**NANOTECHNOLOGY**

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**INTRODUCTION**

In last few decades nanotechnology has delivered extensive researchwith emergence in Engineering, Biotechnology, Food-technology,medical sciences and Agriculture. It also forming impact on all formsof life with significant advances owing to wide range of applicationsin the field of electronics, optical fibers, sensors, semi-conductors,automobiles, nano-fabrics, bio-medical, catalysts, agriculture,cosmetics, packaging, bio-engineering, medicines, drug delivery, andother areas [Baker, 2012; Iravani, 2011; Song, 2009; Shankar et al., 2004]. In 1959 the concept ofnanotechnology was first begun; when Richard Feynman conveyed avisionary and prophetic speech at a meeting of the American PhysicalSociety, where he speculated on the possibility and potential of Nanosized materials [Feynman, 1960].

The classic laws of science are different at the nanoscale.Nanoparticles possess large surface areas and essentially no innermass, i.e., their surface-to-mass ratio is extremely high. Nanoscienceis based on the knowledge that particles in the nanometer range,and nanostructures or Nano machines that are developed from thesenanoparticles possess special properties and exhibit unique behavior.These special properties, in conjunction with their unique behavior,can significantly impact physical, chemical, electrical, biological,mechanical, and functional properties [Mukhopadhyay, 2014]. The uses of nanomaterialsspecifically for the agricultural purposes are required for improving thefertilization process, increase in yields through nutrient optimizationand minimized the requirements of plant protection products [Huang et al., 2015]. Almost every industry, including research, engineering, medicine, and health, uses nanotechnology. Despite the fact that nanotechnology is still in its early stages, the consumer market is already bursting with products "nanotechnology enhanced"[Murty et al., 2013].The development of multiple spectroscopic methods has accelerated nanotechnology research and invention. In 1982, IBM researchers produced scanning tunneling microscopy (STM), which made it possible to capture images of a single atom on ''flat'' (i.e., surface without a tip)[Binnig, 1982].While the evolution of nanotechnologies is a contemporary multidisciplinary science encompassing the disciplines of physics, chemistry, biology, and engineering, the creation of NPs by both nature and people dates back to the time before the advent of Christ. For instance, the Romans used metals of nanometric dimensions to make glass. The renowned Lycurgus cup, which is on display at the British Museum and changes color depending on whether it is lit from the outside (green) or from the inside (red), includes NPs of silver andgold[[http://britishmuseum.org/](http://www.britishmuseum.org/), 2015].

Ordinary materials frequently display novel and unpredictable characteristics when sized to the nanoscale, involving extraordinary strength, chemical reactivity, electrical conductivity, superparamagnetic behavior, and other properties that the same material does not have at the micro- or macroscale. Currently, a wide variety of nanomaterials are manufactured on an industrial scale, while others are produced at lesser quantities since they are still in the research and development stage (table 1.1) [JRC Reports., 2010]

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| --- | --- | --- |
| AluminumAluminum oxideAluminum hydroxideAntimony oxideAntimony pentoxideBarium carbonateBismuth oxide Boron oxideCalcium oxideCarbon blackCerium oxideChromium oxideCluster diamondsCobalt and cobalt oxideColloidal goldCopper (II) oxide | DendrimersDimethyl siloxideDysprosium oxideFullerenesGermanium oxideIndium oxideIron and iron oxidesLanthanum oxideLithium titanateManganese oxideMolybdenum oxideNanoclaysNeodymium oxideNickelNiobiumPalladium | PlatinumPolyethylenePolystyrenePraseodymium oxideRhodiumSamarium oxideSilanamineSilicon dioxideSilverCarbon nanotubesTantalumTerbium oxideTitanium dioxideTungstenYttrium oxideZinc oxide |

With an emphasis on the synthetic production and biological techniques of designing nanoparticles, nanotechnology is a significant new field of study that has gained popularity in recent years with substantial momentum in establishing the nano revolution, due to their extensive applications [Abou El-Nour et al., 2010]. Nanoparticles' uses are developing quickly in a variety of fields, including biomedicine, pharmaceuticals, catalytic processes, drug delivery, and antimicrobial research, because of their completely new or improved characteristics [Heiligtag, 2013]. The nanoparticle has been recognized and purified using liquid chromatography with a photo diode array detector. Chromatography is necessary to purify the nanoparticles as the biosurfactants and biosurfactant stabilized nanoparticles are generated during nanoparticle synthesis or biosynthesis as well as coating nanoparticles [Singh et al., 2017].

