Bioactive Compounds of Soursop (*Annona muricata* L.) Fruit

Luis M. Anaya Esparza and Efigenia Montalvo-González

Contents

L. M. Anaya Esparza
Laboratorio Integral de Investigación en Alimentos, Tecnológico Nacional de México/Instituto Tecnológico de Tepic, Tepic, Nayarit, Mexico

Laboratorio de Microbiología de Alimentos, Departamento de Ciencias Pecuarias y Agrícolas, Centro Universitario de los Altos, Universidad de Guadalajara, Tepatitlán de Morelos, Jalisco, Mexico
e-mail: l_m_ae@hotmail.com

E. Montalvo-González (✉)
Laboratorio Integral de Investigación en Alimentos, Tecnológico Nacional de México/Instituto Tecnológico de Tepic, Tepic, Nayarit, Mexico
e-mail: efimontalvo@gmail.com; emontalvo@ittepic.edu.mx

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Abstract

Soursop (*Annona muricata*) belongs to the family Annonaceae and is widely distributed and commercially cultivated in the tropical and subtropical climates around the world. The stem, leaves, roots, fruits, seeds, peel, and pulp of soursop have been used in traditional medicine for the treatment of diverse ailments. Most of the beneficial activities in human health are attributed to the presence of bioactive compounds (BC) with several in vitro and in vivo biological activities, including anti-inflammatory, antitumoral, and analgesic effects. This chapter focuses on nutritional quality, traditional uses, and the bioactive compounds from *A. muricata* fruit and their relation with biological activities.

Keywords

Biological activities · Health benefits · Nutritional quality · Soursop fruit · Traditional uses

Abbreviations

AAE	Ascorbic acid equivalent
ACE	Angiotensin-I converting the enzyme
ACGs	Acetogenins
AOX	Antioxidant activity
BC	Bioactive compounds
BC-AMF	Bioactive compounds from *A. muricata* fruit
DSSC	Dietary supplement of soursop capsules
GI	Glycemic index
LD_{50}	Lethal dose
TCA	Trichloroacetic acid
TE	Trolox equivalent
VCE	Vitamin C equivalent

1 Introduction

Annona muricata L. is commonly known as soursop, and it is native from Central America and the West Indies [1]. The plant belongs to the Annonaceae family, and it is widely distributed and commercially cultivated in the tropical and subtropical climates around the world [2, 3]. Additionally, the soursop fruit has been considered to be the most cultivated and delicious fruit of the *Annona* genus; its flavor is more acid and less sweet than cherimoya (*Annona cherimola* Mill) [2, 4].

Several studies have shown the physiological, physicochemical [3], and nutritional [5] characterization from soursop fruit, including the presence of bioactive compounds (BC) in the pulp, seed, columella, and peel [6, 7]. *A. muricata* plant parts have been used in the traditional medicine for the treatment of diverse ailments [1]; nonetheless, scientific evidence shows that the extracts from soursop pulp have great potential for industrial and pharmaceutical applications, due to their in vitro and in vivo biological activities [8].

Table 1 Nutritional composition and energy value (per 100 g of the edible portion on a fresh weight basis) of *Annona muricata* fruit

Components	Moreno-Hernández et al. [9]	Badrie and Schauss [1]	Vwioko et al. [10]
Calories (kcal)	68.17	68.55	64.01
Moisture (%)	80.71	82.8	75.8
Protein (%)	1.03	1	0.26
Fat (%)	0.77	0.67	0.85
Carbohydrates (%)	14.28	14.63	13.83
Fiber (%)	[a]2.59	0.79	[a]0.36
Ash (%)	3.32	0.6	8.90

[a]Dietary fiber

2 Nutrimental Content

Table 1 shows the nutrimental composition and energy value of the edible part of *A. muricata*. The soursop pulp has high amounts of water (76–83%), carbohydrates (13–15%), low content of lipids (0.67–0.85%), and proteins (0.26–1.03%) [1, 9, 10]. Furthermore, soursop pulp exhibits a good percentage of dietary fiber (0.36–2.59%), which has demonstrated important implications in human nutrition and health [11]. Besides, soursop pulp is very low in calories (64–68 kcal per 100 g of edible portion) (Table 1), and it contains some nutritionally important components to human health such as vitamins, minerals, and amino acids, as shown in Table 2. In this context, the regular consumption of soursop pulp could provide essential nutrients and elements to human health.

