NANOTECHNOLOGY

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INTRODUCTION

Nanotechnology has produced extensive research in the previous eras, with applications in engineering, biotechnology, food technology, medical sciences, and agriculture. A widespread in the fields of electronics, optical fibers, sensors, semi-conductors, automobiles, nano-fabrics, bio-medical, catalysts, agriculture, cosmetics, packaging, bio-engineering, medicines, drug delivery, and other fields have a significant impact on all forms of life [Baker, 2012; Iravani, 2011; Song, 2009; Shankar et al., 2004]. When Richard Feynman gave a visionary and prophetic speech at an American Physical Society meeting in 1959, he first introduced the idea of nanotechnology. He speculated on the potential and possibility of nanosized materials [Feynman, 1960].

At the nanoscale, the conventional laws of science are altered. Nanoparticles have a very high surface-to-mass ratio as they have very little inner mass and a large surface area. Nanoscience is built on the understanding that things with a diameter of less than one nanometer, along with the nanostructures or nanomachines made from them, have unique properties and behaviors. They can have a substantial on the physical, chemical, electrical, biological, mechanical, and functional properties due to their special characteristics and distinctive behavior [Mukhopadhyay, 2014]. Nanomaterials are to be used explicitly for agricultural applications to improve fertilization, boost yields through nutrient optimization, and lessen the need for plant protection products [Huang et al., 2015]. Practically all industry, uses nanotechnology including research, engineering, medicine, and health. Despite the fact that nanotechnology is silent in its early stages, the user market is previously bursting through products "nanotechnology enhanced" [Murty et al., 2013]. The growth of multiple spectroscopical methods has augmented nanotechnology examine and invention. In 1982, IBM researchers produced scanning tunneling microscopy (STM), which made it probable to capture images of a only atom on "flat" (i.e., surface without a tip) [Binnig, 1982]. Although 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 liable on whether it is lit after the outside (green) or from the inside (red), includes NPs of silver and gold [http://britishmuseum.org/, 2015].

When scaled down to the nanoscale, common materials frequently revelation novel and unpredictable properties, including extraordinary strength, chemical reactivity, electrical conductivity, superparamagnetic behavior, and other traits that the similar material does not have at the micro- or macroscale. Many different kinds of nanomaterials are currently produced on an industrial scale; others, which are still in the investigate and progress stage, are produced in smaller quantities (table 1.1) [JRC Reports., 2010].

Aluminum	Dendrimers	Platinum
Aluminum oxide	Dimethyl siloxide	Polyethylene
Aluminum hydroxide	Dysprosium oxide	Polystyrene
Antimony oxide	Fullerenes	Praseodymium oxide
Antimony pentoxide	Germanium oxide	Rhodium
Barium carbonate	Indium oxide	Samarium oxide
Bismuth oxide	Iron and iron oxides	Silanamine
Boron oxide	Lanthanum oxide	Silicon dioxide
Calcium oxide	Lithium titanate	Silver
Carbon black	Manganese oxide	Carbon nanotubes
Cerium oxide	Molybdenum oxide	Tantalum
Chromium oxide	Nanoclays	Terbium oxide
Cluster diamonds	Neodymium oxide	Titanium dioxide
Cobalt and cobalt oxide	Nickel	Tungsten
Colloidal gold	Niobium	Yttrium oxide
Copper (II) oxide	Palladium	Zinc oxide

With an emphasis on the synthetic production and biological techniques of designing nanoparticles, nanotechnology is a significant innovative of study that has become more well-known 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].

