

# A review on ‘Nanotechnology for the Development of Nanomedicine’

Saurabh Sharma\*, Swapnil Goyal

Mahakal Institute of Pharmaceutical Studies Ujjain M.P.

Submitted: 15-03-2022

Accepted: 28-03-2022

## ABSTRACT:-

Nanotechnology is the science which used materials at nanoscale. It's new but fleetly developing science where materials in the nanoscale range are employed to serve as means of diagnostic tools or to deliver therapeutic agents to specific targeted spots in a controlled manner. Nanotechnology in pharmaceutical field have numerous advantages like enhanced solubility, increased dissolution rate, enhanced stability, reduction in dose, increase in bioavailability and rapid onset of action. And also offers multiple benefits in treating chronic human conditions by site-specific, and target-acquainted delivery of precise drugs. Recently, there are a number of outstanding usages of the nanomedicine (chemotherapeutic agents, biological agents, immunotherapeutic agents etc.) in the treatment of various diseases. This review paper presents, presents an updated summary of recent advances in the field of nanomedicines and nano based drug delivery systems, approaches of medication, advantages and usage of nanomaterials in upgrading both the efficacy of new and old medicines.

**Keywords:-** Nanotechnology, Nanoparticles, Liposomes, drug delivery system,

## I. INTRODUCTION

Over the past decades, there has been considerable exploration interest in the area of developing nano technology by using nano particles as carriers for the development of nanomedicine. The word ‘Nano’ is deduced from Latin word, which means dwarf. Nano size refers to one thousand millionth of a individual unit therefore nanometer is one thousand millionth of a meter ( i.e.  $1\text{ nm} = 10^9\text{ m}$ ). The term “nanotechnology” has been derived from the Latin and Greek words “ nanus” and “ nanos,” independently, meaning “ dwarf.” In general, nanotechnology is concerned with confines with forbearance limits of 1 – 100nm as well as with the

manipulation of materials at atomic and molecular levels (Figure 1). Hence, nanotechnology is frequently defined as the purposeful design, characterization, production, and application of materials, structures, devices, and systems by controlling their size and shape in the nanoscale range. Since nanomaterials are analogous in scale to natural molecules, they can be engineered to have various useful medical functions and applications. There's growing advancement in nanotechnology that will bring crucial vital changes in the diagnosis, treatment, and prevention of diseases.<sup>1-3</sup> All features of nanomedicine grounded on progress in nanomaterials research and the nanoengineering essential to produce devices to recognize their goals.

The field of nanomedicine aims to use the properties and physical characteristics of nanomaterials for the diagnosis and treatment of diseases at the molecular levels.<sup>4</sup> Nanomedicine permits the cure of disease within the body and at the cellular or molecular level and is one of the most promising fields within the implicit new technological advances in drug. This technology is also revolutionizing medical areas similar as monitoring, tissue repair, disease evolution control, protection and enhancement of human biological systems, diagnosis, treatment and prevention, pain relief, health prevention, delivery of medicines to cells, positioning it as a revolution in the medical scientific and healthcare fields.<sup>5-8</sup>

Major advantages of nano sizing include

- Rapid onset of action
- Enhanced solubility
- Protection of encapsulated medicine
- Increase surface
- Less amount of drug needed
- Reduce toxin
- Increase rate of dissolution and oral bio availability
- Retention of medicine at the active place.
- Reduction in fed/ dieted variability.