3 Traditional Uses and Health Importance

Soursop pulp is commonly eaten raw (fresh) or processed [1, 12]. The processed pulp is available in the market in the preserved form [13, 14]. However, due to its excellent sensory properties (taste, flavor, and odor), the pulp has been suitable for processing in food and beverage products such as juice, nectar, ice cream, jelly, jam, puree, syrup, fruit bar, flakes, milkshakes, yogurt, and alcoholic beverages [12, 15–18].

A. muricata fruit (pulp and seeds) has been used as a natural medicine by native people of various cultures for a wide range of illnesses [19]. The fruit and fruit juice have been consumed in some part of the world (Jamaica, Haiti, the Dominican Republic, Colombia, Bolivia, the West Indies, Suriname, the Philippines, and Brazil) due to several health benefits against fever, diarrhea, dysentery, hematuria and urethritis, asthma, and parasitic and liver diseases, and it also exerts antispasmodic, antiemetic, and antisudorific properties [1, 20–22]. Soursop pulp is used as lactagogue, which increased the mother's milk during the postpartum period [1, 22].

Table 2 Vitamins, minerals, and amino acid content of *Annona muricata* fruit

Minerals (mg/100 g)		Vitamins (mg/100 g)		Amino acids (mg/100 g)	
Calcium	10.3[a]	Vitamin A (retinol)	14.45[b]	Tryptophan	11[a]
Phosphorus	27.7[a]	Vitamin B1 (thiamin)	0.11[a]	Methionine	7[a]
Iron	0.64[a]	Vitamin B2 (riboflavin)	0.05[a]	Lysine	60[a]
Magnesium	0.04[c]	Vitamin B3 (niacin)	1.28[a]		
		Vitamin C (Ascorbic acid)	29.6[a]		
		Vitamin E (tocopherol)	29[c]		

Source: [a]Badrie and Schauss [1]; [b]Pinto et al. [2]; [c]Onyechi et al. [5]

4 Phytochemicals Present in *A. muricata*

Extensive qualitative and quantitative phytochemical screening on different parts (leaves, barks, roots, stems, and fruits that include the seeds, peel, columella, and pulp) of *A. muricata* plant has been conducted [8]. The types of compounds include alkaloids, terpenoids, kauranes, lignans, megatigmanes, phenols, flavonoids, tannins, cyclopeptides, glycosides, and essential oils, among others [8, 22, 23]. All these compounds have great potential for use in industry and medicine [8].

4.1 Phytochemical Present in Soursop Fruit

A. muricata fruit contains a wide range of natural compounds, identification, and quantification of the phytochemicals that have gained importance in the recent years, mainly by their potential biological activities and benefits to the human health [19, 24]. Phytochemicals such as phenols [6, 7, 25], flavonoids [5, 7, 26–29], carotenes [28, 30], alkaloids [23, 31–34], saponins [35], and acetogenins [36–39] have been identified by qualitative or quantitative methods in *A. muricata* fruit (Table 3).

Additionally, a qualitative screening on unripe *A. muricata* fruit revealed the presence of saponins, tannins, terpenoids, flavonoids, anthraquinone, and cardiac glycoside, while the quantitative screening showed that cardiac glycoside (27.19 mg/g) was the highest occurring phytochemicals in the extract followed by terpenoid (19.3 mg/g), tannin (13.1 mg/g), flavonoid (9.09 mg/g), saponin (4.63 mg/g), and anthraquinone (1.1 mg/g) [40]. Additionally, soursop pulp has esters of aliphatic acids (51%), 2-hexanoic acid methyl ester (24%), and 2-hexenoic acid ethyl ester (8.6%) as main compounds, which are classified as essential oils [41].

