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Application of Nanoparticles and Nanotools in Pharmaceutics and Medicine

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ABSTRACT: The advancements in the field of nanotechnology has significantly contributed in the evolution of its associating fields that consists of synthesis and applications of nanoparticles in field of medicine and pharmaceutics. Nanoparticles have size that ranges from 0.2 to 100 nm also they have increased surface to volume ratio. Additionally, the biological, physical and chemical properties of nanoparticles can be altered in accordance with their applications. Different types of nanoparticles exhibit a broad array of applications in various fields of pharmaceutics and medicine including tissue engineering, cancer treatment and diagnosis, drug delivery, nanorobots, biosensors, biomolecules detection, regenerative medicine and as antimicrobial agents. Nanotechnology provides intelligent devices, materials and systems for better pharmaceutical applications also it delivers the opportunity to improvise medical devices and materials that help in creating new nanotools when existing and more conventional technologies may be approaching their limits. The traditional methods of diagnosis and treatment of diseases are slow, less accurate and precise and they have large number of side effects. In this review we will be discussing various nanoparticles and their mechanism of action along with their applications in the field of medicine and pharmaceutics. The property of biocompatibility contributes to the sustainable usage of nanoparticles in the field of medicine and pharmaceutics. This review focuses to shed light on the crucial contributions of nanoparticles to pharmaceutical, modern medicine and nanotools development in treatment and diagnosis of various diseases and ailments.

Keywords: Nanotools, Magnetic resonance imaging, Nanoparticles, Drug delivery systems, Cellulose nanocrystals, Personalized medicine, Biological labelling and detection, Cancer treatment and diagnosis

INTRODUCTION

A scientist named Norio Taniguchi from Tokyo (Japan), invented the term "Nanotechnology" for the first time in the year 1974, when he referred to matter in nanometres. Nanotechnology is a branch of technology that deals with materials and substances having dimensions less than 100 nanometres, it includes the alteration of individual atoms and molecules in order to create any technology on a nanoscale that has utilization in any field. The characteristics of matter at the nano scale can be distinct from those at macroscale. Materials can be nano-structured for new and novel characteristics. Nanoparticles dosage offer plethora of advantages over traditional dosage forms, which includes reduced toxicity, enhanced bio distribution, improved efficacy and improved patient compliance.

Nanotechnology refers to studying the phenomena and manipulation of materials at macromolecular, molecular and atomic scales, as at this stage particles differ from properties in bulk stage along with the technologies that design, characterize, produce the structures, devices and systems by monitoring the shape and size at nanometer scale (Hakkani *et al.*, 2020).

Nanotechnology is a field that merges nanomaterial in biotechnology that is field of material science and biology. Nanoparticles demonstrate unique structural and surface properties which makes them suitable to be utilized for a wide range of therapeutic applications. The distinct properties and utilization of nanoparticles arises from a large variety of characterstics that they possess such as size of nanoparticles and biomolecules (proteins and polynucleic acid). Moreover, nanoparticles have the potential to be altered and manipulated to impart them with useful properties like magnetic behaviour and fluorescence (De *et al.*, 2008).

Nanoparticles have subnanosize structure, they contain bioactive substances or drug and are constituted of several atoms or molecules with a diversity of sizes (ranging from 5 nm to 300 nm) and varied morphologies (spherical, needles amorphous, crystalline, etc). Nano scale devices and materials can be manufactured through top-down or bottom-up methods. In bottom-up approach, nanoparticles are manufactured from cluster of atoms or molecules in a supervised manner that is synchronized by thermodynamic means through self-assembly. These methods are collectively called as top down nanofabrication techniques, they include nano molding, photolithography, nano fluidics and dippen lithography. Nanotechnology is broadly seen as having a great

ability to bring benefits to many areas of applications and research.

The major research gap that has not been explored yet includes the production of nanoparticles of same size and colour as well as production of single-size nanoparticles. Additionally, most of the nanoparticles utilized in medicine and pharmaceutics today are synthesized from chemical resources rather, green synthesis approach should be adopted and utilized and for the synthesis of nanoparticles from plants, animals and microorganisms resources as they offer least cytoxicity and are more safe, for this more biological entities should be researched upon that can be suitable for nanoparticle synthesis.

A. Synthesis of nanoparticles

Constant progression in the field of nanotechnology has establish a diversity of approaches to produce nanoparticles (NPs) from various series of materials, including metals, semiconductors, ceramics, metal oxides, polymers, etc. Depending upon their origin and synthesis methods, NPs possess unique physicochemical, structural and morphological characteristics, which are important in a wide variety of applications concomitant to electronic, optoelectronic, optical, electrochemical, environment and biomedical fields.

Nanostructured materials are very different from their multidimensional counterparts due to their physical, chemical, electronic and magnetic properties, and depend on their shape and size, so they have attracted much attention. Many methods have been developed to synthesize and manufacture nanostructured materials with controllable shapes, structure, dimensionality and sizes. The performance of materials depends on their properties. The properties in tern depend on the atomic structure, composition, microstructure, defects and interfaces which are controlled by thermodynamics and kinetics of the synthesis.

Top-down approach: In the top-down approach, bulk commodities are broken down into nanoscale structures or particles. The top-down synthesis method is an extension of the method used to produce micron-sized particles. The top-down approach is inherently simpler and relies on the removal or decomposition of bulk materials or on miniaturization of bulk fabrication processes to produce the desired structure with appropriate properties. The biggest problem with the top-down approach is the imperfection of surface structure. For example, photolithographic nanowires are not smooth and may contain many contaminants and structural defects on their surface. Examples of such technologies are high-energy wet ball mills, electron beam lithography, atomic force manipulation, vapour-phase condensation, aerosols, etc.

Bottom-up approach. The bottom-up approach is the most cost-effective alternative that can create lesser waste. The bottom-up method refers to the accumulation of the nanoscale substances: atom-by-atom, molecule-by-molecule, or cluster-by-cluster. Many of these methods are still under development or are increasingly being used in the commercial production of nano powders. Organometallic chemical route, revere-micelle route, sol-gel synthesis, colloidal precipitation, hydrothermal synthesis, template assisted sol-gel, electrodeposition etc, are some of the well-known bottom–up techniques reported for the preparation of luminescent nanoparticles. The top down and bottom up approach for nanoparticle synthesis is demonstrated in Fig. 1.

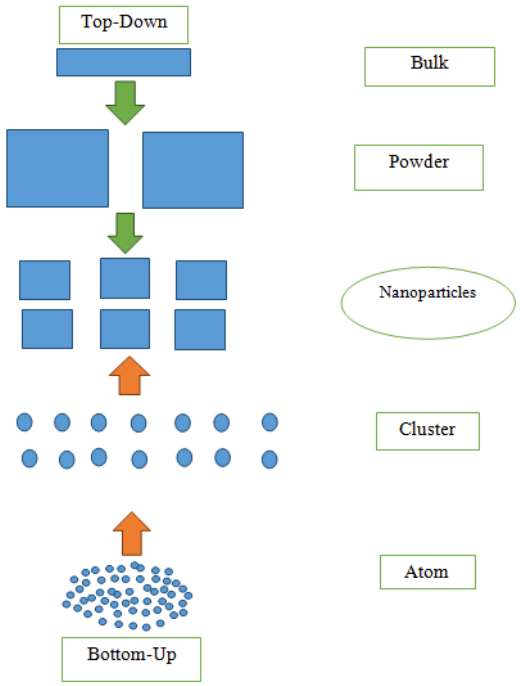

Fig. 1. Schematic representation of top down and bottom up approaches.

