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Annona senegalensis Persoon (Annonaceae): A review of its ethnomedicinal uses, biological activities and phytocompounds

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Abstract
Annona senegalensis, also known as wild custard apple and wild soursop is a member of Annonaceae family. It is a fruit tree native to Senegal and found in semi-arid to subhumid regions of Africa, with a long history of traditional use. Numerous ethnomedicinal uses have been attributed to different parts of *A. senegalensis*, as well as its use as food and food additives. All parts of the plant contain varying amounts of essential oils. Annogalene, annosenegalin, acetogenins, kaurenoic acid and (-)-roemerine are the major bioactive constituents of *A. senegalensis*. Biological activities of phytoconstituents from various parts of *A. senegalensis* include anticonvulsant, cytotoxic, antimicrobial, antispasmodic, anti-inflammatory and analgesic activities; others are antioxidant, antivenomous, hypnotic, anthelmintic, antiplasmodial, haemostatic, spermatogenic and insecticidal activities.

Keywords: *Annona senegalensis*; Annonaceae; ethnomedicine; biological activity; acetogenins

1. Introduction
Natural products, especially those derived from plants, have been used to help mankind sustain its health since the dawn of medicine. Over the past century, the phytochemicals in plants have been a pivotal pipeline for pharmaceutical discovery. The importance of the active ingredients of plants in agriculture and medicine has stimulated significant scientific interest in the biological activities of these substances [1]. One such plant with abundance of phytochemicals is *Annona senegalensis* Persoon (Annonaceae). This review therefore seeks to describe the morphology and ecology of the plant, its ethnomedicinal uses, biological activities and phytoconstituents, especially the acetogenins.
Annona senegalensis, commonly known as Wild Custard Apple and Wild Soursop is a shrub or small tree 2-6 m tall but may reach 11 m under favourable conditions. The bark is smooth to roughish, silver grey or grey-brown. Leaves are alternate, simple, oblong, ovate or elliptic, green to bluish green, almost without hairs on upper surface but often with brownish hairs on the lower surface. Flowers are up to 3 cm in diameter on stalks 2 cm long, solitary or in groups of 2-4, arising above the leaf axils. The fruits are formed from many fused carpels, fleshy, lumpy, egg shaped, 2.5-5 by 2.5-4 cm, ovoid or globose, unripe fruit green, turning yellow to orange on ripening (Fig. 1). Wild fruit trees of this species are found in semi-arid to sub-humid regions of Africa. The species occur along river banks, fallow land, swamp, forests and at the coast. It commonly grows as a single plant in the understorey of savannah woodlands [2].
It is found growing throughout Nigeria. It is very common in Northern Nigeria, primarily in Nasarawa, Kaduna, Kano, Plateau, and Niger States and in the Federal Capital Territory, Abuja and usually known as Gwándàn dààjìì (Hausa) or dukuu-hi (Fulani) [3].

2. Ethnomedicinal Uses
All parts of *A. senegalensis* plant have been found useful for traditional medicine applications. The leaves have been used in treating yellow fever, tuberculosis, and small pox [4, 6]. The stem bark has been used in snakebite and hernia treatment [7]. The root is used in conditions such as difficulty in swallowing, gastritis, snake bites, male sexual impotence, erectile dysfunction, tuberculosis, and as antidote for necrotizing toxins; the root bark is effective in infectious diseases [5, 8, 12]. Juice from the tree is used in the treatment of chicken pox [13]. Many of the plant parts are used as antidotes for venomous bites and in the management of diabetes [14, 15].
In Guinea, *A. senegalensis* has been employed in the treatment of malaria [16]. In Swaziland, the bark is used to treat open sores [17].

Among the Igede people of Benue State in North Central Nigeria, the plant is used in combination with *Ageratum conyzoides* for diarrhoea and in combination with *Nauclea latifolia* for dysentery [18].

Use of *A. senegalensis* for pest control in Nigeria and Tanzania has also been documented [18, 19]. In the Republic of Benin, the fresh leaves are spread in poultry houses and left until they are dried. This is repeated once or twice a week for the control of parasites such as fleas and lice [20].

