

PHYTOCHEMICAL AND PHARMACOLOGICAL POTENTIAL OF ANNONA SPECIES: A REVIEW

AMUDHA P, VANITHA VARADHARAJ*

Department of Biochemistry, School of Life Sciences, Vels University, Pallavaram, Chennai, Tamil Nadu, India.

Email: vanitha.sls@velsuniv.ac.in

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ABSTRACT

Herbal plants and phytochemical products have been used for the treatment of various diseases from ancient times in the folklore medicine worldwide. Crude extracts from plants now play an important and valuable source for natural products that are used in the advancement of medicines against various diseases, for the improvement of pharmaceutical preparations and for novel bioscience research. One such plant genus is *Annona*, such as *Annona muricata*, *Annona cherimola*, *Annona reticulata*, *Annona squamosa*, and *Annona senegalensis* are some species widely cultivating in India and tropical regions of Asia for their edible fruits and medicinal values. These plants have been used for centuries as traditional folk medicine for the treatments of various diseases. The plants are considered to be a good source of vitamins, minerals, plant proteins, fibers, etc., as well as the plant is supposed to have many biological activities. This review describes the morphology and ecology of the plant, its ethnomedicinal uses, pharmacological activities, and phytoconstituents.

Keywords: *Annona muricata*, *Annona cherimola*, *Annona reticulata*, *Annona squamosa*, *Annona senegalensis*, Phytochemicals and pharmacological properties.

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INTRODUCTION

Plants and plant-derived medicinal products have been used to help humankind to continue its healthiness from the dawn of medicine. Over the past century, the phytochemicals in plants play an important role in pharmaceutical discovery. The importance of the active ingredients of plants in medicine has inspired and denoted scientific interest in the biological activities of these substances [1].

Under the classification of flowering plants, the family *Annonaceae* also called as custard apple family [2] has many traditional values, mainly composed of trees, shrubs and rarely lianas [3]. The word genus *Annona* is derived from a Latin word "anon" which means "yearly produce" that specifies the production of fruits to the plants of this family. Under the family *Annonaceae*, encompassing 2300-2500 species and around 130 genera are currently classified [4]. The family *Annonaceae* mostly found in tropic regions and few species found in temperate regions also. Around 900 species are Neotropical, 450 species are Afrotropical and some species are Indo-Malaysian.

In the family *Annonaceae* [5]: *Annona*, *Anonidium*, *Rollinia*, *Uvaria*, *Melodorum*, *Asimina*, and *Stelechocarpus* are most commonly available and widely distributed genera. In India, the genus *Annona* is frequently available. Hence, the present review was outlined on some species of *Annona* from the available literature and depending on the accessibility of the plants. The family *Annona* comprises a number of tropical and subtropical habitats worldwide but its further territorial extension is limited, due to the environmental conditions of the *Annonaceae*, to geographical areas with very precise characteristics of altitude, temperature, relative humidity, and soil. The most significant species with profitable importance of *Annonaceae* family including *Annona squamosa* Linn., *Annona reticulata* Linn., *Annona muricata* Linn., *Annona senegalensis* Linn., and *Annona cherimola* Linn. were listed in Table 1 and selected for the review.

VERNACULAR NAMES***A. muricata* L.**

A. muricata also known as graviola, guyabano, or soursop in English; asguanabana in Spanish; huanaba in Guatemala; zopote de viejas in

Mexico; cabeza de negro in Venezuela; catoche in Argentina; jaca do para in the Netherlands; lakshmanaphal or jangli or mullaraamaphala in India [6].

***A. cherimola* L.**

A. cherimola also known as cherimoya, custard-apple, and cherimoya in English; anonaposhte, cherimolia, cherimoyer, cherimolla, and cherimoya in Spanish; anone, cherimolier, and cherimole in French; cherimoya, cherimolia, cherimoyabaum, and cherimoya in German; grabiola, graveola, and graviola in Portuguese; cherimoa and cherimoya in Japanese; cherimolia, Mexico Pox or poox in Italian; hanuman phal and marytiphall in Hindi; hanuman phalamu in Telugu [6].

***A. reticulata* L.**

A. reticulata also known as Jamaican apple, bullock's heart, netted custard apple, and Sweetsop in English; lonang and nona kapri in Malaysia; noinong in Thailand; anonacolorada, anona de seso, anonaroja in Spanish, corossolsauvage, bois cachiman, and cachiman in French; luvun, ramphal, and nona in Hindi [7].

***A. squamosa* L.**

A. squamosa also known as custard apple, sugar apple, and sweet apries in English; sharifa in Hindi; sitaphalam in Telugu; corossolier, cailleux, and pommiercannelle in French [8].

