IJNRD.ORG ISSN : 2456-4184
INTERNATIONAL JOURNAL OF NOVEL RESEARCH AND DEVELOPMENT (IJNRD) | IJNRD.ORG
An International Open Access, Peer-reviewed, Refereed Journal

A REVIEW ON NANOPARTICLE- A DRUG DELIVERY SYSTEM

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Abstract:-

Nanoparticles are novel approach to drug delivery system in which drug particle is very small ranging from 1 to 100 nm in size which help to formulate a dosage form which can reach site of action and show its pharmacological effect, Nanoparticles are very useful in case of tumor cell specially such tumor in which anti-cancer drug or chemotherapeutic drug cannot reach due to large particle size & small pore size of tissue like Brain in which BBB (Blood Brain Barrier) which is a main barrier for drug therapy, in these review we briefly discuss Nanoparticles, types of Nanoparticles, classification of nanoparticles, Application of Nanoparticles in pharmaceuticals as well as in other fields.

There are many unique carriers in novel drug delivery systems (NDDS) that outperform traditional dose forms. Conventional dosage forms exhibit high dose and poor availability, instability, a first pass effect, fluctuations in plasma drug level, and rapid drug release (Buzea et al., 2007). One crucial tool for the pharmaceutical industry's expansion of the medication market is NDDS. By improving efficacy, safety, patient compliance, and product shelf life, NDDS can reduce issues.

Nano particles [(1-4)]:

In the past ten years, the prefix "nano" has found increased use across a variety of knowledge domains. The terms "nanoscience," "nanotechnology," "nanomaterials," and "nanochemistry" are only a few of the new nano-related terms that are often used in scientific reports, popular literature, and newspapers, and that are now known to a large audience, including non-experts. According to the National Nanotechnology Initiative's definition, nanoparticles are objects with at least one dimensional size between 1 and 100 nm. However, particles up to several hundred nanometers in size are frequently referred to as "nano" particles. Nanotechnology is the study of very small objects. It involves the usage and tinkering with of matter. At this scale, atoms and molecules function differently and have a number of unexpected and intriguing purposes. Pharmaceutical nanoparticles are solid, submicron-sized drug carriers

with a diameter of less than 100 nm that may or may not be biodegradable. Nanosphares and nanocapsules are collectively referred to as nanoparticles. In contrast to nanocapsules, which have a special polymeric membrane surrounding the drug, nanospheres are matrix systems in which the drug is uniformly spread. The classification, preparation method, characterization, application, health implications, and pharmacological features of nanoparticles are the main topics of this systematic review. Nanocarriers with optimized physicochemical and biological properties are taken up by cells more easily than larger molecules, so they can be successfully used as delivery tools for currently available bioactive compounds.

For decades, polymeric nanoparticles have been manufactured for usage in a variety of high performance materials, such as high impact resistant polymers and specialized coatings for these uses. We can measure structure and create control methods to make structured particles thanks to sophisticated analytical approaches and computer simulations of the activities taking place during particle production. By changing the carrier's shape, chemical makeup, internal structure, and morphology of the nanoparticles, for example, we can achieve new degrees of product performance in the targeted drug delivery system.

Nanotechnology applies the principles of engineering, electronics, physical science, and material science & manufacturing at a molecular and supra-micron level. The phrase is derived from the Greek word "Nano," which means dwarf. Particulate dispersions or solid particles with a size between 10 and 1000 nm are referred to as nanoparticles. A nanoparticle matrix is used to dissolve, trap, encapsulate, or attach the medication. Depending on the preparation technique, one can produce nanoparticles, nanospheres, or nanocapsules. Nanospheres are matrix systems in which the drug is physically and uniformly spread, whereas nanocapsules are systems in which the drug is confined to a cavity and enclosed by a special polymer membrane.

Advantage of Nanoparticle [5-6]:-

1) Particle size and surface characteristics of nanoparticles can be easily manipulated to achieve both passive and active drug targeting after parenteral administration.

2) They control and sustain release of the drug during the transportation and at the site of localization, altering organ distribution of the drug and subsequent clearance of the drug so as to achieve increase in drug therapeutic efficacy and reduction in side effects.