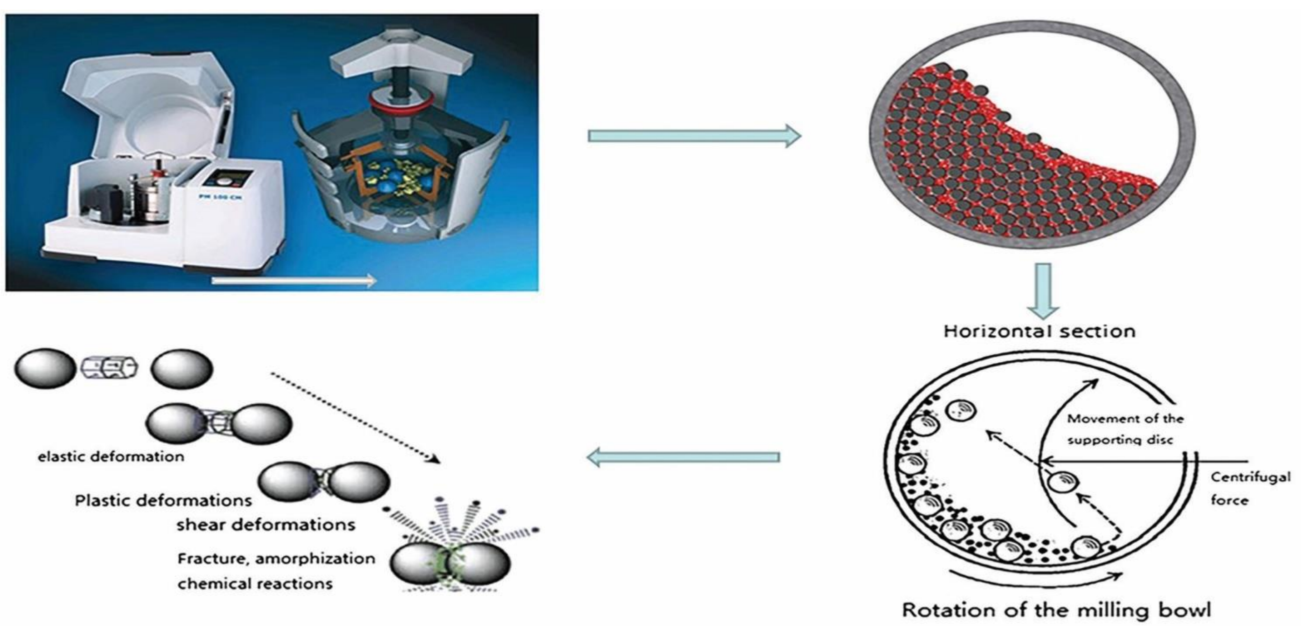
Approach in synthesis of nanomaterials:

Top-down approaches

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

Machine-driven pounding

An applied method for making materials at the nanoscale from bulk materials is machine-driven pounding. Mechanical milling is an effective method for producing blends of different phases and nanocomposites [Zhuang et al., 2016]. Mechanical production is used to create a variety of nanocomposite materials, including aerosol coatings that resist wear, nanoalloys based on aluminum, nickel, magnesium, and copper, and many others [Prasad Yadav et al., 2012].

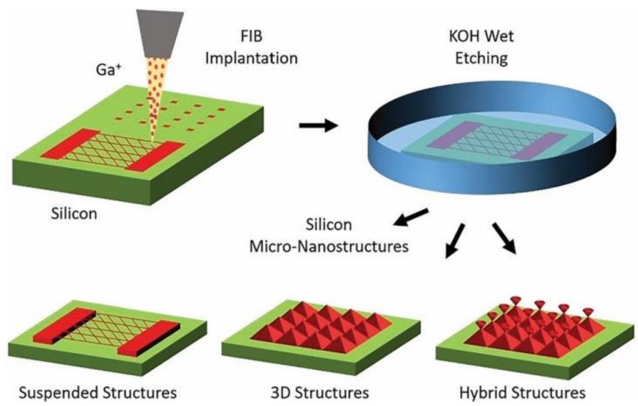


The ball milling method's basic idea. Reprinted from ref. 25 with permission. John Wiley & Sons, Ltd., 2016-2017.

Lithography

Lithography uses a focused electron or light beam to create nanoarchitectures in a practical way. The two main subcategories of lithography are mask- and maskless-lithography [Pimpin and Srituravanich, 2012]. Using a specific mask or template, nanopatterns are transferred over a sizable area in masked nanolithography [Szabo et al., 2013].

In maskless lithography, nanopatterns are written arbitrarily without the use of a mask. By combining wet chemical etching and ion implantation with a focused ion beam, 3D freeform micro nanomachining can be accomplished [Garg et al., 2020].



