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Review articles

Eco-Friendly Nanoparticle Synthesis Using *Annona* Species: A Comprehensive Review

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ABSTRACT
Nanotechnology has emerged as a transformative field with applications spanning medicine, environmental remediation, and materials science. However, conventional chemical and physical synthesis methods pose significant environmental and health concerns due to the use of toxic chemicals and high energy consumption. Green synthesis using plant extracts offers a sustainable, cost-effective, and eco-friendly alternative. The genus *Annona*, comprising species rich in bioactive phytochemicals, has gained considerable attention as a biogenic source for nanoparticle synthesis. The review identified extensive research on green synthesis of metallic and metal oxide nanoparticles using *Annona muricata*, *A. squamosa* and *A. reticulata.* Various plant parts including leaves, fruits, peels, seeds, roots, and bark have been successfully utilized. Silver nanoparticles (AgNPs), zinc oxide (ZnO), copper oxide (CuO), gold (AuNPs), and nickel oxide (NiO) nanoparticles. Phytochemicals such as flavonoids, phenolics, alkaloids, and terpenoids act as reducing, capping, and stabilizing agents. *Annona*-mediated nanoparticles demonstrate potent antimicrobial activity against diverse pathogens, significant anticancer properties with selective cytotoxicity, strong antioxidant capacity, and excellent photocatalytic performance for environmental remediation. *Annona* species represent promising biogenic resources for sustainable nanoparticle synthesis with multifunctional applications. The green synthesis approach offers environmental benefits, biocompatibility, and enhanced biological activities compared to conventional methods. However, challenges related to standardization, scalability, and mechanistic understanding require further investigation to facilitate clinical translation and industrial implementation.

Keywords: *Annona* species, green synthesis, nanoparticles, antimicrobial activity, anticancer activity, photocatalysis, bioactive compounds, sustainable nanotechnology, phytochemicals.

INTRODUCTION

Nanotechnology has revolutionized multiple scientific disciplines, offering unprecedented opportunities in medicine, electronics, environmental science, and materials engineering. Nanoparticles, defined as particles with at least one dimension between 1 and 100 nanometres, exhibit unique physicochemical properties.

Conventional nanoparticle synthesis methods, including chemical reduction, physical vapour deposition, and sol-gel processes, have dominated industrial and research applications for decades. However, these approaches present significant limitations that compromise their sustainability and safety. Chemical synthesis typically requires toxic reducing agents such as sodium borohydride, hydrazine, or dimethylformamide, along with hazardous stabilizers and organic solvents. Physical methods demand high energy consumption, specialized equipment, and controlled atmospheric conditions. Both approaches generate hazardous waste, pose environmental pollution risks, and raise concerns about biocompatibility for biomedical applications. The accumulation of toxic residues on nanoparticle surfaces can trigger adverse biological responses, limiting their clinical utility.

Green synthesis has emerged as a sustainable alternative that addresses these limitations by utilizing biological entities—including plants, microorganisms, algae, and fungi—as reducing and stabilizing agents. Among these biogenic sources, plant-mediated synthesis offers distinct advantages such as rapid reaction kinetics, cost-effectiveness, scalability potential, elimination of microbial culture requirements, and the presence of diverse phytochemicals that confer multifunctional properties to the synthesized nanoparticles. Plant extracts contain a rich repertoire of secondary metabolites, including polyphenols, flavonoids, alkaloids, terpenoids, proteins, and enzymes, which serve as natural reducing agents, capping agents, and stabilizers during nanoparticle formation.

The genus *Annona*, belonging to the family Annonaceae, comprises approximately 166 species distributed across tropical and subtropical regions. Several *Annona* species, particularly *Annona muricata* (soursop), *Annona squamosa* (sugar apple) and *Annona reticulata* (custard apple), have been extensively studied for their medicinal properties. Traditional medicine systems have long recognized *Annona* species for their antimicrobial, anticancer, anti-inflammatory, antidiabetic, and antioxidant properties. This bioactive potential, combined with widespread availability and agricultural waste generation (peels, seeds, leaves), positions *Annona* species as ideal candidates for green nanoparticle synthesis.

