al., 2019).

These actions reduce the incidence of inflammation. Second, due to the existence of dietary fibers in fruit pulp (Schwertz et al., 2012). Dietary fibers regulate the intake of energy, control satiety, increasing the food cake, controlling the transport and absorption of fats.

In addition to reducing the secretion of hormones that act during digestion. Factors peculiar to the development of obesity. Another form of antioxidant action of the camu camu and in the comorbidities caused by obesity such as diabetes (Souza Schmidt et al., 2010).

De Gonçalves et al.(2019) tested camu camu in a type 1 diabetic rat model receiving either 1 or 3 g/kg per body weight of fruit pulp extract by gavage over 30 days. Using the combination of camu camu pulp and soymilk. (Gonçalves et al., 2014; Fujita et al., 2013).

Another form pulp extract powder (spray-dried and frozen) was used by Anhê et al. (2019) in rats on a high-fat, high-sucrose diet. In studies of healthy individuals supplemented with oral administration of juice or pulp and lyophilized capsules (Vargas, 2012). The results in these experiments showed that the camu camu blocked weight gain, increased glucose tolerance and insulin sensitivity.

The anti-diabetic capacity present in the camu camu by the possibility of polyphenols present in the fruit, inhibits disaccharides (α -amylase and α -glucosidase), modulates sodium-dependent glucose carriers (SGLT1-SGLT6, SLC5A family genes) in the intestinal lumen and increases the availability of Glut 2 which reduces post-prandial hyperglycemia (Akter et al., 2011; Nascimento et al., 2018; Lavle et al., 2016; Donado-Pestana et al., 2018).

Another form of action of the polyphenols and ascorbic acid present in the camu camu against diabetes is the defense barrier mechanism of the antioxidant enzymes. Anthocyanins, cyanidin-3glucoside, ascorbic acid, total polyphenols, flavonoids quercetin, myricetin, catechin, xarinic acid and the present gallic acid ripe fruits have the highest antioxidant activity (De Azevêdo et al., 2014; Ferreira, 2020).

After analyzing and comparing the antioxidant capacity of other Brazilian fruits such as acerola, jabuticaba (*Plinia cauliflora*), cagaita (Stenocalyx dysentericus), açaí (*Euterpe oleracea*), java plum (*Syzygium cumini*), with camu camu, there was a positive correlation between ascorbic acid and total polyphenols in the oxygen radical absorbance capacity (ORAC) assay (r = 0.795; p < 0.001) and DPPH (r = 0.989; p < 0.001) [49].

Moreover, during the review, there was only a report of a possible injury or the presence of hepatitis associated with camu camu ingestion. After viral testing, magnetic resonance and biopsy, there was no evidence of such statement; the case was reported. Evidence suggests that camu camu may be a viable support option to mitigate anti-inflammatory processes and increase antioxidant defenses.

Another form of action of the polyphenols and ascorbic acid present in the camu camu against diseases is the defense barrier mechanism of antioxidant enzymes (Anhê et al., 2019). Kaneshima et al.(2013) state that C-glycosidic elastin together with the ascorbic acid of the camu camu fruit seeds may be responsible for the antioxidant activity of the fruit.

Studies using wister rats with hyperdislipedimia and supplemented with fruit pulp (Schwertz et al., 2012 Pereira et al., 2014) a mixture containing several tropical fruits containing 5% camu camu fruit pulp showed high levels of glutathione peroxidase, superoxide dismutase and catalase when compared to the non-supplemented group. Since obese and diabetic individuals are liable to develop hypertension, camu camu may pose a solution.

Balisteiro et al. (2017) and Fidelis et al., (2018) indicated that camu camu fruit pulp (spray-dried) (0.5-1.0%) together with samples of soy milk fermented by lactic acid bacteria inhibited the effect on angiotensin converting enzyme (ACE).

The authors agree on the hypothesis of a synergistic activation between camu camu and an active ingredient of soy milk. In table 1 and 2 demonstrates the action of the camu camu in metabolic diseases.

Although more studies are lacking, the 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 can be part of daily treatment prescriptions, as well as an alternative nonphytotherapic option. It is therefore important to be clear in what way and how the camu camu can not only be a food supplement but also possibly add core values in metabolic disease interventions.

