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A REVIEW ON NANOPARTICLES

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ABSTRACT
Nanoparticles are tiny particles with unique properties, classified into organic, inorganic, and carbon-based categories.The surface characteristics and particle size of Nanoparticle can be modified to target medications passively and actively. nanoparticles also exhibit strong reactivity due to their small size and large surface area, which can lead to biologically harmful effects. Carbon-based nanoparticles, including fullerenes, graphene, carbon nanotubes, and carbon nanofibers, have distinct mechanical, chemical, and physical characteristics.Silver, gold, and copper nanoparticles have also been extensively studied for their antibacterial and antiviral properties.The applications of nanoparticles are diverse, ranging from biomedical and pharmaceutical to The environmental and industrial uses. Various polymers have been used in the formulation of nanoparticles for drug delivery research to increase therapeutic benefit, while minimizing side effects. Nanoparticles are tiny materials having size ranges from 1 to 100 nm.They can be classified into different classes based on their properties, shapes or sizes. The nanoparticles are synthesized by various methods for research and commercial uses that are classified into three main types namely physical, chemical and mechanical processes that has seen a vast improvement over time. This paper presents a review on nanoparticles, their types, properties, synthesis methods and its application
KEYWORDS: *Nanoparticles, Drug Delivery, Targeting, Drug Release*

INTRODUCTION

Nanoparticles are defined as particulate Dispersions or solid particles with a size in the Range of 10-1000nm. The drug is dissolved, Entrapped, encapsulated or attached to a Nanoparticle matrix. Depending upon the method Of preparation, nanoparticles, nanospheres or Nanocapsules can be obtained. Nanocapsules Are systems in which the drug is confined to a Cavity surrounded by a unique polymer Membrane, while nanospheres are matrix Systems in which the drug is physically and Uniformly dispersed. The major goals in designing nanoparticles as a Delivery system are to control particle size, Surface properties and release of Pharmacologically active agents in order to Achieve the site-specific action of the drug at the Therapeutically optimal rate and dose regimen.

Advantages

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. 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.
4. Site-specific targeting can be achieved by Attaching targeting ligands to surface of particles Or use of magnetic guidance.
5. The system can be used for various routes of Administration including oral, nasal, parenteral, Intra-ocular etc.

Types of Nanoparticle

Inorganic nanoparticles: In the field of Modern material science Inorganic nanoparticle has been developed the role based upon their unique physical properties and particularly in biotechnology. Based upon these two factors of inorganic nanoparticles they have certain physical properties that mainly include size dependent optical, magnetic, electronic, and catalytic properties. Bio related application are involved for the preparation of these interesting nanoparticles like iron oxides, gold, silver, silica, quantum dots etc. Novel physical properties mainly related because of their size approaches nanometer scale dimension.

Polymeric Nanoparticles: Polymeric nanoparticle it is also a type of nanoparticle. In the recent year polymeric nanoparticle has a tremendous development in the field of research. The dispersion of preformed polymers and the polymerization of monomers are two strong strategies mainly involved for preparation. 10 1000nm it is the range of size involved with solid particles.

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Solid Lipid Nanoparticles: For controlling the drug delivery in 1990 s Solid lipid nanoparticles played a dominant role. There are certain alternate emulsions, liposomes and polymeric nanoparticles as a colloidal Carrier system.

Liposomes: Liposomes are one of the methods based upon the different types of nanoparticles. Structure of liposomes consists of one or more phospholipid bilayers and they are sphere-shaped vesicles to carry compound of interest. Today liposomes have been useful in the field of reagent and tool in various scientific disciplines. Since many features involved in liposome they made their own way in the market. Cosmetic and pharmaceutical industries numerous molecules act as a carrier, and in the field of Food and farming industries liposomes involved in encapsulation to grow delivery system that can entrap unstable Compounds.

Nanocrystal: A nocrystal is a type based upon material particle having at least one dimension smaller than 100 nanometres and mainly composed of atoms in either a single or poly-crystalline arrangement. Nanocrystals are aggregates of around hundreds or thousands of molecules that combine in a crystalline form, composed of pure drug with only a thin coating comprised of surfactant or combination of surfactants.