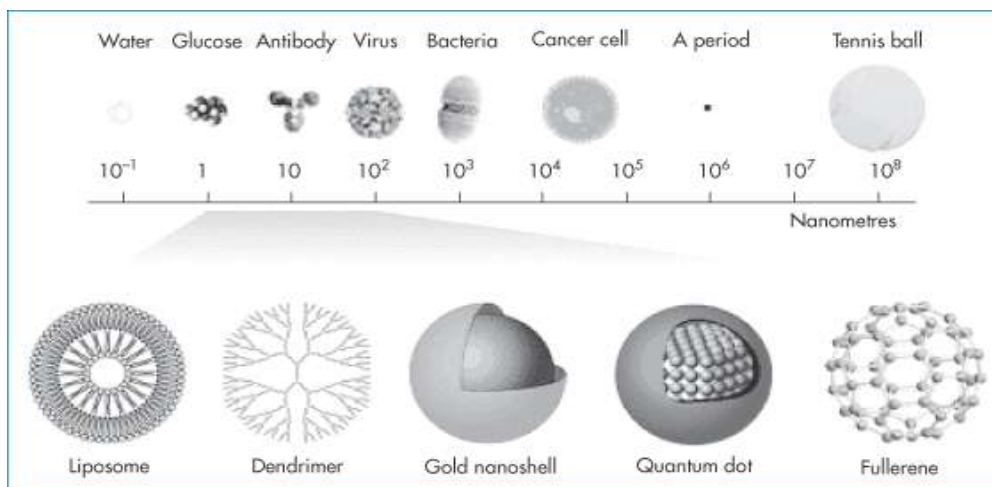


Figure 1: Structures of nanoparticles

### History of Nanomedicines

The production and use of nanosized particles was initiated hundreds of years ago in early times, still, the past few decades in particular have witnessed notable progress in the interdisciplinary operation of this technology.<sup>9,10</sup> In the early 2000s, it was the sanguinity of scientists in nanotechnology that urged governmental and financing associations to shoulder strategic reviews of the present significance of nanomedicine (pivotal objects, implicit openings for bettered health care as well as the threat – benefit analysis of these new technologies) to determine precedences for future financing. The European Science Foundation launched its Forward Look on Nanomedicine (2003), which was the first foresight study on medical usages of nanosciences and nanotechnology. In the same year, the UK government carried out a study to probe whether nanotechnology could raise new ethical, health, and safety issues. The final report of this study was published in 2004 with generally regarded as safe recommendations for a sure, safe, and responsible development of nanotechnology.<sup>11-14</sup>

The European Technology Platform Nanomedicine was launched in 2004 from the innovativeness of the European Commission. This group of experts from industry, investigation centers, and academia convened to prepare the vision regarding future investigation priorities in nanomedicine. In 2005, its vision paper and strategic exploration docket for nanomedicine were released, as a first step toward setting up an multinational platform on nanomedicine, aiming at enhancing the quality of life and health care of patients. The European Foundation for Clinical Nanomedicine was established in Basel (Switzerland; in 2007) as a nonprofit association which aimed at advancing drug for the benefit of individualities and society through the usage of nanoscience.<sup>15-19</sup> The Foundation reached its objectives through support of clinicians and this led to lightning advancement in the medical usages of nanosciences (Figure 2). This Foundation created the atmosphere for focused research, interdisciplinary commerce, and information flow between clinicians, experimenters, the public, and confederated stakeholders.<sup>20</sup>

