IJP (2024), Vol. 11, Issue 7 **(Review Article)**

Received on 01 July 2024; received in revised form, 23 July 2024; accepted, 28 July 2024; published 31 July 2024

ANNONA RETICULATA (RAMPHAL): A REVIEW ON ITS MEDICINAL USES AND HEALTH BENEFITS

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Keywords:

Annona reticulata (Ramphal), Medicinal use, Inflammatory conditions, Antioxidant properties

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ABSTRACT: *Annona reticulata* (Ramphal), also known as custard apple, is a tropical fruit-bearing tree with a long history of traditional medicinal use. This review article comprehensively examines the medicinal properties and health benefits associated with various parts of the Annona reticulata (Ramphal) tree, including its fruit, leaves, seeds, and bark. The fruit of Annona reticulata is rich in vitamins, minerals, and antioxidants, and have been traditionally used to treat various ailments such as diabetes, inflammation, and microbial infections. Scientific studies have highlighted its antioxidant properties and potential therapeutic effects against diabetes and inflammatory conditions. The leaves of the Annona reticulata tree have been utilized in traditional medicine for their hypoglycemic and antimicrobial properties. Research on related species suggests potential benefits for managing diabetes and combating microbial infections. Annona reticulata seeds, have often been overlooked, but they show activity as antimicrobial agents based on limited research. Studies have explored their potential effectiveness against certain bacteria and fungi, suggesting their utility in traditional medicinal practices. The bark of the Annona reticulata tree has been traditionally used for its antipyretic, antidiabetic, and antimicrobial properties, although scientific research specifically on Annona reticulata bark is lacking. While traditional uses of Annona reticulata parts suggest potential health benefits, further scientific research is necessary to validate these claims and elucidate their mechanisms of action. Understanding the medicinal properties of Annona reticulata could contribute to the development of novel therapeutic agents for various health conditions.

INTRODUCTION: Annona reticulata, commonly known as custard apple or bullock's heart, is a tropical fruit tree revered for its deliciously sweet and creamy fruits. Belonging to the Annonaceae family, this evergreen tree is native to the tropical regions of the Americas, particularly the Caribbean, Central America, and parts of South America. The fruit is known for its sweet and creamy flesh, which is often compared to a combination of mango and banana flavors [1].

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.IJP.11(7).343-53

Article can be accessed online on: www.ijpjournal.com

DOI link: https://doi.org/10.13040/IJPSR.0975-8232.IJP.11(7).343-53

The custard apple tree is characterized by its medium to large-sized canopy, with glossy, dark green leaves that provide ample shade. Its flowers are unique, with three outer fleshy petals and three smaller inner petals, often greenish-yellow or reddish in color. The fruit, which typically matures in late summer to fall, is a compound fruit composed of numerous individual segments, each containing a glossy, black seed surrounded by soft, white, custard-like pulp.

Cultivated for centuries by indigenous peoples and later by European settlers, custard apple has gained popularity worldwide not only for its exceptional taste but also for its nutritional and medicinal properties. The fruit is rich in essential vitamins and minerals, including vitamin C, vitamin B6,

potassium, and magnesium, making it a valuable addition to a healthy diet. Beyond its culinary uses, custard apple has a long history of traditional medicinal use. Various parts of the tree, including the fruit, leaves, seeds, and bark, have been employed in herbal remedies for ailments ranging from digestive disorders to skin conditions. Additionally, scientific studies have identified bioactive compounds in custard apple, such as annonaceous acetogenins, flavonoids, and phenolic compounds, which exhibit antioxidant, anti-inflammatory, and anticancer properties [2].

In addition to its cultural and culinary significance, custard apple holds promise for sustainable agriculture and agro forestry practices. The tree is relatively low-maintenance, adaptable to a range of soil types, and can thrive in both tropical and subtropical climates. Its fruits provide a valuable source of income for farmers in many regions and contribute to biodiversity conservation efforts by providing habitat and food for wildlife [3, 4]. Overall, Annona reticulata stands as a testament to the richness of tropical biodiversity, offering not only delectable fruits but also ecological, cultural, and economic benefits to communities around the world.