Nanotube: A nanotube is a nanometer scale tube like structure. Nanotubes are members of the fullerene structural family. Their name is derived from their long, hollow structure with the walls formed by one-atom-thick sheets of carbon called graphene. These sheets are rolled at specific and discrete ("chiral") angles and the combination of the rolling angle and radius decides the nanotube properties; for example, whether the individual nanotube shell is a metal or semiconductor. Nanotubes are categorized as single-walled nanotubes (SWNTs) and multi-walled nanotubes.

Dendrites: Dendrimers arise from two Greek words: Dendron meaning tree and Meros meaning part. Structure of dendrimers has a well-defined size, shape and defined molecular weight and also Dendrimers are hyper-branched, globular, monodisperse, three dimensional nanoscales synthetic Polymers. Molecular chemistry and polymer chemistry both exhibit well-defined characteristics features of Dendrites

Polymeric nanoparticles are colloidal structures composed of synthetic or semi synthetic polymers. The drug is dissolved, entrapped, encapsulated or attached to a nanoparticle matrix. Depending upon the method of preparation, nanoparticles, nanospheres or nanocapsule can obtained. Nanocapsules are systems in which the drug is confined to a cavity surrounded by a unique polymer membrane, while nanospheres are matrix systems in which the drug is physically and uniformly dispersed.The general synthesis and encapsulation of polymer are represented in this Figure

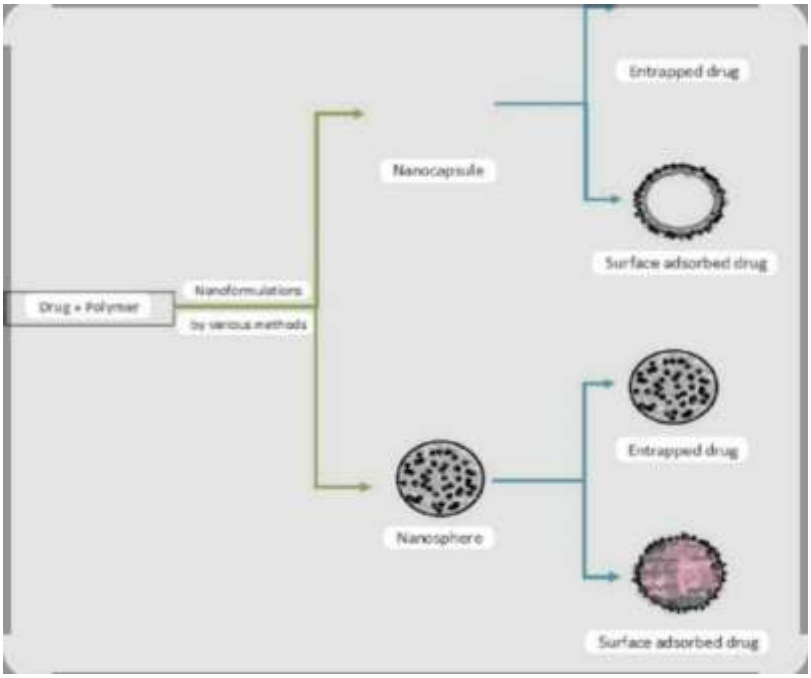


Fig1 . Types of Polymeric Nanoparticle

Classification of Nanoparticle

In general, there are three types of nanoparticles: organic, inorganic, and carbon-based.

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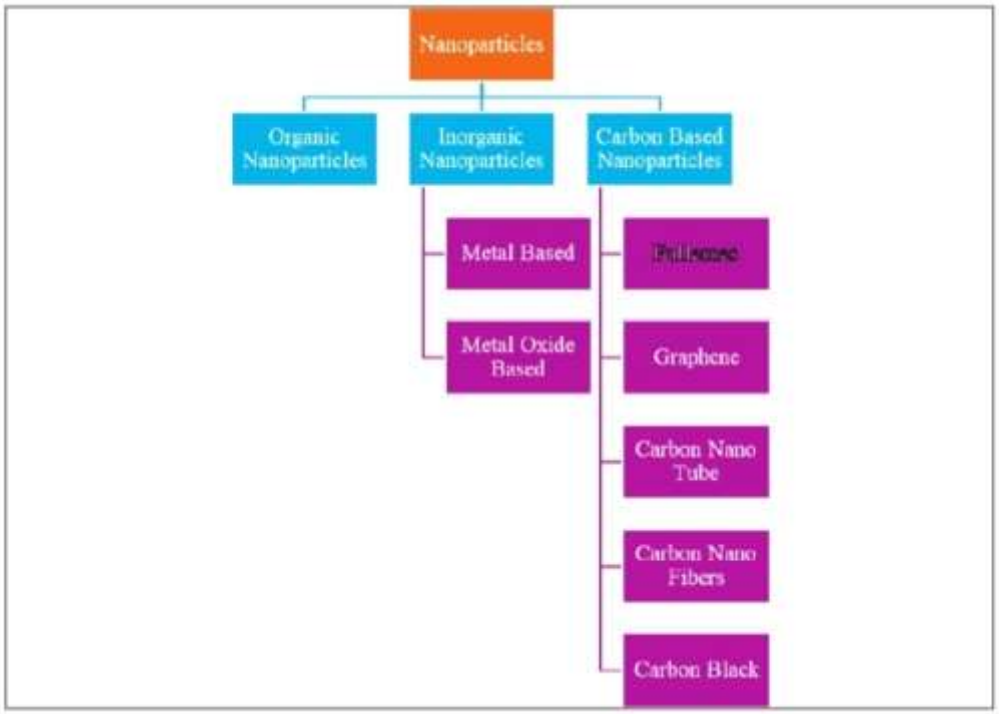