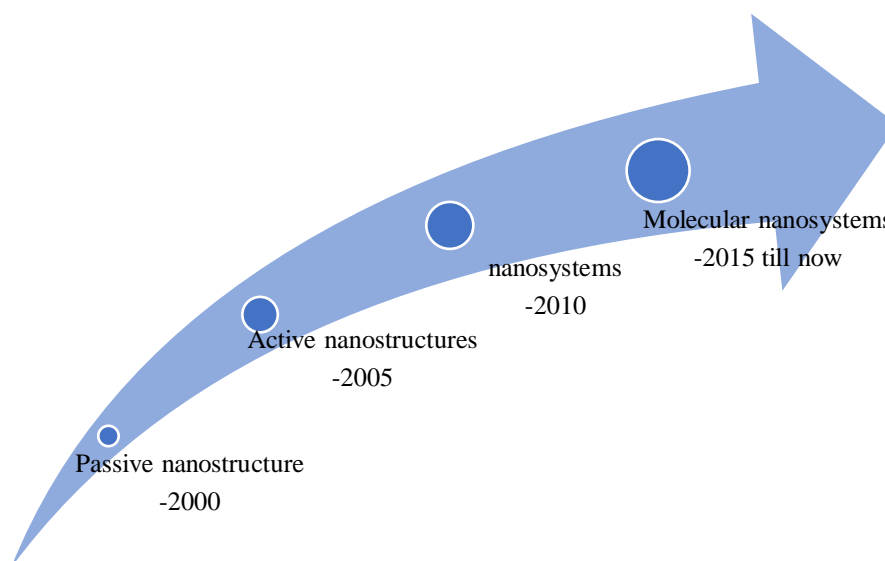


Figure 2: Timeline for Generations of nanoparticles

**Rationale for the Development of Nanomedicine**

The aim of nanomedicine is to monitor, control, construct, form, defend, and enrich humanbiological systems at the molecular level using engineered devices and nanostructures, to achieve medical benefit. For this, the nanocarriers should be engaged with active constituents similar as therapeutic agents, radionuclides, and gene/genome siRNA in the size range from one nanometre to hundreds of nanometres.<sup>21-25</sup> These may be included in a microdevice (that have a macro interface) or in a biological atmosphere. The focus, still, is always on nanocarrier interactions within the frame of a larger device or directly within a cellular or natural system of the body. Nanotechnology is applied highly to give targeted

medicine remedy, diagnostics, tissue rejuvenescence, cell culture, biosensors, and other tools in the field of molecular biology. varied nanotechnology platforms like fullerenes, nanotubes, QDs, nanopores, dendrimers, liposomes, magnetic nanopores, and radio-controlled nanoparticles readily interact with biomolecules located on both the cell surface and within. Therefore, nanocarriers acting as a vehicle can't only transport encapsulated or grafted small chemotherapeutic medicines, but also convey them inside cells once they've penetrated those.<sup>26</sup> Similar systems can also be anchored with ligand, peptide, and fractions of antibodies on their surface to target-specific tissues, therefore enhancing the specificity of the delivered drug molecule.<sup>27</sup>

Table 1: FDA approved Nano formulation available in pharmaceutical industry

Commercial Nano formulations	Nanocarrier	API	Applications in medicine
Avinza®	Nanocrystal	Morphine sulphate	Psychostimulant
Doxil®	Liposome	Doxorubicin	AIDS-related KS, multiple myeloma, ovarian cancer
Lipocurc™	Liposome	Curcumin	Inflammatory diseases
Genexol®	Micelles	Paclitaxel	Metastatic breast cancer, pancreatic cancer
Emend®	Nanocrystal	Aprepitant	Antiemetic
Inflexal® V	Liposomes	Influenza virus antigens	Influenza vaccine
Taxotrel®	Micelles	Docetaxel	Antineoplastic

Copaxone®	Polymer-based nano formulations	Polypeptide	Multiple sclerosis
Abraxamel®	Protein Nanoparticles	Paclitaxel	Breast cancer, Non-small cell lung cancer, Pancreatic cancer
Fungizone®	Colloidal dispersion micellar	Amphotericin B	Systemic fungal infections
Feridex®	Inorganic nanoparticles	Iron oxide	Liver/spleen lesion MRI
NanoTherm®	Inorganic nanoparticles	Iron oxide	Iron deficiency anemia, glioblastoma, prostate, and pancreatic cancer
Adagen®	Polymeric nanoparticles	Pegademase bovine	Severe combined immunodeficiency disease
Estrasorb™	Micelles	Estradiol	Menopausal therapy
Nanocurc™	Polymeric nanoparticles	Curcumin	Pancreatic cancer
Visudyne®	Liposomes	Verteporfi	Ocular histoplasmosis, myopia, decreased visio

### Nanomaterials Used for the Development of Nanomedicines

Use of novel bionanomaterials like nanoparticles, liposomes, metal nanoparticles, dendrimers, and carbon nanotubes (CNTs), nano shells, nanopores,

nanorobots, and nanosuspension for drug delivery purposes constitutes a burgeoning new field called “nanomedicines” that seeks to address the issue in order to maximize the therapeutic response with improved patient compliance.<sup>28</sup>(Figure 3)