***A. senegalensis* L.**

A. senegalensis also known as wild custard apple and wild soursop in English; wildsuikerappel in Africa; gishta and gishta gaba in Arabic; pomme cannelle du senegal, annone in French; mchekwa, mkonokono, mtomoko-mwitu, mutopetope, mwitu, mtomoko in Swahili; sinkuongo and jumbukungo in Mandinka.

ECOLOGY***A. muricata* L.**

A. muricata found mainly in the humid tropical and subtropical lowlands and common on the coastal areas and slopes. It is commonly seen in the roadsides and also found in pastures and cultivated mainly for the fruit. The species cultivated mainly in home gardens and also

Table 1: Taxonomic classification of *Annona* species

Binomial name	<i>Annona muricata</i>	<i>Annona cherimola</i>	<i>Annona reticulata</i>	<i>Annona squamosa</i>	<i>Annona senegalensis</i>
Order	Magnoliales	Magnoliales	Magnoliales	Magnoliales	Magnoliales
Family	Annonaceae	Annonaceae	Annonaceae	Annonaceae	Annonaceae
Genus	<i>Annona</i>	<i>Annona</i>	<i>Annona</i>	<i>Annona</i>	<i>Annona</i>
Species	<i>Annona muricata</i>	<i>Annona cherimola</i>	<i>Annona reticulata</i>	<i>Annona squamosa</i>	<i>Annona senegalensis</i>
Common name	Soursop	Cherimoya	Custard apple	Sugar apple	Wild soursop

found in rural gardens on volcanic and raised limestone islands. They are poor in withstanding frost. *A. muricata* found throughout the West Indies except in the Bahamas and also occurs from Mexico to Brazil. It is common in the West but infrequent on the southern Florida. It is found in Puerto Rico, mostly on the slopes of Cordillera. *A. muricata* is native to tropical areas in South and North America and also found in the tropical and subtropical countries such as India, Malaysia, and Nigeria [9].

A. cherimola L.

A. cherimola is mainly found in the highlands from sea-level up to approximately 1400 m altitude. In Colombia and Ecuador, it occurs naturally at elevations between 1400 and 2000 m where the temperature ranges lie between 17 and 20°C [6].

A. reticulata L.

It is cultivated throughout India up to an altitude of 900 m. It is found growing abundantly and widely in the hilly areas, wastelands, and found in several districts of Andhra Pradesh, Punjab, Rajasthan, Uttar Pradesh, Madhya Pradesh, Bihar, West Bengal, Assam, Gujarat, Maharashtra, Karnataka, Kerala, and Tamil Nadu. It is a native plant of South America and West Indies [10].

A. squamosa L.

It is widely cultivated in India and found in Thailand and originates from the West Indies and South America. *A. squamosa* is primitive to tropical South America and the West Indies and originated in lowland Central America where it is home-grown, and from there it was distributed to Mexico and throughout tropical America.

A. senegalensis L.

It is widely found in semi-arid to sub-humid all over the parts of Africa. The species occurs along riverbanks, fallow land, and swamp forests and at the coast. Commonly grows as a single plant among the savannah woodlands [11].

BOTANICAL DESCRIPTION

A. muricata L.

A. muricata is an evergreen tropical tree and bushy grows up to 9 m in height. Found in tropical America and Caribbean region of West Indies. Leaves found to be leathery with displeasing odor, broadly elliptic to obovate, 5.8-19.0 cm × 3.7-8.1 cm, and sometimes lightly unequal. Flowering starts during the 3rd year and flowers leaf-opposed on the old wood, greenish yellow, usually three, fleshy, triangular, saccate at the base. Fig. 1 shows the fruit of *A. muricata* and the fruit skin is found to be leathery and covered with curved, soft, pliable spines with white colored pulp inside divided into many segments. Seeds found to be black, oval with smooth finishing surface [7].

A. cherimola L.

A. cherimola is erect but low branched and partially shrubby and it grows up to 5-9 m. Due to the mitriform petiole concealing the bud, leaves are deciduous to semi-deciduous. Leaves are alternate, two-ranked, contains hairy petioles; ovate to elliptic, short blunt narrow at the apex; somewhat hairy on the top surface, smooth on the lower surface [12]. Flowers are pleasant, solitary or in group of two or three, on short hairy stalks, have three outer greenish, fleshy, oblong petal-like tepals, and three smaller inner tepals. Fruits are syncarp, formed by pistils and receptacle, conical or slightly heart-shaped, 10-20 cm long

Fig. 1: Fruit of *Annona muricata*

and up to 10 cm in width, weighing on average 150-500 g. Skin looks smooth having finger print-like markings and covered with conical or rounded protuberances. Fig. 2 shows the fruit of *A. cherimola* and the fruit is easily broken, exposing snow-white, juicy flesh with pleasing aroma and tasteful, sub acid and contain many hard, brown or black beanlike seeds with 1.25-2 cm long.