FIG. 1: IMAGE OF *ANNONA RETICULATA*

Biogeographical Distribution: Its biogeographical distribution spans across several countries in Central America, South America, and the Caribbean. Here is an overview of the geographical distribution of *Annona reticulata*.

Central America: Custard apple is native to the countries of Central America, including:

Mexico: Particularly in the southern regions of Mexico, including states like Chiapas, Oaxaca, and Veracruz.

Guatemala: Found in various regions throughout the country, especially in the southern and coastal areas.

Belize: Distributed in the lowland areas and along riverbanks.

Honduras, Nicaragua, Costa Rica, and Panama: Custard apple trees can be found in forests, as well as cultivated in gardens and orchards.

South America: Annona reticulata is also native to several countries in South America, including:

Colombia: Found in both wild and cultivated settings, especially in the northern regions.

Venezuela: Distributed in tropical areas, including the Amazon rainforest and coastal regions.

Brazil: Native to the Amazon basin and other parts of the country's tropical and subtropical regions.

Peru: Found in the Amazon rainforest and other forested areas.

Caribbean: Custard apple is indigenous to various islands in the Caribbean, including:

Jamaica: Widely cultivated and found in the wild in forested areas.

Cuba: Cultivated in gardens and small orchards, as well as found in the wild.

Puerto Rico: Distributed in forested regions and cultivated in home gardens.

Dominican Republic: Found in both wild and cultivated settings, especially in the southern and coastal areas. Trinidad and Tobago, Barbados, Haiti, and other Caribbean islands: Custard apple trees can be found in both wild and cultivated environments [5, 8].

Botanical Characteristics: Botanical characters of Annona reticulata, commonly known as custard apple or bullock's heart, include a combination of distinctive features of its leaves, flowers, fruits, and overall growth habit. Here's an overview:

Leaves:

- The leaves of Annona reticulata are simple, alternate, and broadly elliptic to ovate in shape.

- ❖ They are leathery in texture, glossy dark green on the upper surface, and lighter green underneath.
- ❖ Leaf margins are entire (smooth) and may be slightly undulate (wavy).
- ❖ Leaves typically measure 5 to 20 centimeters in length and 3 to 10 centimeters in width.

FIG. 2: IMAGE OF *ANNONA RETICULATA* LEAVES

Flowers:

- ➢ The flowers of custard apple are bisexual, meaning they contain both male and female reproductive structures.
- ➢ They are solitary or grouped in clusters in the leaf axils.
- ➢ Each flower has three outer, fleshy, greenish-yellow to reddish petals and three smaller, inner petals.
- ➢ The inner petals are densely covered with fine, woolly hairs.
- ➢ The flowers are protogynous, meaning the female parts mature before the male parts, which helps prevent self-pollination.

FIG. 3: IMAGE OF *ANNONA RETICULATA* FLOWERS

Fruits:

- o The fruit of Annona reticulata is a compound fruit composed of numerous individual segments or carpels, each containing a single seed.
- o The fruit is spherical to heart-shaped and may measure 6 to 12 centimeters in diameter.
- o The surface of the fruit is covered with knobby, diamond-shaped or polygonal protrusions, giving it a distinct reticulated (net-like) appearance.
- o When ripe, the skin of the fruit turns from green to yellow or brownish-yellow, and it becomes soft and fragrant.
- o The pulp is creamy-white to pale yellow in color, soft, and sweet, with a flavor reminiscent of a blend of banana, pineapple, and strawberry.

FIG. 4: IMAGE OF *ANNONA RETICULATA* FRUIT

Overall Growth Habit:

- ✓ Annona reticulata is an evergreen tree that typically reaches a height of 5 to 10 meters, although it can grow taller under optimal conditions.
- ✓ It has a rounded to spreading canopy with dense foliage.
- ✓ The trunk is short, usually with a diameter of about 30 to 60 centimeters, and may be slightly buttressed at the base [6, 8].