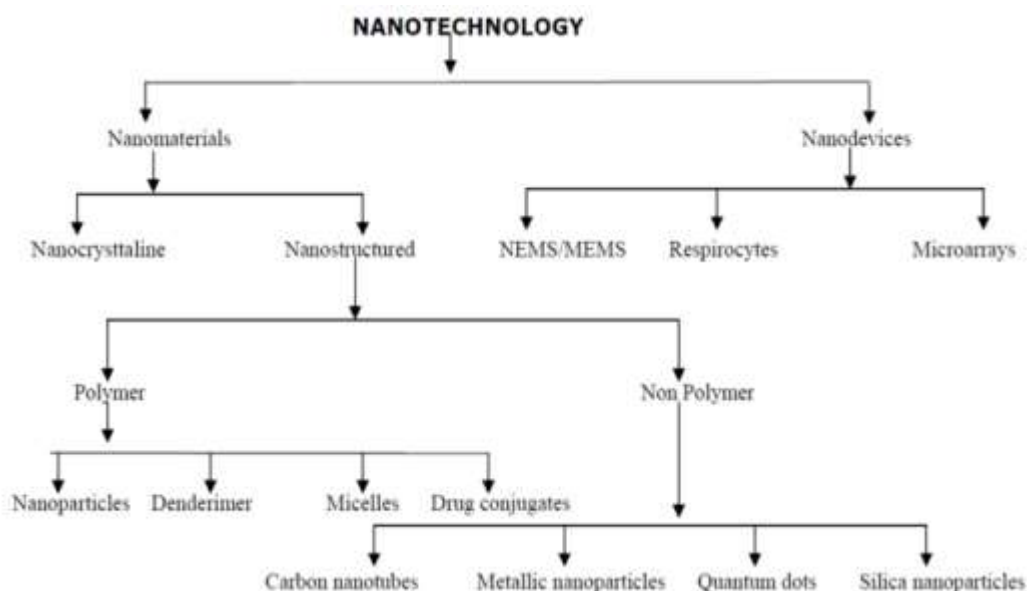


Figure 3: Types of nanoparticles

Table 2: Indexing if different types of nanoparticles

Types	Nature
Nanosuspensions	Nanosuspensions are submicron colloidal biphasic dissolutions of pure drug particles ( lower than 1 $\mu\text{m}$ ) that are stabilized by a small percentage of excipients, similar as surfactants and polymers, without any matrix material, which could dramatically enhance the saturated solubility, dissolution rate, and adhesion of drug particles to cell membranes. Nanosuspensions are most suitable for medicines that bear high dosing or have limited administrative volume. Nanosuspensions have been demonstrated to be a superior replacement over other approaches presently available for enhancing bioavailability of a number of inadequately soluble drugs due to high dissolution rate, amplified rate and extent of absorption, area under plasma versus time curve, onset time, peak drug level, reduced variability, and reduced fed/dieted effects. The best option is for topical preparations, i.e., the higher penetration capability. For oral preparations nanoparticles can cleave to the gastrointestinal mucosa extending the contact time of the medicine therefore enhancing its absorption (Attarietal., 2016)
Polymeric nanoparticles	<p>Polymeric nanoparticles are colloidal solid particles prepared from biodegradable polymers similar as chitosan and collagen or nonbiodegradable polymers similar as poly (lactic acid) (PLA) and poly (lactico-glycolic acid) (PLGA). The unique sizes of nanoparticles are amenable to surface functionalization or alteration to achieve desired characteristics. This was achieved by varied approaches to form the corona to increase medicine retention time in blood, reduce nonspecific distribution, and target tissues or specific cell surface antigens with targeting ligands (peptide, aptamer, antibody, and small molecule). Different materials/ particles are used for the preparation of nanoparticles leading to a distinction in surface properties (Kumarietal., 2010)</p> <ul style="list-style-type: none"> <li>• Gelatin Nanoparticles</li> <li>• Chitosan Nanoparticles</li> <li>• Albumin Nanoparticles</li> </ul>
Superparamagnetic iron oxide nanoparticles	Superparamagnetic iron oxide nanoparticles (SPIONs) are new drug-delivery vehicles. SPIONs are small synthetic $\gamma\text{-Fe}_2\text{O}_3$ (maghemite) or $\text{Fe}_3\text{O}_4$ (magnetite) particles with a core ranging between 10 and 100nm in periphery. These magnetic particles are covered with certain biocompatible polymers, similar as dextran or polyethylene glycol, which give chemical handles for the conjugation of therapeutic agents and also enhance their blood distribution profile
Metal nanoparticles	<p>Metal nanoparticles are nanosized inorganic particles, especially nanoparticles of the alkali metals and the noble metals, copper, silver, and gold of either simple or composite nature; they display unique physical chemical and visual properties and represent an progressively important material in the development of new nanodevices which can be used in multitudinous physical, biological, biomedical, and pharmaceutical usages.</p> <ul style="list-style-type: none"> <li>• Silver Nanoparticles</li> <li>• Gold Nanoparticles</li> </ul>