Nano formulations: Nanomedicine formulations have aroused many researchers' interest in drug delivery applications. These nano formulations improve the performance of conventional drugs and are specific to the delivery target site destination.

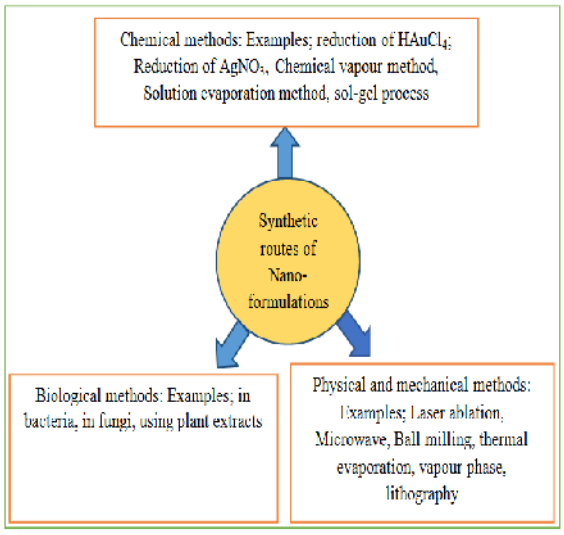

Fig. 2. Diagrammatic representation of preparation routes of nano-formulations.

Dendrimers, polymer nanoparticles, liposomes, nano emulsions, and micelles are a few nano-formulations, which are increasingly important in improving drug formulations in the pharmaceutical industry. Synthesis routes of nano-formulations are depicted in Fig. 2.

There are many synthetic methods to prepare nano formulations for drug delivery into biological systems. The choice of synthesis technique depends on the size and shape, the composition of the particle form, the biochemical properties of the drug, and the target site.

Biological synthesis of Nano-formulations: Recently, green synthesized nano-formulations have appeared, in which biological objects (microbes and plants) play a leading role in the synthesis of various nano-formulations. This is the beginning of the development of a new field of nanobiotechnology. Thus, it is a path of sustainable development, which is being developed thanks to growing success and ease of formulation. It is both cost-effective and environmentally friendly. The use of organic matter to produce nano-agriculture has paved the way for new and innovative methods of developing these natural nano-products (Iravani 2011; Pirzadah *et al.*, 2019).

The biological systems for synthesis of nano-formulations utilize mostly microbes because they naturally produce intracellular or extracellular inorganic, such as magnetostatic bacteria for magnetite, diatoms for silicon-containing materials. S-layer bacteria used for gypsum and calcium carbonate (Sastry *et al.,* 2003). Nanobiotechnology methods for the synthesis of nanoformulations have many advantages, such as the use of known microbial technologies and methods of scaling biomass, which leads to economic feasibility, the ability to easily cover large surfaces due to the correct growth of microorganisms, which is an advantage. The huge advantages in the agricultural field make the production of biologics easier...In the green synthesis of nanopreparations, microbial enzymes are used to break down the corresponding salts into nanoparticles (Duhan *et al.*, 2017).

The synthesis of nano-formulations using plants includes a mixture of the corresponding salt and plant extract that undergoes a redox reaction, and the formation of nanoparticles is indicated by the color change of the reaction mixture. The extract involves the transfer of electrons to metal ions and leads to the formation of nanoparticles. During the biosynthesis of nano-formulations, there is an initial activation period when processed metal ions are changed into their elemental form (zero valent) from mono or divalent oxidation states and later on nucleation of the reduced metal atoms takes place (Malik *et al.*, 2014). This is rapidly followed by the amalgamation of smaller nanoparticles resulting in the formation of thermodynamically more stable larger nanoparticles while the process of reduction of metal ions continues and further growth processes lead to the production of nanoparticles in varied shape and size viz., hexagons, rods, wires, spheres, and cubes and the energy in the form of heat plays a key role in the reaction (Akhtar *et al.,* 2013). This reaction continues until the capping agent from the biological entity (plant extracts), which will eventually inhibit the growth of the high-energy atomic growth planes which in turn leads to the formation of specific type of nanoparticles.

B. Application of nanoparticles in medicine

Different nanoparticles have been documented with a wide range of applications in various fields of medicine and biology including cancer therapy, drug delivery, tissue engineering, regenerative medicine, biomolecules detection, and also as antimicrobial agents. Moreover, the development of stable and effective nanoparticles requires a deep knowledge of both physico-chemical features of nanomaterials and their intended applications. Moving further, the health risks associated with the use of engineered nanoparticles needs a serious attention.

Silver nanoparticles. Silver nanoparticles (AgNPs) are most importantly used in field of medicine as bacterial and therapeutic agent. These ions are used in the formation of connections regarding dental, that is in the medical devices installation, as a cover for germs in water filters as an antibacterial agent in air sanitizers, pillows, and respirators, and socks, soap, shampoos, toothpaste, washing machines, and much more than other consumer products as cement made up of bone and for such other dressing wounds.

Role of these nanoparticles in medicine: AgNPs classify these mammalian cells which called as aggregates in particular through endocytosis and due to their small-size it can easily cross the blood-brain barrier, when it enters into the cell with the help of an endocytic vesicle, still it is distributed in the cytoplasm of the cell as well as the nucleus by cell trafficking because of the diversity of their physio-chemical elements, in which they can also affect different kind of cells with different cellular processes. Toxins donate cancer cells by lowering the mitochondrial activity, oxygen-producing production (ROS), releases that is lactate dehydrogenase (LDH), decreases the metabolism of cell cycle. Among AgNPs and antibodies the interaction has been demonstrated in specific known studies. Inflammation can occur due to the AgNPs in the portable cell. Importing of AgNPs to the site where inflammation response is started by macrophages, this release of macrophages. Other than these such cellular mechanisms, AgNPs also exhibit anti-angiogenic and anti-proliferative characterstics. In case of normal cells, vascular endothelial growth factor (VEGF) simultaneously associate to its receptor in endothelial cells to activate angiogenesis. This is done by opening up the signalling pathway of (PI3K / Akt). AgNPs anti-angiogenic as it inhibits Akt phosphorylation is PI3K because the signing method that unable to complete, ultimately ending angiogenesis, starving of the cell, oxygen deprivation or expropriation and tumour cell death takes place here.

Nanoparticles provide targeted drug delivery, enhance drug availability, enhance drug or genetic effect on targeted tissues, and improve stability. Chemical

reduction from these silver nitrate using various biological compounds produced silver nanoparticles (Tri-ethyl-amine, Alpha-Terpineol) as well as biological foundations (reaction promoter). Carob plant crops and *Rumex hymenosepalu* plant which is highly known for the usage of integration. With these silver nanoparticles which is larger than 23% of all nanoproducts and particles are also broadly used in diagnostics & therapeutic application here, (example wound healing, arthritis, etc.). This is mainly known for antibacterial & antifungal, and antiviral effects.