Nanotechnology has an emerging and remarkable application for a variety of problem-solving. Nanomaterials of metals (Au, Ag, Se, etc.) and their oxides have been exploited as antibacterial agents, drug delivery agents for targeted therapy, antioxidant agents, anticancer agents, etc. Specifically, Au and Ag nanoparticles are favourable because of their small size and distinct properties, which allow them to penetrate cell walls and cell membranes of pathogenic microbes. Gold (Au) and silver (Ag) nanoparticles are highly valued for their unique properties, making them widely used as anti-inflammatory, antibacterial, and antifungal agents in various medical applications, including coatings for dental care, catheters, antimicrobial filters, medical devices, eye treatments, wound dressings, etc.[1]

1. Botanical & Geographical Distribution

1.1. *Annona squamosa:*

Annona squamosa is the botanical name that comes under the family of Annonaceae. It is native to tropical America but has spread widely across Asia's tropical and subtropical regions, including Malaysia, Thailand, Laos, and Vietnam. In India, it thrives abundantly in the Aravalli Hills of Rajasthan.[2] Depending on the area, Annona squamosa is known by the following names: in Telugu/Kannada: Seethaphala, Sitaphala; Malaysia/Indonesia: Nona, Sri kaya, or Sarikaja; Hindi: Sharifa, Sita-phal, Ata; Spanish/French: Corossolsauvage, bois cachiman, Cachiman, Anonacolorada, and Anona de seso.[3] The tree is 3–8 meters tall, with thin gray bark. The leaves are 5-17 cm long and 2-6 cm wide. Fruits are aggregated, 5-10 cm in diameter, heart-shaped, yellow-green, or knobby, with 30-40 carpels, each with one 1.3-1.6 cm dark brown or black seed.[4]

Figure: 1

1.2. *Annona reticulata:*

Annona reticulata has been naturalized in Mexico, South America, and the West Indies. This species has also been introduced to Australia, Brazil, Africa, Taiwan, Bangladesh, India, Pakistan, Malaysia, Cuba, Colombia, and other countries.[5] Annona reticulata is known by the following names: in Malayalam: Manilanilam, Portuguese: Frutoda-Condessa, Telugu: Ramasitapalam, English: Bullock's heart, Corazon, Kannada: Ramaphala, Tamil: Ramachita, Indonesian: Buah Nona and India: Ramphal.[6] The young branches of the compact tree Annona reticulata are attached by 1-2 cm stalks; its oblong-lanceolate leaves measure 10-15 cm in length and 3-6 cm in width. The rough exterior of the heart-shaped or rounded fruits changes from yellow to yellowish-red as they ripen.[7]

Figure: 2

1.3. *Annona Muricata:*

Annona muricata originated in Central America; it is now grown in many tropical and subtropical regions, including parts of Africa, Asia, Australia, and South America. The medium-sized, exotic fruit-bearing evergreen tree has enormous, glossy, dark-green leaves and can grow up to 8 meters in height. The tree has edible, heart-shaped, green fruits that are 15–20 cm in diameter.[8] The leaves have a smooth, shiny dark green upper surface and a light green underside. They are usually elliptic, oblong, or narrowly oval, pointed at both ends, and measure 6.25-20 cm long and 2.5-6.25 cm wide.[9] Around the world, A. muricata is known by a variety of names. In English: A. muricata is called soursop; Latin America: guanabana; Portuguese: graviola; in Indonesia: sirsak or nangka belanda. Other names for it include corossol, anona, anoda, annone, araticum, and araticum-manso.[10]