Although new studies should be made. Furthermore, this review should support the fruit of the camu camu as an antioxidant with viable action against metabolic diseases, restoring inflammatory and immune functions.

Knowing that there will be questions from doctors and agencies that regulate the effectiveness of doses and synergism with other drugs. However, the fruit camu camu is surrounded by the literature in evidence that proves its biochemical and nutritional properties in addition to the high content of vitamin c recognized.

Finally, the gap and possibilities are open to reinforce what has been reviewed, especially with human studies taking into account the specific states and phases of the disease, thus increasing confidence among consumers, patients and physicians seeking a drug-free strategy.

Table 1. Effects of Camu-camu	(Myrciaria dubia McVaugh) on the				
prevention of obesity and its comorbidities in animals					

Reference	Population	Experimental Protocol/ Use of the fruit	Methods	Main results	
Nascimento et al, 2013	Rats	Experimental obesity Camu-camu ^a	Two groups. One experimental group, which ingested 25 mL / day of camu-camu pulp (GCC) for 12 weeks and another untreated group (CG).	After 12 weeks, the animals that received the pulp: ↓ BMI, of the fat in white adipose tissues.	
Fidelis et al., 2019	Rats	Antihypertensive activity Camu-camu ^b	Camu-camu seed as antioxidant activity and inhibition of angiotensin converting enzyme (ACE).	The aqueous extract: ↓antihypertensive action in vitro.	
Anhê et al., 2019	Rats	Metabolic tests Camu-camu ^a	The effect of a crude extract of camu camu on obesity and associated immunometabolic disorders	The camu camu: ↓ fat accumulation and glucose tolerance and insulin sensitivity	
Nascimento et al., 2018	Rats	Experimental obesity Camu-camu ª	Foour groups: sedentary group S (no treatment), exercise group E (continuous swimming training), Camu-camu group C (25mL of pulp of Camu- camu/day) and exercise and Camu-camu group EC (25mL of pulp of Camu-camu/day, continuous swimming). After 12 weeks.	After 12 weeks, the Camu- camu in obese rats, showing: \leftrightarrow TC, TG, \downarrow glucose and \uparrow HDL-c and in all groups there was a significant reduction except for the control group.	
Murta, 2017	Rats	Experimental diabetes Camu camu ^e	The shake of skimmed milk powder and camu camu lyophilized. The Wistar rats were treated with the shake of camu-camu oral gavage for about 28 days.	The results indicate the action of the fruit: ↓ hypercholesterolemia	
Gonzales Saldaña, 2018	Rats	Experimental hyperlipidemia and type 2 diabetes ^d	The experimental group received dubious Myrciaria (camu camu) 0.6g / kg for 30 days.	The experimental group shows: \downarrow TC, LDL and TG and \uparrow HDL.	
Goncalves et al., 2014	al., Experimental diabetes ^d		The animals were divided into two main groups. TI: diabetic rats receiving a dose of 1 g/kg of aqueous. camu-camu frozen pulp extract by gavage for 30 days; TII: diabetic rats receiving a dose of 3 g/kg of aqueous. camu-camu frozen pulp extract by gavage for 30 days.	The camu-camu: ↑ plasma antioxidant activity, ↓ triacylglycerol and total cholesterol and lipid peroxidation in the plasma.	

a pulp; **b** seed; c pulp lyophilized; d extracts of camu-camu ; \leftrightarrow , without difference; \uparrow , increased; \downarrow , reduced; ; **BMI**, body mass index; **TC**, total cholesterol; **TG**, triglycerides; **HDL-c**, high-density lipoprotein cholesterol ratio; ; **LDL-c**, low-density lipoprotein cholesterol;

