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An Review of Nanotechnology

T.Vyjayanthimala[1*], Snehalatha[1], T.S. Nagaraja[1], T.Mallamma[1]

1.Department of Pharmaceutics, S.J.M. College of Pharmacy,JMIT Campus Chitradurga, Karnataka -577502

ABSTRACT

For the past few decades, there has been a considerable research interest in the area of drug delivery using particulate delivery systems as carriers for small and large molecules. Particulate systems like nanoparticles have been used as a physical approach to alter and improve the pharmacokinetic and pharmacodynamic properties of various types of drug molecules. Nanoparticles promise to revolutionize medicine and increasingly used in drug delivery. The purpose of this review is to explore the design, development of nanotechnology, different method of preparation and application. By making the drug into nanoparticles by using different method of preparation, which may alleviate the manifestations of disease with minimal dose and less toxicity. These drug delivery systems can be potentially translated into targeted cellular and tissue-specific clinical applications designed to achieve maximal therapeutic efficacy with minimal side effects.

Keywords: nanotechnology, methods of preparation, applications in drug delivery.

*Corresponding Author Email: rawalvyjayanthi93@gmail.com

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INTRODUCTION

The platform for nanotechnology is believed to have been laid down by Richard Feynman a physicist at California Institute of technology, in 1959.He presented a technological vision of miniaturization of materials, manipulating and controlling things on a small scale called "nanotechnology". The term nanotechnology was first used in 1974 by Norio Taniguchi, a researcher at the University of Tokyo who used it to refer to the ability to engineering materials at nanoscale.

Nanotechnology is a breakthrough technology expected to bring revolutionary changes in the field of life sciences, including drug delivery, diagnostics, pharmaceuticals and production of biomaterials; in the field of medicines is one of the most fascinating areas that include new career therapies, drug delivery systems and biomaterials for implants or prosthesis.[1]Nanotechnology can be defined as the science and engineering involved in the design, synthesis, characterization and application of materials and devices whose smallest functional organization is on nanometre scale. In the past few years, nanotechnology has grown by leaps and bounds and it have a huge potential in the development of new and effective medical treatments. At present 95% of all new potential therapeutics have poor pharmacokinetics and biopharmaceutical properties. Therefore there is a need to develop suitable drug delivery systems that distribute the therapeutically active drug molecule only to the site of action, without affecting healthy organs and tissues. Nanotechnology plays an important role in the therapies of the future as 'nanomedicine' thus lowering doses required for efficacy as well as increasing the therapeutic indices and safety profiles of new therapeutics.[2]

Nanoparticles

Nanoparticles are solid colloidal particles ranging in size from 1 to 1000nm . They consist of macromolecular materials and can be used therapeutically. In this drug or biologically active material dissolved, entrapped or encapsulated and to which the active principle is absorbed or attached. Nanoparticle has emerged as a promising strategy for the efficient delivery of drugs used in the treatment of cancer by utilizing the enhanced permeability and retention effect and tumor specific targeting. They are especially designed to release the drugs in the vicinity of the target tissue.[1]

The major goals in designing nanoparticles as a delivery system are to control

- Particle size
- Surface properties

- Release of pharmacologically active agents in order to achieve site-specific action of the drug at the therapeutically optimal rate and dose regimen[1]

Types of Nanoparticles Applied in Drug Delivery [3]

Sr.no	Type of Nanoparticles	Material used	Applications
1	Nanosuspensions and Nanocrystals	Drug powder is dispersed in surfactant solution	Stable system for controlled delivery of poorly soluble drug
2	Solid lipid Nanoparticles	Melted lipid dispersed in Aqueous surfactant	Least toxic and more stable Colloidal carrier systems as alternative materials To polymers
3	Polymeric nanoparticles	Biodegradable polymers	Controlled and targeted drug delivery
4	Polymeric micelles	Amphiphilic block copolymers	Controlled and systemic delivery of water insoluble drugs
5	Magnetic Nanoparticles	Magnetite Fe2O3,Meghe Mite coated with dextran	Drug targeting diagnostics to in medicine
7	Liposomes	Phospholipids vesicles	Controlled targeted drug delivery
8	Nanoshells	Dielectric core and metal shell	Tumor targeting
9	Ceramic Nanoparticles	Silica,alumina,titania	Drug and biomolecule delivery
10	Nanopores	Aerogel,which is produced by cell gel chemistry	Controlled release drug carriers
11	Nano wires	Silicon, cobalt, gold or Copper based nanowires	Transport electron in nano Electronics
12	Quantum dots	cdSe-cdS core shell	Targeting ,imaging agent
13	Nano films	polypeptides	Systemic or local drug Delivery.
14	Ferrofluids	Iron oxide magnetic Nanoparticles surrounded by polymeric layer.	For capturing cells and other biological targets.