Fig2. Classification of Nanoparticles

Organic nanoparticles :- Ferritin, liposomes, dendrimers, and other organic nanoparticles or polymers are well-known examples. These nanoparticles are non-toxic and biodegradable, yet some, like micelles and liposomes, have a hollow core and are Susceptible to electromagnetic and thermal radiation, including heat.

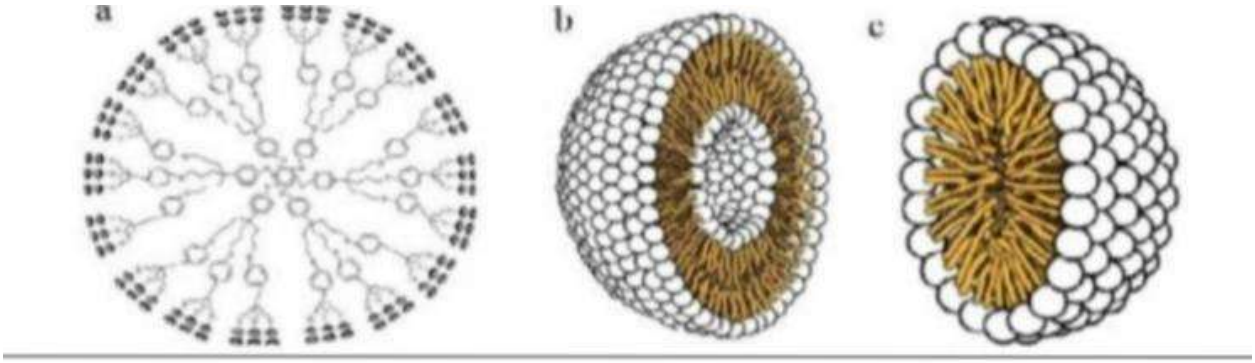


Fig3. Organic Nanoparticles: A) Dendrimers, B) Liposomes, C) Micelles

Inorganic nanoparticles :- Non-carbon-based particles are known as inorganic nanoparticles**.** Inorganic nanoparticles are often defined as those based on metal and metal oxides

1.Metal nanoparticles :- Metallica nanoparticles are manufactured from metals by either constructive or destructive processes**.** The pure metal nanoparticles are produced using the metal precursors**.**Because of the plasma on resonance characteristics, the metal nanoparticles have special optoelectrical capabilities. The shape, facet, and size of metal nanoparticles govern their production.

2. **Metal Oxides Based Nanoparticles:-** Metal oxides-based NPs are NPs made from metals that can be transformed into their corresponding Oxides**.** When compared to their metal equivalents, nanoparticles based on metal oxides exhibit remarkable features

Carbon based nanoparticles :- There are two main categories of carbon-based NPs**:** fullerenes and carbon nanotubes **(**CNTs).

Fullerenes :- C60 is one of the most well-known and often used fullerenes, Buckminster fullerene. It has the shape of a soccer ball due to the cage-like arrangement of its 60 carbon atoms, each of which has three bonds. Twelve pentagons and twenty hexagons are utilized in the C60 structure.It can be included into systems to enhance particular behaviours due to its special characteristics.

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Graphene :- One carbon allotrope is graphene. Carbon atoms arranged in a hexagonal network on a two-dimensional flat surface constitute graphene. Graphene sheets typically have a thickness of one nanometer .