**Approach in synthesis of nanomaterials:**

*Top-down approaches*

Bulk materials are separated in top-down methods to create nanostructured materials. Mechanical milling, laser ablation, etching are some top-down techniques.

**Mechanical milling**

A practical method for creating materials at the nanoscale from bulk materials is mechanical milling. In order to create blends of various phases and to create nanocomposites, mechanical milling is a useful technique [Zhuang et al., 2016]. Aluminum alloys enhanced by oxide and carbide, spray coatings that resist wear, nanoalloys based on aluminum, nickel, magnesium, and copper, and a variety of other nanocomposite materials are all produced mechanically [Prasad Yadav et al., 2012].



The principle of the ball milling method. Reprinted with permission from ref. 25. Copyright: r2016, John Wiley & Sons, Ltd.

**Lithography**

Lithography is a practical method for creating nanoarchitectures with a concentrated electron or light beam. Masked and maskless lithography are the two primary categories of lithography [Pimpin and Srituravanich, 2012]. In masked nanolithography, nanopatterns are transferred over a large area using a specific mask or template [Szabo et al., 2013].

In maskless lithography, arbitrary writing of nanopatterns is done without a mask. 3D freeform micro nanomachining can be achieved by ion implantation with a focused ion beam combined with wet chemical etching [Garg et al., 2020].



A schematic diagram of the fabrication of 3D micro-nanostructures with an ion beam through bulk Si structuring. This involves implantation in Si through Ga FIB lithography and mask-writing at nanometer resolution, subsequent anisotropic wet etching in KOH solution, and the fabrication of Si micro-nanostructures via the selective removal of the unimplanted region.

**Laser Ablation**

Laser ablation synthesis involves the formation of nanoparticles using a strong laser beam on a target material. During the laser ablation process, due to the high energy of the laser radiation, the starting material or starting substance evaporates, resulting in the formation of nanoparticles. The use of laser ablation to produce precious metal nanoparticles can be considered a green technology because no stabilizers or other chemicals are required [Amendola and Meneghetti, 2009]. This technique can be used to produce a variety of nanomaterials, such as metal nanoparticles [Zhang et al., 2017], carbon nanoparticles[Ismail et al., 2020], oxide compounds[Duque et al., 2019] and ceramics[Su and Chang, 2018].

**Bottom-up Approaches:**

*Chemical vapor deposition*

Chemical vapor deposition methods play an important role in the creation of carbon-based nanomaterials. In CVD, a thin film is formed on the surface of the substrate through a chemical reaction of vapor phase precursors.A precursor is considered suitable for CVD if it has sufficient volatility, high chemical purity, good evaporation stability, low cost, harmless nature, and long shelf life [Jones and Hitchman, 2008].

To produce carbon nanotubes by CVD, the substrate is placed in an oven and heated to a high temperature. After that, carbon-containing gas (e.g., hydrocarbons) is slowly brought into the system as precursor molecules. At high temperatures, the decomposition of the gas releases carbon atoms, which join together on the substrate to form carbon nanotubes [Shah and Tali, 2016].

**Solvothermal and hydrothermal methods:**

The hydrothermal process is one of the best known and widely used methods for the production of nanostructured materials. In the hydrothermal method, nanostructured materials are obtained by a heterogeneous reaction carried out in an aqueous medium at high pressure and temperature around a critical point in a closed container [Wu et al., 2011; Cao et al., 2016; Li et al., 2015]. The solvothermal method is like the hydrothermal method. The only difference is that it is carried out in a non-aqueous environment. Hydrothermal and solvothermal methods are usually performed in closed systems [Chen and Holt-Hindle, 2010].

**Emergent field of Nanotechnology**

Numerous innovative uses for metal NPs have been investigated in a variety of fields. Metal NPs exhibit optical absorption, which is connected to the pattern of electronic vibrations on the metal NPs surface. Plasmons is a term used to define this occurrence [Prashant, 2013; Pradeep et al., 2011]. A remarkable model system for exploring the world of colloidal solutions was provided by gold NPs. The manufacture of sensors, electronic devices, and charge storage are just a few of the many uses for gold nanoparticles. The methods for creating monodisperse metal NPs with certain sizes and shapes are still limited, which presents a challenge to the scientific community [Kamlesh et al., 2012a; 2012b].