Wound treatment is a multi-step process that involves the integration of various tissue functions with cell lines. As we are observing that most common use of these silver nanoparticles are used as a dressing. First trade wear, ACTi coat consisting of double layered polyamide ester that is coated with crystalline silver ions. Very low minimum Inhibitory concentration and minimum bactericidal concentration figures has been recognized by ACTi coat. In addition, opportunities to improve tolerance to silver with bacteria is low due to the continuous discharge of silver nanoparticles from the product. Using these silver nanoparticles (coatings) are also has been proven in treatment of different chronic diseases and conditions like wounds for example, leg ulcers, diabetic foot ulcers as well pressure ulcer etc.

Nowadays the joint replacement method has immerged as a common treatment for most of arthritic patient's diseases. Bone cement that contains PMMA (polymethylmethacrylate) implants in human body having a high risk of this to improve this infection. Therefore, the increase in joining infection with many conflicting germs means that proper prophylaxis against these microorganisms is essential. A nanosilver-filled biomaterial has been shown to increase antibacterial activity against methicillin-resistant S. aureus (MRSA) and all other types of resistant which are used for testing. This is a new approach to nanoscale drug delivery systems (nanocarriers) have the ability to insert a human cell into detect possible changes that occur at the cellular level at the onset of the disease. Nanocarriers and nano drugs can do it used for detection, diagnosis, treatment, and prevention of many human diseases including cancer (Midha *et al.*, 2015).

Magnetic nanoparticles. Magnetic particles range from nanometre to micrometre scale are used in a growing count of medical therapeutic applications. The key components of the magnetic particles of applications are non-toxicity, bio-compatibility, injections, and high concentration in targeted tissue; the most vital asset among the above is non-toxicity. Ferric oxide is crucial component of magnetic nanoparticles, although other metals like cobalt and nickel are mainly utilized in such applications. High magnetic flux attracts magnetic nanoparticles in humans. This property is being utilized in drug administration as well as classification that includes cell filtering. Over the past few years, magnetic nanoparticles are retrieving attention due to their ability of being used as agents for prophetic magnetic resonance imaging (MRI) and heating mediators for hyperthermia.

Magnetic nanoparticles are also utilized as contrast agents, such as dextran magnetite in MRI. On comparison with paramagnetic ions and super-paramagnetic ions, the iron oxide particles possess a higher molar release. When it used as a pool of blood as well as tissue-specific agents, and can provide benefits in lower concentration. Monoclonal antibodies (MAbs) that targeted directly to cancer cells or tissues which can serve as an effective identification tool. They developed a comparative MRI agent named MAb-magnetite which is prepared by associating magnetite bound with poly-ethylene glycol and MAb anti-cell glioma surface antigen (Shinkai *et al.*, 2005).

Magnetic nanoparticles mainly consist of metal nanoparticles and nanoparticle metal alloys. Nanoparticles are common in gold, silver, iron, nickel and cobalt. Metal oxide nanoparticles mainly including iron oxides (γ-Fe_2O_3 and Fe_3O_4) & ferrites ($CoFe_2O_4$, $MnO.6ZnO.4Fe_2O_4$), and also alloy metal nanoparticles covered FePt, FeCo, and so on. The Fe_2O_3 and Fe_3O_4 magnetic nanoparticles are mostly used magnetic nanoparticles, which manually synthesized as well as easily controlled by particle shape and size. Other metals such as manganese (Mn) and Zinc (Zn) also can be added to the nanosized an iron oxide structure for ferrite nanoparticles ($Mn_3Zn_7Fe_2O_4$, $MnO.6ZnO.4Fe_2O_4$, etc.). These ferrite nanoparticles have strong magnetic fields and a high degree of relaxation, which usually contributes to application for magnetic resonance imaging (MRI). First, magnetic nanometre materials have non-virulence and non-immunogenicity. Secondly, magnetic nanoparticles possess a higher impact. In detail, they have a very important site, ready to carry large quantities of DNA fragments, drugs and medicines, and altered genes. After this alteration, can be utilized as vectors. Thirdly, altered magnetic nanoparticles have very good biocompatibility. Fourth, some magnetic nanoparticles have super-para-magnetism (Hrdy *et al.*, 2009).

Gene therapy is the only treatment by moving an exogenous gene into the patient's target gene. Hereby mentioned another novel treatment known for tumours after conventional surgery, radiotherapy and chemotherapy. But gene transfer metabolism is crucial to gene therapy with safety, efficacy and control. DNA inside is very unstable and outside the cell is highly volatile and downgraded by nucleotidase. Transfer of exogenous genes to target cells which are to be used in gene therapy are dependent on the gene transfer system and the importance of a consistent and effective gene vector for gene therapy.

There are two types of gene vectors namely viral and non-viral vectors. Viral genetic carriers (such as adenovirus, herpes simplex virus, and smallpox virus) are those that can transport the targeted gene to the cell through a viral vector for genetic expression. The viral vector is associated with a high transfer efficiency (Ting Guo *et al.*, 2018).

In recent years, tumour morbidity has been on the rise and early tumour diagnosis has become increasingly important. Magnetic Resonance Imaging is one of the frequently used method for diagnosing tumours. It is

due tothe recent advancements in field of nanotechnology, nanomaterials are systematically being applied for the detection and treatment of tumours. In combining purpose nanotechnology majorly with MRI which is only to diagnose tumours has significant effects. In MRI, magnetic nanoparticles exhibit specific sensitivity to magnetic fields. Magnetic nanoparticles attached with magnet and nucleic acid is demonstratedin Fig. 3.

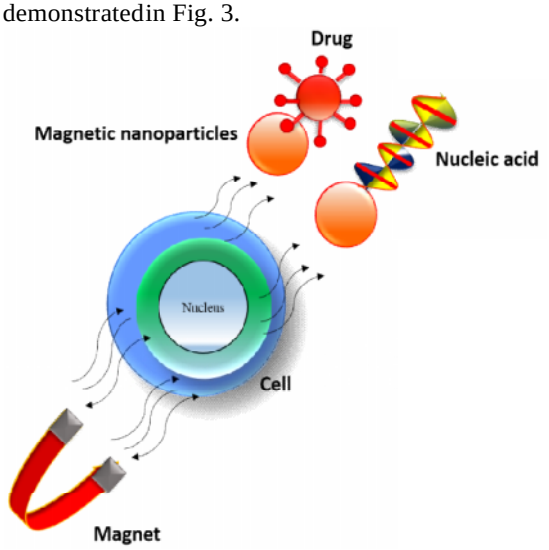

Fig. 3. Magnetic Nanoparticles attachedwith magnet and nucleic acid demonstration.

Polymeric nanoparticles. They range from 10 to 1000 nm and are made of polymers and copolymers. Drug protection, covered in a cell or absorbed on the surface or chemically attached. For the surface, effectively. It is said to have a core-shell structure with an interior Polymer matrix containing hydrophobic drugs and surface made of hydrophilic Polymers such as PEG and PVP provide stearic stability, reducing immunogenesis and phagocytosis. Nanoparticles through reticuloendothelial systems. PLA coated nanoparticles with PEG increased their residence time in GI fluids by preventing enzymatic degradation.