Reference	Population	Experimental Protocol/Use of the fruit	Methods	Main results	
Salomão Oliveira et al, 2018	Voluntee Adult	Experimental study including individuals adults ^a	Two groups were formed: experimental (EG) (n=29) and control (CG) (n=29). The EG group received a capsule containing camu-camu, holding approximately 442 mg of vitamin C for 45 days, and CG received a capsule (placebo) for the same time period	There was a significant reduction in some indicators of MS diagnosis, such as: ↓ BBP, TG , abdominal circumference and ↓ HDL-c.	
Balisteiro et al, 2017	Voluntee Adult	Experimental study including 23 healthy individuals were selected to consume seven meal tests, with a 1 week interval between them, consisting of 50g of adults ^b white bread plus 300mL of water (control) or clarified fruit juice of camu -camu and jaboticaba.		The results indicate that native Brazilian fruit juices can be considered as adjuvant treatment for postprandial blood glucose reduction.	
Vargas, 2012	Volunteer adults	Experimental study including young adults ^a	The volunteers were divided into two groups: 1) intervention group that received capsules of lyophilized camu-camu containing 320 mg of vitamin C; 2) control group that received capsules containing 320 mg of synthetic vitamin C.	At the end of the intervention a significant ↓ in fasting glucose, TC and ↑ HDL-c	
Fujita et al, 2013	In vitro ^c	The camu-camu targeting early stages type 2 diabetes (T2D) and associated hypertension ^c	Dried camu-camu powder combined and with soymilk	Overall, fermentation of camu-camu and soymilk combination resulted in high soluble phenolic ↑ antioxidant activity.	

Table 2. Effects of Camu-camu (Myrciaria dubia McVaugh) on the prevention of obesity and its comorbidities in humans and in vitro

a capsules of lyophilized camu-cam; b larified fruit juice of camu-camu and jaboticaba.; c extracts of camu-camu; MS, metabolic syndrome; \uparrow , increased; \downarrow , reduced; TC, total cholesterol; TG, triglycerides; HDL-c, high-density lipoprotein cholesterol ratio; ; LDLc, low-density lipoprotein cholesterol; AH, arterial hypertension; DBP, diastolic blood pressure

CONCLUSION

The presented review gathers the evidence that camu camu may be a viable alternative for the prevention or treatment of metabolic diseases. Despite the promising results of this fruit, its indication may be based

not only on the nutritional balance present in the fruit, but also because it is a natural source of vitamin c, which can act on several metabolic pathways which give immune responses, besides the anti-inflammatory and antioxidant action of flavanoid and phenolic compounds responsible for the prevention of various diseases.

However, even with the considerable amount of research indicating the effectiveness of the fruit, further studies should be carried out in order to add the existing evidence.

REFERENCES

1.NCD Risk Factor Collaboration. (2019). Rising rural body-mass index is the main drivof the global obesity epidemic in adults. *Nature*, 569(7755), 260.

NCD Risk Factor Collaboration. (2019). Rising rural body-mass index is the main driver of the global obesity epidemic in adults. *Nature*, *569*(7755), 260.

2.BRASIL. Ministério da Saúde. Secretaria de Atenção à Saúde. Departamento de Atenção Básica. Cadernos de Atenção Básica: estratégias para o cuidado da pessoa com doença crônica obesidade. n. 38, Brasília, 2014.

3. Chooi, Y. C., Ding, C., & Magkos, F. (2019). The epidemiology of obesity. *Metabolism*, 92, 6-10.

4. Even, P. C., Virtue, S., Morton, N. M., Fromentin, G., & Semple, R. K. (2017). are rodent Models Fit for investigation of Human obesity and related diseases?. *Frontiers in nutrition*, *4*, 58.

5. Bakirova, R. Y., Muravlyova, L. Y., Koichubekov, B. K., Grigorevskaya, L. A., Bekov, E. K., & Suleimenova, S. B. (2016). The method of "research based learning" on "1.NCD Risk Factor Collaboration. (2019). Rising rural body-mass index is the main abdominal obesity", the students specialty "general medicine". *European Journal of Natural History*, (6), 18-20.

6. Nascimento, O. V., Boleti, A., Yuyama, L. K., & Lima, E. S. (2013). 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*, *85*(1), 355-363.

7. Gonçalves, F. A., Vargas, B. L., Aguiar, J. P. L., & Souza, F. D. C. D. A. (2019). Efeito do néctar de camu-camu (Myrciaria dubia (Kunth) McVaugh) sobre o perfil lipídico e a glicemia de adultos normocolesterolêmicos. *Volume 19, Pags. 27-35.*

8. Langley, P. C., Pergolizzi Jr, J. V., Taylor Jr, R., & Ridgway, C. (2015). Antioxidant and associated capacities of Camu camu (Myrciaria dubia): a systematic review. *The journal of alternative and complementary medicine*, 21(1), 8-14.

