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Screening of antidiabetic and antioxidant potential along with phytochemicals of Annona genus: a review

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Abstract

Background: Annona species can be found in the subtropical and tropical parts of the world. Because of their medicinal capabilities and highly exotic edible fruits, they are one of the most important members of the Annonaceae family. Isoquinolines, pyrimidine-β-carboline alkaloids, lectins, acetogenins, and volatile oils are among the active metabolites found in this genus, all of which have been shown to have anti-diabetic and antioxidant activities.

Main body: The fundamental objective of this review was to summarize the antidiabetic and antioxidant activity based on reported secondary data from different plants of the genus Annona. These species include *Annona cherimola*, *Annona squamosa*, *Annona macroprophyllata*, *Annona muricate*, *Annona reticulata*, *Annona carcans*, *Annona coriacea*, *Annona cornifolia*, and *Annona senegalensis*. The Annona species investigated had significant antihyperglycemic and antioxidant properties.

Conclusion: The available evidence, both in vitro and in vivo, confirms the ability of Annona species to treat diabetes in addition to producing oxidative damage.

Keywords: Annona, Antioxidants, Medicinal plants, Antidiabetic

Background

The Annona genus is named after the Latin phrase "annual harvest." Among the Annonaceae families, this genus provides the most food. It contains approximately 162 species of trees and shrubs. These species are thin, 5 to 11 m tall, upright or slightly disseminated, and sometimes rough, with gray to brown bark [1]. With around 2400 species in 108 genera, Annonaceae are mainly pantropical, are a larger family than any other Magnoliidae group. The botanist Jussieu published his classification of the Annonaceae family in 1789 [2, 3]. Different analytical methods have documented terpenoids (mainly diterpenes) and alkaloids (isoquinoline alkaloids) in this family species [4]. The family has several plant species of economic value as they are edible worldwide, including tropical America, Australia, Africa, India, Europe, and the Mediterranean [5], which makes this genus economically the most important because of its foodstuffs and medicinal properties. The fruits of a number of Annona species are edible, including *Annona crassiflora* (araticum), *Annona squamosa* (Fruita do conde), and *Annona muricata* (Graviola). In Brazil, several of the Annonas' fruits are highly prized. It is frequently consumed "naturally" or in the form of juice, cake, or ice cream [6]. Earlier molecular and medicinal studies of the species have shown substantial biological activities, such as cytotoxicity to various cell lines, anti-platelet, antiparasitic, antibiotics, and antimicrobial properties. The existence and reason for these activities is due to the presence of alkaloids, acetogens, and terpenes [7]. As a result, the purpose of this study was to examine the Annona genus

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species that have anti-diabetic and anti-oxidant capabilities.

Methods

We reviewed scientific articles published in journals by electronic databases (Google Scholar, PubMed, Medline, Web of Science, DOAJ, and Scopus) using specific keywords such as "Annona"; "Diabetes mellitus"; "Antioxidants"; "Medicinal plants"; "Antidiabetic". We reviewed 76 articles that provided data on the use of Annona species to treat diabetes and oxidative damage. The synonyms, taxonomy, and several other botanical distribution and descriptions were retrieved from "The Plant List" (http://www.theplantlist.org/), "Flora of Bangladesh" (http://bnh-flora.gov.bd/species-list/), and "CABI" (https://www.cabi.org/isc/).

Main text

Botanical distribution

Nine species of the Annona genus were characterized in this study, whose botanical representation is summarized in Table 1.

Annona cherimola

Annona cherimola Miller belongs to the genus Annona in the Annonaceae family in magnolias order, which is also provides edible fruit species. It is a steep, semi momentary but low bunched tree. The plant, highly prevalent in Ecuador and Peru is widely distributed throughout the tropics and subtropics of America, Africa, Asia, and even South Europe [8, 9]. Alone or in combination with others, it has been used in Mexican Traditional medicine to treat several diseases like fever, cough, worms, headache, and inflammation. Currently, this is utilized in the treatment of diabetes [10–12].

Annona squamosa

Annona squamosa L., known as custard apple, generally is an endemic of the West Indies, and throughout India, it is well grown. Annona squamosa is renowned for its anti-diabetic properties among tribal men in and around Aligarh district's village in Uttar Pradesh [13].. There, native people make a mixture of 4–5 newly emerged leaves with five grains of black pepper early in the morning to treat diabetes. Continuing the therapy ensured up to 80% positive results [13].

Annona macroprophyllata

Annona macroprophyllata Donn. Sm. is yet another species that is known to be classified under the genus Annona. It is referred to as "ilama," a common tree in central Mexico. It is familiar by "papauce" or "anona blanca" in the Southeast [14, 15]. Its fruits are consumed as food, but its leaves are used as anticonvulsants [16]. In traditional medicine, it is also prescribed as an analgesic and anti-inflammatory agent [17].

Annona muricata

Annona muricata is a well-known member of the Annonaceae family and the Annona genus. It is commonly known as sour-sop. It is employed for treating diabetes, hypertension, fever, pain, and against worms and vomiting [18]. Several pharmacological studies showed that *Annona muricata* possess vasodilator, cardio-depressive, antispasmodic, antihypertensive, antimutagen, anticonvulsant antiviral, antidiabetic, and antioxidant properties [26–30].

Annona reticulata

Annona reticulata in India is typically known as "custard apple" or "heart bullock." It is locally useful in the treatment of epilepsy, dysentery, cardiac problem, parasite and worm infection, constipation, and bacterial infection [19].

Annona carcans

Annona carcans is a member of the Annonaceae family, which comprises woody, arbustive, or arborist plants and many fruits [21, 31] and also known as *Annona amambayensis* Hassl. It is commonly known as "araticum-caga - reso" or "cortic - a reso." It is used as purgative in folk medicine, and found in the Brazil [21].

Annona coriacea

Annona coriacea is a fruit tree native to Brazil. The ecoregions of Cerrado, Caatinga, and Pantanal are part of their original habitat. Buildings and toys are made from the wood. Synonyms of this plant are *Annona coriacea* var. cuneata R.E. Fr and *Annona geraensis* Barb. Rodr [32].

Annona cornifolia

Annona cornifolia is part of the family of Annonaceae and *Annona walkeri* S.Moore is used as a synonym of this plant. It is commonly referred to as "aratian-mirim." The fruit pulp is mature, orange, and sweet and aromatic. The green fruit is well-known for its ability to treat ulcers [24].

Annona senegalensis

Annona senegalensis, referred to as sour soup (English), abo (Yoruba, Western Nigeria), and uburuocha (Igbo, Eastern Nigeria), is commonly found in Nigeria [25]. The bark of the stem is silvery gray or gray-brown. The leaves are simple, alternate, and oblong, and they're hairless on top with brownish hair on the underside. Leaves are used to treat diarrhea, joint disease, respiratory disease, conjunctivitis, burns, snakebite sores, trypanosomiasis, jaundice, bleeding, female barrenness, seizures, asthenia, and fever [25].