Ocular Drug Delivery: Cyclodextrin (CD) and polymeric vesicles (PV) are types of polymeric nanocarriers. CDs bind to a specific cyclic oligo- or six or more units of glucose α-1,4 glycosidic bonds. This configuration has a hydrophilic character with an outer surface in the curtail cone geometry and an internal cavity with a hydrophobic characteristic. Furthermore, the polarity of these systems is modified based on the different types of cyclodextrin and the number of glucose units that make up their substitutes (Ahlawat *et al.*, 2018).

Diagnosis and Imaging: The ordinary imaging and diagnostic methods can only detect early-stage cancer when the mass of the tumour is at least one centimetre in size. Polymeric nanoparticles have the ability to limit the common contrast agents as a virtue of their surface capabilities and their potential to control the solubility of agents that is to improve the imaging of cancer cells (Park *et al.*, 2009).

Polymeric Nanoparticles in Oncologic Treatment: Classic therapies to combat cancer include severe surgery, chemotherapy and radiotherapy of cells. Chemotherapy is used for treatment of most cancers, but it is also more toxic due to its affection for healthy and cancer cells. Nanomedicine is a more specific alternative. Its main purpose in oncology is to transfer cancer cells only to cancer cells, improving its efficiency and reducing toxins. The potential application of nanomedicine may lead to combination therapy along with cancer detection, resulting in improved treatment and immunity (Prabhu *et al.*, 2015).

Diagnostics of Particles: Magnetic nanoparticles attached to a decent antibody which are employed to label specific molecules. Gold polymeric nanoparticles combined with small fragments of DNA can be utilized to identify the genetic sequence. PNPs promise to produce carriers capable delivering drugs to a specific destination, by making it easier to convert vehicles for delivery drug delivery, to improve drug safety.

Polymer-based nano-particles effectively transport drugs, proteins, and DNA to target cells and organs. Their nano-size encourages efficient transmission across cell membranes and stability in the bloodstream. Polymers are suitable materials for the production of innumerable and diverse molecular models that can be integrated into the manufacture of nano-particles with many applications (Singh *et al.*, 2018).

Nano-emulsion. Nano-emulsions are submicron-sized emulsions that are widely considered as drug carriers to improve the distribution of therapeutic agents. These are the most sophisticated nanoparticles for the delivery of active agents for controlled drug delivery and targeting. Nano-emulsions are thermodynamically stable isotropic systems in which two impure liquids (water and oil) are combined by a suitable surfactant to form a mixture in a single-phase or with a droplet diameter in the range of 0.5–100 um. Nano-emulsion droplet sizes typically fall in the range of 20–200 nm and reflect narrow dimensional distributions. Nano-emulsion has great promise for the future of cosmetics, diagnostics, drug treatment, and biotechnology.

Component of nano-emulsion: Oils, lipids, surfactants, water-soluble co-solvents, and water are the components of nano-emulsion systems. In the preparation of nano-emulsions, the oil phase containing triglycerides (such as tri-, D-, or mono-acetylsalicylic, vegetable oils, mineral oils, and free fatty acids) of high-loading oil phases of the drug are commonly used for the development of nano-emulsions. Surfactants utilized in nano-emulation systems for delivery and food delivery are span (sorbitan fatty acid esters), polyoxymethylene (derivatives of sorbitan fatty acid esters), chromophore (polyoxyl-35) And starch derivatives), phospholipids (egg, soy or milk lecithin) and amphiphilic proteins.

Formulation techniques of nano-emulsion drug delivery systems: High energy methods are widely used to make nano-meters. High mechanical energy is used, which provides strong interfering energy, which breaks down large-sized droplets into nano-droplets and produces nano-emulsions with high kinetic energy. Ultrasonic

devices such as ultrasonic, microfluidizers, and high-pressure homogenizers are used to generate disruptive forces. Using high-power methods, greater control over particle size can be achieved with formula composition selection. High power also provide stability, rheology and control of the colour of the emulsion. (Kumar *et al.*, 2019).

Albumin based nanoparticles. Albumin, a multifaceted protein carrying molecule for delivery drugs, has exhibited non-toxic, non-immune, bio-friendly, and biodegradable characterstics. Albumin nanoparticles have high binding capacity of various drug drugs and are well tolerated and have minimal side effects.

There are five different strategies for synthesizing albumin-based nanoparticles namely: template, nanocarrier, scaffolding, stabilizer, and albumin-polymer conjugate. Albumin is used as a template for production of fluorescent metal clusters. The metal ions bind with the free thiol group of albumin amd trap them. The reduction capacity of albumin molecules can be activated at approximately pH 12. Alkaline pH plays an vital role in the formation of clusters. At neutral pH, each albumin molecule is trapped in 13-14 Au (III) ions. The Au (III) ions are reduced to Au (0), when pH is more than 12. Albumin reduces the intracellular production of reactive oxygen species (ROS) and enhances the stability of albumin-gold nanoclusters against ROS in living cells. The brad tunable emission wavelength is appropriate for a variety of bioimaging applications, including cell imaging and in vivo fluorescence imaging. Albumin acts as a template during the synthesis process and facilitates surface changes that are synthesized with functional ligands. Other contrast agents and drugs can be altered on the surface of albumin-tempered clusters for multimodal imaging and treatment.

The development of albumin-based nanoparticles for drug delivery and bioimaging helps to guarantee the biostructure of the obtained nanoparticles and to increase the clinical acceptance of such materials. Loaded active ingredients include chemotherapy drugs, pulmonary drugs, inhibitors, dyes, contrast agent. Albumin-based nanoparticles prepared for a variety of chemotherapy, PTT, PDT, combination therapy, optical imaging, MRI, photo coastal tomography, multimodal imaging or therapeutics can be used. On comparison with small molecular drug formulations, albumin-based nanoparticles perform specific functions such as drug resistance and effective treatment of orthotopic brain tumours. Albumin-based nanomedicine exhibits tumour-targeted delivery and also reduces in vivo drug toxicity. The in vivo drug of albumin-based nanomedicine has good performance in reducing toxicity which gives the patient the opportunity to give high doses but without excessive side effects.

Quantum Dots. The quantum dots are also known as semiconducting nanoparticles, the display unique shape and size dependent optoelectronic properties. It is an attribute of these properties that since the last decade quantum dots are being utilized in biomedical field for bioimaging (real-time tissue imaging), single molecule probes, diagnostics, drug delivery and among various other areas. The optical properties possessed by quantum dots can be manipulated by their composition and size, resistance to photobleacing, their brightness, high surface to volume ratio, multiplexing capacity these all properties make them apt for diagnostics, in vivo imaging, intracellular tracking, therapeutic delivery in biomedical imaging, inorganic particles such as iron oxide and gold quantum dots, have gathered considerable attention over the past few years. These are being studied and explored extensively for applications such as diagnostic agents (for tumor detection), DNA functionalized probes (for real-time analysis of diseased biomolecules) and molecular probes (for tracking and monitoring of drug delivery) (Cormode *et al.*, 2008).

Quantum dots can be synthesized by using two important methods. The first method is top-down approach that utilizes techniques such as electron beam lithography and MBE (molecular bean epitaxy) (Mattoussi *et al.*, 2011). The second method of synthesis is bottom-up approach, in this method precursor material get self-assembled in order to react with a solution to yield colloidal quantum dots (Murray *et al.*, 1993).