A. reticulata L.

A. reticulata are small deciduous or semi-deciduous tree grows up to 10 m height. The bark looks rough, thin and dark brown, 1.4-4.0 mm thick, and if dried it becomes double quilled. Leaves are found to be oblong, lanceolate, reticulate, pellucid punctate, with bad odor; when young it looks glabrous above and glaucous and pubescent beneath, lateral nerves having 8-11 pairs, petiole grows up to 2 cm long. Flowers are found to be bisexual, drooping, greenish white, fleshy, solitary, leaf found to be opposite or 2-4 on short extra axillary branchlets. Fig. 3 shows the fruits of *A. reticulata* and the fruit found to be globose, 5-10 cm in diameter and when ripe it looks yellowish-green color. Berries looks heart-shaped syncarpium with pentagonal areoles, seeds found to be smooth and black in color. The tree has deep penetrating root system with abundant root fibers [7].

A. squamosa L.

A. squamosa trees are semi evergreen well branched shrub grows up to a height of 7 m. The bark found to be thin, gray, and woody and having extensively branched tap root system. Leaves found to be simple, alternate, oblong lanceolate or elliptic, and pellucid-dotted, peculiarly scented, and 5.0-15.0 cm × 1.9-3.8 cm in size. Flowers found to be green in color, fleshy, drooping, extra axillary, more on the leafy shoot than on the older wood. Fig. 4 shows the fruit of *A. squamosa*, and the fruits has many carpels with lozenge shaped on a central torus and fused into an irregular globose or heart-shaped tubercled, yellowish green in color and syncarpium with thick scaly skin. The pulp is sweet and pleasing odor and looks light yellow in color. The seeds found to be oblong and deep brownish black in color and covered with whitish pulp.

A. senegalensis L.

A. senegalensis is a wild shrub grows up to 7 m, but this plant is not resilient in nature. It is cultivated for its leaves, fruits, flower, bark, and



Fig. 2: Fruits of *Annona cherimola*



Fig. 4: Fruit of *Annona squamosa*



Fig. 3: Fruits of *Annona reticulata*



Fig. 5: Fruit of *Annona senegalensis*

stem for medicinal purpose. Leaves are alternate, simple, oblong to ovoid in shape, 6-185 × 25-120 mm in size. The stem looks gray in color when young and smooth to coarsely in older trees. The undeveloped branches have yellow hairs and lost during development. The flowers grows up to 35 mm in diameter, on stalk grows up to 30 mm long and directly above the leaf axils. Fig. 5 shows the fruit of *A. senegalensis* and the fruit is formed from several fused and ovate carpels about 45 mm in diameter. At early stage, it looks dark green and yellow when ripe and finally to orange during the later stage of life. It has a curved inner whorl around the stamens and ovary and with several stamens.

ETHNOMEDICINAL USES

A. muricata L.

A. muricata is extensively used as traditional medicines against many human diseases, especially cancer and parasitic infections. The fruit is a good source of natural medicine for arthritic pain, neuralgia, arthritis, diarrhea, dysentery, fever, malaria, parasites, rheumatism, skin rashes, and worms. It is given to elevate mother's milk after childbirth. Leaves are used to cure cystitis, diabetes, headaches, and insomnia. Leaf's decoction is used to treat antirheumatic and neuralgic effects and cooked leaves are used to treat abscesses and rheumatism [13]. Seeds should be crushed can be used to treat anthelmintic activities against worms and parasites both internally and externally. *A. muricata* is used for astringent, insecticide and pesticide and also used to cure coughs, pain and skin diseases in tropical Africa. Fruits and flower are used to cure catarrh and the root-bark and leaves are used to treat antiphlogistic and anthelmintic activities in India [14]. Leaves

of *A. muricata* mixed with *A. squamosa* and *Hibiscus rosa-sinensis* are applied on the head to protect against fainting in Malaysia. *A. muricata* leaves are used as an ethnomedicine for tumors and cancer in South America tropical Africa and Nigeria. Leaves, barks, and roots are used to treat the anti-inflammatory, hypoglycemic, sedative, smooth muscle relaxant, hypotensive, and antispasmodic effects.