3) Site-specific targeting can be achieved by attaching targeting ligands to surface of particles or use of magnetic guidance.

4) Controlled release and particle degradation characteristics can be readily modulated by the choice of matrix constituents. Drug loading is relatively high and drugs can be incorporated into the systems without any chemical reaction; this is an important factor for preserving the drug activity.

5) The system can be used for various routes of Administration including oral, nasal, parenteral, intra-ocular etc.

Limitation of Nanoparticle:-

1) Small size and large surface area can lead to particle particle aggregation, making physical handling of nanoparticles difficult in liquid and dry forms

2) Small particles size and large surface area readily result in limited drug loading and burst release

Types of Nano particles:-

1. Lipid-based nano delivery systems [7- 12] :-

Increased oral, topical, and intravenous medication administration has frequently utilised lipid-based Nanaoparticle . Solid lipid NPs (SLNs) and liposomes are the most popular lipid-based nanodelivery methods. The particle size range of liposomes, which are spherical vesicles made of phospholipid bilayers, varies between 10 and 1000 nm, When phospholipids are spread in an aqueous solution, liposomes are created. The hydrophilic head group of phospholipids interacts with the polar medium when they are in water, creating multi- and unilayered vesicles. These vesicles have a spherical shell made of biological lipid bilayers. Because of their entrapment capabilities, liposomes are a highly useful tool for pharmaceutical delivery. Liposomes are normally developed by drying down lipids from an organic solvent, then dispersing the lipids through aqueous medium in the presence of a detergent, followed by purification Probe or bath sonication is the technique that is most frequently employed for dispersion in liposome production. The liposome's lipid bilayer properties may enable it to fuse with cell membranes, resulting in the direct administration of substance (in this case, a medication) inside the cell . Studies on the liposomal effects of anticancer medications have shown that greater tissue retention increases total drug circulation and tumour exposure length.

2. Polymer-based nanodelivery systems ([13-17]):-

Tissue- and organ-specific targeting makes polymer-based NPs preferable than liposomes. Researchers and drug development experts have a wide range of options for reducing toxicity and inducing particular functions for a given drug or compound thanks to the ability to absorb and coat polymeric formed NPs with various substances, such as target-specific ligands for tissue specificity and polyethylene glycol for increased hydrophilic properties**.** For the creation of polymer-based NPs with a lipophilic core, numerous biodegradable polymers are accessible some of the more widely used biodegradable polymers include poly (lactic acid) (PLA), poly (glycolic acid) (PGA), and poly (lactic acid) (PLGA) polymers**.** Commercially available materials for use in different drug delivery systems include PLGA, PLA, and PGA. Because PLA, PGA, and PLGA are all biodegradable polymers that hydrolyze to lactic acid and/or glycolic acid during hydrolysis, their usage in NP formulations enables particle modification without increasing toxicity. The formation of Krebs cycle intermediates associated with these polymers creates minimal physiological toxicity as they are easily and efficiently metabolized. Differing NP characteristics such as particle size, shape and zeta potential can be produced according to parameters set forth by the specific synthesis process.

3) Metal-based systems [18- 22] :-

In both industry and academia, metal-based NPs are often used. The use of gold-based NPs for the treatment of cancer has attracted a lot of attention. They are an excellent tool for future study in cancer therapy and treatment because of the distinctive sheen that is common to gold NPs and the simplicity of localisation and visibility. Superparamagnetic iron oxide nanoparticles (SPION) have made a promising entrance into the realm of biomedicine as a therapeutic and diagnostic tool due to their magnetic characteristics and biocompatibility. Due to their strong magnetism, SPIONs provide ideal image probes for MRI contrast and imaging. Comparing SPION-based contrast agents to more traditional contrast agents like gandolinium, it has been discovered that the former resulted in a longer delineation of tumour margins and improved tumour localisation. As a result, the FDA has approved the use of many iron-oxide-based imaging agents, including Lumiren and Endorem, in the medical industry. Additionally, gold nanoparticles have been employed to induce hypothermic damage in a number of cancer cell lines and have been proven successful in the management of superficial tumours. As a result, clinical trials using gold NPs and hypothermic procedures are now being conducted for patients with oropharyngeal cancers. Hexachloroplatinate can be easily reduced using hydrogen gas to produce platinum nanoparticles (NPs). Platinum nanoparticles' surprise antioxidant effects are among their best qualities. During experimental research, it was discovered that platinum NPs emit antioxidant

