

Queries for Author

Paper: **cabi.91923.029**

The proof of your manuscript appears on the following page(s).

Please read the manuscript carefully, checking for accuracy, verifying the reference order and double-checking figures and tables.

During the preparation of your manuscript for publication, the questions listed below have arisen. Please attend to these matters and return the answers to these questions when you return your corrections.

Please note, we will not be able to proceed with your article and publish it in print if these queries have not been addressed.

No	Query
AQ1	'Acetogenin in soursop fruit (annonacin) is a neurotoxin' - In context, singular, yes?
AQ2	R1 Please provide an in-text citation for reference Adefegha, 2015.

29 Soursop (*Annona muricata* L.)

Annegowda Hardur Venkatappa¹ and Rajeev Bhat^{2*}

¹Sri Adichunchanagiri College of Pharmacy, Adichunchanagiri University, Nagamangala, Mandya, Karnataka, India; ²ERA-Chair for Food (By-) Products Valorization Technologies, Estonian University of Life Sciences, Tartu, Estonia

Abstract

Soursop (*Annona muricata* L.) is one of the widely consumed and marketed fruit of the Annonaceae family. It possesses high nutraceutical and biopharmaceutical value (nutritional and therapeutic value). Soursop fruit are sweet with an exotic flavour, and loaded with essential vitamins, minerals and antioxidant-rich polyphenolic compounds. The fruit are established for their bioactivity such as antioxidant, anticancer, antimicrobial, larvicidal and insecticidal properties. However, soursop fruit have been linked with induced toxicity, owing to some of the compounds present. The waste portions, mainly peel and seed, have been recognized to encompass ample amounts of bioactive components. Soursop fruit are climacteric and perish rapidly, thus necessitating the application of various postharvest techniques to preserve them for an extend period. In this chapter, information on botanical aspects, cultivation, traditional uses, presence of bioactive components, nutraceutical value and postharvest preservation along with potential applications is discussed.

Introduction

Ever since the beginning of human civilization, fruit and vegetables have been considered as two important components of a healthy diet. Regular consumption of fruit and vegetables not only provides nutrition and energy, but also helps in the prevention of various degenerative diseases related to cardiovascular systems, inflammation, cancer and others. Among a wide range of popular fruit available on the international market, fruit belonging to Annonaceae family remain the most popular and are widely admired for their smooth and creamy flesh, exotic flavour and sweet taste (Márquez Cardozo *et al.*, 2013). Soursop fruit is native to Central and South America, but often encountered in the majority of tropical and subtropical regions, such as

Australia, Bermuda, Brazil, China, Colombia, Cuba, India, Malaysia, New Zealand, Panama and Vietnam. The fruit contributes partially to regional economic growth, being sold as fresh fruit or exotic processed products (Shashirekha *et al.*, 2008; Rabelo *et al.*, 2016). The top three producers of soursop are Mexico, Venezuela and Brazil (Pinto *et al.*, 2005; Márquez Cardozo *et al.*, 2013).

This fruit has more importance in comparison with other species of Annonaceae family members, mainly due to commercial importance, nutritional and medicinal values (Pinto *et al.*, 2005). Thus, it can be considered as a fruit with nutraceutical or biopharmaceutical value. However, the seeds of the fruit are toxic (1–2 cm in length and 0.3–0.6 g in weight) and occur from very few to up to 200 in number (; Moghadamtousi *et al.*, 2015). Soursop fruit have

*Corresponding author: rajeev.bhat@emu.ee

a tinge of papaya, apple, pineapple, mango and strawberry flavour with the edible portion being 67% of the total weight. The fruit have an attractive aroma and exotic taste of the flesh part (pulp) and can be used either fresh or frozen. The fruit are used to prepare juice (sherbets), smoothies, ice cream, milkshake and as an ingredient to make desserts. In South America, this plant is also grown as an ornamental/garden plant.

Though many research works are available on this fruit, information remains scattered on the composition, nutraceutical value and postharvest technologies employed for its preservation for an extended time, emphasizing the importance of recording this information in a single document, as done in this book chapter, wherein information regarding the nutritional and therapeutic values, food applications and postharvest technologies are covered.

Botanical Description

Annona muricata L. belongs to the family Annonaceae and is popularly known as soursop, graviola, guyabano, durian belanda and mamphal. The plants are small, slender, erect evergreen trees reaching a height of up to 5–8 m at full maturity. Leaves are oblong to ovate to cylindrical, 14–16 cm in length and 5–7 cm in width. Soursop trees are highly sensitive to frost and temperatures below 5°C (Mishra *et al.*, 2013). The fruit are large, oval, heart-shaped, dark green coloured when unripe, and slightly light green-coloured on ripening. It is one of the larger fruit of the genus *Annona* weighing up to 10 kg (average weight being 3–4 kg) (Tovar-Gómez *et al.*, 2011). The rind or skin portion of the fruit has short, soft and pointed spines. The pulp is white, cottony, fibrous and juicy, surrounded by a central soft pith/core (Fig. 29.1).

Traditional Uses

Since time immemorial, soursop fruit has been traditionally used as a natural medicine to cure various ailments. Immature fruit are used to treat skin diseases, skin rash, cankers, fever, malaria, peptic ulcer, dysentery and colic diseases. In addition, the peel of the immature

fruit is used in treating atonic dyspepsia (Khan *et al.*, 1998). The acidic pulp of the immature fruit is used to treat liver diseases and to cure foot parasite (Pinto *et al.*, 2005). In Jamaica and the West Indies, the fruit has been used to reduce fever, dysentery and gastric ulcers (Badrie and Schauss, 2010), to treat malaria and as an antiviral and abortifacient agent (Osorio *et al.*, 2007). In the Philippines and Uganda, it is used to treat hypertension, cancer and diabetes (Ong and Kim, 2014), while in Brazil, the fruit is used as a galactagogue. In Bolivia, soursop fruit are used to treat kidney disorders, and in the Dominican Republic to treat asthmatic symptoms, arthritis pain, neuralgia and rheumatism (Badrie and Schauss, 2010; Vandebroek *et al.*, 2010; Hajdu and Hohmann, 2012; Moghadamtousi *et al.*, 2015). In South America, the fruit are claimed to have a tranquillising effect (Hasrat *et al.*, 1997). In Malaysia, the fruit juice is used to treat stomach pain and hypertension. In the Philippines the fruit is used in the management of diabetes, while in Peru it is used to treat obesity, gastritis, dyspepsia and inflammation (Daddiouaissa and Amid, 2018).

Nutritional Composition

The fruit harvest season can influence the biochemical composition of soursop fruit. Those harvested during the dry season are reported to have higher values of sugar, acidity and ascorbic acid than fruit harvested during the wet season. However, the volume of alcoholic components and protein were much higher when harvested during the wet season (Omoifo, 2004). The quantity of fruit pulp accounts for 75% of the total weight followed by peel (20%) and seed (5%). The edible pulp portion contains ~81% of water, 17% carbohydrates, 1% protein, 0.5% lipids and 3.3% fibre. The amount of crude protein and crude fibre was detected to be higher in the peel, whereas the amount of crude fat, moisture and carbohydrate was greater in the pulp (Akomolafe and Ajayi, 2015). The fruit has 1% acidity and mainly contains citric acid and slight amounts of ascorbic, malic and isocitric acid. The acidity of the fruit pulp was recorded to increase corresponding with the increased production of ascorbic acid, and