A. cherimola L.

A. cherimola is a dessert fruit that can be eaten fresh. Due to its enzymatic characteristics, *A. cherimola* fruits cannot be used for thermal processes and its processing should utilize refrigerating or freezing, with addition of antioxidants to avoid enzymatic oxidation and subsequent coloring [15]. *A. cherimola* seeds are used as an insecticide to kill lice and to cure parasitic skin problems. *A. cherimola* seeds has an important alkaloid, acetogenins [16], which has antiparasitic and cytotoxic activities. The annonaceous acetogenins are a new group of powerful phytochemical agents, and more than 300 of these compounds have been found which has antimicrobial, antitumor, cardiotoxic, and insecticidal properties. The fruit contains low cholesterol and sodium. It is rich in dietary fiber, vitamin B6, vitamin C and potassium. Fruit is used traditionally for antimicrobial and insecticidal activities and to cure stomach-ache and pancreatic ulcers. Dried flowers are used as flavoring for snuff in Jamaica. Immature fruit is used for cooked vegetable and bark is used as a decoction for diarrhea. For toothache, root can be chewed and decoction from root can be used to treat fevers. Decoction from leaves can be used to treat worms and leaves are used to tan leather.

A. reticulata L.

Decoction from bark can be used for the treatment of dysentery and diarrhea. *A. reticulata* leaves can be used to prepare tea for relieving

colic. Leaves should be warmed and applied over the abdomen to get relief from indigestion in babies and children in Philippines. Leaves should be crushed can be used as poultice for abscesses and to cure ulcers. Fruits possess anthelmintic properties. Root bark is used to cure toothache and is placed around the gums to get relief from toothache and decoction from roots can be used to cure fever. Decoction from leaves can be used in treating malaria and syphilis. The roots can be used for epilepsy. *A. reticulata* has been used as an anti-inflammatory agent, antianxiety, antistress, antimutagenic, and spasmolytic agent. Leaf and stem extract possess inotropic, positive for chronotropic and spasmolytic properties [6].

A. squamosa L.

A. squamosa has lots of medicinal values. Unripe fruit can be used as an astringent and root can be used for drastic purgative and seeds can be used to treat antifertility activity. Leaves can be used as a vermicide, for treating tumors and applied to abscesses, insect bites and skin problems. For toothache, root and bark scrapings can be used. Seeds should be powdered can be used to kill head-lice and fleas and proper care should be taken to avoid the powder to come in contact with eyes since it causes severe pain. Fruits, seeds, and leaves possess vermifugal and insecticidal properties. Pulp can be used as a flavoring agent in ice creams. Between 50% and 80% of the fruit are edible. Since *A. squamosa* has the biochemical substances such as alkaloids, glycosides, resins, volatile oils, gums and Tannins and ascorbic acid the plant possess excellent medicinal properties [17]. *A. squamosa* contains more of vitamin C (35-42 mg/100 g) than in grapefruit. The nutrient value of thiamine, potassium, and dietary fiber is also found to be higher.

A. senegalensis L.

A. senegalensis has an excellent source for traditional medicine applications. Leaves can be used for treating yellow fever, tuberculosis, and small pox and stem bark can be used for snakebite and hernia treatment [18]. Root can be used for difficulty in swallowing, gastritis, snake bites, male sexual impotence, erectile dysfunction, tuberculosis, and as an antidote and root bark can be used for infectious diseases [19]. Juice can be collected from the tree can be used for the treatment of chicken pox [20]. Many parts of the plant can be used as antidotes for venomous bites and management of diabetes [21]. *A. senegalensis* has been used for treatment of malaria in Guinea [22], and bark can be used to cure open sores in Switzerland [23]. *A. senegalensis* along with *Ageratum conyzoides* can be used for diarrhea and with *Nauclea latifolia* used for dysentery practiced in the Benue state in North Central Nigeria [24]. Fresh leaves can be used in poultry houses and left until they dry and the process can be repeated once or twice a week for controlling parasites including fleas and lice in Nigeria and Tanzania [25]. *A. senegalensis* can also be used as food and food additives. Leaves can be used as vegetables and edible pulp of the fruit has a pleasant taste and the flowers can be used as spices for various foods.

PHYTOCHEMISTRY

A. muricata L

A. muricata contains carbohydrates, phenols, flavonoids, alkaloids, coumarins, glycosides, phytosterols, quinones, steroids, proteins, saponins, and terpenoids. *A. muricata* contains flavonoids, saponins, tannins, alkaloids, triterpenoids, reducing sugar, and cardiac glycosides in the ethanolic leaf extract [26]. A new acetogenins called cohibins A and B and sabadelin which involves in the biosynthesis of monoterahydrofuran acetogenins were present in the methanolic root extracts and from stem bark a new biogenetic precursor's epoxy-murins A and B isolated. From the seed extract, a new monoterahydrofuran namely murisolin, two new cytotoxic γ -lactones namely corosolone and corosolin, a new acetogenins, muricatetrocins A and B, gigantetrocin B, muricatacin, solamin and epomuricinens A and B Annonaceous acetogenins, C-35 and C-37 mono-epoxy unsaturated compounds epomuricinens A and B, and epomusenins A and B and two new mono-epoxy saturated C-35 representatives, epomurinin A and B were isolated from fruit pulp of methylene chloride extract.