The first ever application of quantum dots in medical diagnostics involved their usage for immunostaining of membrane protein of living cells and immunofluorescent labelling of fixed cells and tissues (Duan *et al.*, 2005). A majority of quantum dots are excited by same wavelength off light this enables different multiplexing potential and high-throughput staining of biological samples (Mott *et al.*, 1936). Emission property and size tunable absorption of quantum dots are essential properties of quantum dots that make them suitable for biomedical imaging as this enables to tune the quantum dots from UV to near-infrared spectrum.

In biomedical application, fluorescence is utilized for imaging, labelling, detection, tracking and therapy. The biological molecules are labelled using quantum dots and organic fluorophore. The quantum dots constitute a new class of fluorophores that are advantageous over traditional fluorophores. The quantum dots exhibit narrow emission and broad absorption spectrum, long life time, stability against photobleaching and high brightness. The most commonly used quantum dots are CdSe, ZnSe and CdTe. The most frequently investigated, studied and utilized quantum dot is Cadmium Selenide. Different sizes of quantum dots with precisely controlled ratios are utilized for multicolour optical coding in biological assays (Gutzwiller *et al.*, 1964). The quantum dots used in biomedical imaging are near infrared luminescent quantum dots that exhibit an emission wavelength ranging from 700 to 900 nm (Hass *et al.*, 1979). The usage of near infrared quantum dots is useful biomedical imaging of living tissue due to enhanced tissue staining without interfering with autofluorescence and longer attenuation distances, as tissue chromophores weakly absorb the light in infrared range. The surface properties and unique optical properties of quantum dots allows them to undergo heteroconjugation

and become biocompatible for biological applications (Gutzwiller *et al.*, 1964).

C. Application of nanoparticles in pharmaceutics

In modern pharmaceutical research, nanotechnology plays an important role in synthesis and development of nanoparticles with unique features having extensive pharmaceutical and medical application in in drug delivery, imaging, diagnostics, sensing, artificial implants, gene delivery and tissue engineering.

Metal oxide nanoparticles. Fluorescent AP-MgO (magnesium oxide synthesized through an aerogel procedure) nanoparticles are synthesized by mixing approximately 0.4g of AP-MgO in fluorescein solution prepared in 100mL of absolute methanol (having concentration 2×10^{-5} M) and then centrifuging the suspension. The pellet was then collected air-dried to obtain AP-MgO aerogel. The prepared aerogel nanoparticles have a very high surface area that contributes to their significantly increased chemical activity. The properties like enhanced surface reactivity and large surface area help AP-MgO nanoparticles to serve a potent disinfectant and bactericidal. These properties contribute to the ability of nanocrystals to adsorb and bear the active halogens. The microscopic size of nanoparticles permits them to engulf the bacterial cells to great extent and also they help in bringing halogens to a functional form in high concentration in close vicinity to the cell. The halogen treated magnesium oxide nanoparticles (AP-MgO/Cl_2 and AP-MgO/ Br_2) exhibit a faster and stronger impact in the eliminating action of both bacteria as well as spores (Stoimenov *et al.*, 2002).

Since the past decade, the role of nanotechnology in virology has been increasing exponentially. In therapeutic, prophylactic and diagnostic approaches, nanoparticles have been employed for imaging purposes and as adjuvants used for transporting drugs. Virucidal nanoparticles and drug delivery models have been utilized for the fighting hepatitis (type A, B, C and E), human immunodeficiency virus (HIV) and herpes simplex virus (HSV-1 and HSV-2) (Yadavalli and Shukla, 2017).

The zinc oxide nanoparticles have inherent anticancer property, due to this zinc oxide nanoparticle are loaded anticancer drug. The synthesis reaction to produce zinc oxide nanoparticles involves reaction of sodium hydroxide and zinc. Solution with varying concentrations of zinc nitrate and sodium hydroxide is prepared by dissolving them in water. Also, a solution of starch prepared in water in different concentrations is mixed with zinc nitrate solution and mixed continuously. Later, there is dropwise addition of sodium hydroxide solution to this mixture with constant agitation until white precipitate is formed. The precipitate was allowed to settle down and separated through centrifugation. The product was calcined and dried to form powder. Drug-loaded nanoparticles (DOX), are added to mixture containing zinc nitrate and starch and is stirred until it dissolves completely. Loading gets saturated at 0.1 mg/ml, and therefore were selected for optimum loading concentration. The drug loaded zinc oxide nanoparticles remain steady till 24 hrs, they release drug in controlled manner. The ZnO nanoparticles loaded with drug is an effective and novel approach towards cancer treatment and daignosis, with greater targeting of the extremely toxic chemotherapeutic drugs, therefore producing minimal side effects (Sharma *et al.*, 2014).

Gold nanoparticles. Among all metallic nanoparticles, gold nanoparticles are object of substantial interest because of their distinct size, shape and surface properties. Gold nanoparticles are advantageous over other nanoparticles due to their biocompatibility and non-toxic nature, also these particles have ability of conjugating with a huge variety of biomolecules such as DNA, proteins and other molecular species. Gold nanoparticles have their application in various biomedical fields such as immunostaining, cell imaging, colorimetric assays, biosensing and drug delivery (Dhar *et al.*, 2008).

Natural gum stabilized nanoparticles synthesized by reaction of aqueous solution of chloroauric acid and gellan gum. An aqueous solution of chloroauric acid (having concentration 1×10^{-4} M) is reduced to gold nanoparticles by boiling them in aqueous solution of gellan gum (0.2% w/v). The pH of solution was adjusted after addition of chloroauric acid by addition of sodium hydroxide (pH between 11-12) to yield ruby-red gold nanoparticles. The gold particles were loaded with doxorubicin hydrochloride (10^{-4}M), loading of DOX onto gold nanoparticles increases their apoptotic activity also they have potential in cancer treatment, particularly brain tumor. The surface of nanoparticle is carbohydrate-rich this eases transfer of loaded drug across blood-brain barrier. It can also be used for transport of other biologically active molecules (Dhar *et al.*, 2008).

The antibacterial gold nanoparticles coated with organic molecules have ability to fight against multi-drug resistant bacteria. The gold nanoparticles are modified using organic molecules such as N-heterocyclic molecules, 4,6-diamino-2-pyrimidinethiol (DAPT), non-antibiotic amines through in-situ synthesis. The synthesized gold nanoparticles are able to inhibit both laboratory strain and clinical strain of multi-drug resistant isolates. The antibacterial gold nanoparticles are effective in curing wounds infected by multi-drug resistant bacteria through an electrospun scaffold containing intermediate-capped gold nanoparticles. These nanoparticles have the ability to withstand bacteria and display biocompatibility. These nanoparticles have the ability to increase antibiotic screening space and to broaden the applications of gold nanoparticles, which in turn provides an alternative against multi-drug resistant bacterial infections. The homogeneous electrospun nanofibers have been utilized in treatment of wound infection (Yang *et al.*, 2017).