FIG. 5: *ANNONA RETICULATA* TREE

Medicinal Uses: While there's limited scientific research specifically on the medicinal uses of each part of the Annona reticulata tree, traditional medicine suggests various applications such as Annona reticulata has a long history of traditional use in various cultures for its medicinal properties. Different parts of the plant, including the leaves, bark, roots, and fruits, have been used in traditional medicine for treating ailments such as diarrhea, dysentery, fever, asthma, and skin diseases.

Fruit: Rich in vitamins, minerals, and antioxidants, the fruit is commonly consumed fresh or processed into beverages like juices or smoothies. Some traditional medicinal uses include its potential as an anti-diabetic, anti-inflammatory, and antimicrobial agent. Medicinally, the fruit is believed to have been use to alleviate gastrointestinal issues like diarrhea and dysentery. Additionally, it's thought to possess antioxidant properties that may help protect cells from damage caused by free radicals. The fruit of Annona reticulata (Ramphal) is not only delicious but also rich in phytochemicals such as flavonoids, alkaloids, and phenols, which contribute to its medicinal properties. Studies have shown that extracts from Ramphal fruit possess significant antioxidant activity, which may help in preventing oxidative stress-related diseases. Research also suggests that Ramphal fruit extracts exhibit antimicrobial activity against various pathogenic bacteria and fungi, indicating its potential as a natural antimicrobial agent [13, 14].

FIG. 6: *ANNONA RETICULATA* FRUIT

Let's delve into the medicinal uses of its constituents:

Acetogenins: Annonaceous acetogenins are a group of natural compounds found in Annonaceae plants, including Annona reticulata. These compounds have been extensively studied for their cytotoxic properties, particularly against cancer cells. They exhibit potential anticancer activity by inhibiting the growth of tumor cells and inducing apoptosis (programmed cell death) in various cancer cell lines. Several studies have demonstrated the cytotoxic effects of acetogenins isolated from Annona reticulata against different types of cancer, including breast, prostate, and liver cancer. [XVI]

Flavonoids: *Annona reticulata* fruits contain flavonoids, which are known for their antioxidant properties. Flavonoids help to neutralize free radicals in the body, thereby reducing oxidative stress and inflammation. This antioxidant activity may contribute to the fruit's potential health benefits, including protection against chronic diseases such as cardiovascular disease and cancer [17].

Alkaloids: Some alkaloids present in Annona reticulata have shown analgesic (pain-relieving) and anti-inflammatory properties in preclinical studies. These alkaloids may contribute to the traditional use of Annona reticulata in treating pain and inflammation. However, further research is needed to elucidate their specific mechanisms of action and therapeutic potential [18].

Tannins: Tannins are polyphenolic compounds found in Annona reticulata fruits, which possess various pharmacological properties, including antioxidant, anti-inflammatory, antimicrobial, and wound healing activities. Tannins may help in the management of gastrointestinal disorders due to their astringent properties, which can help alleviate diarrhoea and dysentery. Additionally, tannins have been investigated for their potential role in promoting wound healing and preventing infections [19].

Vitamins and Minerals: *Annona reticulata* fruits are rich in vitamins (such as vitamin C) and minerals (such as potassium and magnesium), which are essential for maintaining overall health and well-being. These nutrients play various roles in the body, including immune function, bone health, and energy metabolism. Consuming Annona reticulata fruits as part of a balanced diet can help fulfil daily nutritional requirements and support optimal health [20].

Leaves: The leaves of the Ramphal tree have been used traditionally for their medicinal properties, including their potential as an antidiabetic and antimicrobial agent. The leaves of the Ramphal tree are used in traditional medicine for their potential antidiabetic properties. They are believed to help regulate blood sugar levels. Additionally, the leaves are sometimes brewed into teas or used in poultices to relieve skin conditions like eczema and psoriasis.