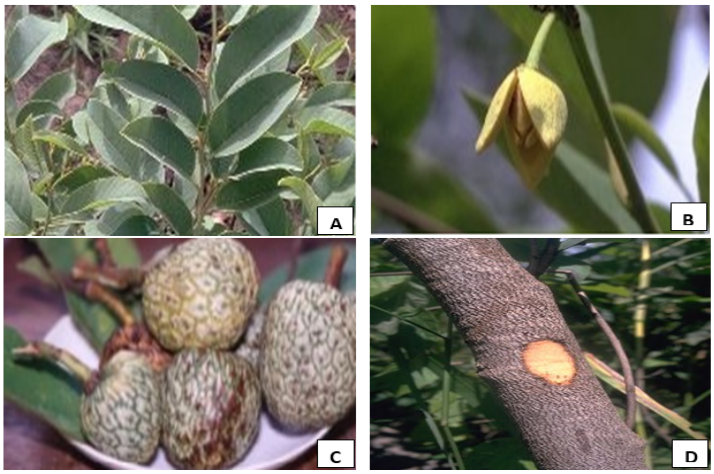


Fig 1: *Annona senegalensis* Pers.; (A) leaves (B) flower (C) fruits and (D) stem. Source: World Agroforestry Database

Table 1: Ethnomedicinal Uses of *Annona senegalensis* Pers. (Annonaceae)

Location	Local Name	Plant Part	Form	Conditions Treated	Ref.
Nigeria	Abo/Abobo (Yoruba) Ubunu-ocha (Igbo) Gwandar-daji (Hausa)	Leaf	-	Yellow fever	[4]
Nigeria	Ukopko (Idoma)	Leaf, Root	Decoction	Tuberculosis	[5]
Nigeria	Gwandan daaji (Hausa) Dukuu-hi (Fulani)	Leaf	Infusion	Small pox	[6]
Nigeria	Gwandar daji (H)	Stem	-	Snake bites, Hernia	[7]
Cameroon	Doukkouhi ladde (Fulfulde)	Root	Infusion	Necrotizing Venoms	[8]
Nigeria	Gwandan daji (Hausa)	Root	Infusion	Erectile Dysfunction	[9]
Nigeria	Gwandan daaju (Hausa) Dukuu-hi (Fulani)	Root	Infusion	Difficulty in swallowing	[10]
Guinea	Sunsuningbe	Root bark	Decoction	Infectious diseases	[11]
Cameroon	Doukouhi	Root	Decoction	Gastritis, Snake bites, Male Sexual Impotence	[12]
Nigeria	Gwandan daji (Hausa)	Tree	Juice	Chicken pox	[13]
Republic of Congo	Moulolo (Kongo) Nlolo (Laadi) Ololo (Mbochi) Tchilolo (Vili)	Leaf, Seed, Bark	Decoction	Diabetes	[14]
Nigeria	Ahur/Anyam hul (Tiv)	Various	Various	Venomous bites	[15]

In addition to ethno medicinal uses, *A. senegalensis* is also used as food and food additives. The leaves are sometimes used as vegetables, while the edible pulp of the ripe fruit has a pleasant pineapple-like taste. Flowers serve as a spice for various meals [2].

3. Phytochemistry

Phytochemical screening revealed the presence of various secondary metabolites including tannins [21], flavonoid [22], saponins [23], alkaloids [24], glycosides, steroids [25], volatile oil [26] and anthocyanins [27]. *A. senegalensis* has also been found to contain various minerals such as Ca, K, Mg, Zn, Fe, Cu, Mn, Pb, Cr as well as ascorbic acid and amino acids, making it an important source of nutrients [28, 29].

3.1 Essential oils

GC and GC–MS analyses showed p-cymene (36.0%), α-phellandrene (25.0%), α-pinene (8.3%), Z-sabinol (6.9%) and limonene (4.8%) as the major constituents of the essential oil of *A. senegalensis* stem bark [30]. In another study, leaf essential oil of *A. senegalensis* had oxygenated monoterpenes (65.0%) as the major constituents along with citronellal (30.0%), citronellol (14.8%), geranial (17.2%), thymol (8.1%), β–caryophyllene (7.8%) and carvacrol (6.92%) [36]. The essential oil, obtained by steam distillation of air dried leaves of *A. senegalensis* growing in Burkina Faso was analyzed by GC and GCMS, the oil was found to contain germacrene D (19.2%), β-caryophyllene (19.1%), γ-cadinene (11.1%) and α-humulene (9.7%) as major components [37].