Table 1 Botanical Information of the species

Scientific name	Local name	Synonym	Local uses	Distribution	References
Annona cherimola	Chirimoya, Atemoya, Chirimolia Cerimoya, cherimoyer, momona	Not reported	Insecticide, fever, cough, worms, anti-inflammatory, headache	Egypt, Eritrea, Somalia, South Africa, China, India, Israel Myanmar, Philippines, France, Italy, Portugal, Spain, Mexico, Ecuador, Peru,	[8–12]
Annona squamosa	Custard apple, chirimoya fruta do conde, tiep baay, amritaphala	*Annona asiatica* L.	Antidiabetic	Egypt, Sudan, China, India, Israel, Pakistan, Thailand, Costa rica	[13]
Annona macroprophyllata	llama, Papauce, Anona blanca	*Annona diversifolia* Saff.	Anticonvulsant, analgesic, anti-inflammatory	Mexico, China, India	[14–17]
Annona muricata	ci guo fan li zhi nangka seberang durian belanda	*Annona macrocarpa* Barb.; *Annona muricata* L.; *Annona muricata* L.;	diabetes, hypertension, fever, pain and against worms and vomiting	China, India, Indonesia, Malaysia, Myanmar, Pakistan	[18]
Annona reticulata	Bullock's heart	*Annona excelsa* Kunt.; *Annona laevis* Kunth.; *Annona longifolia* Moc.; *Annona longifolia* Sesse.; *Annona riparia* kunth.	Epilepsy, dysentery, cardiac problem, parasite and worm infection, constipation, and bacterial infection	India, Bangladesh, China, Indonesia, West indies	[19]
Annona crassiflora	Araticum, marolo, pinha-docerrado (cerrado pine-cone), cabeça de negro, etc	*Annona macrocarpa* Barb., *Annona rodriguesii* Barb.	Astringent, antidiarrheal, rheumatism, treating wounds, snake bites and pediculosis.	Brazil	[20]
Annona carcans	'araticum-caga - reso" or "cortic - a reso,"	*Annona amambayensis* Hassl. ex R.E.Fr., *Annona cacans* var. glabriuscula R.E.Fr, *Annona cacans* subsp. glabriuscula (R.E.Fr.) H.Rainer	Purgative	Minas Gerais, Mato Grosso do Sul, Espı´rito Santo, Parana´,Rio de Janeiro, Rio Grande do Sul, Santa Catarina, and Sa˜o Paulo	[21]
Annona coriacea	Marolo, araticum	*Annona coriacea* var. amplexicaulis S.Moore, *Annona coriacea* var. cuneate, *Annona coriacea* var. pygmaea Warm.	Chronic diarrhea, antimalarial, anti-helmintic	Brazil	[22, 23]
Annona cornifolia	araticum-mirim	*Annona walkeri* S.Moore	–	Brazil	[24]
Annona senegalensis	Sour soup, abo, uburuochaand gwandar	*Annona senegalensis* var. arenaria Sillans, *Annona senegalensis* var. cuneata Oliv, *Annona senegalensis* var. glabrescens Oliv.	Diarrhea, disease of the joints, conjunctivitis, wounds, snakebites, trypanosomiasis, jaundice, hemorrhoids, feminine barrenness, convulsions, fever, and asthenia	Nigeria	[25]

Phytochemicals

Nine species of the Annona genus were characterized in this study, whose phytochemical study is summarized in Table 2.

Annona cherimola

From the ethanol leaf extract of *Annona cherimola*, four flavonoid compounds: kaempferol, quercetin, nicotinflorin, and rutin and phenolic compound caffeic acid was also identified using the TLC method [33]. Chen et al identified Aromin-A; squamocin from the stem extract of *A. cherimola*, along with Cherimolin; dihydrocherimolin; molvizarin;motrilin; itrabin; jetein; cherimolin-2; almunequin from the seeds [34]. In the ethanol extract of the *Annona cherimola* seeds, two new cytotoxic addictive acetogenins, anomolin and annocherimolin, were identified [35].

Annona squamosa

Annona squamosa is proven to have glycosides, alkaloids, saponins, flavonoids, tannins, carbohydrates, proteins, phytosterols, amino acids, and phenolic compounds. Different chemical components have been identified from the plant's leaves, stems, and roots, including 15 alkaloids, 10 cyclopeptides, 39 acetogenins, and 8 diterpenoids [36].

Annona macroprophyllata

Seed extract of *Annona macroprophyllata* constitutes 3 compounds namely, Laherradurin (acetogenin), rolliniastin-2, and cherimolin-2 [47, 48].