PREPARATION OF NANO PARTICLES

The different methods are

Emulsion Polymerization[4]

Emulsion polymerization in a continuous aqueous phase is one of the most frequently used methods to produce nanoparticles. This method has a number of advantages. It represents a rapid production method that can rather easily be scaled up. The most important advantage, however, is that no organic solvents at all or well tolerated solvents like ethanol are employed during this procedure. To produce nanoparticles by emulsion polymerization a sparsely soluble monomer is dissolved in the aqueous phase. Additional monomer above its solubility may be added. This additional monomer can be stabilized by addition of emulsifiers(hence the name "emulsion polymerization") and then is present in emulsifier micelles or in larger emulsion droplets.

However, the presence of an emulsifier is not necessary and does not influence the kinetics of this process.

Interfacial Polymerization[5]

In this the preformed polymer phase is transformed to an embryonic sheath. The polymer that becomes core and drug molecule to be loaded are dissolved in a volatile solvent. The solution is then poured into a non-solvent for both polymer and core phase. The polymer phase is separated as a coacervate phase at o/w inter phase. The resultant mixture turns milky due to formation of nano capsules. This is used for encapsulation of proteins, enzymes, anti-bodies and cells were employed.

Solvent Deposition or Nanoprecipitation[4]

Solvent deposition or nanoprecipitation describes the formation of nanocapsules or nanoparticles by dissolution of poly(lactic acid) or a poly(lactic acid)-copolymer in a water miscible organic solvent, such as Acetoneor benzyl alcohol. Again the drug is dissolved in or admixed to the organic solution. This mixture is then poured into a surfactant-containing water phase under moderate stirring. Surfactants that can be used include poloxamers118, 407, poloxamine 904, 908 and 1504, or stabilizing hydrocolloids such as poly(vinyl alcohol) or gelatin. The aqueous phase turns opalescent due to the formation of nanocapsules. The acetone or a similar water miscible organic solvent is then removed similarly to solvent evaporation. Besides polylactic acid and copolymers, other polymers such as poly(_-caprolactone) Eudragit oranother methyl methacrylic acid copolymer, poly(ß-malic acid-cobenzyl maleate), or cellulose acetate phthalate can be used, and by using acetonitrile as the organic solvent even no surfactants are required.

Emulsification/solvent evaporation[7]

Emulsification-solvent evaporation involves two steps.

The first step requires emulsification of the polymer solution into an aqueous phase (see Figure 1). During the second step polymer solvent is evaporated, inducing polymer precipitation as nanospheres. A polymer organic solution containing the dissolved drug is dispersed into nanodroplets, using a dispersing agent and high-energy homogenization, in a nonsolvent or suspension medium such as chloroform (ICH, class 2) or ethyl acetate (ICH, class 3). The polymer precipitates in the form of nanospheres in which the drug is finely dispersed in the polymer matrix network. The solvent is subsequently evaporated by increasing the temperature under pressure or by continuous stirring. The size can be controlled by adjusting the stir rate, type and amount of dispersing agent, viscosity of organic and aqueous phases, and temperature. Even though different types of emulsions may be used, oil/water emulsions are of interest

because they use water as the nonsolvent; this simplifies and thus improves process economics, because it eliminates the need for recycling, facilitating the washing step and minimizing agglomeration. However, this method can only be applied to liposoluble drugs, and limitations are imposed by the scale-up of the high energy requirements in homogenization. Frequently used polymers are PLA, PLGA, ethyl cellulose (EC), cellulose acetate phthalate, poly(E-caprolactone) (PCL) and poly(h-hydroxybutyrate) (PHB). Drugs or model drugs encapsulated were albumin, texanus toxoid, testosterone, loperamide, prazin- quantel, cyclosporin A, nucleic acid and indomethacin.

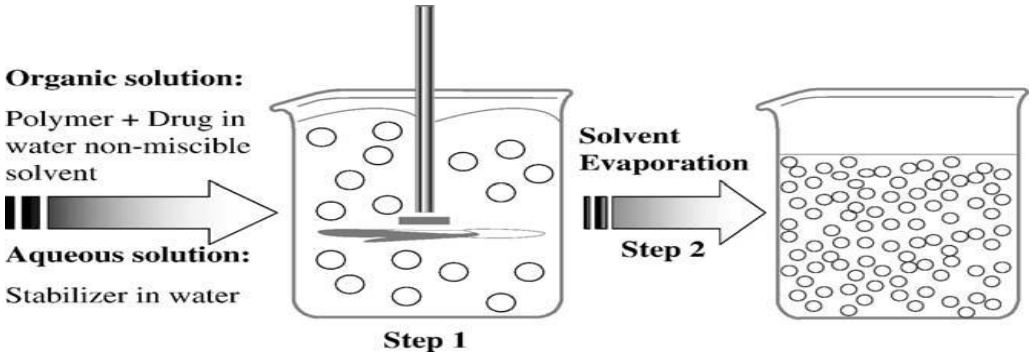

Figure 1. Schematic representation of the emulsification-evaporation technique.