In Brazzaville (Congo), essential oils were found in all parts of *A. senegalensis* including leaves, stem bark, root bark, epicarp and mesocarp [38]. In Nigeria, nineteen monoterpenes and sesquiterpenes were identified in the essential oils of the leaves and fruits of *A. senegalensis*. The major constituents were car-3-ene in the fruit oil and linalool in the leaf volatile oil [42].

3.2 Acetogenins

Annonaceous acetogenins are waxy substances consisting of C_{32} or C_{34} long chain fatty acids which have been combined with a propan-2-ol unit at C-2 to form a gama-lactone. They are only found in several genera of the plant family Annonaceae [39]. Two cytotoxic monotetrahydrofuran acetogenins, namely annogalene and annosenegalin (Fig. 2a) have been isolated from the cytotoxic methanolic extract of *A. senegalensis* and *A. cherimolia* seeds. Their structures were established on the basis of 1D and 2D NMR spectroscopic techniques [43].

3.3 Alkaloids

Identification of alkaloids from *A. senegalensis* leaves had been reported. These included (-)-roemerine (Fig. 2c), an aporphine alkaloid and (-)-isocorydine [24].

Table 2: Chemical compounds isolated from *Annona senegalensis.*

Plant part	Compound	Class	Biological Activity	Ref.
Leaf, stem	Limonene	Terpene	-	[30]
Stem bark	*p*-cymene	Terpene	-	[30]
Stem bark	Z-sabinol	Terpenoid	-	[30]
Stem bark, Fruit	α-phellandrene	Terpene	Antimicrobial	[30, 31]
Leaf, Seed, Stem bark, Fruit	α-pinene	Terpene	Antimicrobial	[30, 31, 36]
Leaf, Seed, Fruit, Root bark	Mycrene	Terpene	Antimicrobial	[31, 32, 36]
Leaf, Fruit	Sabinene	Terpene	-	[32]
Leaf	(-)-Roemerine	Alkaloid	Reverses Multidrug- Resistance Phenotype with Cultured Cells	[33]
Root bark	Kaurenoic acid	Terpenoid	Anticonvulsant, Antibacterial, Cytotoxic, Antiproliferative	[34, 35, 40]
Leaf, Seed	β–pinene	Terpene	-	[36]
Leaf	Linalool	Terpenoid	-	[36]
Leaf	Citronellal	Terpenoid	-	[36]
Leaf	Citronellol	Terpenoid	-	[36]
Leaf	Linalyl acetate	Terpenoid	-	[36]
Leaf	Geranial	Terpenoid	-	[36]
Leaf	Thymol	Aromatic	-	[36]
Leaf	Carvacrol	Aromatic	-	[36]
Leaf	β–caryophyllene	Terpene	-	[36, 37]
Leaf, Seed, stem, root bark	γ-cadinene	Terpene	-	[37, 38]
Leaf, seed, fruit, stem, root bark	α-humulene	Terpene	-	[37, 38]
Leaf, seed, fruit, root bark	Germacrene D	Terpene	-	[37, 38]
Seed	Camphene	Terpene	-	[38]
Seed	Sabinene	Terpene	-	[38]
Seed	α-phellandrene	Terpene	-	[38]
Seed	δ -3-carene	Terpene	-	[38]
Leaf, seed	p-cymene	Terpene	-	[38]
Seed, root bark	β-phellandrene	Terpene	-	[38]
Leaf, seed, fruit	1,8 cineole	Terpenoid	-	[38]
Fruit	Linalool	Terpenoid	-	[38]
Fruit	Terpinen-4-ol	Terpenoid	-	[38]
Fruit	α-terpineol	Terpenoid	-	[38]
Seed	Bornyl acetate	Terpenoid	-	[38]
Leaf, seed, fruit, stem, root bark	α-copaene	Terpene	-	[38]
Seed, fruit, stem, root bark	β -hydroxy-16-Kaurene	Terpenoid	-	[38]
Leaf, seed, fruit, stem, root bark	E-β-caryophyllene	Terpene	-	[38]
Seed, stem, root bark	Kauren-16-ol	Terpenoid	-	[38]
Leaf, seed, fruit, stem, root bark	β-selinene	Terpene	-	[38]
Leaf, stem, root bark	α-selinene	Terpene	-	[38]
Leaf, seed, fruit, root bark	Germacrene A	Terpene	-	[38]
Leaf, seed, fruit, stem, root bark	β-eudesmol	Terpenoid	-	[38]
Leaf, fruit, stem, root bark	δ-cadinene	Terpene	-	[38]
Leaf, seed, fruit, stem, root bark	γ- eudesmol	Terpenoid	-	[38]
Seed, Root bark	Germacrene B	Terpene	-	[38]
Leaf, seed, fruit, stem, root bark	Elemol	Terpenoid	-	[38]
Root	Gigantetronenine	Acetogenin	-	[39]
Leaf	Caryophyllene oxide	Terpenoid	Cytotoxic against Brine shrimp	[41]
Fruit	Car-3-ene	Terpenoid	-	[42]
Seed	Annosenegalin	Acetogenin	Cytotoxic	[43]
Seed	Annogalene	Acetogenin	Cytotoxic	[43]
Root	Squamocine	Acetogenin	Anthelmintic against *Rhabditis pseudoelongata*	[44]
Root	Glaucanisine	Acetogenin	-	[44]
Root	Glaucanetine	Acetogenin	-	[44]
Root	Goniothalamicine	Acetogenin	-	[44]
Root	Liriodenine	Alkaloid	-	[44]
Root	Norolivéroline	Alkaloid	-	[44]