**Nano pesticides:**

With new techniques for creating innovative active components with nanoscale dimensions, as well as their formulation and administration, which are generally referred to as "nano pesticides," nanotechnology is emerging as a highly appealing study topic toward attaining these aims. Recent developments in the field of nano pesticide research can be summed up as the use of nanotechnology in crop protection. The study of the fundamental interactions between nanoscale materials and insects, the formulation of active ingredients into nano emulsions and dispersions using currently available pesticides, the development of new nano pesticide formulations using nanomaterials as active pesticide agents, or the use of these nanomaterials as nanocarriers for their delivery are all included in this field's broad research aspects [Benelli and Lukehart, 2017].To generate NPs in various shapes and chemical compositions, a wide range of substances, including metals, metal oxides, semiconductor quantum dots (QDs), carbon, ceramics, silicates, lipids, polymers, proteins, dendrimers, and emulsions, have been synthesized or utilized from natural resources [Puoci et al., 2008]. Some common advantages of NP-based pesticide formulations include: (a) increased solubility of water-insoluble active ingredients (b) increased formulation stability (c) elimination of toxic organic solvents in comparison to conventionally used pesticides (d) capability for slow release of active ingredients (e) improved stability to prevent their early degradation (f) improved mobility and higher insecticidal activity due to smaller particle size, and (g) substantial implementation of NP-based pesticide formulations [Sasson et al., 2007].

**Nanoencapsulation:**

A chemical, such as an insecticide, is distributed to a specific host plant through the process of nanoencapsulation to control insect pests. Similar to the case with bigger particles, pesticides can be properly absorbed by plants when they are nano encapsulated with nanoparticles [Scrinis and Lyons, 2007]. Additionally, this method can introduce DNA and other desired compounds into plant tissues to protect host plants against insect pests [Torney, 2009].

**Cancer Treatment:**

Advanced cervical carcinoma, one of the most common and aggressive gynecological illnesses in young women globally, is found in over 70% of cases [Catarino et al., 2015]. Targeted medication therapies use nanoparticles (NPs), which are less than 100 nm in size, to transport medicines. Additionally, because the NPs preferentially localize to cancer cell proliferation and readily enter tissue and molecular levels, they target specific polluted sites in order to transport effective amounts of cancer therapy [Vinardell and Mitjans, 2015; Monge-Fuentes et al., 2014; Prabakar et al., 2013]. The specific interactions between nanoscale materials and cell lines can promote the development of more effective and new strategies for lowering chemical concentrations and improving the responsiveness of cancer cells [Tang et al., 2014]. Different stages of apoptosis represent progression through programmed cell death. Recently, researchers looked into using cancer cells that had undergone cell death as a targeted novel treatment for anticancer medicines. A long history of anticancer drugs is readily available, and it is hoped that progressively potent treatments against malignant growth can be developed from commonly obtained therapeutically significant plants [Liu et al., 2014]. Secondary metabolites, which are derived chemicals from terpenoid indole alkaloids and are widely utilized around the world in conventional herbal medicine, are produced by the medicinal plant known as CR. Every year, this plant produces vincristine and vinblastine, the two majors anticancer vinca alkaloids used in chemotherapy regimens to treat various tumors. Traditional medicine uses CR to treat a variety of malignancies as well as skin conditions, menorrhagia, diabetes, hypertension, and cancer. Vinblastine to treat a certain type of cancer and Hodgkin's disease to oxidize leukemia [Pattarachotanant et al., 2014;Koul et al., 2013; Moudi et al., 2013].

**Synthesis of nanoparticles**

**Green Synthesis of Zinc Oxide Nanoparticles from Pomegranate (Punica granatum) Extracts:**

Pomegranate is known to contain a variety of essential biomolecule and metabolite components, including organic acid, polyphenol, flavonoid, anthocyanin, alkaloid, fatty acid and vitamin components. Its high phenolic content has been attributed to its antibacterial, antiseptic, antirheumatic and antioxidant capabilities. However, its efficacy is largely dependent on the stability, size and size distribution of the nanoparticle, its surface function, its morphology, its shape and the material used in its synthesis [Khezerlou et al., 2018; Ismail et al., 2012]. Zinc oxide nanoparticles are among the most well-understood inorganic metal oxides nanoparticles, due to their ability to withstand extreme environmental conditions, strong antimicrobial properties, and low human toxicity [Tang and Ly, 2014].