9. Vidigal, M. C., Minim, V. P., Carvalho, N. B., Milagres, M. P., & Gonçalves, A. C. (2011). 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 International*, 44(7), 1988-1996.

10. Grigio, M. L., Chagas, E. A., Rathinasabapathi, B., Chagas, P. C., da Silva, A. R. V., Sobral, S. T. M., & de Oliveira, R. R. (2017). Qualitative evaluation and biocompounds

present in different parts of camu-camu (Myrciaria dubia) fruit. African Journal of Food Science, 11(5), 124-129.

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

12. Kocot, J., Luchowska-Kocot, D., Kielczykowska, M., Musik, I., & Kurzepa, J. (2017). Does vitamin C influence neurodegenerative diseases and psychiatric disorders?. *Nutrients*, 9(7), 659.

13. Contreras-Duarte, S., Chen, P., Andía, M., Uribe, S., Irarrázaval, P., Kopp, S., ... & Rigotti, A. (2018). 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*, *51*.

14. Villanueva-Tiburcio, J. E., Condezo-Hoyos, L. A., & Asquieri, E. R. (2010). Antocianinas, ácido ascórbico, polifenoles totales y actividad antioxidante, en la cáscara de camu-camu (Myrciaria dubia (HBK) McVaugh). *Food Science and Technology*, *30*, 151-160.

15. de Azevêdo, J. C. S., Fujita, A., de Oliveira, E. L., Genovese, M. I., & Correia, R. T. P. (2014). Dried camu-camu (Myrciaria dubia HBK McVaugh) industrial residue: A bioactive-rich Amazonian powder with functional attributes. *Food Research International*, *62*, 934-940.

16. Ferreira, F. B. (2020). 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.

17. Zanatta, C. F., Cuevas, E., Bobbio, F. O., Winterhalter, P., & Mercadante, A. Z. (2015). Determination of Anthocyanins from Camu-camu (Myrciaria dubia) by HPLC- PDA, HPLC- MS, and NMR. *Journal of Agricultural and Food Chemistry*, 53(24), 9531-9535.

18. Carmo, H. M. O. D., Souza, F. M. A., Soares, A. C. L., Munhoz, J. A. M., Santos, F. G. A., de Siqueira, N. G., & Silva, R. P. M. (2019). Dietary supplementation with Camu-Camu versus sleeve gastrectomy in Wistar rats weight control. *Revista do Colegio Brasileiro de Cirurgioes*, 46(4), e2238-e2238.

 Schwertz, M. C., Maia, J. R. P., Sousa, R. F. S. D., Aguiar, J. P. L., Yuyama, L. K. O., & Lima, E. S. (2012). Hypolipidemic effect of camu-camu juice in rats. *Revista de Nutrição*, 25(1), 35-44.

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

21. Araújo, P. A. D. C. (2019). Estudo da cinética de secagem de resíduo industrial de camu-camu (Myrciaria dubia), caracterização e extração por líquido pressurizado de seus compostos ativos (Doctoral dissertation, Universidade de São Paulo).

22. Akachi, T., Shiina, Y., Kawaguchi, T., Kawagishi, H., Morita, T., & Sugiyama, K. (2010). 1-methylmalate from camu-camu (Myrciaria dubia) suppressed D-galactosamine-induced liver injury in rats. *Bioscience, biotechnology, and biochemistry*, 74(3), 573-578.

23. Pinto, P. M., Jacomino, A. P., da Silva, S. R., & Andrade, C. A. W. (2013). Harvest point and maturation of camu-camu fruit harvested at different stages. *Pesquisa Agropecuária Brasileira*, 48(6), 605-612.

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

25. Aguiar, J. P. L., & Amaral Souza, F. C. A. (2018). Antioxidant capacidant and bioactive compounds and health benefits of camu-camu puree (Myrciaria dubia (HBK) Mc Vaugh). International Journal of Development Research, 8(6), 20742-20745.

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

27. Grigio, M. L., Chagas, E. A., Durigan, M. F. B., de Andrade Sousa, A., Mota Filho, A. B., & Chagas, P. C. (2016). Determination of harvest time and quality of native camucamu fruits (Myrciaria dubia (Kunth) Mc Vaugh) during storage. *Fruits*, 71(6), 373-378.