An illustration showing how bulk Si structuring with an ion beam can be used to create 3D micro-nanostructures. This involves anisotropic wet etching in KOH solution, anisotropic implantation in Si using Ga FIB lithography, mask writing at nanometer resolution, and fabrication of Si micro-nanostructures by selectively removing the un-implanted region.

Laser Ablation

Laser removal synthesis the formation of nanoparticles using a strong optical maser ray on a target material. During the laser removal process, owing to the high energy of the laser radiation, the starting material or starting substance evaporates, subsequent formation of nanoparticles. The use of laser ablation to produce precious metal nanoparticles can be measured a green technology since 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

Methods of chemical vapor deposition are crucial in the production of nanomaterials based on carbon. In CVD, a thin film is created on the substrate's surface by a chemical reaction involving precursors from the vapor phase. According to Jones and Hitchman (2008), a precursor is deemed suitable for CVD if it has enough volatility, high chemical purity, good evaporation stability, low cost, harmless nature, and a long shelf life.

The substrate is heated to a high temperature in an oven to create carbon nanotubes by CVD. Then, carbon-containing gas is gradually introduced into the system as precursor molecules, such as hydrocarbons. Carbon atoms are released when the gas decomposes at high temperatures, and they come together on the substrate to form carbon nanotubes [Shah and Tali, 2016].

Solvothermal and hydrothermal methods:

One of the most well-known and habitually used phases for inventing nanostructured materials is the hydrothermal process. By performing a heterogeneous reaction in an aqueous medium at high pressure and temperature near a critical point in a closed container, the hydrothermal method produces nanostructured materials [Wu et al., 2011; Cao et al., 2016; Li et al., 2015]. Similar to the hydrothermal method is the solvothermal method. The only distinction is that it takes place in a dry environment. The majority of the time, closed systems are used to conduct hydrothermal and solvothermal methods [Chen and Holt-Hindle, 2010].

Emergent field of Nanotechnology

Numerous innovative uses for metal NPs have been studied in a variety of fields. Metal NPs exhibit optical absorption, which is connected to the pattern of automated vibrations on the metal NPs surface. Plasmons is a term used to define this occurrence [Prashant, 2013; Pradeep et al., 2011]. A typical system for reconnoitering the world of colloidal resolutions 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 through nanoscale dimensions, as well as their invention and administration, which are generally denoted to as "nano pesticides," nanotechnology is emergent as an extremely 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 investigation of 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 designs consuming nanomaterials as vigorous 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]. A wide range of materials, including metals, metal oxides, semiconductor quantum dots (QDs), carbon, ceramics, silicates, lipids, polymers, proteins, dendrimers, and emulsions, have been synthesized or used as natural resources to produce NPs in a variety of shapes and chemical compositions [Puoci et al., 2008]. The following are some common benefits of NP-based pesticide formulations: (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) ability 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 (g) substantial impurity removal [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]. Moreover, plants against insect pests are protected in plant tissues by using desired compounds and this technique can present DNA [Torney, 2009].

Cancer Treatment:

Progressive cervical carcinoma, one of the utmost communal and antagonistic gynecological diseases in early 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 differently contain 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]. Cell line and nanoscale materials can interact specifically to promote the growth 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, scientists investigated the use of cancer cells that had experienced 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]. Subordinate metabolites, are consequent 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 Pomegranate (Punica granatum) Extracts derived from Zinc Oxide Nanoparticles:

Pomegranate is known to contain a diversity of essential biomolecule and metabolite components, including organic acid, polyphenol, flavonoid, anthocyanin, alkaloid, fatty acid and vitamin components. Its high phenolic compound has been attributed to its antibacterial, antiseptic, antirheumatic and antioxidant capabilities. However, its efficacy is mostly 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].