Table 2 Phytochemical constituents of the species

Scientific name	Parts used	Compounds	Reference
Annona cherimola	Leave, Stem, Seed	kaempferol, quercetin, nicotinflorin , rutin, caffeic acid, Aromin-A; squamocin, Cherimolin, dihydrocherimolin, molvizarin, motrilin, itrabin, jetein, cherimolin-2, almunequin, acetogenins, anomolin, annocherimolin	[33–35]
Annona squamosa	Leaves, tender stem, Bark, Seeds, Stem bark.	Anonaine,Anolobine,Aporphine,Corydine,Isocorydine,Norcorydine,Norisocorydine, Glaucine,Liriodenine,Norlaureline,Norushinsunine,Reticuline,Roemerine,Samoquasine A, Annosqualine,Cyclosqamosin A, Cyclosqamosin B, Cyclosqamosin C, Cyclosqamosin D, Cyclosqamosin E, Cyclosqamosin F, Cyclosqamosin G, Cyclosqamosin H, Cyclosqamosin I, Squamtin A, Annosquamosin A, Annonacin, AnnonacinA, Annonastatin, Squamocin, Squamocin-O1, Squamocin-O2, Bullatacin, Bullatacinone, 4-deoxyannoreticuin, *cis*-4-deoxyannoreticuin(2,4-*cis* and *trans*)-squamoxinone, (2,4-*cis* and *trans*)-Mosinone A, Mosin B, Mosin C, Squamotacin, Molvizarin, (2,4-*cis* and *trans*)-squamolinone, (2,4-*cis* and *trans*)-9-oxoasimicinone, Bullacin B, Squamostatin D, (2,4-*cis*-and *trans*)-bullatacinone, Squamostatin C, Annonin I, Annonin VI, Squamostene-A, Reticulacin-1, Squamosinin-A, Annotemoyin-1, Annotemoyin-2, Annomosin A, Annosquamosins A,Annosquamosins B, Annosquamosin C, Annosquamosin D, Annosquamosin E, Annosquamosin F, Annosquamosin G.	[36]
Annona macroprophyllata	Seeds	Laherradurin; rolliniastin-2; cherimolin-2	[37]
Annona muricata		Annonaine, nornuciferine, asimilobine, epomusenin-A, epomusenin-B, epomurinin-A, epomurinin-B, *cis*-annoreticuin, muricin J, muricin K, muricin L, cinnamic acid derivative, coumaric acid hexose, 5-caffeoylquinic acid, dihydrokaempferol-hexoside, p-coumaric acid, caffeic acid derivative, e, dicaffeoylquinic acid, feruloylglycoside, 4-feruloyl-5-caffeoylquinic acid, p-coumaric acid methyl ester, annomuricin A, annomuricin B, annomuricin C, annomuricin E, annomutacin, (2,4-*cis*)-10R-annonacin-A-one, (2,4-*trans*)-10R-annonacin-A-one, annohexocin, muricapentocin, (2,4-*cis*)-isoannonacin, (2,4-*trans*)-isoannonacin, muricatocin A, muricatocin B, muricatocin C, gigantetronenin,annopentocin A, annopentocin B,annopentocin C, cisannomuricin-D-one, *trans*-annomuricin-D-one,murihexocin A, murihexocin B, murihexocin C ,muricoreacin, Cis-corossolone, annocatalin, annocatacin B, anonaine, isolaureline, xylopine,Quercetin 3-O-α-rhamnosyl- (1→6)-βsophoroside, gallic acid,epicatechine, quercetin 3-O-rutinosid, quercetin 3-O, neohispredoside, quercetin 3-O-robinoside, catechine, chlorogenic acid, argentinine (1-N,N-dimethylethanyl-4,6-dimethoxy-3,8-dihydroxy-phenanthrene), kaempferol 3-O-rutinoside, quercetin 3-O-glucoside, quercetin, kaempferol, annonamine, (S)-norcorydine, (R)-4′-O-methylcoclaurine (R)-O,O-dimethylcoclaurine, ,annoionol A, annoionol B, annoionol C, annoionoside,, vomifoliol, roseoside,turpinionoside A,citroside A, blumenol C, (+)-epiloliolide, loliolide, ,rutin, kaempferol 3-O-rutinoside, kaempferol 3-O-robinobioside, kaempferol 3-O-β-D-(2′′-O-β-D-glucopyranosyl,6′′-O-α-L-rhamnopyranosylglucopyranoside, montecristin, cohibin A, cohibin B, *cis*-solamin, *cis*-panatellin,*cis*-uvariamicin IV, *cis*-uvariamicin I, *cis*-reticulatacin, *cis*-reticulatacin-10-one, chatenaytrienin 1, chatenaytrienin 2, chatenaytrienin 3, muridienin 3, muridienin 4, muricadienin, coronin, sabadelin, murisolin, muricatacin, donhexocin, cohibin C, cohibin D, muricatenol, 2,4-*cis*-gigantetrocinone, 2,4-*trans*-gigantetrocinone, 2,4-*trans*-isoannonacin-10-one, annomontacin, longifolicin,muricin A, muricin B, muricin C, muricin D,muricin E,muricin F, muricin G, muricin H, muricin I, *cis*-annomontacin, annonacinone, xylomaticin, N-fatty acyl tryptamines, annoreticuin-9-one, epoxymurin A epoxymurin B, corepoxylone, annonacin-10-one, isoannonacin, isoannonacin-10-one, goniothalamicin, gigantetrocin, gigantetrocin A gigantetrocin B, muricatetrocin A, muricatetrocin B,epomuricenin A epomuricenin B, annomuricatin A, annocatacin A, annomuricatin C, annonacin	[38]
Annona reticulata	Leaf, Bark, Stem bark, Root, Root bark, Seed, Fruit	Dopamine, Salsolinol, Coclaurine, Sesquiterpenes mainly Spathenelol, Muurolene, Copaene, Eudesmol, Acetogenin – Squamone, Solamin, Annomonicin, Rolliniastatin 2, Annoreticuin-9-one. Triterpenoid – annonaretin A, Monotetrahydrofuron acetogenins, Reticulatacin, Diterpenes: (–)- kau-M-en-19-oiac cid acid and methyl 1β, 17-dihydro-(–)-kauran-19-oate, Alkaloids: Liriodenine, Copaene, Patchoulane and 1H-cycloprop (e) azulene, (-)Kau-16-en-19-oic acid, Bistetrahydrofurone acetogenin, Bullatacin.Dopamine, Salsolinol, Coclaurine, Diterpenes (–)-kaur-16-en-19-oic acid, 16-α-hydroxy-(–)-kauran-19-oic acid, Methyl-17-hydroxy-16-β-(–)-kauran-19-oate, Reticullacinone, Rolliniastatin-2 (= bulatacin = annonin-VI), Molvizarin.Aporphine alkaloids Liriodenine, Norushinsunine, Reticuline, Acetogenin neoannonin, Sesquiterpenes mainly Spathenelol, Muurolene, Copaene, Eudesmol, Anonaine, Michelalbine, Oxoushinsunine, Reticuline, Unknown phenolic comp, Series of N-fatty acyl tryptamine where acyl portion ranged from hexadecanoyl to hexacosanoyl. Cytotoxic acetogenins as Squamocin, *cis*-/*trans*-isomurisolenin, Annoreticuin, Annoreticuin-9-one, Bullatacin, *cis*-/*trans*-bullatacinone, *cis*-/*trans*-murisalinone, Solamin, Annomonicin, Rolliniastatin-1, 2 squamone and isoannonareticin. Volatile oil constituents like α-pinene, β-pinene, Myrcene, Limonene, Terpinen-4-ol, and	[19, 39]

Table 2 Phytochemical constituents of the species *(Continued)*

Scientific name	Parts used	Compounds	Reference
		Germacrene D. Cycloreticulin A, Cycloreticulin B, Acetogenins mainly *cis* and *trans*isomurisolenin, Annoreticuin, Bullatacin, Squamosine and Rolliniastatin. Aminoacyl triesters of Squamocin 1, N-fatty acyl tryptamines. Annonaceous acetogenins (polykelides): Annonareticin, 2,-4-*cis*-isoannonareticin, 2, 4-*trans*-isoannonareticin, Solamin, Murisolin, Reticulacinone, Annoreticuin, Annomonicin, Sitosterol, Daucosterol, Sucrose, Palmitic acid and Stearic acid. Annonaceous acetogenin: 2, 4-*cis*-isoan-nonareticin,Pinene, Myrcene, Limonene, Terpinen-4-ol, Germacrene D.	
Annona crassiflora		Not reported	–
Annona coriacea	Leaves	Palmitic acid, oleic acid, asitrocinone, annonacin, trilobalicin, annomuricin E, asimicin, bullatacin, annohexocin, murihexocin, goniotriocin, bullatalicinone, annoglaucin, ginsenoside Rh5, salzmanolin, annoheptocin A, annoheptocin B, squamocin glycosilated	[40]
Annona carcans	–	Not reported	
Annona cornifolia	Seeds	9-Hydroxyfolianain, annofolin, folianin B, 4-desoxylongimicin, folianin A, squamocin M, squamocin L	[41]
Annona senegalensis	Seed, Root, Leaves	Annosenegalin, Annogalene; gigantetronenine; squamocine; glaucanisine; glaucanetine; goniothalamicine, Roemerine; anonaine; nornuciferine; liriodenine; coclaurine; isoboldine	[42–46]

Annona muricata

Several plant phytochemicals, such as alkaloids, flavonol, phenols, and essential oils, were evaluated from the *A. muricata* plant. However, acetogenin was found to be a rich source in *A. muricata*. The existence of several key minerals, including Potassium (K), Calcium (Ca), Sodium (Na), Copper (Cu), Iron (Fe), and Magnesium (Mg), demonstrate that the frequent intake of *A. muricata* fruit may assist in providing the human body with essential nutrients and elements [19, 47, 49–55]. According to research findings, *Annona muricata* reported 17 Alkaloids, 100 Annonaceae acetogenin, 10 phenolics, 13 flavonol triglycerides, 17 megastgmane, and 2 cyclopeptides from its fruits, leaves, seeds, and pericarp, respectively [38].