The leaves of the Ramphal tree contain bioactive compounds such as alkaloids, flavonoids, and tannins, which contribute to their medicinal properties. Studies have shown that Ramphal leaf extracts possess antidiabetic activity, potentially through mechanisms such as improving insulin sensitivity and glucose uptake.

Ramphal leaf extracts also demonstrate significant anti-inflammatory and analgesic properties, which may be useful in managing inflammatory conditions and pain [21, 22].

FIG. 7: *ANNONA RETICULATA* LEAVES

Here are the detailed medicinal uses of each constituent found in Annona reticulata leaves.

Alkaloids:

Analgesic: Alkaloids present in Annona reticulata leaves exhibit potential analgesic properties, which may help alleviate pain associated with various conditions.

Antimicrobial: Some alkaloids have demonstrated antimicrobial activity against bacteria, fungi, and parasites, suggesting their potential use in treating infectious diseases.

Antidiabetic: Certain alkaloids show promise in lowering blood sugar levels and improving insulin sensitivity, indicating their potential utility in managing diabetes.

Antimalarial: Studies suggest that specific alkaloids possess antimalarial activity, which could contribute to the development of novel antimalarial agents [23, 26].

Flavonoids:

Antioxidant: Flavonoids in Annona reticulata leaves possess potent antioxidant properties, scavenging free radicals and protecting cells from oxidative damage.

Anti-inflammatory: Some flavonoids exhibit anti-inflammatory effects by inhibiting pro-inflammatory enzymes and cytokines, suggesting their potential in mitigating inflammatory conditions.

Neuroprotective: Certain flavonoids have shown neuroprotective effects, protecting neurons from damage and potentially offering therapeutic benefits in neurodegenerative diseases.

Cardioprotective: Flavonoids may contribute to cardiovascular health by improving endothelial function, reducing blood pressure, and lowering cholesterol levels [26, 27].

Tannins:

Antidiarrheal: Tannins possess astringent properties that help reduce intestinal secretions and alleviate diarrhea, making them useful in the management of gastrointestinal disorders.

Wound Healing: Tannins have been traditionally used topically for wound healing due to their ability to precipitate proteins, form a protective layer, and promote tissue repair.

Antimicrobial: Some tannins exhibit antimicrobial activity against a wide range of pathogens, including bacteria, fungi, and viruses, suggesting their potential in combating infections [28, 29].

Vitamins and Minerals:

Immune Support: Vitamins and minerals in Annona reticulata leaves play crucial roles in immune function, helping the body fight off infections and maintain overall health.

Bone Health: Minerals like calcium and magnesium contribute to bone strength and density, reducing the risk of osteoporosis and fractures.

Metabolic Support: B vitamins play essential roles in energy metabolism, nerve function, and red blood cell production, supporting overall metabolic health [30, 31].

Seeds: Ramphal seeds are not typically consumed due to their toxic compounds. However, they have been used in traditional medicine for their anthelmintic properties, meaning they may help expel parasitic worms from the body. Care should be taken when using the seeds due to their toxicity.

While Ramphal seeds are not typically consumed due to their toxicity, they have been traditionally used as anthelmintic to expel parasitic worms from the body. Studies have reported the presence of bioactive compounds such as acetogenins and alkaloids in Ramphal seeds, which may contribute to their anthelmintic properties.

Due to their toxicity, caution should be exercised when using Ramphal seeds, and they should only be used under the guidance of a qualified healthcare professional [32, 33].

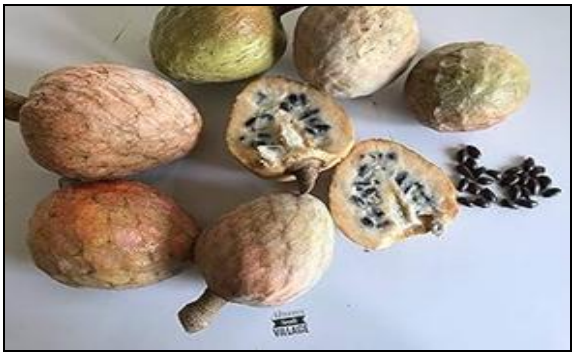

FIG. 8: *ANNONA RETICULATA* SEEDS

An overview of the detailed medicinal uses of each constituent found in Annona reticulata seeds

Alkaloids:

Antiparasitic: Some alkaloids present in Annona reticulata seeds have demonstrated potent antiparasitic activity, particularly against intestinal parasites such as worms.