characteristics and increase Caenorhabditis elegans' lifespan. In the past several years, platinum-based NPs have shown improved chemotherapeutic agent efficacy in the treatment of various breast and ovarian cancer cell lines . It has been demonstrated that platinum nano particles both dramatically improve anticancer medication efficacy and lower the toxicity profiles frequently linked to the use of chemotherapy drugs. These results imply that the advantageous characteristics of platinum NPs may go beyond their antioxidant activities and provide novel benefits in drug delivery.

4) Carbon nanotubes[23,24] :-

Carbon nanotubes (CNTs) are tubes made of one or more walls of grapheme sheets with a hexagonal arrangement of carbon atoms. First-generation CNTs were extremely poisonous, making them unsuitable for use in a range of industries, including medicine delivery. The toxicity profiles often associated with CNT administration, however, have been greatly reduced because to recent improvements in CNT formulation. Researchers may be able to create altered CNTs with altered toxicity profiles by altering the surface and altering covalent and non-covalent intermolecular interactions. Over the past few years, interest in research into medicine delivery utilising CNT has increased due to its potential to reduce hazardous side effects. Improvements in the transport of numerous different compounds have been demonstrated using CNT . Multi-walled CNTs were employed in the reformulation of DOX for the treatment of cancer by Mehra et al. When compared to typical DOX dosages, the study discovered that medication formulations using CNTs had increased total circulation duration, prolonged release, and higher DOX cytotoxicity. There have also been reports of additional compounds being released over time. The movement of CNTs across cellular membranes via endocytosis or non-endocytosis pathways is expected to facilitate cellular absorption. In tumour tissue, CNTs have shown they can increase permeability and extravasate. They are the perfect candidates for novel drug delivery strategies due to their huge surface area and hence great loading capacity.

5) Quantum dots [25- 27]:-

The particle size distribution of quantum dots (QDs), a type of fundamental semiconductor that exhibits electrical properties, ranges from 2 to 10 nm. These particular dots are created and produced via a variety of methods, including manufacturing, inorganic nanocrystal virus assembly, and electrochemical assembly employing ionic reactions between electrolyte and metal structures. The number of places where active material can be attached is greater in QDs. Due to the abundance of active sites on QDs, multifunctional characteristics can be created by attaching and modifying a variety of bioactive substances. According to a recent study, PEGylated QDs promoted NP trafficking and improved cellular uptake by focusing on the caveolae-mediated endocytic pathway. By attaching prostate-specific antigen to QDs, several studies have established the use of QDs in tissue-specific targeting of tumour cells.

6) Super paramagnetic nanoparticles:-

The molecules known as super paramagnetic molecules are those that are drawn to a magnetic field but do not retain any magnetic properties once the field has been removed. For selective magnetic bio separations, iron oxide nanoparticles in the 5-100 nm range have been employed. For separation from the surrounding matrix, typical approaches involve coating the particles with antibodies to cell-specific antigens. Due to their paramagnetic characteristics, super paramagnetic nanoparticles have the ability to be seen in magnetic resonance imaging (MRI), guided to a specific place using a magnetic field, and heated to cause the release of a medication. Super paramagnetic nanoparticles fall within the category of inorganic-based particles with an iron oxide core that is covered in either inorganic substances (silica, gold), or organic substances (phospholipids, fatty acids, polysaccharides, peptides, or other surfactants and polymers). Super paramagnetic nanoparticles differ from ordinary nanoparticles in that they can be heated or guided to a specific place in the presence of an externally generated AC magnetic field due to their inducible magnetization. These

qualities make them appealing for a variety of applications, including magnetically assisted cell transfection, drug delivery systems, magnetic hyperthermia (local heat source in the case of tumour therapy), and various separation techniques and contrast enhancing agents for MRI.