Annohexocin, annomutacin, annomuricin A to E, annonacinone, corosolone, cis-annonacin, annomontacin, annonacin, epomuricin A and B, cis-corosolone, corepoxylone, corepoxylone, annomuricin A and B, cohibin A and D, donhexocin, montanacin, muricatetrocin A and B muricatidin, annopentocin A to C, gigantetrocin A and B, gigantetrocin, goniiothalamycin, montecristin, corosolin, gigantetrocinone, iso-annonacin, muracin A to G, muricatacin, muri-catenol, gigantetrocin, murihexocin 3, muricatacin, muricatocin A to C, muricoreacin, murihexocin A to C, muricapentocin, muricin H, muricin I, rolliniastatin 1 and 2, uvariamicin I and IV, coronin, javoricin, murisolin, solamin, annocatalin, xylomaticin, robustocin, annomonin and murihexol are the few annonaceous acetogens found in graviola [27].

A. cherimola L.

A. cherimola has various phytochemicals including alkaloids, flavonoids, glycosides, saponins, tannins, carbohydrates, proteins, compounds, phytosterols, and amino acids. *A. cherimola* possesses potent antioxidant activity [28]. Stem and seeds possess various chemical constituents including annocherine A, B, cherianoine, aromin-A, N-cis-cafeoyltyramine, dihydro-feruloyltyramine, N-transferuloylmethoxytyramine, and N-cisferuloyltylmethoxytyramine [29]. Seeds have been found to contain cyclooctapeptides, cherimolacyclopeptide A, and cherimolacyclopeptide B [30].

A. reticulata L.

Ethyl acetate, butanol and methanol extract showed the presence of phytochemical components such as alkaloids, tannins, terpenoids, and coumarins [31]. From the leaves contains an alkaloid, tetrahydroisoquinoline which possesses cardiotoxic activity and from the bark, a bioactive acetogenin has been isolated. *A. reticulata* contains aporphine, alkaloids, terpine derivatives, glycoside and a novel diazepam, squamolone [32]. Ethyl acetate extracts of seeds contains 7-lactone acetogenin, cis-/trans-isomurisolenin, along with six known cytotoxic acetogenins, annoreticuin, annoreticuin-9-one, cis-/trans-bullatacinone, bullatacin, cis-/trans-murisolinone, and squamocin [33] and annoreticuin, bullatacin, squamosine, rolliniastatin [34], reticullacinone, rolliniastatin-2, molvizarin [35], 14-hydroxy-25-deoxy-rollinacin [36]. In *A. reticulata*, by the method of bioactivity-directed fractionation, Bullatacin and a novel bioactive monoterahydrofuran acetogenin, reticulatacin, and kaurane diterpenes have been isolated from the bark [37]. From the methanol extracts of seeds, two cyclopeptides, the cycloheptapeptide cycloreticulic C, *cyclo*(Pro¹-Gly²-Gln³-Pro⁴-Pro⁵-Tyr⁶-Val⁷), and the cyclohexapeptide glabrin A, *cyclo*(Pro¹-Gly²-Leu³-Val⁴-Ile⁵-Tyr⁶) have been isolated and sequence and three-dimensional structure of cycloreticulins A and B, new cyclooctapeptides were also identified [33,34].

A. squamosa L.

A. squamosa possesses glycosides, alkaloids, flavonoids, steroids, phenols, tannins, and saponins in the ethanolic seed extracts. Various phytochemical constituents are isolated from leaves, stem and root were glaucine, norcorydine, aporphine, isocorydine, coryeline, and anonaine. From the leaves anonaine, borneol, camphor, benzyltetrahydroisoquinoline, car-3-ene, camphene, carvone, β -caryophyllene, farnesol, 16-hetriacontanone, geraniol, hexacontanol, higemamine, limonine, methylheptenone, p-(hydroxybenzyl)-6,7-(2-hydroxy,4-hydro) isoquinoline, eugenol, linaloolacetate, isocorydine, menthone, methylsalicylate, methyl anthranilate, n-octacosanol, b-pinene, stigmasterol, a-pinene, β -sitosterol, rutin, thymol 4-(2-nitroethyl-1)-1-6-((6-o- β -D-xylopyranosyl-1- β -D-glucopyranosyl)-oxy) benzene and n-triacontanol. Oil extracted from leaves contain germacrene D, b-elemene, sabinene, a and b-pinenes, bicyclogermacrene, T-cadinol, and T-muurolool are isolated. From fruit oil spathulenol, bornyl acetate, germacrene D, borneol and verbenone were isolated. From stem bark, a new acetogenin squamone were isolated which possess bullatacin, bullatacinone, liriodenine and (-) kaur-16-en-19-oic acid. From the bark 1H-cycloprop (e) azulene, bisabolene, germacrene D, bisabolene epoxide, kaur-16-ene and caryophyllene oxide were isolated. From the branches liriodenine, moupinamide, anonaine and sachanolic acid