Antimicrobial: Certain alkaloids exhibit broad-spectrum antimicrobial properties, inhibiting the growth of bacteria, fungi, and protozoa.

Analgesic: Alkaloids may possess analgesic properties, helping to alleviate pain and discomfort associated with various conditions [34, 35].

Flavonoids:

Antioxidant: Flavonoids found in Annona reticulata seeds possess strong antioxidant properties, scavenging free radicals and reducing oxidative stress.

Anti-inflammatory: Certain flavonoids exhibit anti-inflammatory effects, which may help alleviate inflammation and associated symptoms.

Cardioprotective: Flavonoids may contribute to cardiovascular health by improving blood flow, reducing blood pressure, and protecting against heart disease [36, 37].

Tannins:

Antidiarrheal: Tannins possess astringent properties that can help reduce intestinal secretions and alleviate diarrhoea.

Antimicrobial: Some tannins exhibit antimicrobial activity against a wide range of pathogens, including bacteria, fungi, and viruses.

Wound Healing: Tannins have been traditionally used topically for wound healing, forming a protective layer and promoting tissue repair [38, 39].

Vitamins and Minerals:

Nutritional Support: Vitamins and minerals present in Annona reticulata seeds provide essential nutrients that support overall health and well-being.

Immune Function: Certain vitamins and minerals play key roles in immune function, helping the body fight off infections and diseases.

Metabolic Support: B vitamins contribute to energy metabolism, nerve function, and red blood cell production, supporting overall metabolic health [40, 42].

Bark: The bark of the Annona reticulata tree has been used in traditional medicine for its potential as an antipyretic, antidiabetic, and antimicrobial agent. However, scientific research specifically on the medicinal properties of Ramphal bark is scarce. The bark of the Ramphal tree is known for its astringent properties. It has been used topically to treat wounds, cuts, and skin infections. Some traditional medicinal practitioner also use the bark to alleviate fever and reduce inflammation.

The bark of the Ramphal tree contains bioactive compounds such as alkaloids, flavonoids, and saponins, which contribute to its medicinal properties. Studies have also reported the anti-inflammatory and analgesic properties of Ramphal bark extracts, suggesting its potential use in managing inflammatory conditions and pain [45].

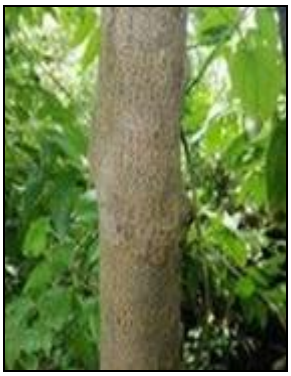

FIG. 9: *ANNONA RETICULATA* BARK

Detailed medicinal uses of each constituent found in Annona reticulata bark.

Alkaloids:

Antiparasitic: Alkaloids in Annona reticulata bark have shown promising antiparasitic activity against various intestinal parasites, including worms and protozoa.

Antimicrobial: Certain alkaloids exhibit broad-spectrum antimicrobial properties, inhibiting the growth of bacteria, fungi, and other microorganisms.

Analgesic: Alkaloids may possess analgesic properties, which could help alleviate pain associated with various conditions [44, 45].

Flavonoids:

Antioxidant: Flavonoids present in Annona reticulata bark exhibit strong antioxidant properties, protecting cells from oxidative damage caused by free radicals.

Anti-inflammatory: Certain flavonoids possess anti-inflammatory effects, which may help reduce inflammation and associated symptoms.