Gold nanoparticles are synthesized by citrate reduction, the aqueous solution of chloroauric acid is boiled. Various volumes of 1% sodium citrate aqueous solution was added to above solution and then stirred for 10 minutes, until formation of coloured gold nanoparticle suspension. These synthesized gold

nanoparticles have size ranging from 57 nm to 346 nm. Gold nanoparticle that are 57 nm size have an increased radiation dose effectiveness. At the concentration of 400 ppm, gold nanoparticles displayed notable anti-bacterial effect. These have potential to function as dose enhancer in radiotherapy. Also it is proven to exhibit anti-bacterial efficacy displayed that gold nanoparticle had considerable effect against *E. coli* clinical strains (Kamiar *et al.*, 2013). Fig. 4 depicts the diagrammatic representation depicting anionic natural gum coated with gold nanoparticles and followed by loading of cationic anticancer drug on natural gum capped gold nanoparticles loading increases the efficiency of drug delivery to targeted site or organ.

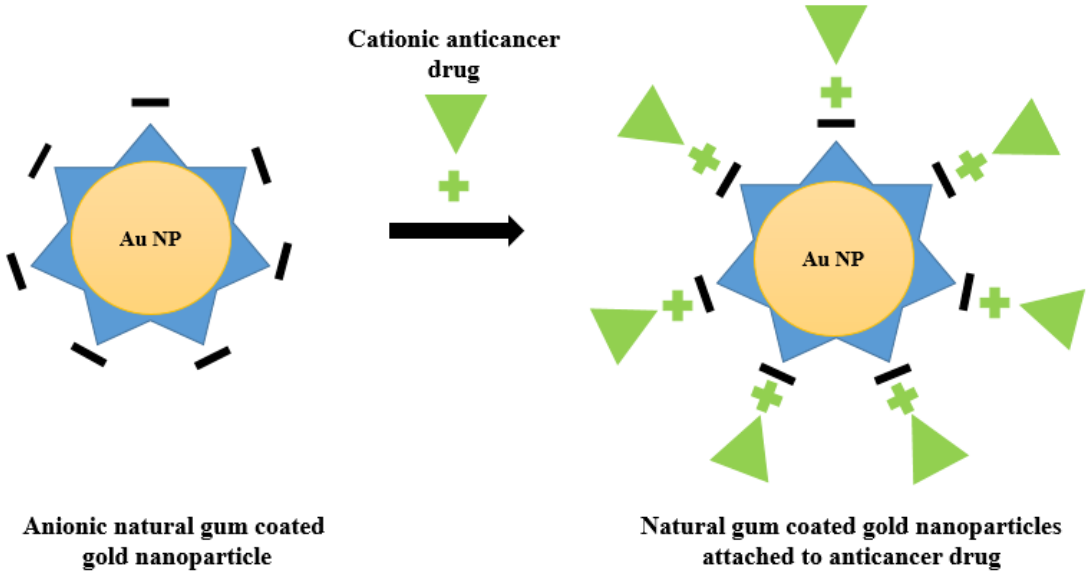

Fig. 4. Diagrammatic representation depicting anionic natural gum coated with gold nanoparticles and followed by loading of cationic anticancer drug on natural gum capped gold nanoparticles loading increases the efficiency of drug delivery to targeted site or organ.

Fluorescent nanoparticles. Fluorescent nanoparticles have controllable optical properties, chemical stability and photostability and larger stokes shift. It is due to their functionability and designability, that fluorescent nanoparticles are extensively utilized as fluorescent probes for wide range of applications (Wang *et al.*, 2020).

In order to amplify selectivity and sensitivity, the fluorescent nanoparticles are combined with the molecularly imprinted fluorescent nanoparticles (MIFN). The sensor based on MIFN, is more adjustable with complex sample matrix, which is especially acquired for medical and biological analysis. The applications of MIFN sensors is in veterinary drugs/drugs residues, pharmaceutical analysis, pesticides/herbicide and human proteins (Wang *et al.*, 2020).

There is utilization of fluorescent dyes combined with targeting molecules that have ability to bind with the receptors that are overexpressed in malignancy can particularly target malignant tumors and also differentiate tumor from normal tissues, which is advantageous for the early diagnosis and precise surgical resection of malignant tumors. Fluorescent dyes such as fluorescein, cyanine, rhodamine, and so on are extensively used because they are effective and simple methods for labelling of tumor cells.

The significant improvements in the field of nanotechnology, different classes of nanomaterials (organic, inorganic, and metallic) are presently used as fluorescent emitters (FNPs). FNPs have better photostability, stronger fluorescent brightness, biocompatibility and water dispersibility which permits FNPs to meet the necessities in order to battle cancer, which has given rise to prominent concern in the past few years. Additionally, the heterogeneity and complexity of tumors is required in selection the applicable FNPs and the effective targeting strategies (He *et al.*, 2019).

The monolein based cubosomes are adsorbed with two fluorescent probes namely dansyl and fluorescein and altered with a hydrocarbon chain in order to enhance their encapsulation efficiency inside the monoolein palisade. The above mentioned nanocarriers can also be filled with quercetin, a hydrophobic molecule which displays anticancer properties. Additionally, the cubosomes filled with the altered fluorescein probe are utilized for imaging living cells. The photophysical and physicochemical characterizations, along with the potential of cubosomes in hosting molecules with can be beneficial in pharmaceutics, promotes their use as fluorescent nanocarriers for theranostic applications (Murgia *et al.*, 2013).

Nanodrugs and nanocrystals. A nanocrystal or nanosuspension is a multifaceted formulation incorporating traditional and inventive features. It consists of drug nanoparticles having particle size in the nanometers, these are usually stabilized with help of surfactants or polymers. Nanosuspensions are generally produced from liquid media through top-down and bottom-up methods or by combination of both methods.

These naoparticles have been created to increase their dissolution rate, solubility and the availability of drugs through different administration routes. It is due to their extremely small size that nanosuspensions can also be regarded as drug delivery nanotechnology in the preparation of nanomedicine. Nanocrystals can be considered a nanoparticle technology for drug delivery. This distinctive feature makes them a zip tool between conventional formulation and nanomedicine products. Nanocrystals constitute a versatile nanotechnology able to improve several aspects, from drug absorption and bioavailability to biodistribution and cellular uptake. They can be used to treat a wide variety of diseases by various administration routes (Leone *et al.*, 2015).

Cellulose nanocrystals (CNCs) are synthesized from natural cellulose through acid hydrolysis or enzymatic method. There are various utilization forms of CNCs as the drug carrier in pharmaceutics, such as the hydrophobic associating with drug, the direct binding with drug, the covalent attachment of drug. Novel approaches have been created to release drug in controlled manner at the molecular level through creating interactions between the ionized drug molecules and CNCs carrying negative charge.