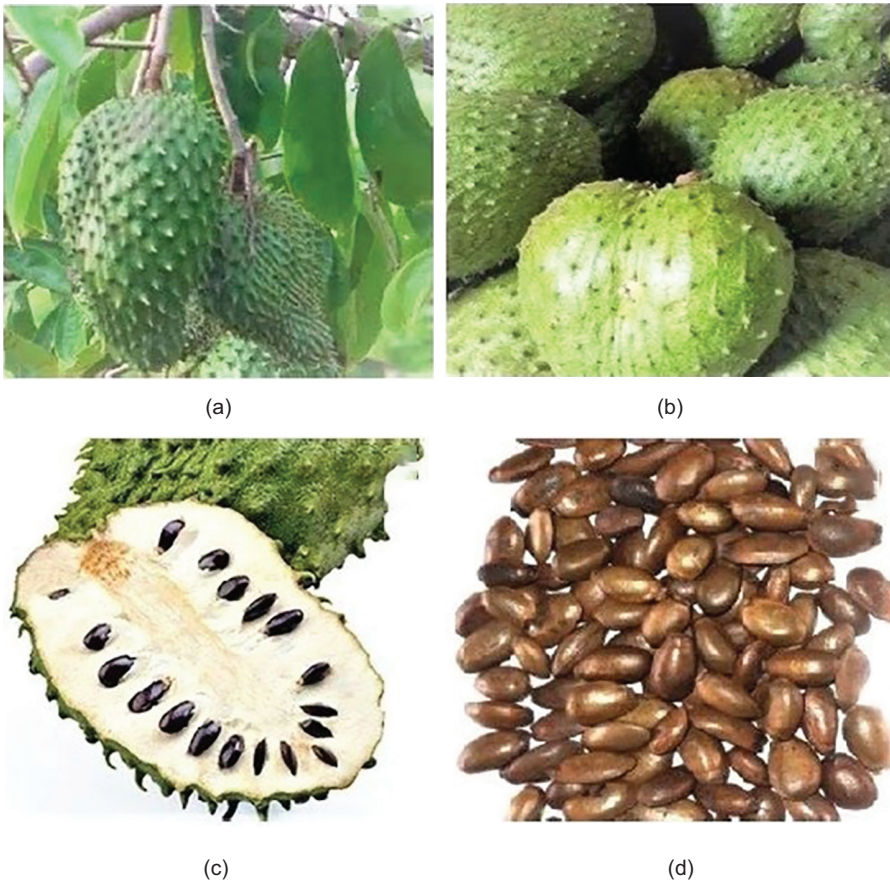


Fig. 29.1. Soursop fruit (*Annona muricata* L.): (a) whole fruit on plant; (b) freshly harvested fruit; (c) cut-open fruit showing white cottony pulp and seeds; (d) dried seeds (photo: authors).

this was maximum after harvesting, which was attributed to increased metabolic activity (Pareek *et al.*, 2011). The total amount of sugars in soursop generally ranges between 16–17%. The sugar level (total soluble solids $1.02 \pm 0.28\%$; sucrose $2.97 \pm 0.24\%$; glucose $3.60 \pm 0.27\%$) has been observed to increase during the ripening process (owing to hydrolysis of starch) (Badrie and Schauss, 2010; Márquez Cardozo *et al.*, 2012). The total amount of sugars reaches concentration approximately five days after harvesting. The increased soluble solids/sugars during ripening is attributed to the breakdown of polysaccharides by enzymes such as amylase, cellulase and polygalacturonase (Paull *et al.*, 1983). The glycemic index and glycemic load is reported to be 32 and 3, respectively, which

is very low and thus requires no dietary restrictions (Passos *et al.*, 2015). In addition, 100 g of fruit contains 2IU vitamin A (retinol), 0.07 mg vitamin B1 (thiamine), 0.05 mg vitamin B2 (riboflavin), 0.08 mg vitamin B12, 0.2 mg vitamin B3, 1.2 mg vitamin B5, 22.6 mg of vitamin C and 0.08 mg of vitamin E (Márquez Cardozo *et al.*, 2012). The vital minerals present in 100 g of fruit pulp are potassium (278 mg), that can help in the prevention of hypertension, calcium (14 mg) and phosphorus (27 mg), both helpful in bone and teeth formation. Further, phosphorus, magnesium, sodium, potassium and zinc are reported to be higher in the peel compared to the pulp (Akomolafe and Ajayi, 2015). Magnesium (0.04 mg/100 g pulp) functions like a co-factor of many enzymes involved

in various metabolic reactions and protein synthesis along with 85 mg of tannins (Coria-Téllez *et al.*, 2017, 2018). Various enzymes like pectinase, catalase and peroxidase are found in the pulp of soursop fruit (Arbaisah *et al.*, 1997). Pectin-esterase is a heat-resistant enzyme that can be used for gelatinization and precipitation of pectin in purées and juice, thus reducing the cloudiness. The amylase formed during ripening helps in converting polysaccharides into simple sugars. Enzymes like polygalactouronase, cellulase and polyphenols oxidase were also found

in the fruit, responsible for cell wall degradation and fruit colour change to brown (Bezerra *et al.*, 2003). In Table 29.1, the nutritional value and bioactive components in an edible portion (100 g) of soursop fruit are compared with other fruit in the Annonaceae family.

During ripening, the green colour (due to chlorophyll pigment) of the fruit peel gets diminished leaving behind a slight yellowish colour (owing to carotenoid pigment). Further, ripening of fruit leads to change in the colour from green to brown due to the oxidation

Table 29.1. Nutritional and other bioactive components in edible portion (100 g) of soursop fruit compared with other fruit of the Annonaceae family (Pinto *et al.*, 2005; Badrie and Schauss, 2010; Márquez Cardozo *et al.*, 2012; Moo-Huchin *et al.*, 2014; Padmanabhan and Paliyath, 2016).

Component	Fruit type (Annonaceae family)			
	Soursop (<i>Annona muricata</i> L.)	Cherimoya (<i>Annona cherimola</i> L.)	Custard apple (<i>Annona reticulata</i> L.)	Sugar apple (<i>Annona squamosa</i> L.)
Moisture content	~81%	~79%	~73–77%	~71%
Protein (g)	~1	1.57	1.7	2.06
Fat (g)	~0.5	0.68	0.60	0.3
Carbohydrates (g)	16.84	17.71	25.20	23.64
Fibre	3.3	3.0	2.4	4.4
Calcium (mg)	14	10	30	24
Potassium (mg)	278	287	382	247
Phosphorus (mg)	27	26	21	32
Iron (mg)	0.64	0.27	0.71	0.60
Magnesium (mg)	21	17	18	21
Vitamin A (IU)	2	5	33	6
Vitamin B5 (mg)	1.2	0.8	0.7	0.9
Thiamine (mg)	0.07	0.101	0.080	0.110
Vitamin B12 (mg)	0.08	0.12	0.12	0.13
Riboflavin (mg)	0.05	0.131	0.100	0.113
Niacin (mg)	0.900	0.644	0.500	0.883
Ascorbic acid (mg)	22.6	11.5	30	37.4
Vitamin E (mg)	0.08	0.27	-	-
Titrateable acidity	1.02	-	0.66	-
pH	3.70	-	-	-
Total soluble solids (°Brix)	~11.0	-	17.75	-
Energy (kilocalories)	65	75	101	94
Anthocyanin (mg/100 g)	6.44	-	1.55	0.73
Flavonoids (mg of quercetin/100 g)	9.32	-	418.24	-

and polymerization of phenols by the enzyme polyphenoloxidase. During this time, the fruit skin becomes smooth and soft. Simultaneously, there is a significant decrease in the pH of the pulp from 5.5 to 3.7 within three to four days of ripening (owing to an increase in ascorbic acid, malic acid and citric acid content, respectively) (Paull *et al.*, 1983). Furthermore, the flavour of the fruit varies and is related to respiration and ethylene production (with the ethylene peak being 250–350 mL/kg/h) accompanied by decreased weight. It was also observed that on the first day of harvest, the fruit start producing CO₂ (100 mL/kg/h), reaching a maximum (350 mL/kg/h) on the fourth day (at 25–30°C). After this, there occurs a bland flavour with loss of astringency, owing to overripening of fruit. During this stage, fermentation of sugars and a decreased level of organic acids and phenols occurs (Badrie and Schauss, 2010; Pareek *et al.*, 2011; Márquez Cardozo *et al.*, 2012).

Chemical Constituents

Systematic phytochemical research has been carried out on the pulp of soursop fruit, which revealed the presence of various types of major phytoconstituents like alkaloids (1.9 mg), tannins (65.98 mg), flavonoids (9.32 mg), saponins (0.17 mg) and anthocyanins (6.44 mg) in 100 g of fruit pulp (Pinto *et al.*, 2005; Onyechi *et al.*, 2012). Each fruit is reported to contain 14–226 µmol annonaceous acetogenins in 100 g of fruit pulp (Bonneau *et al.*, 2017). These are responsible for sporadic atypical Parkinsonism or dementia syndromes (Lannuzel *et al.*, 2007). Studies have revealed the neurodegenerative effects of annonacin (Yamada *et al.*, 2014; Höllerhage *et al.*, 2015). Acetogenins have been isolated from the fruit pulp (by column chromatography and by HPLC), and among them annonacin was the major acetogenin identified (Ragasa *et al.*, 2012; Sun *et al.*, 2014). Acetogenin, the main bioactive compound in soursop, is a lipophilic secondary metabolite derived from long-chain fatty acids, which are responsible for pharmacological activity (Alali *et al.*, 1999).

The by-products of soursop are reported to contain phenolic acids like cinnamic acid,

coumaric acid, syringic acid, procateic acid, gallic acid, caffeic acid, 4-hydroxybenzoic acid, chlorogenic acid and neochlorogenic acid, that serve as a source of antioxidants (Aguilar-Hernández *et al.*, 2019). In Table 29.2, phytoconstituents/bioactive compounds in various parts of soursop fruit and their bioactivities are shown.