Cardioprotective: Flavonoids may contribute to cardiovascular health by improving blood flow, reducing blood pressure, and protecting against heart disease [46, 47].

Tannins:

Antidiarrheal: Tannins possess astringent properties that can help reduce intestinal secretions and alleviate diarrhoea.

Antimicrobial: Some tannins exhibit antimicrobial activity against a wide range of pathogens, including bacteria, fungi, and viruses.

Wound Healing: Tannins have been traditionally used topically for wound healing, forming a protective layer and promoting tissue repair [48, 49].

Vitamins and Minerals:

Nutritional Support: Vitamins and minerals present in Annona reticulata bark provide essential nutrients that support overall health and well-being.

Immune Function: Certain vitamins and minerals play key roles in immune function, helping the body fight off infections and diseases.

Metabolic Support: B vitamins contribute to energy metabolism, nerve function, and red blood cell production, supporting overall metabolic health [50, 51].

Roots: The roots of the Ramphal tree contain bioactive compounds such as alkaloids, tannins, and flavonoids, which contribute to their medicinal properties. Traditional uses of Ramphal roots include their use as antimicrobial agents for treating infections and as antitussive agents for managing respiratory conditions.

Studies have reported the antibacterial and antifungal properties of Ramphal root extracts against various pathogenic microorganisms, supporting their traditional use in folk medicine. Additionally, the roots are sometimes used to alleviate symptoms of asthma and bronchitis [52].

FIG. 10: *ANNONA RETICULATA* ROOTS

Detailed medicinal uses of each constituent found in Annona reticulata roots can provide valuable insights into its potential therapeutic benefits

Alkaloids:

Antimicrobial: Alkaloids present in Annona reticulata roots exhibit antimicrobial properties, which may help combat various pathogens, including bacteria, fungi, and parasites.

Antidiabetic: Some alkaloids have shown potential antidiabetic activity by lowering blood sugar levels and improving insulin sensitivity.

Analgesic: Alkaloids may possess analgesic properties, contributing to pain relief and management [53, 54.]

Flavonoids:

Antioxidant: Flavonoids found in Annona reticulata roots possess strong antioxidant properties, scavenging free radicals and reducing oxidative stress.

Anti-inflammatory: Certain flavonoids exhibit anti-inflammatory effects, which may help reduce inflammation and associated symptoms.

Cardioprotective: Flavonoids may contribute to cardiovascular health by improving blood flow, reducing blood pressure, and protecting against heart disease [55, 56].

Tannins:

Antidiarrheal: Tannins possess astringent properties that can help reduce intestinal secretions and alleviate diarrhea.

Antimicrobial: Some tannins exhibit antimicrobial activity against a wide range of pathogens, including bacteria, fungi, and viruses.

Wound Healing: Tannins have been traditionally used topically for wound healing, forming a protective layer and promoting tissue repair [57, 58].

Vitamins and Minerals:

Nutritional Support: Vitamins and minerals present in Annona reticulata roots provide essential nutrients that support overall health and well-being.

Immune Function: Certain vitamins and minerals play key roles in immune function, helping the body fight off infections and diseases.

Metabolic Support: B vitamins contribute to energy metabolism, nerve function, and red blood cell production, supporting overall metabolic health [59, 60]. The table below provide scientific insights into the medicinal properties of different parts of the Annona reticulata tree, validating some of its traditional uses while also highlighting the need for further research to fully understand its therapeutic potential and safety profile.