Carbon nanotube	Carbon nanotube CNTs are unique sp <sup>2</sup> hybridized three-dimensional tubular structures, conforming exclusively of carbon atoms with C – C distance of 1.4 Å arranged in a series of graphene sheets rolled up into a seamless tubular cylinder with open ends and a periphery of around tens of nanometers. This carbon- based new nanomaterial belongs to the fullerenes family, i.e., the third allotropic form of carbon along with diamond and graphite. CNTs’ unique physicochemical properties make them an ideal applicant for drug delivery and targeting; still, poor dispersibility has been the utmost hurdle to their use in nanomedicines
Quantum dot	QDs are a generation of superior visual property fluorophores that have captivated experimenters in the biomedical field over the last decade. QDs have unique optic properties similar as tunable emission spectra, enhanced brightness, superior photostability, and contemporaneous excitation of multiple fluorescence colors as compared to organic dyes and fluorescent proteins. QDs are colloidal semiconductor nanocrystals with excellent photoluminescent properties, high quantum yields, and high resistance to photo bleaching. The term “ quantum dot” was coined in 1988 and generally produced from groups III – V and II – VI elements of the periodic table. QDs must be highly expanded to include wider categories of nanoparticles more recently established by experimenters and based on carbon, silicon, gold, molybdenum, sulfate, and similar materials, all of which exhibit the quantum confinement event associated with a spectacular change of electron behavior kept at the boundaries of the Bohr radius in ultrasmall objects with size below 10 nm (Wang and Hu, 2014)
Dendrimers	Among the available polymeric nanocarriers, dendrimer is one of the most extensively explored polymeric nanocarriers (Tekade et al., 2015d). Dendrimers are new three-dimensional highly branched polymeric nanocarriers that are synthesized in a reiterative trend. The spherical shape with well- defined multivalent structure, monodispersity, and highly controlled architecture of dendrimers render them an inimitable carrier system which could be successfully explored for targeted medicine delivery. These structures have diameters ranging from 1 to 10 nm. The presence of a large hydrophobic depression can be used for the entanglement of bioactives, giving opportunities for controlled and sustained drug release.

### Preparation of Nano Particles

The different approach involved in the preparation of nanoparticles depends on the proper selection of mainly on two aspects (Figure 4). They are

- ✓ Physicochemical characteristics of the polymer.