The precursor used to create zinc oxide nanoparticles was zinc nitrate hexahydrate [Zn (NO3)26H2O]. Soy tryptic and Mueller-Hinton agar. Sterilized distilled water remained stood for each solution. To remove dust, the leaves and flowers were washed distinctly with tap water, once washed more with distilled water, and then permitted to dry for a minimum of four to six days. Separately shredding and powdering the dried leaves and flowers, they were then placed in a bottle with the appropriate labeling and stored for later use. 100 mL of sterile, twice-distilled water were added to each of the beakers after each contained 10 grams of the leaf and flower powder that had been weighed out and labeled. The mixtures of flowers and leaves were heated for 20 minutes at 60 °C. After allowing the extract to cool, Whatman filter paper was used to filter it. The filtrate was collected and kept at 4 °C in an Erlenmeyer flask with clear labels.

Combination of Zinc Oxide Nanoparticles

6.58g of zinc nitrate was softened in 300 mL of double-distilled water to create the 0.1 M zinc nitrate hexahydrate solution (Zn (NO3)26H2O). To achieve complex formation, ten milliliters of the aqueous pomegranate leaf and flower extracts were each gradually added dropwise into the solution while being magnetically stirred at 60 °C for about two hours. The pellets, after the complex was collected and centrifuged at 10,000 rpm for 10 min. Pomegranate leaf and flower extract was used as a starting material for the biosynthesis of zinc oxide nanoparticles, with zinc nitrate hexahydrate satisfying as a precursor. When indicating the existence colorless zinc nitrate hexahydrate solution was combined with plant extracts (leaf and flower), which have greenish and pinkish-brown hues, respectively, a yellowish-white precipitate formed, of zinc oxide nanoparticles [Rajakumar et al., 2017].

Gold nanoparticles:

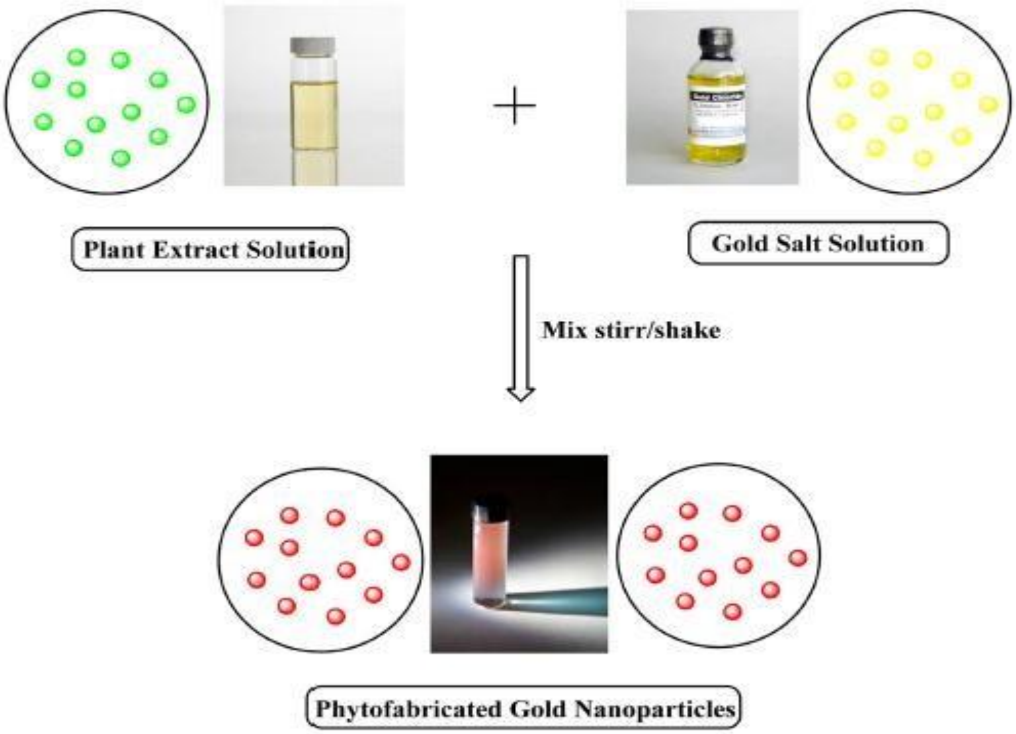
Gold nanoparticles are an extremely coveted material for researchers owing to their compact size, increased surface area-to-volume ratio, magnetic assets, chemical properties, and electronic characteristics. Due to their long-standing medical applications, such as cancer treatment and biocompatibility, 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 ecologically friendly and gainful, great interest to biology, chemistry and materials scientists, predominantly in the situation 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 leading to the detection of a variety of plants with intriguing properties [Morel et al., 2017].