28. Neves, L. C., da Silva, V. X., Chagas, E. A., Lima, C. G. B., & Roberto, S. R. (2015). Determining the harvest time of camu-camu [Myrciaria dubia (HBK) McVaugh] using measured pre-harvest attributes. *Scientia Horticulturae*, *186*, 15-23.

29. Vidigal, M. C., Minim, V. P., Carvalho, N. B., Milagres, M. P., & Gonçalves, A. C. (2011). 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 International*, 44(7), 1988-1996.

30. Rufino, M. S., Alves, R. E., Fernandes, F. A., & Brito, E. S. (2011). Free radical scavenging behavior of ten exotic tropical fruits extracts. *Food Research International*, 44(7), 2072-2075.

31. Bataglion, G. A., da Silva, F. M., Eberlin, M. N., & Koolen, H. H. (2015). Determination of the phenolic composition from Brazilian tropical fruits by UHPLC-MS/MS. *Food chemistry*, *180*, 280-287.

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

33. Myoda, T., Fujimura, S., Park, B., Nagashima, T., Nakagawa, J., & Nishizawa, M. (2010). Antioxidative and antimicrobial potential of residues of camu-camu juice production. *Journal of Food, Agriculture & Environment*, 8(2), 304-307.

34. Fracassetti, D., Costa, C., Moulay, L., & Tomás-Barberán, F. A. (2013). Ellagic acid derivatives, ellagitannins, proanthocyanidins and other phenolics, vitamin C and antioxidant capacity of two powder products from camu-camu fruit (Myrciaria dubia). *Food Chemistry*, 139(1-4), 578-588.

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

36. Villanueva-Tiburcio, J. E., Condezo-Hoyos, L. A., & Asquieri, E. R. (2010). Antocianinas, ácido ascórbico, polifenoles totales y actividad antioxidante, en la cáscara de camu-camu (Myrciaria dubia (HBK) McVaugh). *Food Science and Technology*, *30*, 151-160.

37. Kerimi, A., Gauer, J. S., Crabbe, S., Cheah, J. W., Lau, J., Walsh, R., ... & Williamson, G. (2019). Effect of the flavonoid hesperidin on glucose and fructose transport, sucrase activity and glycaemic response to orange juice in a crossover trial on healthy volunteers. *The British journal of nutrition*, *121*(7), 782-792.

38. Kaneshima, T., Myoda, T., Toeda, K., Fujimori, T., & Nishizawa, M. (2013). Antioxidative constituents in camu-camu fruit juice residue. *Food Science and Technology Research*, 19(2), 223-228

37. Akter, MS, OhS, EunJ.-B, Ahmed M. (2011). Nutritional compositions and health promoting phytochemicals of camu-camu (Myrciaria dubia) fruit: A review. *Food Res Inter* 44 pp. 1728–1732.

Kaneshima, JE, Condezo-Hoyos LA, Asquieri, ER. (2010). Antocianinas, ácido ascórbico, polifenóis totais e atividade antioxidante na casca do camu-camu (Myrciaria dubia (HBK) McVaugh). *Ciência e Tecnologia de Alimentos*, 30 (Suplemento 1), 151-160.
Castro Gómez, J. C., Maddox, J. D., Cobos Ruiz, M., & Imán Correa, S. A. (2018). 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.*

40. Ellinger, S., Gordon, A., Kurten, M., Jungfer, E., Zimmermann, B. F., Zur, B., ... & Stehle, P. (2012). 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*, 60(45), 11292-11300.

41. Babu, P. V. A., Liu, D., & Gilbert, E. R. (2013). Recent advances in understanding the anti-diabetic actions of dietary flavonoids. *The Journal of nutritional biochemistry*, 24(11), 1777-1789.

42. Araújo, P. A. D. C. (2019). Estudo da cinética de secagem de resíduo industrial de camu-camu (Myrciaria dubia), caracterização e extração por líquido pressurizado de seus compostos ativos (Doctoral dissertation, Universidade de São Paulo).

43. Zillo, R. R., Silva, P. P. M. D., Spoto, M. H. F., & Martin, J. G. P. (2019). Camu-camu colhido com a casca verde-avermelhada conserva seus compostos físico-químicos e antioxidantes durante o armazenamento a frio. *Brazilian Journal of Food Technology*, 22.