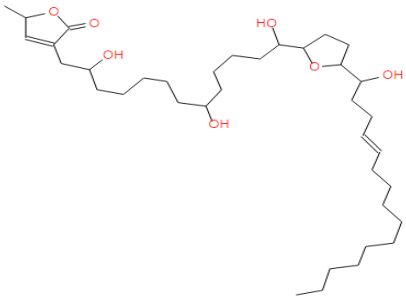
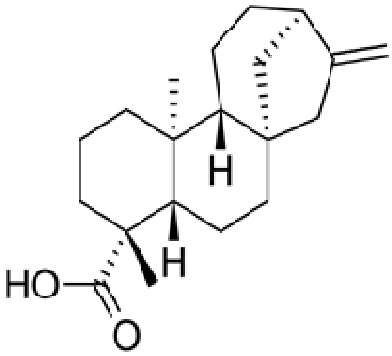
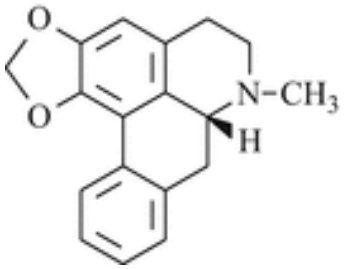


Fig 2: (a) Structure of annogalene. Annosenegalin is 20-epimer, 23, 24-dihydro-annogalene



(b) Structure of Kaurenoic acid



(c) Structure of (-)-Roemerine

4. Biological Activities

4.1 Anticonvulsant Activity

Several studies have proven the anticonvulsant effect of *A. senegalensis* (Table 3). The plant is claimed in traditional medicine in Burkina Faso to be useful in the treatment of epilepsy. In a bid to validate these claims, Konate *et al.* [45], studied the effect of aqueous extract on pilocarpine and picrotoxin induced seizures in mice and rats. Results showed that the plant extract 100 mg/kg and 150 mg/kg i.p had significant (p<0.05) curative effects on the convulsions induced by pilocarpine and at 50 mg/kg i.p had significant (p<0.001) preventive treatment effects on the convulsions induced by pilocarpine. Bioactivity-guided fractionation of the methanol-methylene chloride root bark extract of *A. senegalensis* using pentylenetetrazole (PTZ) induced seizures in mice resulted in the characterization of kaur-16-en-19-oic acid (KA), a diterpenoid. KA dose-dependently delayed onset of myoclonic spasms and tonic-clonic phases of PTZ-induced seizures and maximal electroshock seizures [21].