Annona reticulata

Various phytoconstituents from various parts of the *A. reticulate* have been described through identification of tannins, alkaloids, and phenolic compounds from the stem bark. Leaves are abundant in chemical constituents such as alkaloids, amino acids, carbohydrates, hormones, flavonoids, protein, tannins, glycosides, and phenolics. The root has been discovered to include acids, alkaloids, carbohydrates, proteins, flavonoids, and tannins. This species has also proven rich in Ca, Phosphorus (P), K, Mg, Na, Chlorine (Cl), Sulfur (S), Manganese (Mn), Zinc (Zn), Fe, Cu, Selinium (Se), Cobalt (Co), Nickel (Ni), and Chromium (Cr) [56–58].

Annona coriacea

Gomes et al. 2019 reported, leaves extract of *Annona coriacea* has been found to contain palmitic acid, oleic acid, asitrocinone, annonacin, trilobalicin, annomuricin E, asimicin, bullatacin, annohexocin, murihexocin, goniotriocin, bullatalicinone, annoglaucin, ginsenoside Rh5, salzmanolin, annoheptocin A, annoheptocin B, squamocin glycosylated using analysis of the electrospray ionization Fourier transform ion cyclotron resonance mass spectrometry [40].

Annona cornifolia

The assessment of phytochemicals from various plant parts led to numerous bioactive constituents being found among different Annona species. Acetogenins, alkaloids, essential oils, phenolic compounds, cyclopeptides, amino acids, pigments, and vitamins are among the principal phytochemical components [48]. The study found acetogenins namely 9-Hydroxyfolianain, annofolin, folianin B, 4-desoxylongimicin, folianin A, squamocin M, squamocin L from seed extract of *Annona cornifolia* [41].

Annona senegalensis

The study identified acetogenin and annosenegalin from the seed extract of *Annona senegalansis* and annogalene; gigantetronenine; squamocine; glaucanisine; glaucanetine; goniothalamicine from the root extract. Six alkaloids were also found out, namely roemerine; anonaine; nornuciferine; liriodenine; coclaurine; isoboldine, from the leave extract of *Annona senegalensis* [42–46].

Biological activity

Antidiabetic activity

Annona cherimola Ethanol extract of *Annona cherimola* was tested in alloxan-induced type-2 diabetic rats to study the antidiabetic effect of the leaves of Annona *cherimola*. Plant extract administered at dose 300 mg/kg on alloxan-induced anti-hyperglycemic rats decreased blood glucose level 331.5 mg/dl to 149.2 mg/dl 4 h after

the administration ($P < 0.05$) compared to the acarbose (151.3 mg/dl), an alpha glucosidase inhibitor. The above study proved that rutin, a flavonal glucoside present at the ethanol extract, acts as an alpha glucosidase inhibitor like acarbose, which contributes significantly to the decrease of blood glucose level [59] (Table 3).

Annona squamosa A research study was conducted using the aqueous extract of *Annona squamosa* in streptozotocin-nicotinamide type 2 diabetic rats where symptomatic decrease in plasma glucose level was seen for oral glucose tolerance test from 30 min onwards compared to 250 mg/kg and 500 mg/kg doses administered in normal rats. The result ensured that, aqueous extract of *A. squamosa* has significant potential of antihypoglycemic effect. In that study, the antihyperglycemic effect of that aqueous extract was independent of the dose since no significant difference in results were observed between 250 and 500 mg/kg extract [61].

Annona macroprophyllata A study in Mexico stated that *Annona muricata*, *Annona glabra*, and *Annona cherimola* are used as antidiabetic plants. Based on their research, another study is carried out on *Annona macroprophyllata* as it is a similar species of the Annona genus.

Kamalakkannan, N., & Prince, P. S. M. (2006) isolated a flavonol compound rutin from *Annona microprophyllata* extract which was tested on hyperglycemic rats, and was found to inhibit fasting plasma glucose level, while the insulin and the antioxidant levels were increased [70, 71]. Rutin also reduced the alpha-glucosidase activity in both in vivo and in vitro studies [72]. They demonstrated the same yeast alpha-glucosidase behavior as

Table 3 Result and methods of antidiabetic and antioxidant activity

Scientific name	Parts	Result	Method	References
Annona cherimola	Leaves	Aqueous extract at 300 mg/kg displayed substantial decrease the level of glucose in blood.	Alloxan induced male albinos Sprague-Dawley rats.	[59, 60]
	Juice, Skin, Flesh	Flesh extract at 98.085 Trolox Equivalents per 100 g dose showed maximum scavenging activity.	Oxygen radical absorbance capacity (ORAC) assay	[60]
Annona squamosa	Leaves	Aqueous leaf extract revealed significant Antihyperglycemic effect	Streptozotocin-nicotinamide type 2 diabetic rats (250 and 500 mg/kg)	[61]
		• IC_{50} = 40 µg/ml • IC_{50} = 60 µg/ml • IC_{50} = 110 µg/ml • IC_{50} = 115 µg/ml	• ABTS • Nitric oxide • DPPH • Superoxide	[62]
Annona macroprophyllata	Leave	With a low IC_{50} (1.18 µg/ml) repressed the activity of yeast alpha-glucosidase and reduce blood glucose level.	Streptozotocin induced diabetic male Wistar rats.	[63]
Annona muricata	Leaves	The aqueous extract showed significant blood glucose lowering effect at dose 100 and 200 mg/kg.	Streptozotocin induced diabetic albino Wistar rats.	[64]
	Leaves	Ethanol extract of *Annona muricata* showed significant antioxidant activity in in vitro model.	DPPH, ABTS, nitric oxide, super oxide, hydroxy radical and lipid peroxidation	[65]
Annona reticulata	Leaves	Ethyl acetate fraction from hydroalcoholic extract of *Annona reticulata* at dose 100 mg/kg reduced blood glucose level significantly.	Streptozotocin induced hyperglycemic Wistar albino rats	[66]
	–	Antioxidant activity not reported.	–	–
Annona crassifora	Peel, Seeds, Pulp	Ethanol and aqueous extract express in vitro antioxidant potential.	DPPH and lipid peroxidation assay.	[67]
	–	Not reported Antidiabetic activity.	–	–
Annona coriacea	Seeds, Pulp	• DPPH and beta carotene bleaching test showed free radical scavenging activity of 31.53%, 51.59% respectively in in vitro model.	DPPH, Beta-carotene bleaching and ABTS radical cation.	[68]
Annona carcans	Pulp, Seeds, Leaves	Potent in vitro antioxidant activity was shown by pulp, leaves and seeds extract and fractions.	DPPH, ABTS, and beta-carotene/linoleic acid methods.	[21]
	–	Antidiabetic activity not reported.	–	
Annona senegalensis	Leaves	Aqueous leave extract showed potent antioxidant activity in in vitro model	DPPH, H_2O_2, superoxide ion, ABTS and ferric ion models	[69]
	–	Antidiabetic activity not reported.	–	

Annona macroprophyllata, whereas a low IC_{50} (1.18 μg/ml) was observed [63].

Annona muricata Research has shown that a single dose of 100 mg/kg and 200 mg/kg of an aqueous extract of *Annona muricata* did not significantly affect blood glucose levels in regular rats. The extract administration of single dosing effectively lowered the blood glucose levels in hyperglycemic rats after 2 h of dosing. Plant extracts at 100 mg/kg and 200 mg/kg reduced blood glucose levels by 31.77% and 45.77% after injection of streptozotocin for 14 days, respectively. Repetitive administering of *Annona muricata* aqueous extract at all doses led to a substantial decline of near-normal blood glucose levels on day 7. Also, 76.56% and 58.3% reductions were shown at doses 100 mg/kg and 200 mg/kg, respectively, compared to the initial value. The result also showed that before streptozotocin injection, plant extract's daily administration did not inhibit streptozotocin-induced hyperglycemia during 3 days. However, a significant drop in blood glucose levels during 14 days without treatment has shown that plant extract can work long. The findings also indicate decreased bodyweight loss, fluid and water intake in streptozotocin-induced rats, and blood glucose levels decreased during the four weeks of daily extract administration within one week. The presence of tannins and flavonoids in the phytochemistry of *Annona muricata* confirmed their hypoglycemic activity [64].