Figure: 3

2. Annonaceae Family used in the Synthesis of Nanoparticle:

Heavy metals can be absorbed by plants through their parts, and plant extract-based biological synthesis techniques have become more and more popular for the synthesis of nanoparticles (NPs). Compared to traditional methods, this approach is simpler, more economical, and more efficient. Biological molecules found in plants have a high potential for turning metal salts into nanoparticles.[11]

Green nanotechnology has become a sustainable and environmentally friendly method for synthesizing nanoparticles. The selection of native plant species offers an additional unique biological source. Plants of the Annonaceae family, including Annona squamosa, Annona reticulata, and Annona muricata, have been selected due to their rich phytochemical profiles. Different nanoparticles were synthesized from different parts of these plants, along with their characterization methods, sizes, and shapes.

Table 1: Overview of Nanoparticle Synthesis from Annona Species

<table>
<tr><th>Annonaceae Family</th><th>Parts used for NP Synthesis</th><th>Nanoparticle</th><th>Characterization</th><th>Size Range</th><th>Shape</th><th>Reference</th></tr>
<tr><td rowspan="3">Annona squamosa</td><td rowspan="3">Seed Extract</td><td rowspan="3">CaO</td><td rowspan="3">UV, DLS, FTIR, XRD and FESEM</td><td>DLS – 600-700nm</td><td>-</td><td rowspan="3">12</td></tr>
<tr><td>XRD - 3.72nm</td><td>-</td></tr>
<tr><td>FESEM – under 100nm</td><td>Spherical</td></tr>
<tr><td>Annona squamosa</td><td>Peel</td><td>TiO_2</td><td>UV, XRD, SEM, TEM and EDS</td><td>TEM - 23 ± 2 nm</td><td>Spherical</td><td>13</td></tr>
</table>

				SEM	Aprox. Spherical	
Annona squamosa	Leaf and Fruit Extracts	Ag	XRD, UV-Vis, SEM and Antibacterial analysis.	SEM - 35–90 nm and 15–50nm	Spherical	14
Annona squamosa	Leaf Extract	Cr and Ni	FTIR and UV-visible spectroscopy	UV-Vis spectroscopy	Symmetric	15
Annona squamosa	Seed Extract	CuO	UV-Vis, XRD, FT-IR, AFM, SEM, TEM, HR-TEM and EDX	TEM – 39.8nm	Spherical	16
				XRD – 11nm	-	
Annona squamosa	Seed	MgO	FTIR, UV, XRD, EDX, SEM, TEM and SAED	SEM – Varied from 16 to 120 nm	Flower shape	17
				TEM – 27 and 68nm	Irregular shape	

				XRD – 11.8nm	-	
Annona reticulata	Leaves Extract	Ag	UV, TEM, XRD and FTIR	TEM - 23.84 to 50.54 nm	Some are spherical, rod, and triangular shape.	18
Annona reticulata	Seed Extract	ZnO	XRD, FTIR, UV, DLS and SEM	SEM - 70-85nm	Spherical	19
				DLS – 1620nm	-	
Annona muricata	Root Bark Extract	Ag	UV, TEM, Photon Correlation Microscopy and FTIR	TEM - 22 ± 2 nm	Monodisp-ersed, discrete and topograph-ically spherical.	20
				PCM - 392.10 ± 18.56nm	-	

Annona muricata	Leaf Extracts	Au	UV, TEM and FTIR	TEM - 27 to 32nm	spherical mono-dispersed structure	21
Annona muricata	Leaf Extracts	ZnO	XRD, UV, Raman Spectroscopy, TEM, Photoluminescence and FTIR	TEM – 8nm	-	22
				XRD - 25 g/L : 20.3nm 50 g/L : 9.8 nm 100 g/L : 7.7 nm 200 g/L: 27.6 nm	Hexagonal	
Annona muricata	Fruit Extract	Se	UV, DLS, Zeta Potential, SEM and EDX	DLS – 80-120nm	-	23
				SEM – 120-160nm	Spherical	
Annona muricata	Leaf Extract	MgO	FTIR, XRD and SEM	XRD - 41nm	Hexagonal	24