Zinc nitrate hexahydrate [Zn (NO3)2·6H2O] was used as a precursor to synthesize zinc oxide nanoparticles. Tryptic soy broth and Mueller–Hinton agar. All solutions were prepared using sterile distilled water. The leaves and flowers were washed separately with tap water to remove dust particles, then washed again with distilled water and dried for 4–6 days. The dried leaves and flowers were each separately shredded and ground to a fine powder, then stored in a properly labelled bottle for further use. Ten grams of the leaf and flower powder were weighed out and put into a well-labelled beaker, and 100 mL sterile double distilled water were added to each. The flower and leaf mixtures were heated for 20 min at 60 ◦C. The obtained extract was allowed to cool down and filtered using Whatman filter paper. The filtrate was collected in a well-labeled Erlenmeyer flask and stored at 4 ◦C.

 **Synthesis of Zinc Oxide Nanoparticles**

The 0.1 M zinc nitrate hexahydrate (Zn (NO3)2·6H2O) solution was prepared by dissolving 6.58g in 300 mL double-distilled water. Ten milliliters of the aqueous leaf and flower pomegranate extracts were each slowly added dropwise into the solution under magnetic stirring at 60 °C for roughly 2 h to obtain complex formation. The complex formed after stirring was collected and centrifuged at 10,000 rpm for 10 min and the pellets were collected. The separated pellets were dried in an oven at 80 °C for 8 h and preserved in airtight bottles for further studies. Biosynthesis of zinc oxide nanoparticles was carried out using pomegranate leaves and flower extract and zinc nitrate hexahydrate as a precursor. On addition of the plant extracts (leaf and flower) with a greenish and pinkish-brown color, respectively, to the colorless zinc nitrate hexahydrate solution, a yellowish-white precipitate occurred, indicating the presence of zinc oxide nanoparticles [Rajakumar et al., 2017].

**Gold nanoparticles:**

Gold nanoparticles are a highly sought-after material for researchers due to their compact size, increased surface area-to-volume ratio, magnetic properties, chemical properties, and electronic characteristics. Due to their long-standing medical applications, such as cancer treatment and biocompatibility, gold nanoparticles occupy a prominent position among metallic nanoparticles. Generally, gold nanoparticles are synthesized using physical and chemical methods with well-characterized morphology and size [Magudapathy et al., 2001; Bhattacharya et al., 2008].

**Green synthesis of Au Nanoparticles:**

Nanoparticle synthesis processes that are both environmentally friendly and cost-effective are of great interest to biology, chemistry and materials scientists, particularly in the context of the search for more sustainable methods of synthesis of inorganic materials. Furthermore, the utilization of plants as traditional medicinal products is highly prevalent among local populations, thus these two criteria could potentially lead to the discovery of a variety of plants with intriguing properties [Morel et al., 2017].

**Molecular methodology:**

Materials used for the synthesis of gold and silver nanoparticles are chloroauric acid (HAuCl4), silver nitrate (AgNO3), and Neem (Azadirachta indica) leaf broth prepared by taking 20 g of thoroughly washed and finely cut A. indica leaves in a 500-mL Erlenmeyer flask with 100 mL of sterile distilled water and then boiling the mixture for 2 min before finally decanting it. For reduction of Ag+ ions, 5 mL of Neem leaf broth was added to 45 mL of 10−3 M aqueous AgNO3 solution. Similarly, 5 mL of Neem leaf broth was added to 45 mL of 10−3 M HAuCl4 solution for reduction of AuCl− 4 ions. For synthesis of Ag–Au bimetallic nanoparticles, 90 mL of a 1:1 10−3 M solution of AgNO3 and HAuCl4 was taken along with 10 mL of Neem broth. The reduction of pure Agand Au3+ ions and that of the 1:1 Ag+: AuCl− 4 mixture was monitored by measuring the UV–vis spectra of the solution at regular intervals after diluting a small aliquot (0.2 mL) of the sample 20 times. The Ag, Au, and Au–Ag nanoparticles synthesized after 24 h of reaction of the different salt solutions with the Neem leaf broth were centrifuged at 10,000 rpm for 15 min, following which the pellet was redispersed in sterile distilled water to get rid of any uncoordinated biological molecules. The process of centrifugation and redispersion in sterile distilled water was repeated three times to ensure better separation of free entities from the metal nanoparticles [Shiv Shankar et al., 2004].