Carbon Nano Tubes :- Carbon Nano Tubes (CNT) are made of graphene nanofoil with a honeycomb Lattice of carbon atoms twisted into hollow cylinders. The length of the nanotubes can vary from a few micrometers to 100 nm, with diameters as low as 0.7 nm for single-layered CNTs and 100 nm for multi-layered CNTs. To Many millimeters. A half-fullerene molecule can shut the ends or leave them hollow .

Carbon Nanofiber :- Carbon nanofiber (CNT) is created using the same graphene nanofoils, but they are twisted into cone or cup shapes rather than standard cylindrical tubes

Carbon black :- carbon-based amorphous material with diameters ranging from 20 to 70 nm that is often spherical in shape. Particles interact so strongly with one another that they form agglomerates, which are about 500 nm in size

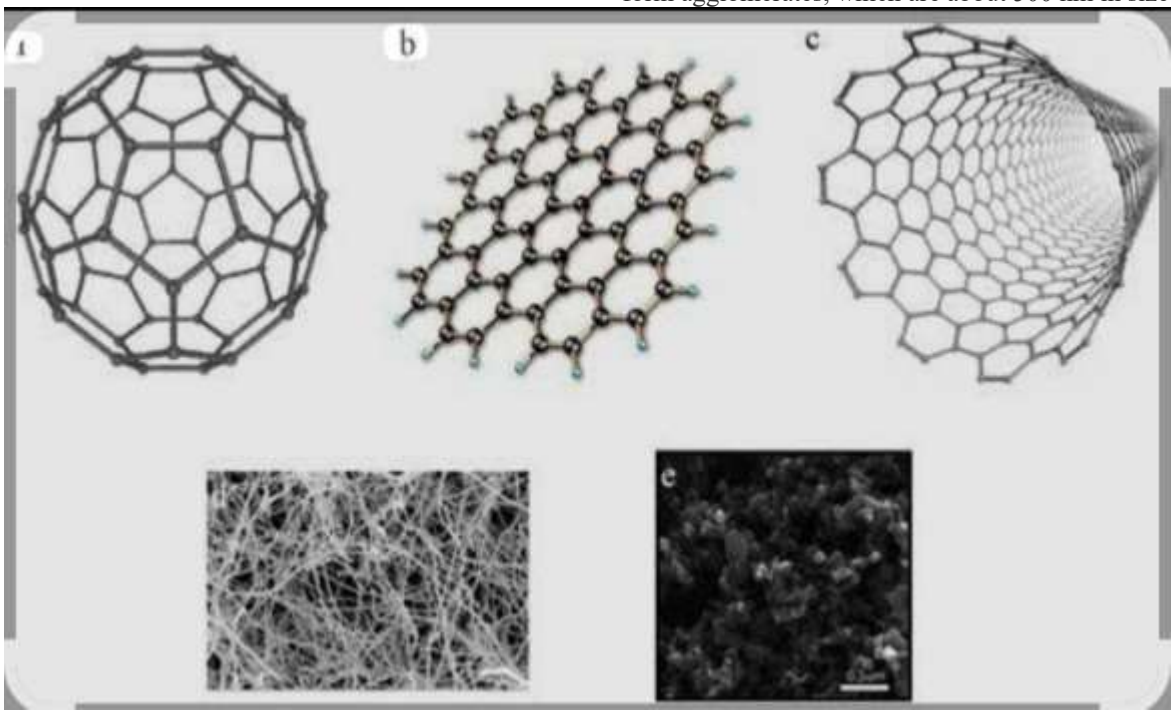


Fig4. Carbon based nanoparticle: a)fullerences, b) graphene, c) carbon nanotubes, d) carbon nanofiber, e) carbon black

Nanoparticle Drug Delivery Systems (DSSs) in Disease Treatment

Nanoparticles used for drug delivery typically range from 10 to 1000 nm, with at least one dimension below 100 nm. Their size and surface characteristics provide pharmaceutical advantages, though they can also contribute to potential toxicity. Smaller nanoparticles are taken up by cells more efficiently larger molecules. However, if nanoparticles are not cleared effectively, they may accumulate in the body. For highly active or cytotoxic nanoparticles, such retention can lead to harmful effects at unintended sites, unlike conventional drugs that are largely eliminated during the first-pass effect. Systemically administered cytotoxic drugs can also damage tissues before reaching their target.