Nanoparticles produced by desolvation of macromolecules[7]

Another technology applicable to a wide range of polymers is based on desolvation by charge and pH changes, or by addition of a desolvating agent (ethanol or concentrated inorganic salt solutions). The main advantage is that this process does not require an increase in temperature and, therefore, may be useful when heat sensitive drugs are used. Nanoparticles were prepared using the process of reversible swelling of macromolecules using gelatin, human serum albumin, bovine serum albumin and casein as the macromolecular materials. This process offers the advantage of producing nanoparticles directly in aqueous suspension, but the use of potentially toxic compounds such as glutaraldehyde and desolvating agents requires subsequent purification. Variations in nanoparticle production by the desolvation process were described, but unfortunately the yield is comparatively low. In the case of gelatin, different methods such as the two-step desolvation method have been applied to produce nanoparticles. Recent reports outline the important use of gelatin as drug delivery systems for DNA and cytostatics.

Coacervation or ionic gelation method [8]

Much research has been focused on the preparation of nanoparticles using biodegradable hydrophilic polymers such as chitosan, gelatin and sodium alginate. Calvo and co-workers developed a method for preparing hydrophilic chitosan nanoparticles by ionic gelation .The

method involves a mixture of two aqueous phases, of which one is the polymer chitosan, a di-block co-polymer ethylene oxide or propylene oxide (PEO-PPO) and the other is a polyanionsodium tripolyphosphate. In this method, positively charged amino group of chitosan interacts with negative charged Tripolyphosphate to form coacervate with a size in the range of nanometer. Coacervates are formed as a result of electrostatic interaction between two aqueous phases, whereas, ionic gelation involves the material undergoing transition from liquid to gel due to ionic interaction conditions at room temperature.

SALTING OUT[5]

It is one of the most commonly adopted methods used to prepare nanoparticles. The method involves the incorporation of a saturated aqueous solution of polyvinyl alcohol (PVA) into an acetone solution of the polymer under magnetic stirring to form an o/w emulsion. The process differs from nanoprecipitation technique as in the latter the polymeric solution (acetone) is completely miscible with the external aqueous medium. But in the salting out technique, the miscibility of both the phases is prevented by the saturation of the external aqueous phase with PVA. The precipitation of the polymer occurs when a sufficient amount of water is added to external phase to allow complete diffusion of the acetone from internal phase into the aqueous phase. This technique is suitable for drugs and polymers that are soluble in polar solvents, such as acetone or ethanol.

INORGANIC NANOPARTICLES[4]

Inorganic nanoparticles made of silica also were produced and their body distribution was investigated. Fumed silica with particle sizes around 16 nm (Aerosil-200) is a frequently used excipient for oral, dermal and rectal dosage forms. However, the use of silica nanoparticles for parenteral application is limited or not feasible due to the non biodegradability of this material. It has to be mentioned that colloidal aluminum hydroxide, phosphate and oxide are contained as adjuvants in a number of intramuscularly or subcutaneously administered vaccines.

Preparation of Nanoparticles in an Oil Emulsion[4]

One of the first methods to produce nanoparticles was the emulsification of an aqueous solution containing a dissolved macromolecule such as albumin, gelatin, chitosan, or a similar macromolecule together with the drug in an oil. The emulsion is then homogenized with a high sheer homogenizer or by ultrasonication and poured into hot oil leading to the denaturation of the macromolecules and the formation of solid nanoparticles. Alternatively to heat denaturation the particles also may be hardened at much lower temperatures, even at room temperature, by cross-

linking with an aldehydes or by gelation. After solidification of the nanoparticles the oil is removed by washing with volatile organic solvents.

Nanoparticles Made by Other Methods[4]

Nanoparticles also may be produced by a variety of other methods. These include polyglutaraldehyde nanoparticles produced by poly condensation techniques, carbohydrate nanoparticles made directly from starch or from polyacryl dextran or polyacryl starch, alginate nanoparticles, chitosan nanoparticles made by electrostatic interaction and complexing method, nanoparticles consisting of poly(ethylene imine)–fatty acid complexes and nanoparticles formed by self aggregation of cholesterol–pullulan copolymers.