Molecular methodology:

Chloroauric acid (HAuCl4), silver nitrate (AgNO3), and Neem leaf (Azadirachta indica) broth are the ingredients used to devise gold and silver nanoparticles. The broth is made by combining 20 g of thoroughly cleaned and finely chopped A. indica leaves with 100 mL of sterile distilled water, boiling the mixture for two minutes, and then decanting it. 45 mL of 103 M aqueous AgNO3 solution was mixed with 5 mL of Neem leaf broth to reduce Ag+ ions. Similar to this, 45 mL of a 10 3 M HAuCl4 solution was mixed with 5 mL of Neem leaf broth to reduce the AuCl 4 ions. 90 mL of a 1:1 103 M solution of AgNO3 and HAuCl4 was taken for the synthesis of Ag-Au bimetallic nanoparticles, along with 10 mL of Neem broth. After diluted a small aliquot (0.2 mL) of the sample 20 times, the UV-vis spectra of the solution were measured at regular intervals to track the reduction of pure Ag and Au3+ ions in addition to that of the 1:1 Ag+: AuCl 4 mixture. After 24 hours of reaction between the various salt solutions and the Neem leaf broth, Ag, Au, and Au-Ag nanoparticles were created. The pellet from the centrifuge was then redispersed in sterilized concentrated water to remove any uncoordinated biological molecules. To effectively separate the free entities from the metal nanoparticles, the centrifugation and redispersion processes were carried out three times in sterilized distilled water [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 efficiency and preserve the resilience 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 conveyance target system while creating the assortment 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

Ovarian cancers are among the most common malignancies diagnosed in the majority of topographical regions of the world. The most prevalent form of cancer in men is prostate cancer, which is also the second leading cause of cancer-related death in developed countries. According to National Statistics and US Cancer Statistics from 2013, reproductive cancer, which includes ovarian, uterine, and cervical types, regularly ranks among the twenty most prevalent and fatal diseases in women worldwide. The use of nano biosensors, which rapidly and directly convert the numerous simultaneous biological events (binding and/or reactions) into electronic signals without necessitating additional labeling steps, has proven advantageous in many areas of bio detection, such as the identification of antigens, proteins, nucleic acids, and reactive oxygen and nitrogen species. Recently, contraceptive field has successfully employed this technique. 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]. Nanomaterials are capable of significantly increasing the efficacy and decreasing the systemic toxicity of chemotherapy delivery. Recent studies have reported the potential of various NP types, such as PLGA and PLA derivatives, bovine serum albumin, magnetic, iron, and gold, functionalized with various targeting ligands, such as 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].

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 and trophoblastic 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 disturbs 2%–22% of females of propagative age and is categorized by the presence of endometrial-like tissue outside of the uterine cavity. It can cause insignificant to unadorned pelvic discomfort and/or sterility. Endometriosis has been shown in recent large-scale epidemiological research to have a profoundly detrimental influence on health-related eminence of life and job productivity, which is aggravated by a typical diagnostic adjournment 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]. Owing to the nonappearance of sensitive blood biomarkers and limitations allied 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:

Uterine fibroids (leiomyomas), which are benign hormone-dependent tumors, are made up of smooth muscle cells from the myometrium. The most prevalent type of pelvic tumor, leiomyomas, affect between 60% and 80% of women of reproductive age. Clinical manifestations of the illness include abnormal uterine bleeding, anemia, genitourinary issues, and infertility, all of which have a negative impact on health.

The majority of current uterine fibroids treatments involve surgery and range from myomectomy to hysterectomy, as well as more invasive procedures like targeted ultrasound ablation and uterine artery embolization. The effects of minimally invasive surgical removal of fibroids have been studied for progression of binding affinity and neuroplasticity using nanomaterial-mediated delivery of anti-tumor cytokines [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 required to investigate 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. Forthcoming diagnoses for plant-mediated nanoparticle preparation comprise 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 consumes consequently grown to be a significant topic of study.

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