**Nanoformulation**

The traditional formulation is originally created using emulsifiable concentrate (EC) or wettable powder (WP) powder mixtures in simple solvent-based solutions. To create homogenous and isotropic dispersions of the formula, new generation formulations may be created using the oil-in-water (EW) emulsion and the microemulsions (MEs) formula [Shao et al., 2018; Patzke and Schieber, 2018; Chin et al., 2012; Puripattanavong et al., 2013; Knowles, 2007; Pirzada et al., 2020; Waghmare et al., 2007]. Typically, slow-release mechanisms are used in nanoformulation and nanoencapsulation delivery formulae to increase efficacy and preserve the durability of the active components on the targets [Kumar et al., 2019; Lade et al., 2019]. Currently, many advancements in the creation of bioinsecticide compounds have been made possible by nanotechnology. Nanotechnology-based biopesticide formulations improve application efficiency and increase delivery efficacy. It is well knowledge that smaller particle sizes increase the active ingredient's surface area and hence enhance its solubility. The issues also include formula stability, mobility, and maintaining the delivery target system while creating the synthesis of the water-based medium [Khandelwal et al., 2021]. The construction of pesticide nanoformulations involves the utilization of a wide range of organic components. To enable delivering active chemicals to the target location, two types of formulations—nanoparticle insecticides and nano-carrier systems—are available. A nanoparticulate polymeric shell, adsorption onto the nanoparticle surface, ligand binding to the nanoparticle core, and entrapment inside the polymeric matrix are all components of the delivery system's structure [Kapinder et al., 2021].

**Applications of Nanotechnology**

**Reproductive medicine:**

*Detection and treatment of cancer: nanobiosensors, contrast agents and targeted delivery tools*

In most topographical areas of the world, reproductive cancers are among the most frequently diagnosed malignancies. Prostate cancer is the most common form of malignancy in men and the second biggest cause of cancer-related mortality in developed nations. Reproductive cancer, comprising ovarian, uterine, and cervical types, routinely ranks among the twenty most common and deadly diseases in women worldwide [National Statistics; US Cancer Statistics, 2013]. In many areas of bio detection, such as the identification of antigens, proteins, nucleic acids, and reactive oxygen and nitrogen species, the use of nano biosensors—which quickly and directly transform the numerous simultaneous biological events (binding and/or reactions) into electronic signals without requiring additional labeling steps—has proven beneficial. This strategy has recently been effectively used in reproductive oncology. For the detection of both well-established and new cancer biomarkers, such as cancer antigen 125 (CA-125) and human epididymis secretory protein 4 (HE4) for ovarian cancer and prostate-specific antigen (PSA) for prostate cancer, respectively, nanoparticle (NP)-based biosensors are now being widely used [Medina-Sanchez et al., 2012; Perfezou et al., 2012; Kumar et al., 2013; Yuan et al., 2012]. Chemotherapeutics can be delivered using nanomaterials in a way that significantly improves their effectiveness and lowers their systemic toxicity. Numerous studies have shown the potential of different types of NPs, including PLGA and PLA derivatives, bovine serum albumin, magnetic, iron, and gold, functionalized with various targeting ligands, including follicle-stimulating hormone receptor-binding peptides, folates, and aptamers, to facilitate the delivery of chemotherapeutic agents into ovarian, endometrial, and prostate cancer cells [Le Broc-Ryckewaert et al., 2013; Dhar et al., 2008; Liang et al., 2011; Zhao et al., 2010; Lee et al., 2013; de Oliveira et al., 2013; Zhang et al., 2013].