APPLICATIONS

Vaccines[4]

A large number of reviews have appeared on the subject of using nanoparticles as delivery systems and adjuvants for vaccines. Poly(methyl methacrylate) nanoparticles were shown tobe very good adjuvants for a number of antigen. Antigens may be incorporated into these nanoparticles by polymerization in the presence of the antigen by gamma irradiation at low temperatures, or they may be adsorbed to previously polymerized particles. Adsorption to previously polymerized particles also allows the employment of heat polymerization since most antigens are heat sensitive. The adjuvant effect depended on the particle size as well as on the hydrophobicity. The adjuvant effect increased with decreasing particle size and with increasing hydrophobicity. Poly(methyl methacrylate) nanoparticles were superior to the conventional aluminum adjuvants which are the most frequently used adjuvants for human vaccination. In addition, nanoparticles may be useful for oral vaccination. Oral administration of plasmid DNA (pCMVArah2) bound to nanoparticles produced secretary IgA and serum IgG2a. Such nanoparticles may be useful for treating food allergies.

Nanoparticles for gene delivery[8]

Polynucleotide vaccines work by delivering genes encoding relevant antigens to host cells where they are expressed, producing the antigenic protein within the vicinity of professional antigen presenting cells to initiate immune response. Such vaccines produce both humoral and cell-mediated immunity because intracellular production of protein, as opposed to extracellular deposition, stimulates both arms of the immune system. The key ingredient of polynucleotide vaccines, DNA, can be produced cheaply and has much better storage and handling properties than the ingredients of the majority of protein-based vaccines. Hence, polynucleotide vaccines are set to supersede many conventional vaccines particularly for immunotherapy. However, there

are several issues related to the delivery of polynucleotide which limit their application. These issues include efficient delivery of the polynucleotide to the target cell population and its localization to the nucleus of these cells, and ensuring that the integrity of the polynucleotide is maintained during delivery to the target site.

Peptides and Proteins[4]

The number of peptide and protein drugs is increasing steadily since they are becoming more and more assessable by using genetic engineering technology. However, their stability in body fluids, especially in the gastrointestinal tract, often is very low. In addition they often encounter difficulties in traversing membranes in the body. Peptides and proteins mostly bind rather well to nanoparticles, which can enable an improvement in the stability as well as in the transport across membranes and into specific cells.

Anti-infective Agents[4]

The treatment of intracellular infections often is difficult or impossible, since a number of drugs cannot reach certain target sites within these cells in which the microorganisms reside. Cells that frequently are infected and are inaccessible to a number of relevant antibiotics include phagocytic cells, such as the Kupffer cells in the liver, cells in the spleen, as well as circulating macrophages. Since nanoparticles are easily taken up by these cells, they are well suited for the delivery of anti-infective drugs to these cells.

Cancer treatment[6]

NPPDSs are reported for the application in cancer therapy, transferring conjugated paclitaxel-loaded NPs, nanovaccines, Adriamycin-loaded NPs for hepatoma treatment, magnetic PBCA nanospheres with aclacinomycin A in gastric cancer, near-infrared absorption nanospheres, polypropylenimine dendrimer NPs for oligonucleotides, lytic-peptide-bound magnetite NPs for breast cancer treatment, ceramic-based NPs entrapping water-insoluble photosensitizing anticancer drugs and poly(epsilon-caprolactone) NPs for the delivery of tamoxifen for breast cancer treatment.

Vascular thrombosis[6]

The formation of blood clots in the circulatory system is associated with a range of serious medical conditions including heart attacks, pulmonary embolisms, strokes and deep vein thrombosis. The main component of the clot is the insoluble protein fibrin. Treatment of vascular thrombosis involves the use of thrombolytic drugs that break up the fibrin, allowing the clot to disperse. Biocompatible NPs are used to develop such delivery systems which can carry the thrombolytic drugs. Chellini explained that the thrombolytic drugs are powerful agents with

serious side effects like causing haemorrhage if they are given systemically. However, orally they are less efficient. If they can be incorporated in NPs, they can be delivered directly to the specific site, using less drug materials and the treatment will be cost-effective with less side effects. The drug will be released from the NPs by diffusion, degradation or erosion.

CONCLUSION

The field of nanotechnology has a bright future with the emergence of several approaches for promising the delivery of therapeutic agents. Some of the marketed formulations like Rapamune®, Emend®, Tricor®, Triglide®, Focalin®, Ritalin are available. Nanotechnology is a most fascinating area where it expected to bring a revolutionary changes in the field of life sciences including, drug delivery, diagnostics, Pharmaceuticals and production of biomaterials for implants and prosthesis. Nanoparticles are much more successful in medical sciences for better drug delivery and patient treatment.

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