Aroma compounds

Gas chromatography/mass spectroscopic analysis (GC-MS) of the fruit pulp during various stages of ripening revealed the presence of esters, aldehydes, alcohols, terpenes and ketones. Further, esters of aliphatic acids were detected to be the dominant odour compound (~51%) followed by 2-hexenoic acid ethyl ester (8.6%), 2-octenoic acid methyl ester (5.4%) and 2-butenic acid methyl ester (2.4%), which were present in the essential oils extracted from fruit pulp (Jirovetz *et al.*, 1998). However, half-ripe and unripe fruit contained ~70% and 60% of esters, respectively. The solid-phase micro-extraction (SPME) and GC-MS study of fruit pulp revealed the presence of 21 compounds among which 12 compounds were identified to be esters like methyl hexanoate, methyl 2-hexenoate, ethyl caproate, ethyl 2-hexenoate, methyl caprylate, methyl crotonate, ethyl butyrate, butyl acetate, ethyl crotonate, methyl caproate, etc. Pulp also contained mono- and sesquiterpenes like β-caryophyllene, 1,8-cineole, linalool, limonene, α-terpineol, linalyl propionate, linalyl propionate, linalyl propionate, α-ocimene, β-myrcene, δ-limonene and calarene. Moreover, alcohol, such as 1-pentanol, 2-hexanol, 2-heptanol, 1-octanol and isopulegol, was detected in the essential oil of the fruit (Augusto *et al.*, 2000; Pino *et al.*, 2001). The compound methyl butanoate is responsible for the pineapple-like, fruity and sweet flavour; compounds like methyl hexenoate, methyl pentenoate and methyl 2-butanoate are responsible for fruity and sweet flavour. Ethyl hexanoate is responsible for fruity flavour; methyl heptenoate and methyl octanoate are responsible for orange flavour; methyl cinnamate for strawberry flavour; β-myrcene for balsamic and spice flavour; δ-limonene for citrus and mint flavour; and linalool for lavender flavour (Santana *et al.*, 2017). Such essential oils are

Table 29.2. Phytoconstituents/bioactive compounds in various parts of soursop fruit and their bioactivities.

Fruit portion	Bioactive compounds	Compounds identified	Bioactivity	Reference
Whole fruit	Flavonoids	Myricetin, fisetin, morin, kaempferol, isorhamnetin, quercetin 3-O-glucoside, and quercetin	Antioxidant activity	Lako <i>et al.</i> (2007) Rubio-Melgarejo <i>et al.</i> (2020)
Whole fruit	Phenolic acids	Ferulic acid and <i>p</i> -coumaric acid	Antioxidant activity	Rubio-Melgarejo <i>et al.</i> (2020)
Whole fruit	Acetogenins	Bullatacin	Potent against L1210 murine leukemia	Badrie and Schauss (2010)
Whole fruit	Acetogenins	Muricin (M and N), muricenin	Muricin M & N shown potent antiproliferative activity against human prostate cancer (PC-3) cells	Sun <i>et al.</i> (2016)
Whole fruit	Acetogenins	Annonamuricin (A, B and C)	Demonstrated potent antiproliferative activity against human prostate cancer (PC-3) cells	Sun <i>et al.</i> (2017)
Pulp	Acetogenins	Cis-annoreticuin, sabadelin	Cytotoxic against human hepatoma carcinoma cell line (Hep G2)	Ragasa <i>et al.</i> (2012)
Pulp	Phenolics	Gallic acid, chlorogenic acid, caffeic acid	Antioxidants	Blancas-Benítez <i>et al.</i> (2019)
Pulp	Phenolics	Gallic acid, cinnamic acid, coumaric acid, 4-hydroxybenzoic acid, chlorogenic acid	Antioxidants	Aguilar-Hernández <i>et al.</i> (2019)
Seeds	Phenolic acids	Gallic acid, chlorogenic acid, caffeic acid, ferulic acid, <i>p</i> -coumaric acid, <i>m</i> -coumaric acid, <i>O</i> -coumaric acid	Antioxidant activity	Menezes <i>et al.</i> (2019)
Seeds	Flavonoids	Rutin, quercetin, catechin	Antioxidant activity	Menezes <i>et al.</i> (2019)
Seeds	Fatty acids	Methyl palmitate, methyl oleate, methyl stearate, 10-nonadecanol	Larvicidal against <i>Aedes aegypti</i>	Komansilan <i>et al.</i> (2012)
Seed	Acetogenins	Annorecticuin-9-one	Cytotoxic to human pancreatic tumour cell line (PACA-2), human prostate adenocarcinoma (PC-3) and human lung carcinoma cells (A-549)	Ragasa <i>et al.</i> (2012)

Continued

Table 29.2. Continued

Fruit portion	Bioactive compounds	Compounds identified	Bioactivity	Reference
Seed	Phenolics	Cinnamic acid, syringic acid, procateic acid, gallic acid, chlorogenic acid, caffeic acid, 4-hydroxybenzoic acid, neochlorogenic acid	Antioxidants	Aguilar-Hernández <i>et al.</i> (2019)

considered to be of use to enhance the flavour of processed food products.

Pharmacological and bioactivity

A wide range of pharmacological and bioactivity has been reported for soursop fruit, thus supporting its use in traditional medicine. Some of the important activities include antimalarial, antiparasitic and anticancer potency (Zafra-Polo *et al.*, 1998; Chih *et al.*, 2001). Acetogenins like annonacin, gigantetrocin, isoannonacin, isoannonain-10-one and goniiothalamycin obtained from the defatted seeds of the fruit are reported to exhibit cytotoxic effects against A-549 lung carcinoma, MCF-7 breast carcinoma and HT-29 colon adenocarcinoma human tumour cell lines (Rieser *et al.*, 1993). The study conducted by Aguilar-Hernández *et al.* (2020a) revealed the peel and seeds to be a potential source of acetogenins, and these researchers identified sonication to be an ideal method for extraction.

The freeze-dried fruit pulp extract exhibited analgesic and anti-inflammatory activities in rodents (Ishola *et al.*, 2014). Methanolic extracts (obtained by Soxhlet extraction) of seeds and pulp of *A. muricata* possess potential cytotoxic effect against cell lines of prostate (PC3) and cervical cancer (HeLa). Besides, moderate activity against breast cancer cell lines (MCF-7) were recorded (Raybaudi-Massilia *et al.*, 2015). Acetogenins like muricins M and N, and muricenin, have been reported to exhibit cytotoxic activity against human prostate cancer cells (PC-3) (Sun *et al.*, 2016). Aqueous extract of the fruit inhibited proliferation of breast cancer cells (T47D) with least toxicity in comparison with tamoxifen (Fidianingsih and Handayani,

2014). The bioactive acetogenin was identified as bullatacin, which was found to be 10^4 to 10^5 times more effective than doxorubicin against A549 and MCF-7 cell lines (Hopp *et al.*, 1997). Bullatacin was also found to be 300 times more active as taxol in L1210 murine leukemia-bearing mice (Ahammadsahib *et al.*, 1993). Acetogenins of the fruit extract induced cytotoxicity by inhibiting the mitochondrial complex I (NADH: ubiquinone oxidoreductase) of the electron transport chain which decreases ATP production causing apoptosis (Miyoshi *et al.*, 1998). In addition, acetogenin nanosuspension (144.4 nm particles) prepared using hydroxypropyl-beta-cyclodextrin and soybean lecithin significantly increased the cytotoxicity against both HeLa and HepG2 cancer cell lines compared to normal acetogenins. The cytotoxic effect of acetogenin nanosuspension in H22 tumour-bearing mice was 1/10th in comparison with normal acetogenins. Additionally, intravenous administration of the acetogenin nanoparticle shown good efficacy compared to the oral administration of the same (Hong *et al.*, 2016). Fruit extracts also selectively inhibited the human breast-cancer cell lines via down-regulation of EGFR (Dai *et al.*, 2011). Annonacin obtained from fruit extract led to growth arrest and apoptosis of MCF-7 cell lines and attenuated MCF-7 xenograft tumour growth in nude mice (Ko *et al.*, 2011). A beverage prepared using the pulp of soursop and blackberry with yogurt inactivated the breast tumour cells (MCF-7) and prostate tumour cells (PC3) along with exhibiting good antioxidant activity (Zambrano *et al.*, 2018). The methanolic and aqueous extracts of fruit pulp induced apoptosis as well as G₀/G₁ cell cycle arrest in MCF-7 cell lines. They also showed good antioxidant and anti-inflammatory activities (Prasad *et al.*, 2020). Methanolic extracts of

fruit pulp showed potential anticancer activity against human hepatic cancer cells (HepG02) (Hemalatha *et al.*, 2020).