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| Reproductive oncology | Non-cancer conditions |
| Cancer detection: | • Endometriosis |
| • Nanobiosensors for cancer biomarkers | ○ Contrast agents for MRI |
| • Contrast agents for clinical diagnostic imaging | ○ Targeted delivery of experimental treatment agents, including gene therapy |
| Cancer treatment: | • Uterine fibroids |
|  • Targeted delivery for improved efficacy and decreased toxicity | ○ Nanosensitisation during minimally-invasive surgery |
|  • Combined therapy: simultaneous delivery of therapeutic payloads | ○ Targeted delivery of experimental treatment agents |
| • Reversal of resistance to chemotherapy | • Ectopic pregnancy andtrophoblastic diseases |
| •Nanosensitisation: potentiation of antitumor effect of chemotherapy by simultaneous exposure of cancer cells to nanomaterials | ○ Targeted delivery of chemotherapy drugs |
| • Effective delivery of drugs with poor biodistribution profile | • Drug delivery systems |
| • Experimental gene therapy | ○ Topical○ Transdermal○ Transplacental○ Intravaginal |

**Non-cancer applications: diagnostic imaging and alternatives to surgical treatment**

**Endometriosis:**

Endometriosis is a chronic gynecological condition that affects 2%–22% of women of reproductive age and is characterized by the presence of endometrial-like tissue outside of the uterine cavity. It can cause mild to severe pelvic discomfort and/or infertility. Endometriosis has been shown in recent large-scale epidemiological research to have a profoundly detrimental influence on health-related quality of life and job productivity, which is aggravated by an average diagnostic delay of 7 to 10 years across all healthcare levels [Johnson and Farquhar, 2007; Kennedy et al., 2005; Nnoaham et al., 2011; Hudelist et al., 2012]. Due to the absence of sensitive blood biomarkers and restrictions associated with imaging tools, such as ultrasound and MRI, in peritoneal endometriosis, early non-invasive detection of this illness is still very difficult [Stratton et al., 2003]. Recently, a rat model of surgically induced endometriosis was used to test the effectiveness of intravenously delivered ultra-small superparamagnetic iron oxide nanoparticles (USPIO-NPs) as MRI signal enhancers. Due to the USPIO-NPs' affinity for macrophages, MRI applications may now be extended to the identification of ectopic endometrial lesions without a clear haemorrhagic component, such as pelvic adhesions or intraperitoneal implants.A potential method for the non-invasive diagnosis of endometriosis, according to study results, is the use of USPIONPs, which boosted the diagnostic precision of MRI in the detection of non-haemorrhagic ectopic endometrial lesions [Lee et al., 2012].

**Uterine fibroids:**

The benign hormone-dependent tumors known as uterine fibroids (leiomyomas) are derived from the smooth muscle cells of the myometrium. Between 60% and 80% of women of reproductive age are affected with leiomyomas, which are the most common kind of pelvic tumor. Clinical signs of the condition include abnormal uterine bleeding, anemia, genitourinary problems, and infertility, which together lower the quality of life in terms of health.

The majority of current uterine fibroids treatments are surgical and include a variety of more invasive procedures: targeted ultrasound ablation, uterine artery embolisation, myomectomy, and eventually hysterectomy. Nanomaterial-mediated delivery of anti-tumour cytokines has been investigated for the improvement of selectivity and potentiation of the effects of minimally-invasive surgical removal of fibroids [Laughlin et al., 2010; Williams et al., 2006; Falcone and Parker, 2013].

**Conclusion**

Researchers and scientists working in several fields have been drawn to nanotechnology and nanoscience. The environmental destiny of active compounds is likely to be significantly impacted by nanoformulations, and novel substances whose environmental fate is unknown are also expected to be discovered. To identify, classify, and measure the active component and adjuvants coming from nanoformulations, advanced technology is required. The need for detailed risk evaluations of nanopesticides is urgent. In order to assess the risk posed by nanoparticles, it is also necessary to conduct research on environmental the future and to analyze it under various circumstances. Plant extracts promise an environmentally benign way to prepare AuNPs that has several uses in various scientific domains and, ultimately, in daily life. For the production of shape- and size-controlled nanoparticles, green sources act as a reducing and stabilizing agent. Future prospects for plant-mediated nanoparticle preparation include scaling up laboratory-based research to an industrial level, elucidating the phytochemicals used in the preparation of the nanoparticles using bioinformatics tools, and determining the precise mechanism used to inhibit pathogenic bacteria. The plant-based nanoparticle has several uses in the pharmaceutical, food, and cosmetic sectors and has consequently grown to be a significant topic of study.

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