Table 3: Anticonvulsant activity of *A. senegalensis*

Plant part	Test	Result	Ref.
Aqueous extract of root bark	Pilocarpine-Induced Seizures in mice Picrotoxin-Induced Seizures in mice	Curative and preventive effects Protective effects	[45]
Methanol/Ethylacetate extract of twigs/leaves	Pentylenetetrazole-induced convulsion in mice.	Delayed seizure onset; reduction in seizure duration; delayed time of death	[46]
Methanol extract of leaves	Pentylenetetrazole-induced convulsion in mice.	non-dose-related inhibition of PTZ-induced seizures: increased seizure latency, prolonged duration of seizure and increased survival time	[47]
Methanol extract of root bark	Pentylenetetrazole-induced convulsion in albino mice.	Prolonged onset of tonic and clonic phases of seizure	[48]

4.2 Cytotoxic Activity

The *in vitro* cytotoxicity evaluation of methanol extract of the leaves was performed using A2780 ovarian cancer cells. *A. senegalensis* exhibited low cytotoxicity with an IC_{50} of 28.8µg/ml [49]. Similarly, the seeds have been tested against KB and VERO cell lines and bioassay-guided fractionation of seed extracts suggested that acetogenins were responsible for this activity [50]. These have been identified as annosenegalin and annogalene in another study [43]. Recently, kaurenoic acid (Fig. 2 (b)) from the root bark possessed antiproliferative effect against HeLa and PANC-1 cell lines [40]. Various fractions of the leaf extracts have showed mild to moderate cytotoxicity in different brine shrimp lethality bioassays [41, 51, 52].

4.3 Antimicrobial Activity

In a study of methanol-methylene chloride extract of the root bark of *A. senegalensis*, the ethyl acetate fraction on further fractionation gave two active subfractions, a lipophilic oily and another fraction (AS2) which on purification precipitated white crystalline compound, later characterized to be kaurenoic acid. MICs of the ethyl acetate fraction, the lipophilic oily fraction and kaurenoic acid against *Bacillus subtilis* were 180, 60, and 30µg/ml respectively. AS2 exhibited activity against *Staphylococcus aureus* with an MIC of 150µg/ml, while the lipophilic oily fraction was active against *Pseudomonas aeruginosa* with an MIC of 40µg/ml. However, the extract and kaurenoic acid exhibited no effects against *Candida albicans* and *Aspergillus niger* [22]. Ethanol extract of the plant had *in vitro* antimicrobial activity against some oral pathogens [55]. An extract of recipe containing six plants including *A. senegalensis* had significant antibacterial activity with (MIC) of 62.5µg/ml against *S. aureus* and 250µg/ml against *C. albicans* [4].

Table 4: Antimicrobial Activities of *A. senegalensis*

Plant part	Test	Result	Ref.
Methanol extract of Plant	*in vitro* activity against attenuated strains of *Mycobacterium bovis* (BCG).	MIC at 1250 µg/ml	[54]
Crude Tannins Isolated from the Leaf	Antibacterial activities against tested bacteria	(MIC) gave 6.25 mg/ml on *Shigella dysenteriae* and 12.5 mg/ml on both *Escherichia coli* and *Salmonella typhi*.	[21]
Crude Flavonoids Isolated from Stem Bark	Antibacterial activities against tested bacteria	(MIC) against *Shigella* specie and *Escherichia coli* at 100 mg/ml while against *Salmonella typhi* at 50 mg/ml	[22]
Crude extract of root bark	Antibacterial activities against tested bacteria	MIC of methanol extract at 62.5 mcg/ml against *S. aureus*; No activity against *E. coli* and *P. aeruginosa*	[56]
Crude Extract from Stem Bark	Antibacterial activities against clinical isolates of bacteria	(MIC) of the methanol extract: 0.39mg/ml on *E. coli*, 3.17 mg/ml on *S. enteriditis* 25.00 mg/ml on *S. dysenteriae*.	[53]

4.4 Antiplasmodial Activity

The *in vivo* animal antimalarial activity of the methanol extract of *A. senegalensis* in mice was investigated. The extract at 100 mg/kg weight of mice gave 57.1% suppression of parasitaemia. At doses of 800 mg/kg weight of mice, it induced the highest chemosuppression of parasitaemia (91.1%) compared to chloroquine, which had a chemosuppression of 96.2%. The roots extract of *A. senegalensis* showed activity against the chloroquinoresistant strain of *Plasmodim falciparum* [57].