The fruit pulp extracted with methanol-acetone has been reported to exhibit potent antioxidant activity (González *et al.*, 2017). Fruit peel possessed significant chelating ability, hydroxyl radical scavenging activity and ferric reducing antioxidant properties compared to pulp (Akomolafe and Ajayi, 2015). The fruit pulp inhibited α -amylase and α -glucosidase and reduced the assimilation of glucose into blood in diabetic patients (Agu *et al.*, 2019). Administration of fruit juice to experimental rabbits revealed dose-dependent hypocholesterolemic activity (Jimoh *et al.*, 2018). The fruit extract also exhibited a neuroprotective effect by maintaining the transmission of various neurotransmitters in scopolamine-induced amnesia with the enhancement of cellular glutathione antioxidant enzymes in an animal model (Al-Brakati *et al.*, 2019).

The fruit pulp showed significant antibacterial activity against *Enterobacter aerogenes* and *Salmonella typhimurium*, and antifungal activity against *Colletotrichum gloeosporioides* and *Rhizopus stolonifer* (León-Fernández *et al.*, 2019). The fruit fermented for over a week exhibited higher antimicrobial activity in comparison with unfermented fruit (Otto *et al.*, 2015). In one of the studies, the pericarp of the soursop fruit significantly inhibited α -amylase and α -glucosidase enzymes, and showed antidiabetic activity and inhibition of angiotensin-converting enzymes under *in vitro* conditions. The result of this study also showed the free radical scavenging and ferrous chelating activities to be strongly correlated with polyphenolic compound and flavonoid content in the pericarp.

Alkaloids present in the fruit (e.g. annonaine, nor-nuciferine, asimilobine) are reported to possess antidepressant activity (proved in animal models), and this was attributed to their moderate affinity towards 5-HT_{1A} receptor and to the inhibitory effect on dopamine reuptake (Hasrat *et al.*, 1997). Freeze-dried unripe fruit extract did not show any mortality even at a dose of 4000 mg/kg in acute toxicity studies. The fruit extract with a dose of 200 mg/kg possessed peripheral and central analgesic activity through acting on opioid systems

and exhibiting anti-inflammatory activity via inhibiting cyclooxygenase activity and nitric oxide generation (Ishola *et al.*, 2014). Soursop fruit extract mitigated caffeine-induced toxicity on weight of testes, epididymes, sperm motility, count and sperm head abnormalities. This effect was correlated to the presence of rich amounts of vitamin C and the antioxidant potency of the fruit (Ekaluo *et al.*, 2013).

Bioassay guided isolation of bioactives from soursop fruit seeds against parasitic *Leishmania* sp. like *donovani* and *Mexicana*, which led to the isolation of acetogenins like annonacinone and corosolone (Vila-Nova *et al.*, 2011). Annonacin isolated from pulp of soursop fruit is reported to induce nigral and striatal neurodegeneration *in vivo* (Champy *et al.*, 2004) and was also found to cause neuronal cell death in neuron culture (Escobar-Khondiker *et al.*, 2007). Acetogenin in soursop fruit (annonacin) is a neurotoxin responsible for 'Guadeloupean' typical Parkinsonism. This is mainly because of neurodegeneration potency of the annonacin as it depletes the ATP supply to mitochondrial cells of rat striatal neurons (Escobar-Khondiker *et al.*, 2007; Bonneau *et al.*, 2015). It is also suggested that the amount annonacin accumulated by the daily consumption of soursop fruit for over a year (as recorded after administering intravenously in rats) can lead to brain lesions (Champy *et al.*, 2004).

Ethanol extracts of soursop fruit seeds in combination with *Piper nigrum* showed five times higher synergistic larvicidal activity (Grzybowski *et al.*, 2013). In addition, seed extracts demonstrated good larvicidal and insecticidal effects against *Aedes albopictus* and *Culex quinquefasciatus* (Ravaomanarivo *et al.*, 2014).

Implications of Food Processing and Preservation on Nutrients, Phytochemicals and Overall Fruit Quality

After attaining market maturity, the fruit are handpicked and washed with fresh or chlorinated water to remove adhering dust, soil particles and pesticides (if any) present on the surface. Later the fruit are peeled by hand followed by extraction using a blender without mixing the peel and without breaking the seeds as they

contain toxic chemicals. The soursop fruit are usually processed into juices, ice creams, nectar (sweetened pulp) or sherbet (Pinto *et al.*, 2005). A refreshing drink is prepared in Cuba and Brazil using fruit pulp, milk and sugar, served as 'champol' (Badrie and Schauss, 2010). In these regions, the fruit pulp is used in preparation of ice cream, juice blends, sherbets, nectars, syrups, milkshakes, jams, jellies and yoghurts. The fruit powder is also used in the preparation of fruit bars and fruit flakes (Umme *et al.*, 1999, Umme *et al.*, 2001; Gratão *et al.*, 2007).

The fruit pulp is processed and preserved either by freezing or by pasteurization for commercial purposes. If the pulp and nectar are pasteurized at 85°C and 90.6°C, respectively, they can be preserved for over a year. The quality of the processed products mainly depends on the amount of total sugars, vitamin C retained, pectinesterase activity, acidity and viscosity. Higher temperatures (around 93°C) decreased the quality of processed (frozen) fruit and this was opined to be altered by varying the vitamin C content and pectinesterase activity. During the preparation of juice, jam and marlamade, nearly 18% of the pulp is mixed with 11% of sugar and 0.02% of sodium benzoate and sodium metabisulfide. This is mixed with water and heated (at 100°C for 15 minutes). The soursop nectar (of 10 and 15%), on incorporation with yoghurt, showed good acceptance levels and had appreciable amounts of zinc, calcium and phosphorus (Lutchmedial *et al.*, 2004).

Pasteurization of soursop purée (at 78.8°C for a period of 69 s at a pH of 3.7) retained its sensory qualities along with improvement in the colour and appearance compared to non-pasteurized purée (Umme *et al.*, 1999). Soursop puree stored at -20°C showed higher stability in comparison with the puree stored at 4 and 15°C (Umme *et al.*, 1999). Addition of ascorbic acid to the pasteurized purée retained the flavour of the nectar; an antioxidant inhibited the polyphenols oxidase mediated pulp darkening of the fruit (Umme *et al.*, 2001).

For long-term preservation, the juice was subjected to pasteurization at 85°C followed by storing at various temperatures (4, 10 and 25°C). The pasteurized juice retained its consistency and quality without any visual changes for 12 weeks when preserved at temperatures of 4 and 10°C, whereas in the case of juice

stored at 25°C after three to five weeks there was a decrease in the pH, total soluble solids and increased titratable acidity along with spoilage (Ampofo-Asiama and Quaye, 2019). In the majority of cases, soursop fruit juice viscosity is high and turbid. Addition of α -amylase to fruit juice reduced the viscosity along with a reduction in turbidity. This was attributed to the liquefaction of starch found in the fruit by α -amylase enzyme (Atolagbe *et al.*, 2016).

The amount of soursop fruit harvested globally is meeting only a small proportion of global demand, and this necessitates sustainable production and increased cultivation of this species. Around 30% of soursop fruit loss occurs during the postharvest period. After harvesting, the fruit need to be processed and preserved for longer, but various constraints like short storage life, the fragile nature of the peel, loss occurring in flavour due to thermo-sensitiveness, inactivation of enzymes (cell wall degrading and browning enzymes) and uneven ripening of fruit render these steps very tedious. When stored at 15°C, nearly nine days are required for ripening, while at 21°C ripening takes seven days and at 22–23°C it takes six days (Lima *et al.*, 2004).

Postharvest management technologies can help to overcome the problems associated with the marketing of the fruit only in the regions close to the cultivating areas and this helps to provide consumers with excellent quality of the product. Some of the techniques include selection of the fruit, disinfection, pre-cooling, drying of residual moisture, waxing, storage and transport (Jiménez-Zurita *et al.*, 2017). Understanding the postharvest physiology of soursop fruit is necessary for the establishment of handling procedures and for recognition of ideal packaging conditions. Fruit can be preserved for a long time at room temperature ($25 \pm 1^\circ\text{C}$) if subjected to postharvest preservation technologies like refrigeration, coating and modified atmosphere. In addition, accurate harvest time of the fruit is also important to find out the shelf life of the fruit. Soursop, being a climacteric fruit, have different periods of maturity and ripen at different intervals. Therefore, immature fruit are often harvested and subjected to forced ripening in storage. In Colombia, the fruit is verified for its maturity by pressing the fruit between the thumbs. Great care must be taken to ensure that the fruit is physiologically mature otherwise it can exhibit irregular maturation

with off-taste. If fruit are harvested when they are ripened then they have reduced shelf life. It is not recommended to leave the fruit on the tree until maturation as it may fall and not meet the requirements for successful sale (Pareek *et al.*, 2011).

