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Review Article

Annona senegalensis Pers (Annonaceae): exploring the underutilized potentials of an African medicinal plant

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This extensive study delves into the many facets of *Annona senegalensis*, a plant species that has been well-respected in traditional African medicine and is now gaining attention in modern pharmacology. The review takes a methodical look at four main areas: pharmacological characteristics, phytochemical profile, geographical distribution and ecological environment, and ethnomedical uses. The medicinal properties of *Annona senegalensis* have earned it a place of adoration in many African traditions. According to historical records, it was used to cure a wide variety of illnesses, including fevers, skin problems, gastrointestinal problems, and malaria. The tapestry of indigenous medicine and culture highlights the plant's centrality to traditional healing practices. The assessment emphasises the plant's widespread presence throughout many African biomes, demonstrating its capacity to adapt to different ecological circumstances, in terms of dispersion. This review also examines the environmental conditions important for its growth, providing a better knowledge of its ecological niche and possible vulnerabilities in the face of environmental changes. The phytochemical examination of *A. senegalensis* reveals a broad array of bioactive chemicals, including but not limited to alkaloids, flavonoids, saponins, and terpenes. These elements are painstakingly connected with their unique therapeutic potentials, revealing insights into the metabolic underpinnings of the plant's medicinal characteristics. Finally, the review synthesizes a range of pharmacological research that evaluate the effectiveness of *A. senegalensis* in diverse medicinal applications. Notable results include its antibacterial, anti-inflammatory, antiparasitic, and anticancer effects, which are critically studied in light of modern scientific methodology and therapeutic significance. This review not only articulates the historic and contemporary relevance of the plant but also acts as a springboard for future research initiatives. It underlines the need for greater study into its latent potential, notably in drug discovery and development, while also increasing awareness about the protection of this unique species in its native environment.

Keywords: *Annona senegalensis, ethnomedicine, phytochemistry, pharmacological activities, toxicity*

Introduction

Annona senegalensis, also known as African custard apple, has gained substantial attention in the domains of ethnobotany and pharmacology due to its broad traditional uses and possible medicinal implications. Indigenous to several African countries, this species has been crucial to traditional medicine systems, addressing a range of health conditions from malaria to gastrointestinal illnesses (Mustapha, 2013; Moghadamtousi,, et al., 2015; Adjakpa,, et al., 2016; Okhale,, et al., 2016; Lawal, et al.,2021). Despite its ubiquitous usage in traditional contexts, the scientific world has only lately begun to untangle the complex phytochemical profile and pharmacological potentials of *A. senegalensis* (Philipov,, et al., 1995; Khallouki,, et al., 2002; Ijaiya, et al., 2014) The plant displays a rich array of bioactive chemicals, including alkaloids, flavonoids, saponins, and terpenes, which contribute to its therapeutic benefits (Mackie & Misra, 1956; Mackie & Ghatee, 1958; Bamba et el., 1984;You, et al., 1995; Yisa et al., 2010; Djoza et al., 2017). This rich phytochemical makeup has prompted interest in its potential for drug development, particularly in areas where traditional medicine is seeking innovative therapeutic agents.

However, the increased attention and exploitation of *A. senegalensis* have also highlighted concerns over its conservation and sustainable use. The rising demand, coupled with habitat loss and environmental changes, poses a danger to its availability and ecological stability (Orwa et al., 2009;). Furthermore, the absence of extensive scientific investigations on its pharmacological actions and safety profile creates a substantial vacuum in the literature, preventing its incorporation into current medical procedures. Given this backdrop, the present review seeks to give a complete evaluation of the ethnomedical usage, geographical distribution, phytochemical composition, and pharmacological properties of *A. senegalensis*. By synthesizing existing knowledge and identifying areas for future research, this paper seeks to contribute to the understanding of this species' potential in both traditional and modern medical contexts, while also emphasizing the need for its conservation and sustainable use.

Distribution and habitat of *Annona senegalensis*

Annona senegalensis, is a botanical gem tucked amid the various landscapes of Africa. This plant, belonging to the Annonaceae family, has acquired importance in ethnobotanical and ecological research owing to its rich ethnomedicinal history and ecological value. Understanding its range and habitat is crucial not just for conserving its cultural relevance but also for establishing sustainable conservation methods and investigating its latent potential in contemporary medicines. The geographical distribution of *A. senegalensis* spreads across a vast length of Africa, comprising a patchwork of nations and biological zones (Orwa et al., 2009). It finds its home in the tropical and subtropical zones of the continent, occupying territories from West Africa, including nations like Nigeria and Senegal, to the East African highlands and as far south as South Africa (Dalziel, 1937; Arnold & Gulumia, 1984; Chhabra, et al., 1987; Klaus & Adala, 1994). This broad spread highlights its resilience to a multitude of environmental circumstances. The plant demonstrates a significant versatility in its ecological requirements, typically surviving in various settings. It is typically found in savannas, woods, and gallery forests (Dalziel, 1937). These ecological niches give essential insights about its optimal habitat characteristics, such as well-drained soils and moderate rainfall patterns.