4.1.1 Phenols, Carotenoids, and Flavonoids

Phenolic, carotenoid, and flavonoids are considered as antioxidants with potential health benefit for the human body [42] due to their free radical scavenging activity [7, 28] as discussed below. The main compounds found in *A. muricata* fruit include gallic, chlorogenic, 4-hydroxybenzoic, protocatechuic, syringic and ellagic acids, kaempferol, epicatechin, quercetin, lutein, tocotrienol, and tocopherols [5–7, 28, 30]. Evidence indicates that *A. muricata* fruit is rich in antioxidant compounds, and the

Table 3 Bioactive compounds present in *Annona muricata* fruit (mg/100 g of edible part dry weight)

Bioactive compound	Content (mg/100 g DW)	Activity	References
Phenolic compounds			
Soluble polyphenols	2470	Antioxidant	[6]
Hydrolyzable polyphenols	568	Antioxidant	[6]
Condensed tannins	286	Antioxidant	[6]
Total polyphenols	3324	Antioxidant	[6]
Cinnamic acid	42.04	Antioxidant	[6, 7]
Coumaric acid derivative	X	Antioxidant	[7]
5-Caffeoylquinic acid	X	Antioxidant	[7]
p-Coumaric acid	0.07	Antioxidant	[6, 7]
Caffeic acid derivative	X	Antioxidant	[7]
Dicaffeoylquinic acid	X	Antioxidant	[7]
Cinnamic acid hexose	X	Antioxidant	[7]
Feruloylglycoside	X	Antioxidant	[7]
p-Coumaric acid methyl ester	X	Antioxidant	[7]
Coumaric acid hexose	X	Antioxidant	[7]
4-feruloyl-5-caffeoylquinic acid	X	Antioxidant	[7]
Gallic acid	15.86	Antioxidant	[6]
Chlorogenic acid	12.80	Antioxidant	[6]
4-hydroxybenzoic acid	131.63	Antioxidant	[6]
Protocateic acid	25.37	Antioxidant	[6]
Syringic acid	148.83	Antioxidant	[6]
Neochlorogenic acid	72.32	Antioxidant	[6]
Ellagic acid	74	Antioxidant	[26]
Coumarin	X	Antioxidant and anti-uricemic	[27]
Flavonoids	5.24	Antioxidant	[5]
Anthocyanins	7.35	Antioxidant	[5]
Apigenin	0.0194	Antioxidant	[29]
Myricetin	0.1257	Antioxidant	[28, 29]
Luteolin 37-di-O-glucoside	X	Antioxidant	[29]
Morin	X	Antioxidant	[31]
Kaempferol	325	Antioxidant	[26]
Kaempferol 3-O-rutinoside	X	Antioxidant	[29]
Fisetin	X	NR	[28]
Dihydrokaempferol-hexoside	X	Antioxidant	[7]
Epicatechin	151	Antioxidant	[26]
Quercetin	171	Antioxidant	[26]
Rutin	36	Antioxidant	[26]
Carotenes			
α-Carotene	0.002	Antioxidant	[30]

(*continued*)

Table 3 (continued)

Bioactive compound	Content (mg/100 g DW)	Activity	References
β-Carotene	0.005	Antioxidant	[30]
β-Cryptoxanthin	0.005	Antioxidant	[28, 30]
Lycopene	0.008	Antioxidant	[28, 30]
Lutein	0.006	Antioxidant	[28, 30]
Tocopherol α	0.012	Antioxidant	[28, 30]
Tocotrienol α	∗0.005	Antioxidant	[28, 30]
Tocotrienol γ	0.011	Antioxidant	[30]
Alkaloids	2		[23]
Annonaine	X	Antidepressive	[31, 32]
Nornuciferine	X	Antidepressive	[31, 32]
Asimilobine	X	Antidepressive	[31, 32]
N-methylcoculaurine	0.0088	NR	[33]
Reticuline	0.091	NR	[33, 34]
Saponins	1.40	Antioxidant	[35]
Acetogenins			
Annonacin	X	Neurodegenerative	[36]
Annonacin-10-one	X	NR	[36]
cis-annoreticuin	X	Cytotoxic	[38]
Epomusenin A	X	NR	[37]
Epomusenin B	X	NR	[37]
Epomurinin A	X	NR	[37]
Epomurinin B	X	NR	[37]
Montecristin	X	NR	[36]
Corossolone	X	Cytotoxic	[36]
Montanacin H	X	Cytotoxic	[36]
Muricatin C	X	NR	[36]
Muricenin	X	Cytotoxic	[39]
Muricin J	X	Cytotoxic	[39]
Muricin K	X	Cytotoxic	[39]
Muricin L	X	Cytotoxic	[39]
Muricin M	X	Cytotoxic	[39]
Muricin N	X	Cytotoxic	[39]
Murihexocin A	X	Cytotoxic	[36]
Xylomatenin	X	Cytotoxic	[36]
Montanacin D	X	NR	[36]
Montanacin E	X	NR	[36]

X = detected (qualitative), *NR* = not reported

diets rich in phytochemicals have been associated with a reduced risk of non-transmittable diseases [43]. Therefore, the regular consumption of *A. muricata* fruit can provide capability of preventing degenerative diseases and improve human health [44].