The shelf life of soursop fruit can be prolonged either by covering with waxes (carnauba wax, candelilla wax, polyethylene wax, etc.) or by refrigeration. In fruit covered by candelilla wax, maturity is delayed and the fruit weight loss during ripening reduced. Similarly, post-harvest shelf life of fruit was extended up to eight days when fruit were stored at 15–22°C (Berumen-Varela *et al.*, 2019). Another study revealed a seven-day delay in reaching maturity after treating fruit with 1-methylcyclopropene (1-MCP) followed by storing at 16°C without chilling injury (Espinosa *et al.*, 2013). Soursop fruit, when treated with 1-MCP and polyethylene wax and stored at 15.4°C, retained total soluble solids, titratable acidity, pH, soluble sugars and reducing sugars during storage up to 15 days (Lima *et al.*, 2004). The emulsion prepared using 1-MCP with carnauba wax, candelilla wax and silicone oils when applied on soursop fruit delayed the ripening up to 15 days of storage compared to a control batch reaching ripening stage within six to seven days (Tovar-Gómez *et al.*, 2011). The flash-pasteurized nectar could be stored for a period of a year at 30°C without any noticeable loss in the quality of the nectar (Benero *et al.*, 1974). Soursop purée if maintained at –23°C, is reported to be preserved for nearly 400 days (Pinto *et al.*, 2005).

Soursop fruit when coated with the emulsion of 1-methylcyclopropene (1-MCP) and beeswax (15:85 v/v) were preserved for a period of 14–15 days at 16°C when compared to the preservation at 25°C for only a period of six days (Moreno-Hernández *et al.*, 2014). Application of 1.0 and 1.5% of chitosan on harvested soursop fruit prevented fungal infection and weight loss after three, six and nine days. Additionally, the pH, total soluble solids, firmness and titratable acidity was not altered by chitosan application (Ramos-Guerrero *et al.*, 2020).

Browning of soursop is very common as it is a climacteric fruit and browning of fruit is mainly catalysed by the enzyme polyphenoloxidase. Browning of fruit along with the preservation of its nutrients and flavour can be ensured by adapting advanced green technologies like

microwaves and ultra-sonication. Exposure to microwaves reduced polyphenoloxidase enzyme activity in the fruit by 57% at 70 W in 30 s and ultrasound treatment reduced the activity of polyphenoloxidase by 43% at 120 W in 220 s (Palma-Orozco *et al.*, 2019). So, soursop fruit pulp can be preserved for an extended time by converting it into dry powder. Fruit pulp dried by spray-drying method maintained antioxidant potency and nutritional value with minimal changes in aroma and volatile components (Neta *et al.*, 2019).

Conclusion and Outlook

Soursop is a recognized nutraceutically valued fruit imparting rich health benefits. The edible pulp encompasses appreciable amounts of vital minerals, vitamins and antioxidant-rich polyphenolic compounds. The fruit imparts a rich exotic flavour that makes it popular. Since the fruit is widely consumed, development of quantitative assays to identify bioactives is needed. Although soursop is a good nutritional source, the presence of various toxic acetogenins affects dopaminergic and other neurons that are responsible/contribute towards developing atypical Parkinsonism when this fruit is consumed in large quantities. The neurotoxic effect is restricted only to the isolated acetogenins, not the pulp of the fruit, and hence future study is required to ensure the safety of the fruit. However, these acetogenins are also reported to possess cytotoxic potency against various human cancer cell lines that necessitates studies to decide the amount of fruit to be consumed to obtain the required therapeutic effect with minimal side effects. When it comes to overall safety, the amount of soursop fruit consumption mainly depends on the individual's age and associated comorbid diseases, if any. Consumption of this fruit needs to be strictly avoided among pregnant and breastfeeding mothers. There is great scope to explore the waste and by-products of soursop fruit with a view to obtaining value-added bioactive compounds. Overall, to conclude, soursop fruit can be a power-packed nutraceutically valued source if consumed with certain precautions.

References

- A02** Adefegha, S.A., Oyeleye, S.I. and Oboh, G. (2015) Distribution of phenolic contents, antidiabetic potentials, antihypertensive properties, and antioxidative effects of soursop (*Annona muricata* L.) fruit parts in vitro. *Biochemistry Research International* 2015, 347673. DOI: 10.1155/2015/347673.
- Agu, K.C., Eluehike, N., Ofeimun, R.O., Abile, D., Ideho, G. *et al.* (2019) Possible anti-diabetic potentials of *Annona muricata* (soursop): inhibition of α -amylase and α -glucosidase activities. *Clinical Phytoscience* 5(1), 1–13. DOI: 10.1186/s40816-019-0116-0.
- Aguilar-Hernández, G., García-Magaña, M. de L., Vivar-Vera, M. de L.Á., Sáyago-Ayerdi, S.G., Sánchez-Burgos, J.A. *et al.* (2019) Optimization of ultrasound-assisted extraction of phenolic compounds from *Annona muricata* by-products and pulp. *Molecules* 24(5), 904. DOI: 10.3390/molecules24050904.
- Aguilar-Hernández, G., Vivar-Vera, M. de L.Á., García-Magaña, M. de L., González-Silva, N., Pérez-Larios, A. *et al.* (2020a) Ultrasound-assisted extraction of total acetogenins from the soursop fruit by Response Surface Methodology. *Molecules* 25(5), 1139. DOI: 10.3390/molecules25051139.
- Ahmmadsahib, K.I., Hollingworth, R.M., McGovren, J.P., Hui, Y.H. and McLaughlin, J.L. (1993) Mode of action of bullatacin: a potent antitumor and pesticidal annonaceous acetogenin. *Life Sciences* 53(14), 1113–1120. DOI: 10.1016/0024-3205(93)90547-g.
- Akomolafe, S.F. and Ajayi, O.B. (2015) A comparative study on antioxidant properties, proximate and mineral compositions of the peel and pulp of ripe *Annona muricata* (L.) fruit. *International Food Research Journal* 22(6), 2381–2388.
- Al-Brakati, A.Y., Al Omairi, Kassab, R.B., Lokman, M.S., Elmahallawy, E.K. *et al.* (2019) Soursop fruit extract mitigates scopolamine-induced amnesia and oxidative stress via activating cholinergic and Nrf2/HO-1 pathways. *Metabolic Brain Disease* 34(3), 853–864. DOI: 10.1007/s11011-019-00407-2.
- Alali, F.Q., Liu, X.X. and McLaughlin, J.L. (1999) Annonaceous acetogenins: recent progress. *Journal of Natural Products* 62(3), 504–540. DOI: 10.1021/np980406d.
- Ampofo-Asiama, J. and Quaye, B. (2019) Effect of storage temperature on the physicochemical, nutritional and microbiological quality of pasteurised soursop (*Annona muricata* L.) Juice. *African Journal of Food Science* 13, 38–47.
- Arbaisah, S.M., Asbi, B.A., Junainah, A.H. and Jamilah, B. (1997) Purification and properties of pectinesterase from soursop (*Annona muricata*) pulp. *Food Chemistry* 59(1), 33–40. DOI: 10.1016/S0308-8146(96)00043-X.
- Atolagbe, O.M., Ajayi, A.A. and Edegbo, O. (2016) Characterization of α -amylase from soursop (*Annona muricata* Linn.) fruits degraded by *Rhizopus stolonifer*. *Pakistan Journal of Biological Sciences* 19(2), 77–81. DOI: 10.3923/pjbs.2016.77.81.
- Augusto, F., Valente, A.L., dos Santos Tada, E. and Rivellino, S.R. (2000) Screening of Brazilian fruit aromas using solid-phase microextraction-gas chromatography-mass spectrometry. *Journal of Chromatography. A* 873(1), 117–127. DOI: 10.1016/S0021-9673(99)01282-0.
- Badrie, N. and Schauss, A.G. (2010) Soursop (*Annona muricata* L.): Composition, nutritional value, medicinal uses, and toxicology. In: Watson, R. and Preedy, V. (eds) *Bioactive Foods in Promoting Health*. Academic Press, Cambridge, Massachusetts, USA, pp. 621–643.
- Benero, J.R., Collazo de Rivera, A.L. and De George, L.M.I. (1974) Studies on the preparation and shelf-life of soursop, tamarind, and blended soursop-tamarind soft drinks. *The Journal of Agriculture of the University of Puerto Rico* 58(1), 99–104. DOI: 10.46429/jaupr.v58i1.10709.
- Berumen-Varela, G., Hernández-Oñate, M.A. and Tiznado-Hernández, M.E. (2019) Utilization of biotechnological tools in soursop (*Annona muricata* L.). *Scientia Horticulturae* 245, 269–273. DOI: 10.1016/j.scienta.2018.10.028.
- Bezerra, V.S., de Lima Filho, J.L., Montenegro, M.C.B.S.M., Araújo, A.N. and da Silva, V.L. (2003) Flow-injection amperometric determination of dopamine in pharmaceuticals using a polyphenol oxidase biosensor obtained from soursop pulp. *Journal of Pharmaceutical and Biomedical Analysis* 33(5), 1025–1031. DOI: 10.1016/S0731-7085(03)00412-6.
- Blancas-Benítez, F.J., Montalvo-González, E., González-Aguilar, G.A. and Sáyago-Ayerdi, S.G. (2019) In vitro bioaccessibility and release kinetics of phenolic compounds from guava (*Psidium guajava* L.) and soursop (*Annona muricata* L.) pulp. *TIP Revista Especializada En Ciencias Químico-Biológicas* 22, 1–7.
- Bonneau, N., Schmitz-Afonso, I., Brunelle, A., Touboul, D. and Champy, P. (2015) Method development for quantification of the environmental neurotoxin annonacin in Rat plasma by UPLC-MS/MS and