The species is also known to flourish in disturbed habitats, especially regions damaged by human activity (Orwa et al., 2009). Such tolerance to human alterations underlines its resilience and raises issues about its function in ecosystem dynamics. In addition to ecological resilience, *A. senegalensi* exhibits a significant affinity for elevations ranging from sea level to higher altitudes, further contributing to its extensive distribution (Klaus & Adala,1994). Understanding the range and habitat preferences of *A. senegalensis* is crucial for conservation efforts. As human activities continue to encroach onto its natural habitats, conservation plans must be informed by an accurate knowledge of its biological requirements. Additionally, the cultivation potential of this species in agroforestry systems might provide a sustainable way of satisfying both conservation and commercial objectives (Orwa et al., 2009). *Annona senegalensis*, with its broad range and ecological flexibility, stands as a rich botanical resource with various ecological consequences. The delicate interaction between its distribution, habitat, and human activities highlights the necessity for a holistic approach to its protection and sustainable exploitation.

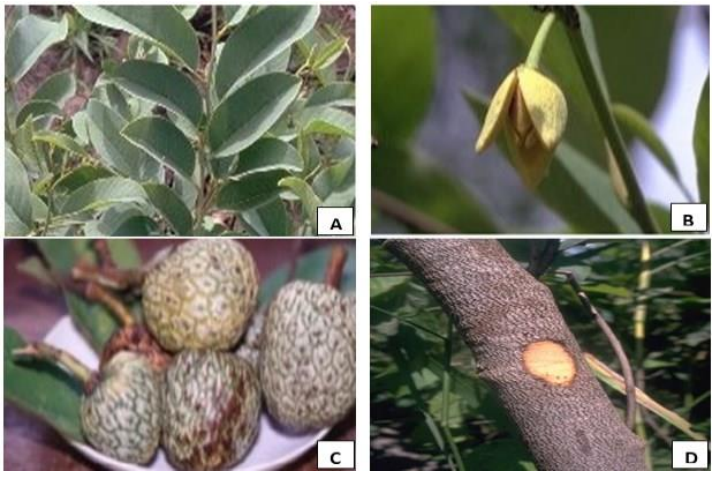

Figure 1. *Annona senegalensis* Pers.; (A) leaves (B) flower (C) fruits and (D) stem (Orwa et al., 2009)

Ethnomedical uses of *Annona senegalensis*

Annona senegalensis maintains a venerable position within the tapestry of traditional African medicine (Aiyeloja & Bello, 2006; Konate et al., 2012; Mustapha et al., 2013). For millennia, this plant gem has been valued for its broad and strong ethnomedical uses. The empirical information passed down via communities and healers offers a vast pool of

wisdom, sometimes functioning as a key healthcare resource for numerous conditions. A full study of the ethnomedical applications of *A. senegalensis* not only elucidates its cultural relevance but also begs investigation into its therapeutic possibilities within modern medicine (Ofukwu et al., 2008; Mustapha, 2013).

Traditional uses across cultures

Across the African continent, the plant has been utilised for its extraordinary medicinal powers. Its fruits, leaves, and roots find application in a plethora of medical applications, illustrating the varied character of this botanical marvel (Bassam et al., 2022). Perhaps one of its most recognised applications, *Annona senegalensis* has been applied in the treatment of malaria. Preparations produced from the plant's leaves and bark are commonly used to treat the symptoms of this prevalent and severe disease (Traore et al., 2013; Ngbolua et al., 2014). The custard apple's roots have long been recognized for their usefulness in addressing many gastrointestinal problems (Attig et al., 2017), delivering relief from ailments like dysentery and diarrhoea (Igoli et al., 2005; Suleiman et al., 2008). *A. senegalensis* also finds its place in the treatment of skin disorders. Pastes and ointments made from its fruits and leaves are administered topically to treat skin ailments, suggesting its dermatological potential (Mustapha et al., 2013). The plant is also mentioned to be used in tuberculosis (Ofukwu et al., 2008), diabetes (Ahombo et al., 2012), erectile dysfunction (Faleyimu et al., 2010), snake bites (Ogoli et al., 2011) and infections (Magassouba et al., 2007; Mustapha et al., 2013). Beyond its specialised usage, the plant has been exploited to reduce general malaise and fever, highlighting its position as a panacea in several traditional medicinal systems.