				SEM - 36.7 and 69.6nm	Hexagonal	
Annona muricata	Stem Extract	CuO	UV-Visible, FTIR, XRD and SEM	XRD – 31-146nm	-	25
				SEM – 100nm	Spherical	

3. Phytochemicals:

The success of *Annona*-mediated green nanoparticle synthesis is fundamentally attributed to the rich diversity of bioactive phytochemicals present in various plant parts. These secondary metabolites serve multiple critical functions during nanoparticle formation, including reduction of metal ions, capping of nascent nanoparticles, and stabilization of the final colloidal system.

3.1. Polyphenols and Flavonoids:

Polyphenolic compounds and flavonoids represent the most frequently identified phytochemical classes responsible for nanoparticle synthesis. Chinnathambi et al. identified flavonoids and phenolics as the primary reducing and capping agents in *A. reticulata* fruit-mediated Ag NP synthesis.[26] Ezealisiji et al. demonstrated that polyphenols, flavonoids, and lignins from *A. muricata* root bark act as reducing and capping agents, with antioxidants, particularly polyphenols, reducing Ag^+ to Ag^0, while alkaloids and flavonoids primarily serve as stabilizing and capping agents.[20] Mokhtar et al. identified functional groups including OH, C aliphatic, and C=O from phenolic acids and flavonoids, along with polyphenols and aromatic compounds, as responsible for reduction reactions and stabilization during Ag NP formation.[27]

3.2. Alkaloids:

Alkaloids, characteristic secondary metabolites of *Annona* species, contribute significantly to nanoparticle stabilization. Ezealisiji et al. specifically noted that alkaloids and flavonoids primarily serve as stabilizing and capping agents, facilitating the formation of spherical, discrete silver nanoparticles.[20] The presence of alkaloids in *Annona* extracts is well-documented, with species like *A. muricata* containing diverse alkaloid profiles including isoquinoline and aporphine derivatives.

3.3. Functional Groups:

FTIR analysis across multiple studies has consistently identified key functional groups involved in nanoparticle synthesis. Mokhtar et al. detected OH groups, C aliphatic bonds, C=O bonds, polyphenols, and aromatic compounds through FTIR measurements, indicating their involvement in reduction and stabilization.[27] These functional groups provide electron-donating capacity essential for metal ion reduction and surface coordination for nanoparticle stabilization.

3.4. Proteins and Enzymes:

Proteinaceous compounds present in plant extracts can serve as both reducing and stabilizing agents. The presence of amide bonds and amino acid residues provides multiple coordination sites for metal ion binding and reduction.

3.5. Specific Compounds Identified:

GC-MS analysis by Santhosh et al. identified specific compounds in *A. muricata* leaf extract, including dioctyl phthalate (21.23%) and tetracosane (9.63%).[28] González-Pedroza et al. identified the lactone functional group in A. *muricata* leaf and fruit peel extracts as likely reducing agents for Ag NP biosynthesis.[29] Ruddaraju et al. noted that *A. squamosa* possesses renowned phytochemicals with medicinal properties, proposing that mounting of secondary metabolites onto ZnO nanoparticles during synthesis acts as reducing, stabilizing, and capping agents.[30]

4. Applications of *Annona*-Mediated Nanoparticles:

4.1. Antimicrobial Activities:

Annona-mediated nanoparticles demonstrate potent antimicrobial activities against diverse bacterial and fungal pathogens, positioning them as promising alternatives to conventional antibiotics in an era of increasing antimicrobial resistance.