4.1.2 Alkaloids

Alkaloids are secondary metabolites characterized by the presence of a nitrogen atom, preferentially synthesized and stored in the leaves of the *A. muricata* plant, but their presence also has been reported in the soursop fruit [33]. The alkaloids reported in *A. muricata* fruit are mainly isoquinoline derivatives including annonaine, nornuciferine, asimilobine, N-methylcoculaurine, and reticuline [31, 32]. Some of these compounds are toxic to SH-SY5Y neuroblastoma cells and inhibitors of the mitochondrial respiratory complex [36], and alkaloids can act as an antidepressant agent [31, 32].

4.1.3 Acetogenins

Acetogenins (ACGs) are secondary metabolites found in Annonaceae family; they are constituted of a long aliphatic chain bearing oxygenated groups, terminated by a γ-methyl-γ-lactone, which is most generally α, β-unsaturated, with one or two tetrahydrofurans located along the hydrocarbon chain [36]. ACGs are considered as the main bioactive compounds of Annonaceae family; it has been identified >120 ACGs from leaves, roots, stems, and fruit pulp and peel of *A. muricata* [8]. Nonetheless, more than 20 ACGs were identified in the pulp, where annonacin is the most representative ACGs [36–39]. The ACGs exhibit extensive biological activities where the antitumoral activity is one of the most studied as discussed below [36–39].

Additionally, the extraction of ACGs is an extensive process, where the yield is mainly dependent on the solvent and the extraction method is employed [45]. León-Fernández et al. [46] evaluated different solvents (chloroform, methanol, ethyl acetate, and water) and extraction methods (Soxhlet, sonication, and microwave) to obtain ACGs from *A. muricata* fruit. They reported that sonication or microwave was adequate to obtain ACGs from *A. muricata* in short times and few solvent costs (chloroform and ethyl acetate). Furthermore, the presence of ACGs in soursop products such as soursop yogurt (38 ng/g) and soursop-frozen dessert (15 ng/g) has been reported by Virgen-Ceceña et al. [18].

5 Biological Activities of Bioactive Compounds from *A. muricata* Fruit

Several biological activities of *A. muricata* have been reported in the association of bioactive compounds (raw extracts, fraction or isolated compounds) from the fruit, and its parts are described below.

5.1 Antioxidant Activity

The antioxidant activity (AOX) of foods is determined by the presence of different antioxidant compounds, with a different mechanism of action to inhibit radicals [47]. AOX has been investigated in *A. muricata* fruit by different in vitro methods as ABTS (1200 μmol TE/100 g) [3], FRAP (382 mmol AAE/100 g) [45], ORAC (14. 5 μmol TE/g) [30], and DPPH (830 μmol of VCE/100 g) [48]. That may give credence to the folklore use of the plants for a myriad of disease conditions. The AOX of *A. muricata* fruit is highly correlated mainly with the phenolic compounds and total flavonoids [49]. However, several other antioxidant compounds have been identified, such as tannins, saponins, glycoside, and acetogenins [5, 8, 46, 50].

Zamudio-Cuevas et al. [51] reported a decrease in the expression of a member of the NADPH oxidase family by the antioxidant activity of bioactive compounds from *A. muricata* fruit (BC-AMF). Also, the BC-AMF proved not to be cytotoxic in fibroblast cultures and showed cytoprotective capacity against hydrogen peroxide-induced stress; in cell culture, it reduced the generation of ROS significantly by inhibiting a sub-unit of the NADPH oxidase enzyme (p47phox) and mentioned that BC from *A. muricata* fruit could prevent damage caused by cellular oxidants.