TABLE 1: MEDICINAL USES OF *ANNONA RETICULATA*

Medicinal Use	Description
Antioxidant	Annona reticulata is rich in antioxidants, which help in neutralizing free radicals in the body. It also contains antioxidants like vitamin C, vitamin A, and phenolic compounds. These antioxidants help neutralize harmful free radicals in the body, which can prevent oxidative stress and damage to cells
Anti-inflammatory	Its anti-inflammatory properties can help reduce inflammation and pain. Studies have shown that certain compounds present in Annona reticulata possess anti-inflammatory properties. These properties can help reduce inflammation in the body, which is associated with various chronic diseases and conditions.
Digestive Aid	Annona reticulata contains dietary fiber, aiding in digestion and preventing constipation. Annona reticulata is rich in dietary fiber, which aids in digestion by promoting regular bowel movements and preventing constipation. The fiber also helps maintain a healthy digestive system by supporting the growth of beneficial gut bacteria.
Fever Reducer	Some traditional medicine systems useAnnona reticulata to reduce fever. It is believed that certain compounds in Annona reticulata have antipyretic properties, which help lower body temperature during fever episodes.
Anti-diabetic	Research suggests that Annona reticulata may have hypoglycemic effects, meaning it can help lower blood sugar levels. This makes it potentially beneficial for individuals with diabetes or those at risk of developing diabetes.
Anti-cancer	Compounds in Annona reticulata have shown potential in fighting cancer cells. Some studies have indicated that certain bioactive compounds found in Annona reticulata, such as acetogenins and flavonoids, may exhibit anti-cancer properties. These compounds have shown promising results in inhibiting the growth of cancer cells in laboratory studies.

Immune Booster	It is believed to boost the immune system, aiding in overall health. Annona reticulata is believed to have immunomodulatory effects, meaning it can help regulate and strengthen the immune system. Regular consumption of Annona reticulata may help enhance the body's defense mechanisms against infections and diseases.
Respiratory Support	Annona reticulata leaves are used to alleviate respiratory issues such as coughs, colds, and bronchitis. The leaves are often brewed into a tea or decoction and consumed for their respiratory benefits.

While traditional uses of Annona reticulata parts suggest potential health benefits, further scientific research is needed to validate these claims and understand the specific mechanisms of action. It's important to note that while Annona reticulata has a long history of traditional medicinal use, scientific research on its efficacy and safety is limited.

CONCLUSION: In conclusion, the review underscores the remarkable medicinal and health benefits of Annona reticulata (Ramphal), a fruit deeply rooted in traditional medicine and culinary practices across various cultures. Through an extensive exploration of its phytochemical composition and pharmacological properties, it is evident that Annona reticulata possesses a diverse array of bioactive compounds, including annonaceous acetogenins, alkaloids, flavonoids, and phenolic compounds, which contribute to its therapeutic potential. The findings synthesized in this review highlight *Annona reticulata's* efficacy in managing a spectrum of health conditions, including its antimicrobial, antioxidant, anti-inflammatory, antidiabetic, and anticancer properties. Moreover, its traditional uses in alleviating gastrointestinal disorders, respiratory ailments, and skin conditions underscore its versatility as a natural remedy. Despite the wealth of knowledge accumulated on the medicinal properties of *Annona reticulata*, there remain significant gaps in our understanding, necessitating further research to elucidate its mechanisms of action, optimize extraction methods, and explore its potential synergistic effects with conventional therapies. Additionally, clinical trials are warranted to validate its efficacy and safety profile in humans, thereby paving the way for its integration into mainstream medicine. In light of the growing interest in natural remedies and the escalating burden of chronic diseases, Annona reticulata emerges as a promising candidate for drug development and nutraceutical formulations. Its accessibility, affordability, and minimal adverse effects underscore its potential to complement existing healthcare strategies and improve global health outcomes. In conclusion, the multifaceted medicinal and health benefits of Ramphal underscore its significance as a valuable resource in traditional medicine and a potential source of novel therapeutic agents. Continued research efforts are imperative to unlock its full therapeutic potential and harness its benefits for the betterment of human health.

ACKNOWLEDGEMENT: Nil

CONFLICT OF INTEREST: Nil

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How to cite this article:
Khorjuwenkar RS and Singh S: *Annona reticulata* (Ramphal): a review on its medicinal uses and health benefits. Int J Pharmacognosy 2024; 11(7): 343-53. doi link: http://dx.doi.org/10.13040/IJPSR.0975-8232.IJP.11(7).343-53.