were isolated. Chloroform extract of the plant possesses Annotemoyin. Annonacin A, annonastatin, saponins like stigma-5,24 (28)-dien-3b-ol-a-L-rhamnoside, squamostatin A, annonin I, VI, VIII, XIV and XVI. Nearly 30 acetogenins were isolated like squamocins B to N, coumarinoligans, annotemoyin and squamocin, annonastatin, squamocin etc from the seeds. From the roots alkaloids such as liriodenine, oxoanabolone and β caryophyllene, α -humulene, α pinene, α -gurjunene were isolated [38]. Alkaloids, fixed oils, tannins, carbohydrates, and phenols also present in *A. squamosa* [39].

A. senegalensis L.

A. senegalensis contains the phytochemicals constituents such as sterols and/or triterpenes, anthocyanes, glucids, coumarins, flavonoids, and alkaloids. From the water and ethanol extract of leaves and roots contains flavonoid, tannis, cardiac glycoside, saponins, alkaloid, steroid, and volatile oils, and negative for saponins, glycoside and antraquinone. The ethanol extract of leaves and root has higher phytochemical activity than compared to the aqueous extract [40]. *A. senegalensis* found to contain minerals such as Ca, K, Mg, Zn, Fe, Cu, Mn, Pb, and Cr as well as ascorbic acid and amino acids, important source of nutrients [41,42]. Stem bark contains 1, 2 benzenediol, butylated hydroxytoluene, phenol, 2, 6 bis (1, 1-dimethylethyl-4methyl, methylcarbamate, n hexadecanoic acid, hexadecane, 13-hexyloxacyclotridec-10-en-2-one, oleic acid, tetracosane, 9-octylheptadecane, heneicosane, 12-methyl-E, E-2, 13-octadecadien-1-ol, octadecanoic acid, 9, 17-octadecandienal, pentadecane, tetratriacontane, and squalene from the GC/MS study [43]. From the root bark, Okoye and coworkers [44] identified diterpenoid, kaur-16-en-19-oic acid or kaurenoic acid as phytochemical constituents responsible for the antibacterial effects. *A. senegalensis* possess wax, alkaloids [45] proteins, amino acids, antraquinones [46], sterols, glycosides, flavonols, terpenoids [47] and terpenes [48].

PHARMACOLOGICAL STUDIES

A. muricata L.

Several studies suggest that flavonoids and phenols are present in *A. muricata* are free radical scavengers that prevent oxidative cell damage and have strong anticancer activities [49,50]. Due to the presence of redox property and presence of conjugated ring structures and carboxylic group which inhibits lipid peroxidation [51]. The traditional uses such as anticancerous, antidiabetic, antibacterial, antifungal, antimutagenic, emetic, anticonvulsant, sedative, insecticidal, and urine stimulant. It also has antiviral (against Herpes simplex), cardiogenic, digestive stimulant, nerviness, febrifuge, vermifuge, pediculocidal, and analgesic properties. The extracts of this plant screened for antiparasitic, astringent, antileishmanial, antidepressant and cytotoxic activities. Aqueous extracts of leaves and seeds show high content of proteins, phenols, non-enzymatic components such as vitamin-C and vitamin-E, enzymatic components such as superoxide dismutase and catalase was having high antioxidant power. Aqueous extracts of *A. muricata* exhibit an antibacterial effect. Methanolic extracts of *A. muricata* shows potent antidiabetic activity by reducing serum total cholesterol, low-density lipoprotein (LDL) and very LDL and a significant increase in high-density lipoprotein and antiatherogenic index [52]. *A. muricata* leaf ethanol extract has hypoglycemic and hypolipidemic effects [53]. Tannins are useful in preventing cancer as well as treatment of inflamed or ulcerated tissues. Saponins can react with cholesterol-rich membranes of cancer cells; thereby inhibit their growth and viability [54].