Cetyl trimethylammonium bromide (CTAB) can neutralize negative zeta potential and therefore CNCs modified with CTAB, can combine to considerable quantities of the anticancer drugs such as paclitaxel, docetaxel and etoposide, which were discharged in a supervised manner over a period of few days. The chitosan (a cationic polysaccharide) is capable of binding to the surface of CNCs, this has led to the development of a new polyelectrolyte macro-ion complex (PMC), which can be used for drug delivery. CNCs carrying cationic b-cyclodextrin (CD) on their surface via ionic association in order to form CD-CNCs complexes that is used to encapsulate the curcumin (hydrophobic drug). These nanoparticles display enhanced cytotoxic activity against colorectal and prostatic cancer cell lines when compared to natural curcumin. The covalent association of folic acid molecules to the surface of CNCs is also a method for delivering chemotherapeutic agents to targeted site. The primary alcohol moieties of CNCs can be oxidized to carboxyl groups which are then reacted with chitosan oligosaccharide (CSOS). CNC–CSOS particles carrying procaine hydrochloride displayed release of drug in 1 h, which indicates that CNC–CSOS particles have the ability to be used as fast response drug carriers in local drug delivery and wound-dressings. CNCs can be embedded into alginate-based nanocomposite microspheres with the targets in regulating drug release behaviour increasing mechanical strength.

Table 1: Different types of nanoparticles and their application in pharmaceutics

Sr. No.	Type of nanoparticle	Application	References
1.	Iron oxide nanoparticles	Advances in magnetic resonance imaging (MRI) Magnetic hyperthermia Drug delivery Tissue repair Diagnostic separation and selection Cell separation and detection Magnetorelaxometry	Bruschi *et al.*, 2019
2.	Metal oxide nanoparticles	Cancer treatment and diagnosis Microbial infections Diabetes Neurodegenerative and cardiovascular diseases Fabrication of dental and orthopaedic implants Bioimaging and biosensors Antimalarial and antilarval, Anti-inflammatory	Andra *et al.*, 2019
4.	Gold nanoparticles	Immunostaining Cell imaging Colorimetric assays Biosensing Drug delivery Radiotherapy Antibacterial activity	Dhar *et al.*, 2008 Kamiar *et al.*, 2013
5.	Pegylated Nanoparticles	Drug delivery Biological labelling and detection Surface plasmon resonance biosensing	Otsuka *et al.*, 2012
6.	Fluroscent nanoparticles	Pesticides/herbicide analysis Veterinary drugs analysis Human related proteins analysis Biosensing Biolabelling Theronostic applications	Wang *et al.*, 2020 Murgia *et al.*, 2013

CNCs increase the stability of the cross-linked network structure, and therefore the alginate based microspheres displayed prominent sustained release profiles (Leone *et al.*, 2015). Table 1 summarises the different types of nanoparticles and their application in pharmaceutics.

Nanotechnology tools

Nanotools in research and development: The rise of nanotechnology that is the manipulation of nanometric scaled material into producing and utilizing the tools has dramatically influenced various industries and especially the pharmaceutical businesses. In general, two types of nanotools are being utilized first one is nano-materials like in dental implants, in orthopaedics or tissue-engineered scaffolds products. These nanomaterials can also be further divided into nano-crystalline and nanostructured materials. Nano-crystals are eagerly produced and could substitute the low activated bulk materials. Drug encapsulation, implants, man-made limbs all is possible with the help of raw nano-material. Raw nano-material will form nanostructured materials which will deliver distinct forms and functions, for instance, carbon nanotubes quantum dots, fullerenes and dendrimers. Another type is nano-devices which are of nanometric -scale and include micro-and nano-electromechanical system (MEMS and NEMS) and microarrays and microfluid (Bailey *et al.,* 2004).

Nanotools for process development: Process development term is described as syntheses of both medicines, medicine intermediary, and to the advancement of analytical tools for diagnosis. There are various nano-tools accessible that could be used in the process development. Two examples of one of the most influential nanotools of miniaturization and computerization in biological screening and synthesis on a nanometric scale are the X-cube system and the NanoSynTest-system. The skills of these two systems are to manipulate the nano-sized titer plate reaction whose density is 100 wells/cm2 and nanoliter volume handling capability (Schober *et al.,* 2004). The X-cube system allows the organic reaction to being executed in a flowing manner at high pressures and temperatures and the NanoSynTest system proposes numerous modules for real-time drug synthesis and ultra-high-throughput screening. These automation and miniaturization tools are likely to carry out effective price decreases in the progressive development of current and also the new products.

Additionally, to automation and miniaturization techniques, nanomaterials are also developed as a resourceful catalytic agent and support solid-phase syntheses. The Magnetic nano-particle helps chiral Ru complexes which help in catalyzing the hydrogenation of heterogeneous asymmetric of the ketone's aromatase with unusually high movement and enantioselectivity (Hu *et al.,* 2005). An anti-inflammatory agent Nabumetone is produced by residue-free catalytic procedure with the help of the utilization of Magnesium oxide. (Climent *et al.,* 2007). A new study has reported about functionally cobalt core-based carbon nanoparticles having great magnetized property and great stability in the atmosphere and not only that but could withstand up to 190°C temperature (Grass *et al.,* 2007). The rapid removal ability from the reaction mixture and the great capacity for ligand binding of these nanobeads make them brilliant supports in organic syntheses and biotech applications.

Nanotools for product development: Product development is defined as the incorporation of drug discovery along with drug development of diagnostic tools. One of the product development's utmost important nano-tool is that the chance to transform the present dugs which are having low water dissolution and solubility proportion into smoothly water-soluble removal by shrinking them to the nanometric scale drugs (Kharb *et al.,* 2006). By shrinking the particle size, the surfaced area is increased leading to greater efficiency in absorbing. A nano-sized converted drug is transformed into a special dosage form like injectable, inhalable, oral, and nasal (Bieri *et al.,* 2008).

The noteworthy claim of this method is to increase the lifetime of the present drugs for this market. There are many drugs already being commercialized within the market. as an example, Elan Corporation using nanocrystal technology for Immunosuppressant drug Rapamune (sirolimus) which utilizes a P antagonist substance (SPA) for inhibition of delayed and acute chemotherapy-induced nausea and vomiting (CINV) and for inhibition of vomiting and nausea, uses nano-metric scale drugs. NanoMed Pharmaceuticals develops nano-sized drugs with the help of their patented Nanotemplate Engineering technology which utilizes solid nanoparticles using microemulsions as templates. SkyePharma utilizing the (IDD) insoluble drug delivery technology on market drugs like PAXIL CR an anti-depressant drug and carcinoma drug SOLARAZE. Lastly NanoCeuticals, A skincare and nutritional supplement from RBC Life Sciences which ensure they produce products that on consumption reduces the surface tension of diet and complements the rise in absorption and moisture of nutrient.

On importance to controlled drug delivery system, there are many nanotools available that can transform the existing drug. The market value of these drug delivery nanotools is around three hundred billion dollars seizing quite the health sector market. Mullica, DermaSal, and MatrixSal from the Salvona industry are the ones that are based on the encapsulated drugs polymer are simplest in this category. These factors pH, temperature, and water can stimulate the encapsulated drugs in the delivering drug. Also, a recent study displayed an innovative tactic utilizing a core-shell style were for curing angiogenesis wherein phospholipid block-copolymer are neighboring by the encapsulation of the anti-angiogenesis agent and cytotoxic agent of polymer core (Sengupta *et al.,* 2005). Fig. 5 depicts the diagrammatic representation of various nanotools for process development.

Nanotools for personalized medicine: With the progress in the genetic field, gene mapping, and the various bio-markers and group together with the nanotools, there is a surge in personalized medicine and so the focus of the pharmaceutical sector is also coming on personalized medicine.