✓ Drug to be loaded

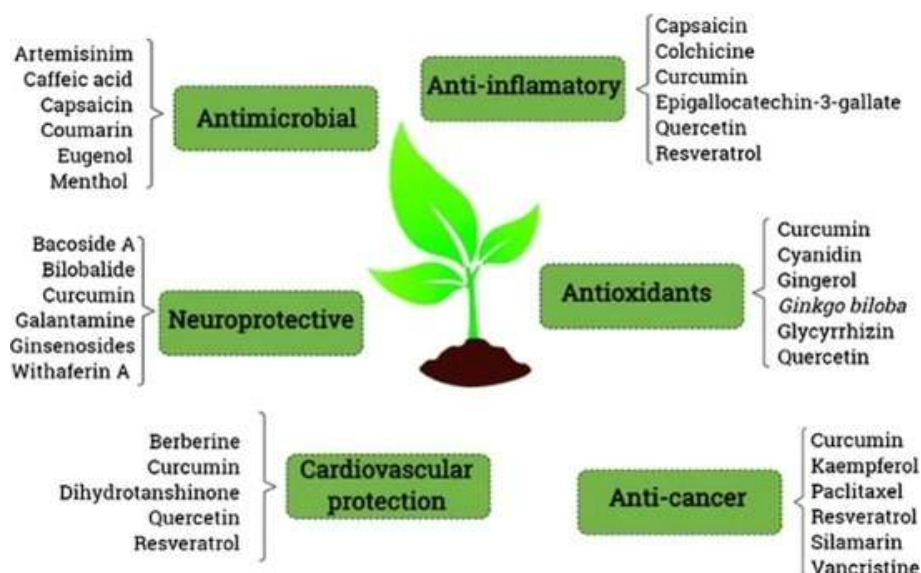


Figure 4 Different plant sources used in Nanomedicine

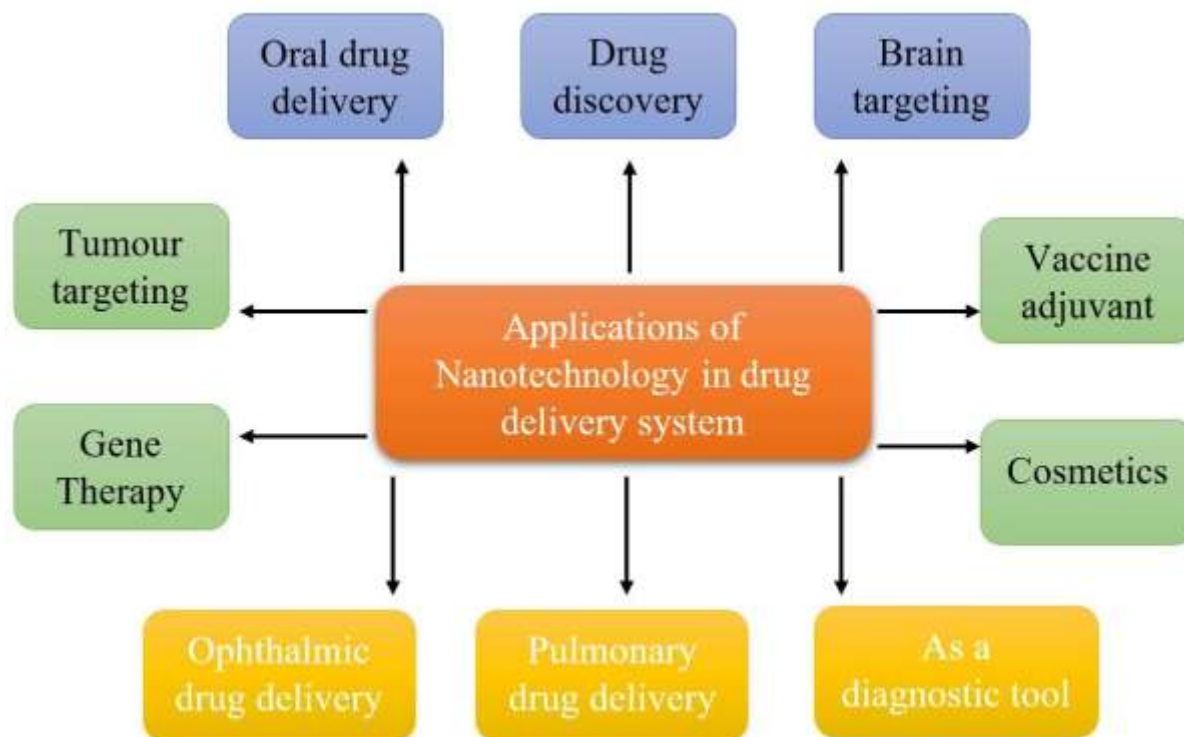
The different methods are

- 1) Amphiphilic macromolecule cross linking.
  - Heat cross linking.
  - Chemical cross linking.
- 2) Polymerization based methods.
  - Polymerization of monomers in-situ.
  - Emulsion (micellar) polymerization.
  - Dispersion polymerization.
  - Interfacial condensation polymerization.
  - Interfacial complexation.
- 3) Polymer precipitation methods.
  - Solvent extraction or evaporation.
  - Solvent displacement (nano precipitation).
  - Salting out

### Applications of Nanotechnology

Nanostructured biomaterials have incomparable physicochemical properties similar as being ultrasmall with controllable size, large surface area to mass ratio, high reactivity, and functionalizable structure. They modify and widen the pharmacokinetic and pharmacodynamic properties of various types of medicine molecules.<sup>29-32</sup> Thus, nanomaterials with such inconceivable properties have been exhaustively investigated in a broad array of biomedical applications, in particular targeted delivery of both imaging agents and anticancer medicines and early finding of cancer lesions, determination of molecular signatures of the tumor by noninvasive imaging and most importantly molecular targeted cancer therapy regenerative drug and tissue engineering. (Figure 5)