4.5 Antivenomous Activity

The potency of the methanol extract of the root bark of A. *senegalensis* was tested against cobra (*Naja nigricotlis nigricotlis* Wetch venom in rats. The extract caused reduction in the induced hyperthermia and directly detoxified the snake venom used by 16–33%. It, however, failed to restore the biochemical functions (serum glutamate-oxalate-transminase (sGOT) and serum-pyruvate-transaminase (sGPT)) of the liver [58]. In another study, a fraction of A. *senegalensis* leaf methanol extract neutralized lethal toxicity induced by *Echis ocellatus* venom. The key phytochemicals mediating the activity of this fraction were flavonoids and tannins [59].

4.6 Spermatogenic Activity

Oladele *et al*. [60], tested the aqueous leaf extract of *A. senegalensis* at different doses of 200, 300, and 500mg/kg body weight for its spermatogenic effect. Results showed the weight of the testes and epididymis increased significantly for the 300 and 500 mg/kg doses. The sperm concentration for the 200, 300 and 500 mg/kg doses also significantly increased and the sperm motility at 300 and 500 mg/kg also increased significantly. Decrease in abnormal sperm morphology was not significant for any of the doses. However, another study revealed that aqueous leaf extract of *A. senegalensis* may possess the potential to adversely affect testicular function in rat [61].

4.7 Anti-Inflammatory and Analgesic Activities

In a bid to provide a scientific validation of the use of *A. senegalensis* against asthma and cough in the Ivorian Pharmacopoeia, Yeo *et al*. [62], evaluated the anti-inflammatory effect of the ethanol extract of the leaf. It was observed that the extract induced a significant decrease in the number of inflammatory cells. Suleiman *et al*. [63], studied the analgesic and anti-inflammatory properties of the methanol stem bark of *A. senegalensis*. The extract at 100, 400 and 1000 mg/kg orally, produced significant (p<0.05) dose dependent reduction in writhes induced by acetic acid, increased nociceptive reaction latency in hot plate test, caused significant (p<0.05) dose and time dependent decrease in the size of the paw oedema caused by egg albumin; and caused significant (p<0.05) inhibition of permeability of blue dye into the peritoneal cavity of mice induced by acetic acid. These results were comparable to those of standard drugs pentazocine and piroxicam.

4.8 Hypnotic Activity

Effect of extract and fractions of *A. senegalensis* leaves on pentobarbitone-induced sleeping time was assessed. The extract and fractions significantly (p<0.05) shortened the sleep onset time (sleep latency) and prolonged sleeping time in a dose-related manner. A bioactive fraction significantly (P<0.05) prolonged sleep time but increased sleep latency in a dose-related manner [47]. Extracts of the root bark also potentiated the central nervous system depressant effect of phenobarbitone in a dose dependent fashion [64].

4.9 Antioxidant Activity

In a study designed to investigate the antioxidant and drug detoxification potential of *A. senegalensis* leaf, aqueous extract of A. *senegalensis* leaf scavenged free radicals *in vitro* and reversed CCl_4-induced hepatocellular damage in rats [65]. Extract from the leaf of *A. senegalensis* from Burkina Faso had an improved antioxidant activity compared to that from Togo. This may be due to higher polyphenolic flavonoids in those from Burkina Faso [66].

4.10 Anthelmintic Activity

Ethanol leaf extract of *A. senegalensis* was assessed for egg-inhibition ability as well as toxicity against the infective larval stage of *Haemonchus contortus*. The extract at 0.8%w/v caused a 98.33% mortality of the larva but had no effects on egg hatching [67]. In another study however, where whole ground plant material was used, the extract of *A. senegalensis* showed significant (P<0.001) reduction in egg hatch at a concentration of 7.1 mg/ml. [68]. The root of *Annona senegalensis* showed anthelminthic activity. Five acetogenins namely gigantetronenine, squamocine, glaucanisine, glaucanetine, goniothalamicine and two alkaloids liriodenine and norolivéroline were isolated and characterized. Squamocine was more potent than levamisole, the reference substance [44].

4.11 Antitrypanosomal Activity

As shown in Table 5, several studies have proven that *A. senegalensis* has potent *in vivo* trypanocidal effects, with little or no *in vitro* effects [69-74]. Further investigations have shown that these activities are due to isolated acetogenins from extracts of the seeds [50]. Acetogenins probably responsible for this activity are annogalene, annonacin, annonacin A, annosenegalin and senegalene [75].