4.1.1. Antibacterial Activity Against Gram-Positive Bacteria:

Multiple studies have documented strong activity against Gram-positive bacteria. Santhosh et al. reported that *A. muricata* leaf-derived AgNPs exhibited antibacterial activity against Gram-positive bacteria with zones of inhibition exceeding 24 mm.[28] Ezealisiji et al. demonstrated significant activity against *Bacillus subtilis* and *Staphylococcus aureus*, with zones of inhibition ranging from 10.00 to 20.00 mm at 5 µg/mL, increasing to 26.00 mm at 10 µg/mL.[20] Maulana et al. reported inhibition zones of 15.7 mm against *S. aureus* for *A. squamosa* bark-derived CuNPs.[31] Velidandi et al. demonstrated antibacterial potential against *S. aureus* with a zone of inhibition of 10.05 ± 0.17 mm.[32]

4.1.2. Antibacterial Activity Against Gram-Negative Bacteria:

Gram-negative bacteria, often more resistant due to their outer membrane, are also susceptible to *Annona*-mediated nanoparticles. Santhosh et al. demonstrated activity against Gram-negative bacteria with zones exceeding 24 mm.[28] Ezealisiji et al. reported activity against *Klebsiella pneumoniae*, *Escherichia coli*, and *Pseudomonas aeruginosa*, with *P. aeruginosa* being most susceptible.[20] Maulana et al. achieved inhibition zones of 12.3 mm against *E. coli* for CuNPs.[31] Mokhtar et al. tested antimicrobial activity against *P. aeruginosa* and *E. coli*, demonstrating synergistic effects with gentamicin, producing zones of inhibition up to 20 mm for *P. aeruginosa* and 19 mm for *E. coli*.[27] Velidandi et al. reported activity against *E. coli* with a zone of 9.86 ± 0.24 mm.[32]

4.2. Anticancer Properties:

Annona-mediated nanoparticles exhibit significant anticancer properties with selective cytotoxicity against various cancer cell lines while maintaining biocompatibility with normal cells.

4.2.1. Breast Cancer:

González-Pedroza et al. evaluated antiproliferation activity against breast cancer cell lines, demonstrating that *A. muricata* peel-derived AgNPs achieved destruction of cancer cells at concentrations not exceeding 3 μg/mL.[29] Mahmood et al. biosynthesized copper oxide nanoparticles that induced cytotoxicity and apoptosis in breast cancer cell lines.[33] Maulana et al. reported anticancer activity against MCF-7 breast cancer cells with IC_{50} of 130.39 mg/L for *A. squamosa* bark-derived CuNPs.

4.2.2. Colon Cancer:

Shaniba et al. reported selective cytotoxicity of *A. muricata* root extract-derived AgNPs against HCT116 colon cancer cells without affecting normal human lymphocytes and erythrocytes.[34] Flow cytometry, qRT-PCR analysis of apoptotic genes (PUMA, caspase-3, -8, -9, Bax, Bcl-2), and western blots (p53, p21, cleaved PARP, caspase-3, -9) revealed apoptosis-related cytomorphological changes, elevated ROS levels, decreased colony formation, and induction of mitochondrial apoptosis. Aziz et al. demonstrated cytotoxicity of *A. muricata* fruit-derived ZnO nanoparticles against colon carcinoma cells.[35]

4.2.3. Cervical Cancer:

Santhosh et al. reported cytotoxic activity against HeLa cervical cancer cells with IC_{50} of 36.53 μg/mL for *A. muricata* leaf-derived AgNPs, causing membrane damage and cell shrinkage.[28] Mokhtar et al. demonstrated potent cytotoxicity of *A. squamosa*-derived AgNPs on HeLa cells with IC_{50} values from 0.001 to 1.6 μg/mL, inducing significant apoptosis.[27] Ruddaraju et al. assessed anticancer potential of *A. squamosa* leaf-derived ZnO nanoparticles against HeLa cells.[30]

4.2.4. Ovarian and Prostate Cancer:

Mokhtar et al. evaluated cytotoxic activity against SKOV3 ovarian cancer and PC3 prostate cancer cells, with *A. squamosa* extract and Ag NPs showing potent cytotoxicity (IC_{50}s from 0.001 to 1.6 μg/mL).[27]

4.3. Anti-Inflammatory Activity:

Velidandi et al. demonstrated protein denaturation inhibition (IC_{50} 58.54 ± 1.28 μg/mL) for silver-silver chloride nanoparticles [32] indicating anti-inflammatory potential relevant for treating inflammatory diseases.