5.2 Anti-inflammatory and Analgesic Activity

Ishola et al. [52] investigated the anti-inflammatory (carrageenan-induced rat paw edema and xylene-induced ear edema tests) and analgesic (the mouse writhing, formalin, and hot-plates tests) activities of BC-AMF in rodents. The authors proposed that mechanism of the anti-inflammatory and analgesic effect of BC (200 mg/kg) is related with the inhibition of chemical mediators of inflammation and the interaction with opioidergic pathway; however, these effects were dose-dependent. Al-Brakati et al. [53] evaluated the anti-inflammatory effect of BC-AMF (300 mg/kg) by immunohistochemistry technique on rats exposed to acetaminophen intoxication. The BC-AMF-pretreated rats demonstrated a decrease in the expression of the pro-inflammatory and antioxidant markers, which evidence the anti-inflammatory capacity of the BC-AMF in rats, by a decrease in the level of pro-inflammatory cytokines.

5.3 Anti-amnesic Activity

It has been reported that excessive consumption of soursop products (infusions from leaves, roots, and barks, also the fruit pulp) may cause degenerative disorders and has been correlated with an atypical Parkinsonism [54–56]. Conversely, Al-Omari et al. [57] mentioned that BC-AMF exhibit high potential to be used as an anti-amnesic agent against Alzheimer's disease.

Al-Omari et al. [57] investigated the potential neuroprotective role of BC-AMF in scopolamine (SCO)-induced amnesia (via modulation of the cholinergic pathway and monoaminergic system) and oxidative damage in the hippocampus of rats. BC-

AMF pretreatment markedly ameliorated hippocampal changes, reflecting its efficiency in the improvement of cognitive performance. Their findings revealed that BC-AMF exerts a potential anti-amnestic effect mainly through the activation of the cholinergic system and Nrf2/HO-1 pathway.

5.4 Antidepressant Activity

Hasrat et al. [31] reported that BC-AMF possesses antidepressant effects on test animals, mainly by the presence of isoquinoline alkaloids as annonain, nornuciferine, and asimilobine. These alkaloids exhibit high affinity to serotonergic 5-HT1A receptors and modulate dopaminergic transmission, which is involved in depressive disorders [31].

5.5 Hypoglycemic Activity

A. muricata fruit exhibited a GI of 30; a low GI improves glycemic control in individuals with impaired glucose tolerance and type 2 diabetes [26]. Adefegha et al. [47] evaluated the in vitro antidiabetic and antihypertensive properties of BC-AMF on key enzymes linked to type 2 diabetes (α-amylase and α-glucosidase) and hypertension (angiotensin-I converting enzyme (ACE)). BC-AMF inhibited α-amylase (50%), α-glucosidase (60%), and ACE (50%) activities, and especially, the inhibition of ACE reduces the risk of developing type 2 diabetes [47].

Oboh et al. [26] reported that the inhibition of ACE activity is due to the antioxidant capacity of polyphenol and flavonoid compounds present in BC-AMF (especially by their chelating activity), preventing the oxidative damage of pancreatic *β*-cells which are implicated in impaired insulin production/function. It has been reported that flavonoids can inhibit α-glucosidase through hydroxylation bonding and substitution at β ring; this inhibition decreases carbohydrate hydrolysis and glucose absorption and inhibits carbohydrates metabolism into glucose [58].

5.6 Antihypertensive Effect

Adefegha et al. [47] evaluated the in vitro antihypertensive properties of BC-AMF, which inhibited the activities of the ACE and reported the strong correlation between the ACE inhibition and phenolic content. This lowers blood pressure by a mechanism that does not involve cholinergic, histaminergic, or endothelial-dependent pathways and that the mechanism of action is acting as calcium antagonists [59].

5.7 Anti-uricemic Activity

Ewadh et al. [27] used BC-AMF for natural treatment of gout and reported a considerable inhibition of the xanthine oxidase activity (in vitro test). BC-AMF (70%) was compared with the positive control (67%, allopurinol), which lead to reducing the production of uric acid. Results suggested that coumarin (a significant fraction of phenolic compound) possesses antioxidant and anti-uricemic activity.

5.8 Hepatoprotective Effect

Al-Brakati et al. [53] evaluated the protective effect of BC-AMF against hepatic injury associated with acetaminophen (APAP) exposure (over 2000 mg/kg) in albino rats, and they observed the remarkable restoration of liver biomarkers such as alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase, and total bilirubin in rats after 7 days of oral administration of SPME (300 mg/kg). Authors highlighted substantial prevention of histological damage in the liver of rats and also the anti-inflammatory effect by administration of SPME [53].