- application to a pharmacokinetic study. *Journal of Chromatography. B, Analytical Technologies in the Biomedical and Life Sciences* 1004, 46–52. DOI: 10.1016/j.jchromb.2015.09.039.
- Bonneau, N., Cynober, T., Jullian, J.C. and Champy, P. (2017) ¹H qNMR quantification of annonaceous acetogenins in crude extracts of *Annona muricata* L. fruit pulp. *Phytochemical Analysis* 28(4), 251–256. DOI: 10.1002/pca.2668.
- Champy, P., Höglinger, G.U., Féger, J., Gleye, C., Hocquemiller, R. *et al.* (2004) Annonacin, a lipophilic inhibitor of mitochondrial complex I, induces nigral and striatal neurodegeneration in rats: possible relevance for atypical parkinsonism in Guadeloupe. *Journal of Neurochemistry* 88(1), 63–69. DOI: 10.1046/j.1471-4159.2003.02138.x.
- Chih, H.W., Chiu, H.F., Tang, K.S., Chang, F.R. and Wu, Y.C. (2001) Bullatacin, a potent antitumor annonaceous acetogenin, inhibits proliferation of human hepatocarcinoma cell line 2.2.15 by apoptosis induction. *Life Sciences* 69(11), 1321–1331. DOI: 10.1016/s0024-3205(01)01209-7.
- Coria-Téllez, A.V., Montalvo-González, E. and Obledo-Vázquez, E.N. (2017) Soursop (*Annona Muricata*). In: Yahia, E.M. (ed.) *Fruit and Vegetable Phytochemicals: Chemistry and Human Health*, 2nd edn. Wiley-Blackwell, Chichester, UK, pp. 1243–1252.
- Coria-Téllez, A.V., Montalvo-González, E., Yahia, E.M. and Obledo-Vázquez, E.N. (2018) *Annona muricata*: A comprehensive review on its traditional medicinal uses, phytochemicals, pharmacological activities, mechanisms of action and toxicity. *Arabian Journal of Chemistry* 11(5), 662–691. DOI: 10.1016/j.arabj.2016.01.004.
- Daddiouaissa, D. and Amid, A. (2018) Anticancer activity of acetogenins from *Annona Muricata* fruit. *IIUM Medical Journal Malaysia* 17(3). DOI: 10.31436/imjm.v17i3.236.
- Dai, Y., Hogan, S., Schmelz, E.M., Ju, Y.H., Canning, C. *et al.* (2011) Selective growth inhibition of human breast cancer cells by graviola fruit extract *in vitro* and *in vivo* involving downregulation of EGFR expression. *Nutrition and Cancer* 63(5), 795–801. DOI: 10.1080/01635581.2011.563027.
- Ekaluo, U.B., Ikpeme, E.V., Ibiang, Y.B. and Omordia, F.O. (2013) Effect of soursop (*Annona muricata* L.) fruit extract on sperm toxicity Induced by caffeine in albino rats. *Journal of Medical Sciences* 13(1), 67–71. DOI: 10.3923/jms.2013.67.71.
- Escobar-Khondiker, M., Höllerhage, M., Muriel, M.-P., Champy, P., Bach, A. *et al.* (2007) Annonacin, a natural mitochondrial complex I inhibitor, causes tau pathology in cultured neurons. *The Journal of Neuroscience* 27(29), 7827–7837. DOI: 10.1523/JNEUROSCI.1644-07.2007.
- Espinosa, I., Ortiz, R.I., Tovar, B., Mata, M. and Montalvo, E. (2013) Physiological and physicochemical behavior of soursop fruits refrigerated with 1-methylcyclopropene. *Journal of Food Quality* 36(1), 10–20. DOI: 10.1111/jfq.12011.
- Fidianingsih, I. and Handayani, E.S. (2014) *Annona muricata* aqueous extract suppresses T47D breast cancer cell proliferation. *Universa Medicina* 33(1), 19–26.
- González, E.M., Fernández, A.E.L., Sáyago-Ayerdi, S.G., Estrada, R.M.V. and Vallejo, L.G.Z. (2017) In vitro antioxidant capacity of crude extracts and acetogenin fraction of soursop fruit pulp. *Pharmaceutica Analytica Acta* 8, 1–7.
- Gratão, A.C.A., Silveira, V. and Telis-Romero, J. (2007) Laminar flow of soursop juice through concentric annuli: Friction factors and rheology. *Journal of Food Engineering* 78(4), 1343–1354. DOI: 10.1016/j.jfoodeng.2006.01.006.
- Grzybowski, A., Tiboni, M., Silva, M.A.N., Chitolina, R.F., Passos, M. *et al.* (2013) Synergistic larvicidal effect and morphological alterations induced by ethanolic extracts of *Annona muricata* and *Piper nigrum* against the dengue fever vector *Aedes aegypti*. *Pest Management Science* 69(5), 589–601. DOI: 10.1002/ps.3409.
- Hajdu, Z. and Hohmann, J. (2012) An ethnopharmacological survey of the traditional medicine utilized in the community of Porvenir, Bajo Paraguá Indian Reservation, Bolivia. *Journal of Ethnopharmacology* 139(3), 838–857. DOI: 10.1016/j.jep.2011.12.029.
- Hasrat, J.A., De Bruyne, T., De Backer, J.P., Vauquelin, G. and Vlietinck, A.J. (1997) Isoquinoline derivatives isolated from the fruit of *Annona muricata* as 5-HT_{1A} receptor agonists in rats: unexploited antidepressive (lead) products. *The Journal of Pharmacy and Pharmacology* 49(11), 1145–1149. DOI: 10.1111/j.2042-7158.1997.tb06058.x.
- Hemalatha, G., Sivakumari, K., Rajesh, S. and Shyamala Devi, K. (2020) Phytochemical profiling, anticancer and apoptotic activity of Graviola (*Annona muricata*) fruit extract against human hepatocellular carcinoma (HepG-2) cells. *International Journal of Zoology and Applied Biosciences* 5, 32–47.