4.4. Antifungal Activity:

Annona-mediated nanoparticles also exhibit antifungal properties. Mokhtar et al. tested activity against *C. albicans*, with *A. squamosa*-derived Ag NPs achieving MIC of 0.093 mg/mL.[27] Maulana et al. reported inhibition zones of 13.9 mm against *C. albicans* for *A. squamosa* bark-derived Cu NPs.[31]

5. Benefits of using *Annona* Species:

Annona species rich and varied phytochemical profile makes them extremely useful biogenic resources for the synthesis of nanoparticles. Flavonoids, phenolics, alkaloids, terpenoids, and acetogenins are examples of compounds that work in concert as reducing, capping, and stabilizing agents to enable controlled nanoparticle formation without the need for external chemical additives. Flexibility in synthesis strategies and material selection is made possible by the availability of several usable plant parts, including leaves, fruits, peels, seeds, roots, and bark. Crucially, phytochemicals that are retained on the surface of the nanoparticles improve biological performance, leading to better functionality than nanoparticles made using traditional chemical or physical methods. Multifunctional nanomaterials with simultaneous antimicrobial, anticancer, antioxidant, and catalytic activities are created by combining nanoscale characteristics with bioactive derived from plants.

6. Economic and Environmental Benefits:

Green synthesis of nanoparticles by the Annona species has many environmental and economic benefits. The procedure does not involve the use of toxic reagents and harmful stabilizers, which can result in the production of chemical waste and environmental pollution. The procedure carried out at room temperature or low temperature requirements is environmentally friendly as it consumes low energy, and the use of extracts derived from water helps to eliminate the use of the harmful organic solvent.

Annona plants are readily accessible and cheap. This makes economic sense from the point of view of material cost. The use of agricultural by-products such as fruit peels and seeds adds economic value to agricultural wastes and promotes the concept of the circular economy. Furthermore, the easy methods involved in the synthesis of Annona nanoparticles make them less dependent on expensive laboratory equipment and specialized knowledge. The versatile use of Annona nanoparticles further makes them less dependent on individual substances, which presents economic advantages.

7. Future Perspectives:

For future studies on the synthesis of nanoparticles via Annona, the mechanism behind the process that involves the usage of phytochemicals in nanoparticle synthesis should be given more emphasis. A lot more research is required in understanding the kinetics of reducing agents and hence, the process of stabilizing the formed nanoparticles. Standardization of extraction as well as synthesis procedures will be very essential in making the studies more comparable.

Investigation of other Annona species with less attention, other than A. muricata, A. squamosa, and A. reticulata, may help in designing materials for their applications. Building complex nanostructures like bimetallic nanoparticles and core shell nanostructures may prove to be a prospective area for their applications in biomedicines as well as environmental fields. Toxicology analysis and regulatory acceptance for their safe implementation in their applications may need equal emphasis in future research as well.

CONCLUSION

This review highlights *Annona* species as valuable and sustainable biological resources for the green synthesis of functional nanoparticles. The rich phytochemical composition of *Annona* plants enables efficient reduction and stabilization of metallic and metal oxide nanoparticles without the use of toxic chemicals, while also enhancing their biological performance. Research on *A. muricata*, *A. squamosa* and *A. reticulata*, clearly demonstrates the versatility of this genus across a wide range of nanoparticle systems. The use of renewable plant materials, including agricultural by-products, supports environmentally responsible and cost-effective nanoparticle production. However, challenges related to reproducibility, limited mechanistic insight, large-scale production, and regulatory approval still need to be addressed. Focused mechanistic studies and improved process optimization will be crucial for advancing *Annona*-mediated nanoparticle synthesis from laboratory research toward practical biomedical and industrial applications.

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