A. cherimola L.

Many pharmacological activities and medicinal applications of *A. cherimola* are widely known. Various extracts like ethanolic, methanolic, and dimethyl formamide of *A. cherimola* fruits possess concentration dependent free radical scavenging activity. The antidiabetic activity of leaf extract in streptozotocin (STZ) induced hyperglycemia in rats. The leaf extract is responsible for stimulates the insulin release and observed restoration of blood glucose level. The antihyperglycemic activity of the methanolic extract of leaves was

comparable with glibenclamide, a standard hypoglycemic drug. The methanolic extract of leaves possesses considerable hypoglycemic activity in normal rats. The leaf extract shows antimicrobial activity against *Escherichia coli*. Volatile compound (cherimolacyclopeptide E) of this plant was studied for its antimicrobial activity. From the methanolic extracts of the leaves, a pure compound is isolated which exhibits antiviral activity against herpes simplex virus Type 2 viruses. The cytotoxic compounds such as anomolin and annocherimolin were isolated from the seeds, collected in Peru. Anomolin was selectively cytotoxic against the human prostate tumor cell line (PC-3), when compared with adriamycin. Annocherimolin possesses cytotoxic potencies when compared with adriamycin in the breast (MCF-7) and colon (HT-29) cancer cell lines. The effect of ethanolic extracts from leaf was studied on bovine kidney cells (Madin-Darby bovine kidney [MDBK]) and human larynx epidermoid carcinoma cells (Hep-2). The ethanolic extract from leaves possesses significant antitumor activity *in vitro* against MDBK and Hep-2 cells. Hexane extract of leaves produces antianxiety actions in mice. Methanolic extracted seeds were examined for antiparasitic activity against *Entamoeba histolytica*, *Nippostrongylus brasiliensis*, *Molinema dessetae*, and *Artemia salina*. The acetogenins isolated from the leaves which inhibit the larvae of *M. dessetae* [55].

A. reticulata L.

A. reticulata leaf extract shows high activities in quenching 1,1-diphenyl-2-picryl-hydrazil and superoxide radicals in plant [56]. Annonaceous acetogenins are a group of phytoconstituents obtained from plants, have potent antineoplastic agents. Acetogenins are efficient cytotoxic inhibitors of the mitochondrial nicotinamide adenine dinucleotide: Ubiquinone oxidoreductase (complex I of the respiratory chain). Seeds of *A. reticulata* contains squamocin which has cytotoxic constituent for mostly all the cancer cell lines tested [57,58]. In ethanol extracts, *in vitro* inhibition toward the *vero* cell line proliferation was found to be lower when compared with cancer cell lines [59]. *A. reticulata* leaves show *in vitro* cytotoxic and human recombinant caspase inhibitory effect [60]. Hence, *A. reticulata* has potent chemopreventive agent in cancer therapy. The aqueous leaf extract has anthelmintic activity [61]. Leaves of *A. reticulata* can be used in the treatment of inflammatory diseases, and potent new anti-inflammatory agents [62]. Leaves of *A. reticulata* possess potent glucose lowering effect. The glucose lowering activity is more of corrective in nature than disruptive [63]. By using roots, tea is prepared and used as a treatment for fevers and the bark is used as a powerful astringent for antidiarrheal and vermifuge [52].

A. squamosa L.

Terpenoids, flavonoids, alkaloids, and tannins possess more antioxidant activities that can be used in the treatment of many diseases, including cancer and possess potent antitumor properties [64]. *A. squamosa* Linn. is used as an antioxidant, antidiabetic, hepatoprotective, cytotoxic activity, gene toxicity, antitumor activity, antilice agent. *A. squamosa* leaves found to lower considerable fasting plasma glucose level in STZ nicotinamide induced Type 2 diabetic rats in the aqueous extract [65]. *A. squamosa* contains flavonoids which are responsible for antibacterial activity against bacterial strains [66]. *A. squamosa* leaf analysed for blood glucose, hemoglobin, glycosylated hemoglobin, plasma insulin, antioxidant enzymes and lipid peroxidation in liver and kidney to STZ-induced diabetic rats. *A. squamosa* regulates the blood glucose level, increases the plasma insulin, lipid metabolism, and prevents diabetic problems from lipid peroxidation and antioxidant systems in experimental diabetic rats [61]. *A. squamosa* seeds possess antitumor activity *in vivo* against AD-5 tumor in the aqueous extracts [67]. *A. squamosa* extracts have the property of induction of apoptosis for certain types of cancerous cells [68]. *A. squamosa* bark extracts have anticarcinogenic effect by modulating the status of lipid peroxidation and antioxidants in 7,12-dimethylbenz[a]anthracene painted hamsters [69]. *A. squamosa* has hepatoprotective activity and could be an effective remedial for chemical-induced hepatic damage [70]. *Annona* species are potent antimosquito agents [71]. The pure compound annotemoyin-1 isolated from chloroform extract of the seeds of *A. squamosa* Linn. was tested for its pesticidal activity [72]. In mouse