- Höllerhage, M., Rösler, T.W., Berjas, M., Luo, R., Tran, K. *et al.* (2015) Neurotoxicity of dietary supplements from Annonaceae species. *International Journal of Toxicology* 34(6), 543–550. DOI: 10.1177/1091581815602252.
- Hong, J., Li, Y., Xiao, Y., Li, Y., Guo, Y. *et al.* (2016) Annonaceous acetogenins (ACGs) nanosuspensions based on a self-assembly stabilizer and the significantly improved anti-tumor efficacy. *Colloids and Surfaces. B, Biointerfaces* 145, 319–327. DOI: 10.1016/j.colsurfb.2016.05.012.
- Hopp, D.C., Zeng, L., Gu, Z.M., Kozlowski, J.F. and McLaughlin, J.L. (1997) Novel mono-tetrahydrofuran ring acetogenins, from the bark of *Annona squamosa*, showing cytotoxic selectivities for the human pancreatic carcinoma cell line, PACA-2. *Journal of Natural Products* 60(6), 581–586. DOI: 10.1021/np9701283.
- Ishola, I.O., Awodele, O., Olusayero, A.M. and Ochieng, C.O. (2014) Mechanisms of analgesic and anti-inflammatory properties of *Annona muricata* Linn. (Annonaceae) fruit extract in rodents. *Journal of Medicinal Food* 17(12), 1375–1382. DOI: 10.1089/jmf.2013.0088.
- Jiménez-Zurita, J.O., Balois-Morales, R., Alia-Tejacal, I., Juárez-López, P., Jiménez-Ruiz, E.I. *et al.* (2017) Topics of postharvest handling of soursop fruit (*Annona muricata* L.). *Revista Mexicana de Ciencias Agrícolas* 8, 1155–1167. DOI: 10.29312/remexca.v8i5.115.
- Jimoh, O.A., Ayedun, E.S., Oyelade, W.A., Oloruntola, O.D., Daramola, O.T. *et al.* (2018) Protective effect of soursop (*Annona muricata* linn.) juice on oxidative stress in heat stressed rabbits. *Journal of Animal Science and Technology* 60, 28. DOI: 10.1186/s40781-018-0186-4.
- Jirovetz, L., Buchbauer, G. and Ngassoum, M.B. (1998) Essential oil compounds of the *Annona muricata* fresh fruit pulp from Cameroon. *Journal of Agricultural and Food Chemistry* 46(9), 3719–3720. DOI: 10.1021/jf980204n.
- Khan, M.R., Kornine, K. and Omoloso, A.D. (1998) Antibacterial activity of some Annonaceae. *Part 1. Fitoterapia (Milano)* (69), 367–369.
- Ko, Y.M., Wu, T.Y., Wu, Y.C., Chang, F.R., Guh, J.Y. *et al.* (2011) Annonacin induces cell cycle-dependent growth arrest and apoptosis in estrogen receptor- α -related pathways in MCF-7 cells. *Journal of Ethnopharmacology* 137(3), 1283–1290. DOI: 10.1016/j.jep.2011.07.056.
- Komansilan, A., Abadi, A.L., Yanuwadi, B. and Kaligis, D.A. (2012) Isolation and identification of biolarvicide from soursop (*Annona muricata* linn) seeds to mosquito (*Aedes aegypti*) larvae. *International Journal of Engineering & Technology* 12, 28–32.
- Lako, J., Trenerry, V.C., Wahlqvist, M., Wattapanpaiboon, N., Sotheeswaran, S. *et al.* (2007) Phytochemical flavonols, carotenoids and the antioxidant properties of a wide selection of Fijian fruit, vegetables and other readily available foods. *Food Chemistry* 101(4), 1727–1741. DOI: 10.1016/j.foodchem.2006.01.031.
- Lannuzel, A., Höglinger, G.U., Verhaeghe, S., Gire, L., Belson, S. *et al.* (2007) Atypical parkinsonism in Guadeloupe: A common risk factor for two closely related phenotypes? *Brain: A Journal of Neurology* 130(Pt 3), 816–827. DOI: 10.1093/brain/awl347.
- León-Fernández, A.E., Martínez-Cárdenas, L., Zepeda-Vallejo, L.G., Arteaga-Garibay, R.I., Gutiérrez-Martínez, P. *et al.* (2019) Antibacterial, antifungal, antioxidant and toxic effect of fractioned extracts from soursop pulp. *Revista Bio Ciencias* (6), 1–17.
- Lima, M.A.C.D., Alves, R.E., Filgueiras, H.A.C. and Lima, J.R.G. (2004) The use of wax and 1-methylcyclopropene on refrigerated storage of soursop fruit (*Annona muricata* L.). *Revista Brasileira de Fruticultura* 26, 433–437.
- Lutchmedial, M., Ramlal, R., Badrie, N. and Chang-Yen, I. (2004) Nutritional and sensory quality of stirred soursop (*Annona muricata* L.) yoghurt. *International Journal of Food Sciences and Nutrition* 55(5), 407–414. DOI: 10.1080/09637480400002800.
- Márquez Cardozo, C.J., Villacorta Lozano, V., Yepes Betancur, D.P., Ciro Velásquez, H.J. and Cartagena Valenzuela, J.R. (2012) Physiological and physico-chemical characterization of the soursop fruit (*Annona muricata* L. cv Elita). *Revista Facultad Nacional de Agronomía Medellín* 65, 6477–6486.
- Márquez Cardozo, C.J., Cartagena Valenzuela, J.R. and Correa Londoño, G.A. (2013) Determination of soursop (*Annona muricata* L. cv. Elita) fruit volatiles during ripening by electronic nose and gas chromatography coupled to mass spectroscopy. *Revista Facultad Nacional de Agronomía Medellín* 66, 7117–7128.
- Menezes, E.G.T., Oliveira, É.R., Carvalho, G.R., Guimarães, I.C. and Queiroz, F. (2019) Assessment of chemical, nutritional and bioactive properties of *Annona crassiflora* and *Annona muricata* wastes. *Food Science and Technology* 39(suppl 2), 662–672. DOI: 10.1590/fst.22918.

- Mishra, S., Ahmad, S., Kumar, N. and Sharma, B.K. (2013) *Annona muricata* (the cancer killer): A review. *The Global Journal of Pharmaceutical Research* 2, 1613–1618.
- Miyoshi, H., Ohshima, M., Shimada, H., Akagi, T., Iwamura, H. *et al.* (1998) Essential structural factors of annonaceous acetogenins as potent inhibitors of mitochondrial complex I. *Biochimica et Biophysica Acta* 1365(3), 443–452. DOI: 10.1016/S0005-2728(98)00097-8.
- Moghadamtousi, S.Z., Fadaeinasab, M., Nikzad, S., Mohan, G., Ali, H.M. *et al.* (2015) *Annona muricata* (Annonaceae): A review of its traditional uses, isolated acetogenins and biological activities. *International Journal of Molecular Sciences* 16(7), 15625–15658. DOI: 10.3390/ijms160715625.
- Moo-Huchin, V.M., Estrada-Mota, I., Estrada-León, R., Cuevas-Glory, L., Ortiz-Vázquez, E. *et al.* (2014) Determination of some physicochemical characteristics, bioactive compounds and antioxidant activity of tropical fruits from Yucatan, Mexico. *Food Chemistry* 152, 508–515. DOI: 10.1016/j.foodchem.2013.12.013.
- Moreno-Hernández, C.L., Sáyago-Ayerdi, S.G., García-Galindo, H.S., Mata-Montes De Oca, M. and Montalvo-González, E. (2014) Effect of the application of 1-methylcyclopropene and wax emulsions on proximate analysis and some antioxidants of soursop (*Annona muricata* L.). *The Scientific World Journal* 2014, 1–7. DOI: 10.1155/2014/896853.
- Neta, M.T.S.L., de Jesus, M.S., da Silva, J.L.A., Araujo, H.C.S., Sandes, R.D.D. *et al.* (2019) Effect of spray drying on bioactive and volatile compounds in soursop (*Annona muricata*) fruit pulp. *Food Research International* 124, 70–77. DOI: 10.1016/j.foodres.2018.09.039.
- Omoifo, C.O. (2004) Biochemical composition of soursop fruit, *Annona muricata* L., as affected by two harvest seasons. *Tropical Agricultural Research and Extension* 7, 1–8.
- Ong, H.G. and Kim, Y.-D. (2014) Quantitative ethnobotanical study of the medicinal plants used by the Ati Negrito indigenous group in Guimaras island, Philippines. *Journal of Ethnopharmacology* 157, 228–242. DOI: 10.1016/j.jep.2014.09.015.
- Onyechi, U., Ibeanu, U., Nkiruka, V., Eme, E.P. and Madubike, K. (2012) Nutrient phytochemical composition and sensory evaluation of soursop (*Annona muricata*) pulp and drink in South Eastern Nigeria. *International Journal of Basic and Applied Sciences* 12, 53–57.
- Osorio, E., Arango, G.J., Jiménez, N., Alzate, F., Ruiz, G. *et al.* (2007) Antiprotozoal and cytotoxic activities in vitro of Colombian Annonaceae. *Journal of Ethnopharmacology* 111(3), 630–635. DOI: 10.1016/j.jep.2007.01.015.
- Otto, R.B., Nankwanga, M. and Sesaaazi, D. (2015) Comparison of antibacterial activities of fermented with those of unfermented *Annona muricata* (L) fruit extracts. *International Journal of Current Microbiology and Applied Sciences* 4, 696–707.
- Padmanabhan, P. and Paliyath, G. (2016) Annonaceous Fruits. In: Caballero, B., Finglas, P.M., and Toldrá, F. (eds) *Encyclopedia of Food and Health*. Academic Press, Cambridge, Massachusetts, USA, pp. 169–173.
- Palma-Orozco, G., Marrufo-Hernández, N.A., Tobías, I. and Nájera, H. (2019) Purification and biochemical characterization of polyphenol oxidase from soursop (*Annona muricata* L.) and its inactivation by microwave and ultrasound treatments. *Journal of Food Biochemistry* 43(3), e12770. DOI: 10.1111/jfbc.12770.
- Pareek, S., Yahia, E.M., Pareek, O.P. and Kaushik, R.A. (2011) Postharvest physiology and technology of Annona fruits. *Food Research International* 44(7), 1741–1751. DOI: 10.1016/j.foodres.2011.02.016.
- Passos, T.U., Sampaio, H.A. de C., Sabry, M.O.D., Melo, M.L.P. de, Coelho, M.A.M. *et al.* (2015) Glycemic index and glycemic load of tropical fruits and the potential risk for chronic diseases. *Food Science and Technology (Campinas)* 35(1), 66–73. DOI: 10.1590/1678-457X.6449.
- Paull, R.E., Deputy, J. and Chen, N.J. (1983) Changes in organic acids, sugars, and headspace volatiles during fruit ripening of soursop (*Annona muricata* L.). *Journal of the American Society for Horticultural Science* 108, 931–934.
- Pino, J.A., Agüero, J. and Marbot, R. (2001) Volatile components of soursop (*Annona muricata* L.). *Journal of Essential Oil Research* 13, 140–141.
- Pinto, A.C. de Q., Cordeiro, M.C.R., de Andrade, S.R.M., Ferreira, F.R., de C. Filgueiras, H.A. *et al.* (2005) *Annona* species. In: Williams, J.T., Smith, R.W., Hughes, A., Haq, N., and Clement, C.R. (eds) *Annona Sp. Monograph*. International Center for Underutilized Crops, Southampton, UK, pp. 1–123.
- Prasad, S.K., Veeresh, P.M., Ramesh, P.S., Natraj, S.M., Madhunapantula, S.V. *et al.* (2020) Phytochemical fractions from *Annona muricata* seeds and fruit pulp inhibited the growth of breast cancer cells through cell cycle arrest at G0/G1 phase. *Journal of Cancer Research and Therapeutics* 16, 1235.