Methods of preparation

The various methods are as follows:-

1. Emulsion Polymerization
2. Desolvation method
3. High Pressure Homogenization
4. Controlled Gellification Method
5. Controlled Nanoprecipitation without Surfactants
6. Solvent Evaporation Method
7. Solvent Emulsification or Solvent Diffusion method
8. Supercritical Fluid Extraction
9. Melt Emulsification and Homogenization following Spray drying of nanodispersions

Application of Nanoparticle:-

1) Tumor targeting using Nanoparticulate delivery system [(28)]

The rational of using nanoparticles for tumor targeting is based on Nanoparticles will be able to deliver a concentrate dose of drug in the vicinity of the tumor targets via the enhanced permeability and retention effect or active nanoparticles. Nanoparticles will reduce the drug exposure of health tissues by limiting drug distribution to target organ.An experiment demonstrated in mice treated with doxorubicin incorporated into poly (isohexylcynoacrylate) nanospheres that higher concentration of doxorubicin manifested in the liver, spleen and lungs than in mice treated with free doxorubicin.

2) Nanoparticles for Gene delivery:-

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.

Nanotechnology in Medicine Application:

3) Anti-Microbial Techniques:-

One of the earliest nanomedicine applications was the use of nanocrystalline silver, which is as an antimicrobial agent for the treatment of wounds, A nanoparticle cream has been shown to fight staph infections. The nanoparticles contain nitric oxide gas, which is known to kill bacteria. Studies on mice have shown that using the nanoparticle cream to

release nitric oxide gas at the site of staph abscesses significantly reduced the infection. Burn dressing that is coated with nanocapsules containing antibotics. If an infection starts the harmful bacteria in the wound causes the nanocapsules to break open, releasing the antibotics. This allows much quicker treatment of an infection and reduces the number of times a dressing has to be changed. A welcome idea in the early study stages is the elimination of bacterial infections in a patient within minutes, instead of delivering treatment with antibiotics over a period of weeks.

4) Nanotechnology in Medicine Application: Cell Repair

Nano robots could actually be programmed to repair specific diseased cells, functioning in a similar way to antibodies in our natural healing processes

5) Nanoparticles for drug delivery into the brain:-

The blood-brain barrier (BBB) is the most important factor limiting the development of new drugs for the central nervous system. Relatively impermeable endothelial cells characterize the BBB with tight junctions, enzymatic activity and active efflux transport systems. It effectively prevents the passage of water-soluble molecules from the blood circulation into the CNS, and can also reduce the brain concentration of lipid-soluble molecules by the function of enzymes or efflux pumps. Consequently, the BBB only permits selective transport of molecules that are essential for brain function. Strategies for nanoparticle targeting to the brain rely on the presence of and nanoparticle interaction with specific receptor-mediated transport systems in the BBB. For example polysorbate 80/LDL, transferrin receptor binding antibody (such as OX26), lactoferrin, cell penetrating peptides and melano transferrin have been shown capable of delivery of a self non transportable drug into the brain via the chimeric construct that can undergo receptor-mediated transcytosis. It has been reported poly(butylcyanoacrylate) nanoparticles was able to deliver hexa peptide dalargin, doxorubicin and other agents into the brain which is significant because of the great difficulty for drugs to cross the BBB. Despite some reported success with polysorbate 80 coated NPs, this system does have many shortcomings including desorption of polysorbate coating, rapid NP degradation and toxicity caused by presence of high concentration of polysorbate 80. OX26MAbs (anti-transferrin receptor MAbs), the most studied BBB targeting antibody, have been used to enhance the BBB penetration of lipsosomes. However, recently, Jiet al. demonstrated that brain uptake of lactoferrin, an iron-binding glycoprotein belonging to the transferrin (Tf) family, is twice that of OX26 and transferrrinin vivo.

6) Nanodrug delivery systems for anti-cancer agents[29] :-

Many researchers have used different approaches and techniques for formulating nanoparticles for anti-cancer agents. Some of these studies along with their prominent findings are mentioned here. 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.

Acknowledgment:- We Sincerely thank to Management of Shakuntala Patil Bahuudesiya Sansatha, Honorable Mrs.Yogita G Patil Mam & Mr.Ganesh G Patil Sir For giving us such World Class Infrastucture & Wi-Fi Facility at Shatabdi Institute of Pharmacy, Bamnod Tal & Dist. Nandurbar

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