Table 2: Pharmacological activities of *Annona species* - *Annona muricata*, *Annona cherimola*, *Annona reticulata*, *Annona squamosa*, and *Annona senegalensis*

Name of the plant	Pharmacological Activities
<i>Annona muricata</i>	Cytotoxicity and antileishmanial activity, antihyperglycemic activity, diabetes and β -cell integrity, hepatoprotective activity, antinociceptive and anti-inflammatory activities, anticancer, antihyper simplex virus, antidepressant, antihyperlipidemia, antimicrobial, antioxidant activity, antihypertensive
<i>Annona cherimola</i> <i>Annona reticulata</i>	Antioxidant activity, antidiabetic activity, antimicrobial activity, antitumor activity, antianxiety activity Antipyretic activity, anthelmintic activity, antiulcer activity, antinociceptive activity, antinociceptive activity, analgesic and anti-inflammatory, antiproliferative activity, antioxidant and antimicrobial activity
<i>Annona squamosa</i>	Regulation of hyperthyroidism and lipid peroxidation, analgesic and anti-inflammatory activity, antibacterial and cytotoxic activity, antioxidant and antilipidemic activity, antiulcer activity, hypoglycemic and antidiabetic activity, molluscicidal properties, genotoxic effect, vasorelaxant activity, antitumor activity, hepatoprotective activity, larvicidal activity, insecticidal activity, anthelmintic activity
<i>Annona senegalensis</i>	Antimicrobial activity, antioxidant activity, anti-inflammatory activity, antimalarial activity, <i>in vivo</i> trypanocidal activity, anti-snake venom activity, antinociceptive activity, anthelmintic activity

model, the methanolic extract of seeds of *A. squamosa* Linn. shows proliferative effect in regulating hyperthyroidism [73]. *A. squamosa* leaves shows antiparasitoid activity, while stem bark shows moderate activity in the methanolic extract [74]. *A. squamosa* Linn. shows abortifacient activities in the seed extract [75]. *A. squamosa* seeds extract shows anthelmintic activity [76]. The bark and leaves possess cytotoxicity, analgesic, anti-inflammatory and antiulcer activities [52].

***A. senegalensis* L.**

The *in vitro* cytotoxicity activity of methanol extract of leaves was performed with A2780 ovarian cancer cells. *A. senegalensis* showed low cytotoxicity with an inhibitory concentration 50% of 28.8 $\mu\text{g/ml}$. Kaurenic acid from root bark possesses antiproliferative effect against HeLa and PANC-1 cell lines. *A. senegalensis* had potent antibacterial activity against *Staphylococcus aureus* (62.5 $\mu\text{g/ml}$) and *Candida albicans* (250 $\mu\text{g/ml}$). *A. senegalensis* shows activity against chloroquine resistant strain of *Plasmodium falciparum* in the root extract. *A. senegalensis* neutralized lethal toxicity induced by *Echis ocellatus* venom in the methanol leaf extracts. Flavonoids and tannins are the key phytochemicals mediated the activity. Extracts of the root bark induces the central nervous system depressant effect of phenobarbitone in a dose-dependent fashion. *A. senegalensis* from Burkina Faso has much better antioxidant activity compared to that from Togo in the leaf extract. This may be due to higher polyphenolic flavonoids in those from Burkina Faso. *In vitro* hemostatic tests on hydroalcoholic extracts of the leaves, an aporphine alkaloid, (-)-roemerine was identified as active principle responsible for the insecticidal activity. Anticoagulant properties which have 39% reduction of plasma recalcification time [55]. Table 2 shows the pharmacological activities of *Annona* species.

CONCLUSION

The family *Annonaceae* has several pharmacological activities such as antiasthmatic, antidiabetic, anti-inflammatory, antioxidant, antimicrobial, anxiolytic, hypoglycemic activity antiarrhythmic, adaptogenic, anthelmintic, antiestrogenic, antimalarial, antiproliferative, antipsoriatic, larvicidal, muscle contractile, hepatoprotective, and anticonvulsant activity. Hexane, ethyl acetate and methanol extracts of *Annonaceae* family (*A. muricata*, *Annona cherimola*, *A. reticulata*, *A. squamosa*, and *A. senegalensis*) contain phytochemical constituents such as sterols, triterpenes, alkaloids, glycosides, saponins, flavonoids, phenolics, and tannins are present. In this review article, effort has been taken to collect and compile the details regarding five species of *Annona* family which will be useful to the society to venture into a field of alternative systems of medicine.

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