Table 5: Antitrypanosomal Activities of *A. senegalensis*

Plant part	Test	Result	Ref.
Various Parts	*Trypanosoma brucei brucei* infection in mice.	Crude and partially purified aqueous extracts of the leaves, at a dose of 200 mg/kg had curative effects	[69]
Maceration and Decoction of dry leaves	*Trypanosoma brucei gambiense* infection in mice.	No trypanocidal or trypanostatic effects	[70]
Extracts of stem bark and roots	*in vitro* trypanocidal activity against *Trypanosoma brucei*	Cessation of motility observed with pet ether and chloroform extracts	[71]
Extract of stem bark	*Trypanosoma brucei brucei* infection in mice.	Hexane extract, at a dose of 400 mg/kg and aqueous extract at a dose of 300 mg/kg, had curative effects	[72]
aqueous extracts of root	*Trypanosoma brucei brucei* infection in mice.	Curative effects at doses of 27.8 mg/kg and 9.5 mg/kg p.o and IM respectively. No trypanostatic effects	[73]
Methanol extract of roots	*in vitro* trypanocidal activity against *Trypanosoma brucei brucei* and *Trypanosoma congolense*	No *in vitro* effects against *T. brucei brucei* Slight reduction in motility of *T. congolense*	[74]

4.12 Insecticidal Activity

Several studies have shown insecticidal properties of *A. senegalensis* (Table 6). An aporphine alkaloid, (-)-roemerine was identified as active principle responsible for the insecticidal activity [51].

Table 6: Insecticidal Properties of *A. senegalensis*

Plant part	Test	Result	Ref.
Essential oils of leaves	Toxicity to *Sitophilus zeamais*	Dose of 2.5 x 10-2 ml/ml, oviposition of *S. zeamais* was reduced LD 25 at, oviposition of *S. zeama*	[26]
Ethanol extracts from Leaves	Larvicidal property against late 3rd instar (is this the right word, instar) of *Culex quinquefascintus*	LC50 value for crude extract was observed to be 23.42 µg/ml. ethyl acetate fractions had mortality of 90% at 50 µg/mL	[51]
Methanolic extract from leaves	Larvicidal activity against *Aedes aegypti*	LC50 value was observed to be 759.6 mg/L for crude extract and 379.3 and 595.2 mg/L for n-hexane and chloroform fractions respectively	[76]
Essential oils of leaves	Toxicity to *Sitophilus zeamais* Motsch, *Sitophilus oryzae* L., *Callosobruchus maculatus* Fab and *Tribolium castaneum* Herbst.	LD 50 at 220.71 ppm against *Sitophilus zeamais*; 159.07 ppm against *S. oryzae*; 206.0 ppm against *Callosobruchus maculates*; 433.89 ppm against *Tribolium castaneum*	[77]
Extracts of leaves	Activity against the seed-beetle *Caryedon serratus* OI.	Ethyl acetate fraction killed 100% of eggs at 0.1 g / ml, methanol fraction killed 33% of eggs at 0.01 g / ml, hexane fraction proved ineffective	[78]
Aqueous extract from leaves	larvicidal activity against *Anopheles gambiae*	LC50 value was observed to be 30.2 µg/ml	[79]

4.13 Haemostatic Activity

A. senegalensis is sold by herbalists in South Benin for treatment of bleeding. Dougnon *et al.* [80], in a bid to find scientific evidence for this use, performed *in vitro* haemostatic tests on hydro alcoholic extracts of the leaves. Results confirmed its anticoagulant properties, as indicated by a 39% reduction of plasma re-calcification time. *A. senegalensis* was also shown to have astringent property, so it could act on primary haemostasis through vasoconstriction.

5. Conclusion

Annona senegalensis possesses a broad spectrum of biological activities as evident from this review. The anticonvulsant, anticancer, antitrypanosomal and insecticidal activity have been most researched on. However, more work still need to be done, especially with regards to isolating active compounds and determining their mechanism of actions, biochemical and physiological effects. It is expected that this review would illuminate potential areas of research with respect to developing active pharmaceutical agents from *A. senegalensis* Pers.

Consent

It is not applicable.

Ethical Approval

It is not applicable.

Competing Interests

Authors have declared that no competing interests exist.

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