The multiplicity of ethnomedical usage of *A. senegalensis* emphasises its cultural value and therapeutic adaptability. These applications are grounded by a rich oral tradition that has maintained communities for generations, underscoring the need for scientific confirmation and investigation of its possibilities within contemporary medicine. In summary, the ethnomedical applications of *A. senegalensis* are a witness to the deep-rooted relationship between indigenous cultures and the botanical riches of Africa. The merging of traditional wisdom with current science offers the potential to reveal the medicinal secrets of this plant, benefitting both cultural heritage and global healthcare. While the traditional usage has been lauded for its efficacy, the integration of this plant into current pharmacological and medical procedures remains an expanding area. The identification of its chemical composition and pharmacological actions provides promising opportunities for medication discovery and healthcare innovation. Scientific investigations proving its traditional usage and investigating innovative applications have the prospect of not just maintaining cultural heritage but also contributing to global health efforts.

Phytochemistry of *Annona senegalensis*

Annona senegalensis, stands as a botanical treasure trove of phytochemical variety. This plant, endemic to many parts of Africa, has caught the attention of researchers and phytochemists for its complicated phytochemical makeup (Khallouki et al., 2002; Yisa et al., 2010; Okhale et al., 2016; Djoza et al., 2017). A detailed investigation of the phytochemistry of *A. senegalensis* exposes a tapestry of bioactive chemicals, each with its distinct features and medicinal potential (Mustapha, 2013; Adayat et al., 2014). This review not only enriches our comprehension of the plant's therapeutic potential but also begs the discovery of novel bioactive compounds for numerous uses. *A. senegalensis* is rich in alkaloids, including anonaine (Li et al., 2013), reticuline (Dholvitayakhun et al., 2013) romerine (You et al., 1995; Magadula et al., 2014), liriodenine and noroliveroline (Fall et al., 2008). These alkaloids have been the topic of pharmacological research, typically showing numerous biological functions, including antibacterial (Lall, et al., 2017), and anti-inflammatory and analgesic characteristics (Adzu et al., 2003; Yeo et al., 2011; Suleiman et al., 2014). The plant's leaves and fruits are rich sources of flavonoids, including quercetin, kaempferol, and catechin (Ameen et al., 2011; Jada et al., 2015).

The plant boasts a considerable saponin content (Afolabi & Afolabi, 2013; Yisa et al., 2010). Saponins have been reported to possess hypocholesterolaemia effect (Price et al., 1987). Tannins, represented by substances like ellagic acid and tannic acid, add to the phytochemical richness of *A. senegalensis* (Jada et al., 2014). Tannins have been connected with antimicrobial, antioxidant and anti-inflammatory actions. Other compounds such as glycosides and steroids (Afolabi & Afolabi, 2013), volatile oils (Khallouki, et al., 2002), anthrocyanins (Mpiana, 2012) and kauronic acid (Okoye et al., 2012, 2013) have been reported in *A. senegalensis*. This extensive phytochemical profile, characterized by a symphony of alkaloids, flavonoids, saponins, terpenoids, polyphenols, coumarins, and tannins, emphasises the multi-dimensional therapeutic potential of the plant. The bioactive elements within this botanical resource not only constitute the core of its traditional therapeutic usage but also urge systematic scientific research, giving exciting opportunities for drug discovery and healthcare innovation