Alzergy et al. [60] evaluated the biological activity of BC-AMF and dietary supplement of soursop capsules (DSSC, sold on the Libyan market as a cancer cure) against trichloroacetic acid (TCA)-induced hepatotoxicity in mice. Mice treated with both (BC-AMF and DSSC) showed ameliorative changes and disappearance of the most pathological changes in the liver tissue (histological examination) compared with the control group [60].

5.9 Antitumoral Activity

Jepkorir et al. [61] evaluated the phytochemical components of soursop fruit and their proliferative activity on the breast (HCC 1395), cervical (Hela), and prostate (DU145) cancer cell lines. The BC-AMF had an LD_{50} of 23.6, 72.5, and 93.6 μg/mL on Hela, DU145, and HCC 1395 cells, respectively. The standard drug used had LD_{50} of 21.1 μg/mL on HCC and 24.8 μg/mL on Hela cells, while a selective inhibition on the growth of HCC cells was observed. On the other hand, Sun et al. [62] isolated ACGs (muricins M and N, and muricenin) from soursop pulp which have shown cytotoxic activity against human prostate cancer cells (PC-3) [62].

In addition, León-Fernández et al. [63] evaluated the toxic effect of BC-AMF (5, 10, 20, 50, 100, and μg/mL) on *Artemia salina*. They reported that BC-AMF showed toxic effects on *A. salina* (LD_{50} ranged from 4 to 33 μg/mL), evidencing the potential cytotoxic effect. The toxicity of BC-AMF might be related to the presence of ACGs [46, 64].

5.10 Antimicrobial and Antifungal Activity

León-Fernández et al. [63] evaluated the antimicrobial activity of BC-AMF against *Enterobacter aerogenes*, *Salmonella typhimurium*, *Bacillus subtilis*, and *Enterococcus faecalis*. They reported that BC exhibited significant inhibitory activity against *E. aerogenes* (17–20 mm) and *Salmonella typhimurium* (18–20 mm). The antibacterial activity was attributed to the presence of alkaloids, acetogenins, and polyphenols. The same authors evaluated the antifungal activity of BC-AMF against *Colletotrichum gloeosporioides* and *Rhizopus stolonifer*. They reported inhibition of 59% in *R. stolonifer* and 38% in *C. gloeosporioides*. The fungistatic or fungicidal effect of BC may be related to the presence of alkaloids, saponins, polypeptides, terpenes, essential oils, and polyphenols, which have a wide spectrum of action [65].

6 Other Studies

6.1 Acute Toxicity

Syahida et al. [66] evaluated the effect of BC-AMF on rats subjected (via force-feeding) to in vivo 28-day repeated doses (0 g/kg = control group; 0.5 g/kg = low dose; 1.0 g/kg = medium dose; 2.0 g/kg = high dose). The authors demonstrated that administration of BC-AMF did not cause any toxicological effects or negative effects on the liver and kidney since the values were in the normal ranges. Similar trends were later reported by Awodele et al. [67] that BC-AMF did not induce any toxic effect on rats at a dose of 2 g/kg after 60 days of administration [68].

7 Conclusions

A. muricata (Soursop) is the most representative fruit of the *Annona* genus; its pulp is low in calories and very digestible and contains vitamins (A, B, C, and D), minerals (calcium, phosphorus, and iron), and bioactive compounds such as alkaloids, phenols, and acetogenins. Traditional uses of *A. muricata* to treat illness such as diarrhea, dysentery, and fever have scientific validation due to their in vitro antimicrobial activity. However, in vivo studies support the widespread traditional use of *A. muricata* as anti-parasitic agent, anti-inflammatory, antinociceptive, anxiolytic, anti-stress, hypotensive, hepatoprotective, gastroprotective, and antitumoral activity. The most extensive bioactivities studied in the *A. muricata* are as hypoglycemic and antitumoral. Until now, the toxic effect of *A. muricata* fruit had not been reported. The increasingly popular use of *A. muricata* fruit is related to their potential biological activities and by their interesting phytochemical profile.

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