- Rabelo, S.V., Quintans, J.D.S.S., Costa, E.V., da Silva Almeida, J.R.G., Júnior, L.J.Q. *et al.* (2016) *Annona* species (Annonaceae) oils. In: Prredy, V. (ed.) *Essential Oils in Food Preservation, Flavor and Safety*. Academic Press, Cambridge, Massachusetts, USA, pp. 221–229.
- Ragasa, C.Y., Soriano, G., Torres, O.B., Don, M.J. and Shen, C.C. (2012) Acetogenins from *Annona muricata*. *Pharmacognosy Journal* 4(32), 32–37. DOI: 10.5530/pj.2012.32.7.
- Ramos-Guerrero, A., González-Estrada, R.R., Romanazzi, G., Landi, L., Gutiérrez-Martínez, P. *et al.* (2020) Effects of chitosan in the control of postharvest anthracnose of soursop (*Annona muricata*) fruit. *Revista Mexicana de Ingeniería Química* 19(1), 99–108. DOI: 10.24275/rmiq/Bio527.
- Ravaomanarivo, L.H.R., Razafindralava, H.A., Raharimalala, F.N., Rasoahantaveloniaina, B., Ravelonandro, P.H. *et al.* (2014) Efficacy of seed extracts of *Annona squamosa* and *Annona muricata* (Annonaceae) for the control of *Aedes albopictus* and *Culex quinquefasciatus* (Culicidae). *Asian Pacific Journal of Tropical Biomedicine* 4(10), 798–806. DOI: 10.12980/APJTB.4.2014C1264.
- Raybaudi-Massilia, R., Suárez, A., Arvelo, F., Sojo, F., Mosqueda-Melgar, J. *et al.* (2015) An analysis in-vitro of the cytotoxic, antioxidant and antimicrobial activity of aqueous and alcoholic extracts of *Annona muricata* L. seed and pulp. *British Journal of Applied Science & Technology* 5(4), 333–341. DOI: 10.9734/BJAST/2015/13587.
- Rieser, M.J., Fang, X.P., Rupprecht, J.K., Hui, Y.H., Smith, D.L. *et al.* (1993) Bioactive single-ring acetogenins from seed extracts of *Annona muricata*. *Planta Medica* 59(1), 91–92. DOI: 10.1055/s-2006-959614.
- Rubio-Melgarejo, A., Balois-Morales, R., Palomino-Hermosillo, Y.A., López-Guzmán, G.G., Ramírez-Ramírez, J.C. *et al.* (2020) Phytochemical and antioxidant dynamics of the soursop fruit (*Annona muricata* L.) in response to colletotrichum spp. *Journal of Food Quality* 2020. DOI: 10.1155/2020/3180634.
- Santana, K.L. de, Galvão, M. de S., Jesus, M.S. de, Nogueira, J.P. and Narain, N. (2017) HS-SPME optimization and extraction of volatile compounds from soursop (*Annona muricata* L.) pulp with emphasis on their characteristic impact compounds. *Food Science and Technology* 37(2), 250–260. DOI: 10.1590/1678-457x.20916.
- Shashirekha, M.N., Baskaran, R., Jaganmohan Rao, L., Vijayalakshmi, M.R. and Rajarathnam, S. (2008) Influence of processing conditions on flavour compounds of custard apple (*Annona squamosa* L.). *LWT - Food Science and Technology* 41(2), 236–243. DOI: 10.1016/j.lwt.2007.03.005.
- Sun, S., Liu, J., Kadouh, H., Sun, X. and Zhou, K. (2014) Three new anti-proliferative Annonaceous acetogenins with mono-tetrahydrofuran ring from graviola fruit (*Annona muricata*). *Bioorganic & Medicinal Chemistry Letters* 24(12), 2773–2776. DOI: 10.1016/j.bmcl.2014.03.099.
- Sun, S., Liu, J., Zhou, N., Zhu, W., Dou, Q.P. *et al.* (2016) Isolation of three new annonaceous acetogenins from Graviola fruit (*Annona muricata*) and their anti-proliferation on human prostate cancer cell PC-3. *Bioorganic & Medicinal Chemistry Letters* 26(17), 4382–4385. DOI: 10.1016/j.bmcl.2015.06.038.
- Sun, S., Liu, J., Sun, X., Zhu, W., Yang, F. *et al.* (2017) Novel Annonaceous acetogenins from Graviola (*Annona muricata*) fruits with strong anti-proliferative activity. *Tetrahedron Letters* 58(19), 1895–1899. DOI: 10.1016/j.tetlet.2017.04.016.
- Tovar-Gómez, B., Mata-Montes de Oca, M., García-Galindo, H.S. and Montalvo-González, E. (2011) Efecto de emulsiones de cera y 1-metilciclopropeno en la conservación poscosecha de guanabana. *Revista Chapingo. Serie Horticultura* 17(SPE1), 53–61.
- Umme, A., Salmah, Y., Jamilah, B. and Asbi, B.A. (1999) Microbial and enzymatic changes in natural soursop puree during storage. *Food Chemistry* 65(3), 315–322. DOI: 10.1016/S0308-8146(98)00215-5.
- Umme, A., Bambang, S.S., Salmah, Y. and Jamilah, B. (2001) Effect of pasteurisation on sensory quality of natural soursop puree under different storage conditions. *Food Chemistry* 75(3), 293–301. DOI: 10.1016/S0308-8146(01)00151-0.
- Vandebroek, I., Balick, M.J., Ososki, A., Kronenberg, F., Yukes, J. *et al.* (2010) The importance of botellas and other plant mixtures in Dominican traditional medicine. *Journal of Ethnopharmacology* 128(1), 20–41. DOI: 10.1016/j.jep.2009.12.013.
- Vila-Nova, N.S., Morais, S.M., Falcão, M.J.C., Machado, L.K.A., Beviláqua, C.M.L. *et al.* (2011) Leishmanicidal activity and cytotoxicity of compounds from two *Annonacea* species cultivated in Northeastern Brazil. *Revista Da Sociedade Brasileira de Medicina Tropical* 44(5), 567–571. DOI: 10.1590/s0037-86822011000500007.
- Yamada, E.S., Respondek, G., Müssner, S., de Andrade, A., Höllerhage, M. *et al.* (2014) Annonacin, a natural lipophilic mitochondrial complex I inhibitor, increases phosphorylation of tau in the brain of FTDP-17 transgenic mice. *Experimental Neurology* 253, 113–125. DOI: 10.1016/j.expneurol.2013.12.017.

- Zafra-Polo, M.C., Figadère, B., Gallardo, T., Tormo, JoséR. and Cortes, D. (1998) Natural acetogenins from annonaceae, synthesis and mechanisms of action. *Phytochemistry* 48(7), 1087–1117. DOI: 10.1016/S0031-9422(97)00917-5.
- Zambrano, A., Raybaudi-Massilia, R., Arvelo, F. and Sojo, F. (2018) Cytotoxic and antioxidant properties in vitro of functional beverages based on blackberry (*Rubus glaucus* Benth) and soursop (*Annona muricata* L) pulps. *Functional Foods in Health and Disease* 8(11), 531. DOI: 10.31989/ffhd.v8i11.541.