Pharmacological activities of *Annona senegalensis*

Annona senegalensis is not just a botanical gem of ethnobotanical value; it also appears as a rich source of medicinal potential. The scientific world has increasingly focused its attention to this species to discover its different medicinal properties. An in-depth analysis of the pharmacological characteristics of *A. senegalensis* reveals a range of bioactivities, each with its particular therapeutic promise. This exploration not only substantiates its traditional therapeutic benefits but also maps a road for further scientific study, medication discovery, and healthcare innovation.
A. senegalensis has received attention for its considerable antibacterial potential. Extracts from various portions of the plant demonstrate inhibitory actions against a range of diseases, including bacteria and fungus (More et al., 2008; Mann et al., 2009; Awa et al., 2012; Okoye et al., 2013; Koggie et al., 2022). Such activities show promise for the discovery of new antibacterial drugs. Pharmacological investigations have uncovered the plant's analgesic and anti-inflammatory potentials (Adzu et al., 2003; Odoh et al., 2004; Konaté et al., 2021) The plant's extracts have proven the potential to modulate inflammatory responses, indicating applications in diseases defined by chronic inflammation (Yeo et al., 2011; Sulieman et al., 2014). Studies have suggested the existence of bioactive chemicals in *A. senegalensis* with potential anticancer activity (Adesogan & Durodold, 1976; Sahpaz et al., 1996, Ajaiyeoba et al., 2006a). These chemicals have exhibited inhibitory effects on cancer cell development, suggesting prospects for further exploration in cancer treatments (Ajaiyeoba et al., 2006a; Magadula et al., 2009; Ahmed et al., 2010). Antioxidant properties have been identified in *A. senegalensis* extracts, suggesting potential advantages in fighting oxidative stress-related disorders (Potchoo et al., 2008; Tamfu et al., 2021). The plant's phytochemical ingredients contribute to its antioxidant capacities (Adisa et al., 2019; Omeke et al., 2019; Tamfu et al., 2021). The bioactive components from the plant displayed antiparasitic capabilities, notably against protozoan parasites (Sahpaz et al., 1994; Ajaiyeoba et al., 2006b). These actions have significance for managing parasite diseases in tropical locations (Sahpaz et al., 1994). Several investigations have documented the insecticidal capabilities of *A. senegalensis* (Ngamo et al., 2007; Gueye et al., 2011; Lame et al., 2014; Mukungulu et al., 2015). An aporphine alkaloid, (-)-roemerine was identified as the active principle responsible for the insecticidal action (Magadula et al., 2009).

The extracts of *A. senegalensis* have been examined for egg inhibition efficacy as well as toxicity against the infective larval stage of *Haemonchus contortus* and the results were encouraging (Monglo et al., 2006; Nukenine et al., 2006). A substantial decrease in egg hatch has also been reported (Alawa et al., 2003). The five acetogenins namely gigantetronenine, squamocine, glaucanisine, glaucanetine, goniothalamicine and two alkaloids liriodenine and norolivéroline from the root of *A. senegalensis* have been reported to display anthelminthic activity (Fall, et al., 2008) .
Multiple reports have established that *A. senegalensis* possesses powerful in vivo trypanocidal activities, with little or no in vitro effects (Youan et al., 1997; Atawodi, 2005; Ogbadoyi et al., 2007; Kabiru et al., 2010). These actions were attributable to the isolated acetogenins from the extracts of the seeds (Sahpaz et al., 1994). Acetogenins potentially responsible for this action include annogalene, annonacin, annonacin A, annosenegalin and senegalene (Setzer & Ogungbe, 2012). The effectiveness of the *A. senegalensis* root bark methanol extract against *Naja nigricotlis nigricotlis* Wetch) venom, was investigated in rats (Adzu et al., 2003; Musa et al., 2017). The extract detoxified the utilised snake venom and reduced the resulting hyperthermia. Another study reported that the methanol extract from the leaves of A. senegalensis prevented the death-inducing effects of the venom from *Echis ocellatus*. The major phytochemicals controlling the activity of this fraction were flavonoids and tannins (Amlabu et al., 2014). Several investigations have reported the effects of *A. senegalensis* extracts on fertility (Mbayo et al., 2023). The weight of the testes and epididymis, and sperm concentration and motility were increase by the extract of *A. senegalensis* (Oladele et al., 2014). Studies have also hinted to the neuroprotective potential, and some central nervous system beneficial effects of *A. senegalensis* (Okoli et al., 2010; Otimenyin & Omeri, 2014) Compounds within the plant have showed to exhibit anticonvulsant (Konate et al., 2012; Dongmo et al., 2014; Okoye et al., 2012), muscle relaxant (Okoye et al., 2012) and hypnotic (Otimenyin & Omeri, 2014) effects which may be significant in neurological illnesses. Other pharmacological activities that have been ascribed to *A. senegalensis* are haemostatic (Dandjesso et al., 2012) and anti-sickling (Mpiana 2012; Kitadi et al.,2020). The varied pharmacological effects of *A. senegalensis* underline its therapeutic adaptability and underscore the necessity for thorough scientific confirmation. Beyond validating its conventional usage, scientific study provides vistas for the creation of new pharmacological drugs. These bioactivities serve as testaments to the plant's extensive phytochemical composition and its ability to contribute to modern healthcare endeavours.