Annona reticulata Various fractions of 100 mg/kg of ethyl acetate, methanol, and residual fractions were obtained from *Annona reticulata* leaves hydro-alcoholic extract and was examined to determine its reduction of blood glucose level potential in streptozotocin-induced diabetic rats. After 14 days of treatment, fasting blood glucose levels decreased in hyperglycemic rats. Fasting blood glucose level decreased by 3.67%, 14.03%, 47.69%, and 50.93% for treatment with residual fraction, methanol fraction, ethyl acetate fraction, and standard drug. The study exhibited a significant ($P < 0.001$) decreased blood glucose level in comparison to the diabetic control group.

The blood glucose levels decreased by a residual fraction and methanol fraction from 417.83 to 402.50 mg/dl and 432.33 to 371.67 mg/dl. Compared to diabetic control groups, these levels were not substantial and the fraction of ethyl acetate was capable of controlling the increase in blood glucose and also attenuating secondary variables with hyperglycemia due to streptozotocin [73].

Antioxidant activity

Annona cherimola The cherimoya skin, flesh, and juice were isolated from *Annona cherimola* and analyzed for antioxidant content using the oxygen radical absorbance capacity (ORAC) assay. The juice showed the highest antioxidant activity, while the flesh exhibited the lowest [60]. Gupta-Elera et al. stated that the cherimoya juice extract enhanced the antioxidant uptake against the burkitt's lymphoma and colon cancer cell lines [60].

Annona crassiflora Ethanol and aqueous extract of *Annona crassiflora* peel, seed, and pulp were screened for in vitro antioxidant activity, whereas antioxidants were measured using DPPH and lipid peroxidation assay. The ethanol extract exhibited substantial and concentration-based scavenging activity in DPPH, together with lipid peroxidation activity inhibition in mice's model. Furthermore, the in-vitro antioxidant activity of peel, seed, and pulp exposed noticeable total phenolic content (TPC), whereas the ethanol peel extract contains the maximum TPC [67].

Annona muricate, A. squamosa, A. reticulata Using different in vitro models (DPPH, ABTS, nitric oxide, superoxide, hydroxyl radical, and lipid peroxidation), the antioxidant potential of leaves of three other species of Annona (*Annona muricata*, *Annona. squamosa*, *Annona reticulata*) were studied. *Annona muricata* ethanol extract displayed a maximum scavenging activity (90.05%) at 500 μg/ml for ABTS, followed by hydroxyl radical scavenging (85.88%) and nitric oxide scavenging (72.60%), whereas a moderate action observed for lipid peroxidation assay. *Annona squamosa* extract showed the least inhibition in all in vitro antioxidant models. The ethanol extract of *Annona reticulata* showed maximum inhibition of 89.37% in DPPH, 89.05% in ABTS, 71.10% in nitric oxide, 77.72% in hydroxyl radical, 80.88% in superoxide radical, and 35.54% in lipid peroxidation at 500 μg/ml. The ethanol extract of *Annona squamosa* showed maximum inhibition of 88.77% in DPPH, 88.06% in ABTS, 68.03% in nitric oxide, 79.79% in hydroxyl radical, 77.21% in superoxide radical, and 50.83% in lipid peroxidation at 500 μg/ml. These findings indicate that *Annona muricata* extracts have strong in-vitro antioxidants efficacy compared to *Annona squamosa* and *Annona reticulata* leaves, which show the function as an effective, free radical scavenger, increasing its therapeutic value [62, 65].

Annona coriacea Seeds and pulp extracts of fruit *Annona coriacea* and *Annona sylvatica* were tested for antioxidant potential. DPPH, Beta-carotene bleaching, and ABTS methods were applied to determine the antioxidant activity. The pulp and seeds of the fruits were extracted by using methanol/water (8:2) for maceration. An excellent extraction yield was shown in the seeds and pulp extracts of fruit *Annona coriacea* (14.5 and

20.5%) and *Annona sylvatica* (8.7 and 5.2%). A moderate antioxidant effect and exhibited free radical scavenging activity of 31.53% by DPPH test was demonstrated by the seed extracts of *Annona coriacea*. By the Beta-carotene bleaching test, the seed further showed 51.59% antioxidant activity. Besides, the ABTS assay afforded 159.50 μM Trolox/g antioxidant activity. Seed extracts of *Annona coriacea* showed significant antioxidant activity. On the other hand, the antioxidant activity of seeds and pulp extract of *Annona sylvatica* was not significant [68].

Annona carcans A research study was done to evaluate the antioxidant effect of the hydro-methanol extract of the leaves, pulp, and seeds of *Annona carcans*. Antioxidant activity was determined by a different model (DPPH, ABTS, and beta-carotene/linoleic acid methods). These three different extracts demonstrated that all of them possess prominent free radical scavenging activity with IC_{50} estimating between 89.67 μg and 26.25 μg/ml, especially the pulp extract with IC_{50} 44.08 μg/ml (DPPH) and 39.32 μg/ml (ABTS). The pulp fraction displayed promising activity in multiple assays with IC_{50} = 47.11 μg/ml (DPPH) and IC_{50} = 26.25 μg/ml (ABTS), relatable to the positive control ascorbic acid. The lipid peroxidation assay also revealed good antioxidant effects of both hydro methanol (51.51 μg/ml) and ethyl acetate (34.34 μg/ml) fractions of pulp. It is observed that due to the presence of quercetin and kaempferol derivative, the pulp extract of *Annona carcans* probably showed antioxidant effects [21].

Annona cornifolia *Annona cornifolia* has been tested for its antioxidant potential against DPPH using seed ethanol extract fractions containing acetogenins, and these compounds exhibited a robust antioxidant activity at 10–100 μg/ml in DPPH assay with a lower IC_{50} [41].

Annona senegalensis The aqueous extract of the *Annona senegalensis* leaves were assessed for in-vitro antioxidant activities using DPPH, H_2O_2, superoxide, 2, 2′-azo-(3-ethylbenzthiazoline-6-sulfonate), and ferric ion models, while the in vivo antioxidant activities were evaluated at the doses of 100 mg/kg, 200 mg/kg, and 400 mg/kg by enzymes and ion levels. In vitro antioxidant activity of the aqueous plant extract of Annona *senegalansis* demonstrated concentration-dependent activity (0.2–1 mg/ml) in 2,2 diphenyl-1 picrylhydration (DPPH), H_2O_2 superoxide ion, 2,2′-azo-(3-ethylbenzthiazoline-6-sulfonate), and ferric ion models. The extract produced maximum inhibitory scavenging activity of DPPH and H_2O_2 which was 96.9% and 77.54% at higher concentration, respectively, while superoxide ion inhibitory activity was 97.4%. Furthermore, the in-vitro antioxidant activity of leaves extract exhibited noticeable total phenolic content (TPC), total flavonoids contents, and proanthocyanidins [69].