44. De Souza Schmidt Goncalves, A. E., Lajolo, F. M., & Genovese, M. I. (2010). Chemical composition and antioxidant/antidiabetic potential of Brazilian native fruits and commercial frozen pulps. *Journal of agricultural and food chemistry*, *58*(8), 4666-4674.

45. Gonçalves, A. E. D. S. S., Lellis-Santos, C., Curi, R., Lajolo, F. M., & Genovese, M. I. (2014). Frozen pulp extracts of camu-camu (Myrciaria dubia McVaugh) attenuate the hyperlipidemia and lipid peroxidation of Type 1 diabetic rats. *Food Research International*, *64*, 1-8.

46. Fujita, A., Borges, K., Correia, R., de Melo Franco, B. D. G., & Genovese, M. I. (2013). Impact of spouted bed drying on bioactive compounds, antimicrobial and antioxidant activities of commercial frozen pulp of camu-camu (Myrciaria dubia Mc. Vaugh). *Food Research International*, 54(1), 495-500.

47. Anhê, F. F., Nachbar, R. T., Varin, T. V., Trottier, J., Dudonné, S., Le Barz, M., ... & Roy, D. (2019). Treatment with camu camu (Myrciaria dubia) prevents obesity by altering the gut microbiota and increasing energy expenditure in diet-induced obese mice. *Gut*, 68(3), 453-464.

48. Nascimento, O. V. D., Boleti, A. P. D. A., Schwertz, M., & Lima, E. S. (2018). Dietary supplementation with camu-camu and continuous exercises in the treatment of obesity. *Revista de Nutrição*, *31*(1), 25-33.

49. Lavle, N., Shukla, P., & Panchal, A. (2016). Role of flavonoids and saponins in the treatment of diabetes mellitus. *Journal of Pharmaceutical Science and Bioscientific Research*, 6(4), 535-541.

50. Donado-Pestana, C. M., Moura, M. H. C., de Araujo, R. L., de Lima Santiago, G., de Moraes Barros, H. R., & Genovese, M. I. (2018). Polyphenols from Brazilian native

Myrtaceae fruits and their potential health benefits against obesity and its associated complications. *Current opinion in food science*, 19, 42-49.

51. Bertoli, R., Mazzuchelli, L., & Cerny, A. (2013). Acute hepatitis associated with the use of natural product camu-camu.

52. Pereira, A. C., Dionísio, A. P., Wurlitzer, N. J., Alves, R. E., de Brito, E. S., Brasil, I. M., & Mancini Filho, J. (2014). Effect of antioxidant potential of tropical fruit juices on antioxidant enzyme profiles and lipid peroxidation in rats. *Food Chemistry*, 157, 179-185.
53. Balisteiro, D. M., de Araujo, R. L., Giacaglia, L. R., & Genovese, M. I. (2017). Effect of clarified Brazilian native fruit juices on postprandial glycemia in healthy subjects. *Food Research International*, 100, 196-203.

54. Fidelis, M., Santos, J. S., Escher, G. B., do Carmo, M. V., Azevedo, L., da Silva, M. C., ... & Granato, D. (2018). In vitro antioxidant and antihypertensive compounds from camu-camu (Myrciaria dubia McVaugh, Myrtaceae) seed coat: A multivariate structure-activity study. *Food and chemical toxicology*, *120*, 479-490.

55. Murta, G. C. (2017). Desenvolvimento e efeito de bebida tipo shake à base de pó de camu-camu (Myrciaria Dubia [HBK] McVaugh) no controle da diabetes, in vivo.

56. Gonzales Saldaña, J. G. (2018). Efecto hipolipemiante de myrciaria dubia (camucamu) en rattus norvegicus cepa holtzman con diabetes tipo 2 inducida.

57. Salomão-oliveira, A., Costa, S. D. S., & Marinho, H. A. (2018). Metabolic syndrome: Intake of Camu-Camu (Myrciaria dubia (Kunth) Mc Vaugh). *Volume 3, Pags. 5-13.*

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

59. Fujita, A., Borges, K., Correia, R., de Melo Franco, B. D. G., & Genovese, M. I. (2013).

Impact of spouted bed drying on bioactive compounds, antimicrobial and antioxidant activities of commercial frozen pulp of camu-camu (Myrciaria dubia Mc. Vaugh). *Food Research International*, 54(1), 495-500.