Figure 5: Application of Nanotechnology in drug delivery system



#### Targeted drug delivery

The anticancer potential of the SQV-loaded folic acid (FA) conjugated PEGylated and nonPEGylated poly (-lactide-coglycolide) (PLGA) nanoparticles (NPs) (SQV – Fol –PEG – PLGA and SQV – Fol – PLGA) reported by Singh et al. on PC-3 ( human prostate) and MCF-7 ( human breast) cancer cell lines. SQV – Fol – PEG – PLGA showed enhanced cytotoxicity and cellular uptake and was most preferentially taken up by the cancerous cells via folate RME mechanism. At 260mM concentration, SQV –PLGA NPs and SQV – Fol – PEG – PLGA NPs showed 20, and 23 cell growth inhibition in PC-3 cells, independently, whereas in MCF-7 cells it was 15, and 14 cell growth inhibition, independently (Singh et al., 2015)

#### Radiotherapy

Radiation sensitization is a process of enhancing the vulnerability of tumor tissues to injury by radiation exposure. Therapeutic rays, employed in the form of radiation remedy, don't distinguish between normal and cancerous cells and must depend on targeting the radiation rays to specific cells. Still, the application of nanoscale

particles in radiation therapy has aimed to develop outcomes in radiation therapy by rising toxin in tumors and lowering it in normal tissues (Atunetal., 2015). The use of nanomaterial radiosensitizers is also called nanoparticle enhancedX-ray therapy. Current progress in nanomedicine and radionuclide therapy has revealed the possibility of designing tumor-targeted nanocarriers that can deliver radionuclide loads to a specific location or in a molecularly particular manner to enhance the efficacy and safety of cancer imaging and therapy (Atunetal., 2015)

#### Photothermal therapy

The use of photo- convinced heat for cancer management is known as photothermalTherapy.These approaches of light-absorbing stains were reutilized to attain photothermal damage of tumor. It has been assumed as a implicit anticancer treatment since it can be controlled spatiotemporally, therefore avoiding damage to nontargeted regions. As most photothermal- converting materials are nanoscaled, photothermal therapy constitutes a class of nanomedicine. First, template nanomaterials to be used for therapy should retain a photothermal effect



that converts light energy into heat energy, i.e., they should have high photothermal conversion effectiveness. Second, the photothermal effects should occur in response to NIR light to assure deep tissue penetration. Finally, the surface of the nanomaterials should be fluently modified to enable effective photothermal therapy. Numerous nanomaterials similar as plasmonic nanoparticles, i.e., gold nanoparticles (AuNPs), silver nanoparticles (AgNPs), sp<sup>2</sup> domain-rich carbon nanoparticles similar as CNTs, and graphene are well known as photothermal converting nanoparticles. In addition, single-layered transition metal dichalcogenides and melanin structure have recently shown great possibility for operation as photothermal therapeutic agents (Kim et al., 2016).

#### Vaccination in AIDS management

Various biodegradable and nonbiodegradable polymeric and liposomal delivery systems have been explored for converting HIV antigens to synthetic NPs to increase their immunogenicity and to defend them against redundant and intracellular degradation. Targeting dendritic cells (DCs) that are essential for initiating immune responses can be achieved by Dermavir, which is the first nanomedicine developed for the treatment of HIV/ AIDS that has demonstrated encouraging phase II clinical safety, immunogenicity, and efficacy results (Kumar et al., 2015).

#### Fungal infection

Fungal infections can attack epithelial tissues, deeper organs, as well as the immunological state of the patient. Topical remedy is desirable since, in addition to targeting the site of infection, it reduces the threat of systemic side effects and increases patient compliance. Nontoxic nanoobjects were also included because they enhance the optical delivery of antifungals. The nanoparticulate agents against cutaneous and ocular mycosis are metallic nanoparticles and nonmetallic nanoparticles (Perera et al., 2015).

## II. CONCLUSION

It's clear that nanotechnology represents a crucial exploration area to face the pharmaceutical industry's R&D challenges. Nanotechnology-based drugs have already found success in the industrial script. This worldwide trend, had increased in the coming times. It offers new tools, chances and scope, which are anticipated to have a great impact on numerous areas in disease,

diagnostics, prognostic and treatment of diseases through its nano- engineered tools. It raises new possibility to industries by delivering new patentive technologies in view of profit loss caused due to off- patent drugs. But still we lack the sufficient data and guidelines regarding safe use of these nanotechnology grounded devices and materials

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