Conclusion

This review involves nine of the Annonaceae species and highlights the antidiabetic and antioxidant ability of Annona plants. Annona species are widely distributed worldwide, while many species are used for both medicinal and food use. As the global scenario is now heading toward non-toxic herbal products with therapeutic applications, comprehensive research into this gold mine of centuries-old expertise should be emphasized. The majority of the plants in this study demonstrated that their antidiabetic and antioxidant activity was potent. Five species were reviewed as having antidiabetic activity, and they demonstrated potent antihyperglycemic effect. Furthermore, antioxidant activity was reviewed from ten species, and they showed potent antioxidant activity with different in vitro models. Though several in vitro studies have confirmed the antioxidant and antidiabetic potential of the species of the Annona genus, still only a few in vivo and clinical trials were performed to date to validate the in vitro outcomes. So their potential in animal and human models should be assessed in the future. Furthermore, the mechanism of action by which they confer antidiabetic and antioxidant activities is still not developed elaborately. This should also be developed in further studies. Moreover, it can be concluded that, since natural medicines have the least side effects and are considered safe for human health, they can substantially substitute synthetic drugs in the future.

Abbreviations

DPPH: 2,2-Diphenyl-1-picryl hydrazyl; ABTS: 2,2′-Azino-Bis(3-ethyl benzothiazoline-6-sulfonic acid); IC_{50}: Half maximal inhibitory concentration; H_2O_2: Hydrogen peroxide; TPC: Total phenolic content; ORAC: Oxygen radical absorbance capacity

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Authors' contributions

SSC and AMT planned and designed the research. SSC and SF conducted the complementary literature searches and reviews. SSC, AMT, and SF wrote the initial draft. SMT and MAS edited and revised the final draft. All authors have read and approved the manuscript.

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Availability of data and materials

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Declarations

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References

1. Pino JA, Agüero J, Marbot R (2001) Volatile components of soursop (annona muricata l.). J Essent Oil Res 13(2):140–141. https://doi.org/10.1080/10412905.2001.9699640
2. Chatrou LW, Pirie MD, Erkens RHJ, Couvreur TLP, Neubig KM, Abbott JR, Mols JB, Maas JW, Saunders RMK, Chase MW (2012) A new subfamilial and tribal classification of the pantropical flowering plant family annonaceae informed by molecular phylogenetics. Bot J Linn Soc 169(1):5–40. https://doi.org/10.1111/j.1095-8339.2012.01235.x
3. FAS (1965) Hutchinson's genera of flowering plants. [The Genera of Flowering Plants (Angiospermae), Based Principally on the Genera Plantarum of G. Bentham and J. D. Hooker. Dicotyledones Volume 1, J. Hutchinson]. Taxon 14(5):166–168. https://doi.org/10.2307/1217553
4. da Silva Almeida JRG, da Cruz Araújo EC, de Araújo Ribeiro LA, de Lima JT, Nunes XP, Lúcio ASSC, de Fátima Agra M, Barbosa Filho JM (2012) Antinociceptive activity of ethanol extract from duguetia chrysocarpa maas (annonaceae). Sci World J 2012
5. Shashirekha MN, Baskaran R, Rao LJ, Vijayalakshmi MR, Rajarathnam S (2008) Influence of processing conditions on flavour compounds of custard apple (annona squamosa l.). LWT Food Sci Technol 41(2):236–243. https://doi.org/10.1016/j.lwt.2007.03.005
6. Dutra LM, Costa EV, de Souza Moraes VR, de Lima Nogueira PC, Vendramin ME, Barison A, do Nascimento Prata AP (2012) Chemical constituents from the leaves of annona pickelii (annonaceae). Biochem Syst Ecol 41:115–118. https://doi.org/10.1016/j.bse.2011.12.011
7. Costa EV, Pinheiro MLB, de Souza ADL, Barison A, Campos FR, Valdez RH, Ueda-Nakamura T, Nakamura CV (2011) Trypanocidal activity of oxoaporphine and pyrimidine-β-carboline alkaloids from the branches of annona foetida mart.(annonaceae). Molecules 16(11):9714–9720. https://doi.org/10.3390/molecules16119714
8. Rao VS, Dasaradhan P, Krishnaiah KS (1979) Antifertility effect of some indigenous plants. Indian J Med Res 70:517–520
9. Arunjyothi B, Venkatesh K, Chakrapani P, Anupalli RR (2011) Phytochemical and pharmacological potential of annona cherimola-a review. Int J Phytomed 3(4):439
10. Andrade-Cetto A, Heinrich M (2005) Mexican plants with hypoglycaemic effect used in the treatment of diabetes. J Ethnopharmacol 99(3):325–348. https://doi.org/10.1016/j.jep.2005.04.019
11. Aguilar A, Camacho JR, Chino S, Jácquez P, López ME (1994) Herbario medicinal del instituto mexicano del seguro social. Información Etnobotánica, México 107
12. Cano L (1994) Flora medicinal indígena de méxicotreinta y cinco monografías del atlas de las plantas de la medicina tradicional mexicana (9682961327)
13. Atique A, Iqbal M, Ghouse AKM (1985) Use of annona squamosa and piper nigrum against diabetes. Fitoterapia:190–192
14. Navarrete A, Gonzalez-Trujano ME, Reyes B, Hong E (1998) Abstracts-some pharmacological effects of an ethanol extract of leaves of annona diversifolia on the central nervous system. Phytother Res 12:600–602
15. González-Trujano ME, Navarrete A, Reyes B, Cedillo-Portugal E, Hong E (2001) Anticonvulsant properties and bio-guided isolation of palmitone from leaves of *annona diversifolia*1. Planta Med 67(02):136–141. https://doi.org/10.1055/s-2001-11504