There is only a limited drug available in the market as of now it will soon take a full turn toward it. The personalized drugs that are available in the market are antidepressant medicines, that are focused on

Cytochrome P450. Another example is the breast cancer drug Herceptin which is only used to treat patients with unusual HER2 gene patient which plays a part in cancer growth. (Beck-Broichsitter *et al.*, 2009).

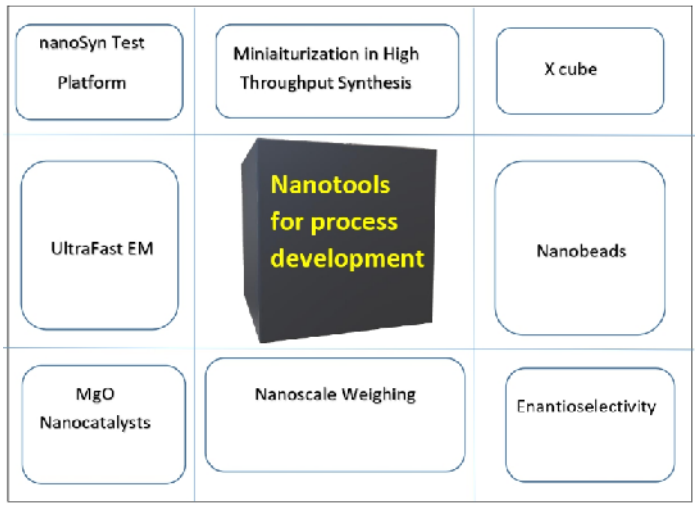

Fig. 5. Diagrammatic representation of nanotools for process development.

The ultrasensitive molecular imaging technique is a very important nanotool for personalized medicine. There are many approaches undergoing research like, for instance, HYPER-CEST (MRI) is a technique that exposures the molecule at a ten-thousand-time lower concentration than the normal magnetic resonance imaging (MRI). This approach utilizes the chemical exchange saturation (CEST) transfer among the free radical Xe with encapsulated biosensor Xe (Schroder *et al.*, 2006).

Lastly, the capability to take out the integrated imaging and therapy-based nanotechnology tools are the most potential nanotool for personalized medicine. Nano-tools grounded on magnetically and optical tunable systems nanotools are still developing, like immune targeted nanoshells comprising of dielectric silica core gold shell nanoparticles together with the targeting agents which has the capability to either absorb or scatter light within the near-infrared region (NIR) and with this advancement, it is very easy to identify tumours utilizing optical imaging and terminate them with the help of photothermal therapy (Gobin *et al.*, 2007).

CONCLUSION

Nanoparticles present a very attractive platform for a wide variety of biological applications. The additional and core structures of these systems can be designed for individual and diverse systems, including biomolecular recognition, medical delivery, biosensing, and bioimaging. Silver nanoparticles have played significant role in the domain of nanomedicine and nanotechnology. Magnetic nanoparticles have the potential to be used as agents for magnetic resonance imaging (MRI) and heating mediators for cancer thermotherapy (hyperthermia). It is evident from this review that the use of nanotechnology in drug delivery and medicine has opened up new avenues and opened many doors to the provision of customized and safe treatment options. Cancer treatment and / AIDS, non-invasive imaging and pharmaceutical delivery have all continued with the use of nanotechnology. Finally, with the use of cellular sizes and surface materials, researchers are able to deliver long-term drugs in extraordinary proportions (continuous extraction) with high accuracy and making tissue difficult to access. Nanoparticles which helps in cancer, ordinary imaging and diagnostic methods can only detect early-stage cancer when the mass of the tumour is at least one centimetre in size. In order to increase the sensitivity and selectivity, the fluorescent nanoparticles are combined with the molecularly imprinted polymer (MIFN). The sensor present on MIFN (the MIFN sensor) is more. Nanotechnology uses therapeutic agents at the nanoscale level to develop nanomedicines. The field of biomedicine including nanobiotechnology, drug delivery, biosensors, and tissue engineering is powered by nanoparticles. Since nanoparticles contain substances formed at the atomic or molecular level, they are usually small nanospheres. Therefore, they exhibit free movement in the human body compared to the other materials used. Nanoscale-sized particles reflect unique structural, chemical, mechanical, magnetic, electrical, and biological properties. New nano-materials and concepts are now being developed that show the potential for energy production from movement, light, temperature variation, glucose and other sources with high conversion efficiency. It is possible that nanomedicine in future would play a crucial role in treatment of human diseases and also in enhancement of normal human physiology. If the same trend continues, nanotechnology will one day become an inevitable part of our everyday life and will make effective contribution in saving many lives.

FUTURE SCOPE

In the present scenario, nanotechnology is a revolutionary field and the advancements in this field

will give rise to usage of nanoparticles in various other fields. The nanoparticles need to be associated with green chemistry route in future. This field explores distinct strategiesand mechanisms involving cultivation mode, strain selection, metabolic engineering, rDNA technology, protein designing and re-engineeringand predictive modelling that permits to create nanobioreactors that helps in creation of new nanobiotechnological field impacting wide range of research areas. The application of nanoparticles in medicine and pharmaceutics had opened gateways to a whole novel therapeutic arena. The presently existing nanoparticles systems in many cases have an elevated therapeutic index of drugs as they are capable of minimising drug toxicity or increasing its efficacy by targeting ligands (like antibodies, aptamers and pesticides) and this may further enhance the therapeutic nanoparticle system in coming years. The multifunctional nature of nanoparticles can be the subject of future research as this multifunctional characteristics makes them a more complex system. The more complicated the functionality of nanoparticles becomes, this will provide aid in creation and redesigning nanoparticles with optimal biological and physiochemical properties that will be more apt for specific functions. Indeed, this was one of the biggest shortcoming for nanoparticles to enter clinical practices. On introduction of safer nanoparticles combined with new emerging methods, in future it is expected that more multifunctional nanoparticles will be created that will have the potential to enter clinical practices. Further, while considering the synthesis of nanoparticles the green synthesis method should be given importanceas it is eco-friendly and economically viable method that has a wide range of applications in nanomedicine, catalysis medicines and many more. This novel and emerging research field in present scenario with day to day developments makes this field to have a bright future. The green synthesis method includes synthesizing nanoparticles that have several advantages such as economic viability, safe, ease of scaled-up process and many more. On the basis of current literature review it can be concluded that synthesis of nanoparticles from plant source specifically, gold and silver nanoparticles synthesized from plant source have clinical benefits. Moreover, the nanoparticle in nano-dimensions will be equally beneficial in medical application as compared to antibiotics and several other drugs. The green synthesis method for production of nanoparticles includes yeast, bacteria, fungi, various plant extracts and plant biomass which have potential application in biology and medicine, along with continued research, nanotechnology is expected to have an enormous impact on the field of medicine and pharmaceutics in the decades to come. The future research should be focused on cytotoxicity and safety of nanoparticles; this could be a critical point to be addressed in future development. In order to make nanoparticles applicable for medicinal and pharmaceutical applications there are still many challenges that needs to be addressed. In future, it is required to create safe, specific and cost effective procedures for producing biocompatible, reproducible and stable nanoparticles from bioresources.

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