Adverse effects and toxicity of *Annona senegalensis*

Although *Annona senegalensis* is acclaimed for its traditional medical usage and possible therapeutic capabilities, few studies have investigated its adverse effects and toxicity (Okoye et al., 2012; Ilboudo et al., 2019). It has been reported that *A. senegalensis* is relatively safe (Adisa et al., 2019; Konaté et al., 2021), but in prolong use may modulate the activity of mitochondrial succinate dehydrogenase (Adisa et al., 2019). However, a full study of its safety profile is required, noting that therapeutic medicines, even of natural origin, may contain undesirable effects and toxicity hazards.

While *A. senegalensis* contains substantial therapeutic potential and has been traditionally utilised for its medicinal characteristics, it is vital to understand the potential detrimental effects and toxicity connected with its ingestion. Caution should be used, and users should stick to approved dosages and customary methods. Further study is needed to create acceptable parameters for the use of *A. senegalensis* in healthcare and traditional medicine.

Clinical trials on *Annona senegalensis*: current status and future prospects

Clinical trials represent the peak of scientific validation in the path from ancient herbal treatment to modern evidence-based healthcare. *Annona senegalensis* has long played a major role in traditional medical systems across Africa. While traditional knowledge has praised its medicinal benefits, scientific studies offer a methodical technique to determine the safety and efficacy of this botanical gem in many medical applications. This study covers the present landscape of clinical studies utilising *A. senegalensis*, offering light on the progress accomplished and the prospects that lay ahead. The small number of therapeutic trials on *A. senegalensis* emphasises the unrealized potential of this botanical resource. As the scientific world increasingly realises its importance, there are various options for further research. Clinical trials can be performed to confirm the traditional usage of the plant, particularly in situations where it has been applied as a treatment for specific diseases. Further clinical study can dive into the pharmacological activities revealed in preclinical investigations, including antibacterial, anticancer, antioxidant, and anti-inflammatory effects. Developing standardized formulations of *A. senegalensis* extracts and assessing their clinical effectiveness might open the road for pharmaceutical development. Comprehensive safety and toxicity evaluations are necessary to ensure the plant's safety profile, permitting its incorporation into contemporary healthcare. Exploring the synergistic potential of *A. senegalensis* with conventional medicines might give insights into complementary therapy options. The rising interest in this plant gives a rare opportunity to combine ancient knowledge with contemporary healthcare, giving great potential for innovative therapeutic agents and evidence-based therapy.

Recommendations

Given the potential pharmacological properties of *A. senegalensis* revealed in preclinical investigations, additional clinical study is advised. Well-designed clinical studies should be done to systematically test its safety and effectiveness in diverse therapeutic applications. Collaboration between traditional healers, academics, and healthcare professionals is vital in this area. To guarantee the safe use of *A. senegalensis*, rigorous safety evaluations and toxicological studies are necessary. These studies should evaluate the possible side effects and toxicity concerns associated with different formulations and doses. The development of standardized formulations and quality control procedures for *A. senegalensis* products is vital. This will assist assure consistency in therapy results and limit fluctuations in bioactive chemical concentrations. There is need to promote education and awareness among communities who utilise *A. senegalensis*. This involves spreading information regarding safe and responsible usage, possible hazards, and the significance of consulting healthcare experts when utilising herbal treatments. Encouraging the integration of traditional medicine, particularly *A. senegalensis*, into modern healthcare systems can promote healthcare access and give more treatment alternatives. Collaboration between traditional healers and medical practitioners should be supported.

Conclusion

Annona senegalensis symbolises a botanical treasure trove of traditional wisdom and medicinal potential. Its ethnomedical applications, rich phytochemical makeup, and pharmacological properties have been appreciated across centuries. While the plant offers promise in addressing different health conditions, it may not be without possible unwanted effects and toxicity hazards. The small number of clinical trials on *A. senegalensis* underlines the need for future study to confirm its traditional applications, check safety, and investigate its medicinal potential in a systematic manner. Collaborative efforts between traditional healers, academics, and healthcare professionals are necessary to bridge the gap between traditional knowledge and current evidence-based treatment. It is vital that consumers exercise caution, stick to specified dosages, and consult healthcare specialists while utilising *A. senegalensis* -based medicines. Standardization, quality control, and safety evaluations should be important to its application in both traditional and modern medicine. As we begin on this path of discovery, the integration of *Annona senegalensis* into contemporary healthcare provides the prospect of not only maintaining cultural legacy but also contributing to global health efforts. With careful investigation and cautious usage, *A. senegalensis* may become a helpful addition to the diversity of therapeutic choices accessible in our quest for greater health and well-being.

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Ethics approval

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