16. Eva González-Trujano M, Tapia E, López-Meraz L, Navarrete A, Reyes-Ramírez A, Martinez A (2006) Anticonvulsant effect of *Annona diversifolia* saff. and palmitone on penicillin-induced convulsive activity. A behavioral and eeg study in rats. Epilepsia 47(11):1810–1817. https://doi.org/10.1111/j.1528-1167.2006.00827.x
17. Carballo AI, Martínez AL, González-Trujano ME, Pellicer F, Ventura-Martínez R, Díaz-Reval MI, López-Muñoz FJ (2010) Antinociceptive activity of *annona diversifolia* saff. Leaf extracts and palmitone as a bioactive compound. Pharmacol Biochem Behav 95(1):6–12. https://doi.org/10.1016/j.pbb.2009.11.017
18. Adjanohoun JE, Aboubakar N, Dramane K, Ebot ME, Ekpere JA, Enow-Orock EG, Focho D, Gbile ZO, Kamanyi A, Kamsu-Kom J (1996) Traditional medicine and pharmacopoeia: contribution to ethnobotanical and floristic studies in cameroon. OUA/STRC, Lagos, p 301
19. Jamkhande PG, Wattamwar AS (2015) *Annona reticulata* linn. (bullock's heart): Plant profile, phytochemistry and pharmacological properties. J Tradit Complement Med 5(3):144–152. https://doi.org/10.1016/j.jtcme.2015.04.001
20. Luzia DMM, Jorge N (2013) Bioactive substance contents and antioxidant capacity of the lipid fraction of *annona crassiflora* mart. Seeds. Ind Crop Prod 42:231–235. https://doi.org/10.1016/j.indcrop.2012.05.027
21. Volobuff CRF, Pederiva MMC, Benites RSR, Lima CJ, Argandona EJS, Cardoso CAL, Pereira ZV, Ruiz ALTG, Foglio MA, de Carvalho JE (2019) Bioguided fractionation, and antioxidant, antiproliferative, and anti-inflammatory activity of *annona cacans* warm. J Med Food 22(10):1078–1086. https://doi.org/10.1089/jmf.2018.0198
22. De Mesquita ML, Grellier P, Mambu L, De Paula JE, Espindola LS (2007) In vitro antiplasmodial activity of brazilian cerrado plants used as traditional remedies. J Ethnopharmacol 110(1):165–170. https://doi.org/10.1016/j.jep.2006.09.015
23. Dos Santos AF, Sant'Ana AEG (2001) Molluscicidal properties of some species of annona. Phytomedicine 8(2):115–120. https://doi.org/10.1078/0944-7113-00008
24. Pio-Correa M (1974) Dicionário de plantas úteis do brasil e das plantas exóticas cultivadas. Ministério da Agricultura, Brazil
25. Neuwinger HD (1996) African ethnobotany: Poisons and drugs: Chemistry, pharmacology, toxicology. CRC Press
26. Feng PC, Haynes LJ, Magnus KE, Plimmer JR, Sherratt HSA (1962) Pharmacological screening of some west indian medicinal plants. J Pharm Pharmacol 14(1):556–561
27. Florence NT, Théophile D, Désiré DDP, Bertin V, Etienne D, Beauwens R, Emmanuel AA, Louis Z, Pierre K (2007) Antidiabetic activities of methanol-derived extract of dorstenia picta twigs in normal and streptozotocin-induced diabetic rats. Asian J Trad Med 2(4):140–148
28. Padma P, Pramod NP, Thyagarajan SP, Khosa RL (1998) Effect of the extract of *annona muricata* and petunia nyctaginiflora on herpes simplex virus. J Ethnopharmacol 61(1):81–83. https://doi.org/10.1016/S0378-8741(98)00013-0
29. Adewole SO, Caxton-Martins EA (2006) Morphological changes and hypoglycemic effects of *annona muricata linn.*(annonaceae) leaf aqueous extract on pancreatic β-cells of streptozotocin-treated diabetic rats. Afr J Biomed Res 9(3)
30. Adewole S, Ojewole J (2009) Protective effects of *annona muricata linn.* (annonaceae) leaf aqueous extract on serum lipid profiles and oxidative stress in hepatocytes of streptozotocin-treated diabetic rats. Afr J Tradit Complement Altern Med 6(1):30–41
31. Kiill LHP, Costa, J. G. d. (2003) Floral biology and reproductive system of *annona squamosa* l.(annonaceae) in petrolina-pe, brazil. Ciência Rural 33(5):851–856. https://doi.org/10.1590/S0103-84782003000500009
32. Pontes AF, Barbosa MR d V, Maas PJM (2004) Flora paraibana: Annonaceae juss. Acta Bot Bras 18(2):281–293. https://doi.org/10.1590/S0102-33062004000200008
33. Calzada F, Correa-Basurto J, Barbosa E, Mendez-Luna D, Yepez-Mulia L (2017) Antiprotozoal constituents from annona cherimola miller, a plant used in mexican traditional medicine for the treatment of diarrhea and dysentery. Pharmacogn Mag 13(49):148–152. https://doi.org/10.4103/0973-1296.197636
34. Chen C-Y, Chang F-R, Chiu H-F, Wu M-J, Wu Y-C (1999) Aromin-a, an annonaceous acetogenin from *annona cherimola*. Phytochemistry 51(3):429–433. https://doi.org/10.1016/S0031-9422(99)00002-3
35. Kim DH, Ma ES, Suk KD, Son JK, Lee JS, Woo MH (2001) Annomolin and annocherimolin, new cytotoxic annonaceous acetogenins from *annona cherimolia* seeds. J Nat Prod 64(4):502–506. https://doi.org/10.1021/np000335u
36. Pandey N, Barve D (2011) Phytochemical and pharmacological review on *annona squamosa* linn. Int J Res Pharmaceut Biomed Sci 2(4):1404–1412
37. Laguna-Hernández G, Brechú-Franco AE, De la Cruz-Chacón I, González-Esquinca AR (2017) A histochemical technique for the detection of annonaceous acetogenins. In: Histochemistry of single molecules. Springer, pp 331–338
38. Moghadamtousi SZ, Fadaeinasab M, Nikzad S, Mohan G, Ali HM, Kadir HA (2015) Annona muricata (annonaceae): a review of its traditional uses, isolated acetogenins and biological activities. Int J Mol Sci 16(7):15625–15658. https://doi.org/10.3390/ijms160715625
39. Nirmal SA, Gaikwad SB, Dhasade VV, Dhikale RS, Kotkar PV, Dighe SS (2010) Anthelmintic activity of *annona reticulata* leaves. Res J Pharm, Biol Chem Sci 1(1):115–118

40. Gomes INF, Silva-Oliveira RJ, Oliveira Silva VA, Rosa MN, Vital PS, Barbosa MCS, Dos Santos FV, Junqueira JGM, Severino VGP, Oliveira BG (2019) Annona coriacea mart. Fractions promote cell cycle arrest and inhibit autophagic flux in human cervical cancer cell lines. Molecules 24(21):3963
41. Lima LARS, Pimenta LPS, Boaventura MAD (2010) Acetogenins from *annona cornifolia* and their antioxidant capacity. Food Chem 122(4):1129–1138. https://doi.org/10.1016/j.foodchem.2010.03.100
42. Sahpaz S, González MC, Hocquemiller R, Zafra-Polo MC, Cortes D (1996) Annosenegalin and annogalene: Two cytotoxic mono-tetrahydrofuran acetogenins from annona senegalensis and *annona cherimolia*. Phytochemistry 42(1):103–107. https://doi.org/10.1016/0031-9422(95)00891-8
43. Zeng L, Ye Q, Oberlies NH, Shi G, Gu ZM, He K, McLaughlin JL (1996) Recent advances in annonaceous acetogenins. Nat Prod Rep 13(4):275–306. https://doi.org/10.1039/np9961300275
44. Fall D, Sambou B, Seck M, Wélé A, Ndoye I, Gleye C, Laurens A (2008) enhancing the anthelminthic activity roots of *annona sengalensis*. Dakar Med 53(1):61–67
45. Magadula JJ, Innocent E, Otieno JN (2009) Mosquito larvicidal and cytotoxic activities of 3 annona species and isolation of active principles. J Med Plants Res 3(9):674–680
46. Lall N, Kishore N, Bodiba D, More G, Tshikalange E, Kikuchi H, Oshima Y (2017) Alkaloids from aerial parts of *annona senegalensis* against streptococcus mutans. Nat Prod Res 31(16):1944–1947. https://doi.org/10.1080/14786419.2016.1263847
47. Rupprecht JK, Hui YH, McLaughlin JL (1990) Annonaceous acetogenins: a review. J Nat Prod 53(2):237–278. https://doi.org/10.1021/np50068a001
48. Bhardwaj R, Pareek S, Sagar NA, Vyas N (2019) Bioactive compounds of annona. In: Murthy HN, Bapat VA (eds) Bioactive compounds in underutilized fruits and nuts. Springer International Publishing, Cham, pp 1–26. https://doi.org/10.1007/978-3-030-06120-3_5-1
49. Leboeuf M, Cavé A, Bhaumik PK, Mukherjee B, Mukherjee R (1980) The phytochemistry of the annonaceae. Phytochemistry 21(12):2783–2813. https://doi.org/10.1016/0031-9422(80)85046-1
50. Yang C, Gundala SR, Mukkavilli R, Vangala S, Reid MD, Aneja R (2015) Synergistic interactions among flavonoids and acetogenins in graviola (*annona muricata*) leaves confer protection against prostate cancer. Carcinogenesis 36(6):656–665. https://doi.org/10.1093/carcin/bgv046
51. Matsushige A, Matsunami K, Kotake Y, Otsuka H, Ohta S (2012) Three new megastigmanes from the leaves of *annona muricata*. J Nat Med 66(2):284–291. https://doi.org/10.1007/s11418-011-0583-1
52. Nawwar M, Ayoub N, Hussein S, Hashim A, El-Sharawy R, Wende K, Harms M, Lindequist U (2012) A flavonol triglycoside and investigation of the antioxidant and cell stimulating activities of *annona muricata linn*. Arch Pharm Res 35(5):761–767. https://doi.org/10.1007/s12272-012-0501-4
53. Jiménez VM, Gruschwitz M, Schweiggert RM, Carle R, Esquivel P (2014) Identification of phenolic compounds in soursop (*annona muricata*) pulp by high-performance liquid chromatography with diode array and electrospray ionization mass spectrometric detection. Food Res Int 65:42–46. https://doi.org/10.1016/j.foodres.2014.05.051
54. Pélissier Y, Marion C, Kone D, Lamaty G, Menut C, Bessière J-M (1994) Volatile components of *annona muricata* l. J Essent Oil Res 6(4):411–414. https://doi.org/10.1080/10412905.1994.9698410
55. Kossouoh C, Moudachirou M, Adjakidje V, Chalchat J-C, Figuérédo G (2007) Essential oil chemical composition of *annona muricata* l. Leaves from benin. J Essent Oil Res 19(4):307–309. https://doi.org/10.1080/10412905.2007.9699288
56. Zaman K (2013) Pharmacognostical and phytochemical studies on the leaf and stem bark of *annona reticulata* linn. J Pharmacog Phytochem 1(5)
57. Suresh HM, Shivakumar B, Shivakumar SI (2011) Inhibitory potential of the ethanol extract of *annona reticulata* linn. Against melanoma tumor. J Nat Pharmaceut 2(4)
58. Leterme P, Buldgen A, Estrada F, Londoño AM (2006) Mineral content of tropical fruits and unconventional foods of the andes and the rain forest of colombia. Food Chem 95(4):644–652. https://doi.org/10.1016/j.foodchem.2005.02.003
59. Calzada F, Solares-Pascasio JI, Ordoñez-Razo RM, Velazquez C, Barbosa E, García-Hernández N, Mendez-Luna D, Correa-Basurto J (2017) Antihyperglycemic activity of the leaves from *annona cherimola miller* and rutin on alloxan-induced diabetic rats. Pharm Res 9(1):1–6. https://doi.org/10.4103/0974-8490.199781
60. Gupta-Elera G, Garrett AR, Martinez A, Robison RA, O'Neill KL (2011) The antioxidant properties of the cherimoya (*annona cherimola*) fruit. Food Res Int 44(7):2205–2209. https://doi.org/10.1016/j.foodres.2010.10.038
61. Shirwaikar A, Rajendran K, Kumar CD, Bodla R (2004) Antidiabetic activity of aqueous leaf extract of *annona squamosa* in streptozotocin–nicotinamide type 2 diabetic rats. J Ethnopharmacol 91(1):171–175. https://doi.org/10.1016/j.jep.2003.12.017
62. Shirwaikar A, Rajendran K, Kumar CD (2004) In vitro antioxidant studies of *Annona squamosa* Linn. leaves. Indian J Exp Biol 42(8):803–807
63. Brindis F, González-Trujano ME, González-Andrade M, Aguirre-Hernández E, Villalobos-Molina R (2013) Aqueous extract of *Annona macroprophyllata*: a potential α-glucosidase inhibitor. Biomed Res Int 2013:591313–591316. https://doi.org/10.1155/2013/591313
64. Florence NT, Benoit MZ, Jonas K, Alexandra T, Désiré DDP, Pierre K, Théophile D (2014) Antidiabetic and antioxidant effects of *annona muricata* (annonaceae), aqueous extract on streptozotocin-induced diabetic rats. J Ethnopharmacol 151(2):784–790. https://doi.org/10.1016/j.jep.2013.09.021
65. Baskar R, Rajeswari V, Kumar TS (2007) In vitro antioxidant studies in leaves of annona species. Indian J Exp Biol 45(5):480–485
66. Rout SP, Kar DM, Mohapatra SB, Swain SP (2013) Anti-hyperglycemic effect *Annona reticulata* L. leaves on experimental diabetic rat model. Asian J Pharm Clin Res 6(1):56–60
67. Roesler R, Malta LG, Carrasco LC, Pastore G (2006) Evaluation of the antioxidant properties of the brazilian cerrado fruit *annona crassiflora* (araticum). J Food Sci 71(2):C102–C107. https://doi.org/10.1111/j.1365-2621.2006.tb08882.x
68. Benites RSR, Formagio ASN, Argandoña EJS, Volobuff CRF, Trevizan LNF, Vieira MC, Silva MS (2015) Contents of constituents and antioxidant activity of seed and pulp extracts of *annona coriacea* and *annona sylvatica*. Braz J Biol 75(3):685–691. https://doi.org/10.1590/1519-6984.21313
69. Ajboye TO, Yakubu MT, Salau AK, Oladiji AT, Akanji MA, Okogun JI (2010) Antioxidant and drug detoxification potential of aqueous extract of *annona senegalensis* leaves in carbon tetrachloride-induced hepatocellular damage. Pharm Biol 48(12):1361–1370. https://doi.org/10.3109/13880209.2010.483247
70. Kamalakkannan N, Prince PSM (2006) Rutin improves the antioxidant status in streptozotocin-induced diabetic rat tissues. Mol Cell Biochem 293(1-2):211–219. https://doi.org/10.1007/s11010-006-9244-1
71. Fernandes AAH, Novelli ELB, Okoshi K, Okoshi MP, Di Muzio BP, Guimarães JFC, Junior AF (2010) Influence of rutin treatment on biochemical alterations in experimental diabetes. Biomed Pharmacother 64(3):214–219. https://doi.org/10.1016/j.biopha.2009.08.007
72. Adisakwattana S, Yibchok-Anun S, Charoenlertkul P, Wongsasiripat N (2011) Cyanidin-3-rutinoside alleviates postprandial hyperglycemia and its synergism with acarbose by inhibition of intestinal α-glucosidase. J Clin Biochem Nutr 49(1):36–41. https://doi.org/10.3164/jcbn.10-116
73. Rout S, Kar D, Maharana L (2016) Anti-hyperglycemic effect of different fractions of *annona reticulata* leaf. Asian J Pharmaceut Clin Res 9:256. https://doi.org/10.22159/ajpcr.2016.v9s2.13710

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