A major challenge in drug development is that around 70% of drugs Worldwide have poor water solubility, resulting in suboptimal pharmacokinetics. Nanoparticle drug delivery systems (DSSs) have been designed to improve targeted Delivery and therapeutic efficiency, minimizing harm to surrounding healthy tissues That could occur if drugs were administered in free form. Over the last few decades, DSS research has progressed considerably, with various systems being developed For treating diseases such as cancer and neurodegenerative disorders.

1.Lipid-Based Drug Delivery Systems (DSSs) :- Lipid-based DSSs vary in composition and size, and are mainly classified Into micelles and liposomes. Micelles are formed when a single layer of lipid Molecules self-assembles in an aqueous environment into nano-sized vesicles Ranging from 5 to 50 nm. They effectively carry hydrophobic drugs by trapping them Within the hydrophobic core, while the hydrophilic heads face the surrounding Water, allowing drugs to be delivered at concentrations higher than their natural Solubility. In contrast, liposomes are bilayer vesicles resembling the cell membrane, With sizes ranging from 10 nm to several microns. The outer layer of Phospholipids interacts with the aqueous environment, while the inner layer Surrounds an aqueous core. The hydrophobic tails of the bilayer align to trap hydrophobic drugs, and the aqueous core can encapsulate hydrophilic drugs.Liposomes have proven

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highly effective in cancer drug delivery, as they transport both water-soluble and insoluble drugs. Conventional small-molecule drugs often diffuse out of tumors due to poor selectivity, causing cytotoxic effects on healthy cells. Liposomes, however, exploit the enhanced permeability and retention (EPR) effect: tumor vasculature has junction gaps between 100 nm and800 nm (compared to 5–10 nm in normal tissue), allowing liposomes to accumulate at tumor sites and release their payloads efficiently.

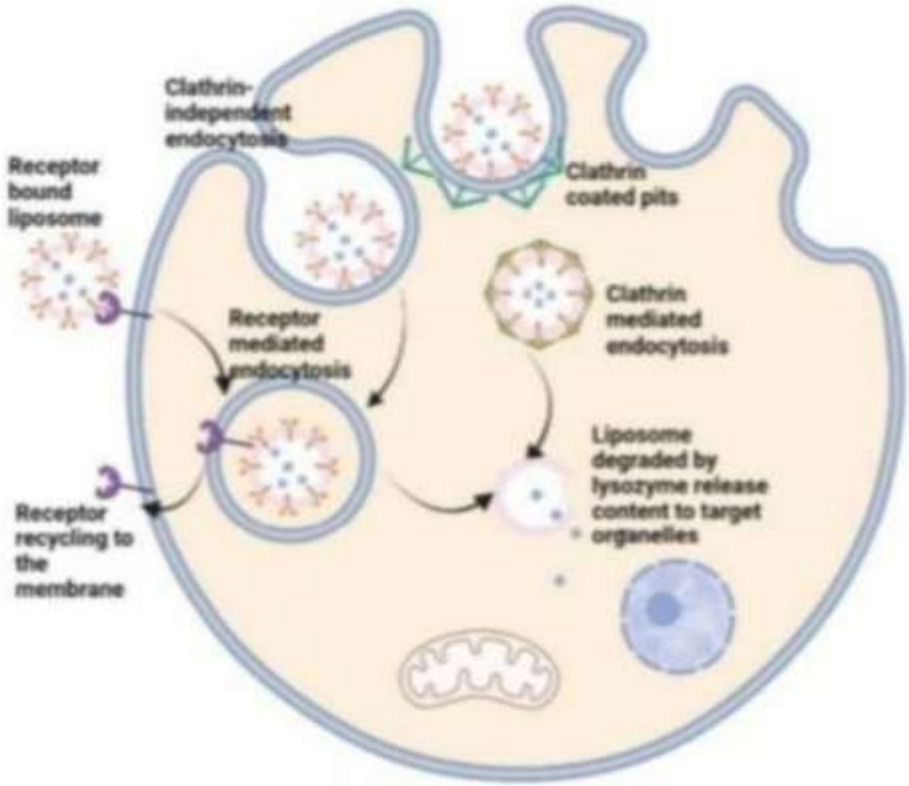


Fig5. Targeted delivery and metabolism of liposome encapsulated drug

Lipid nanoparticles (LNPs) are not only used in gene therapy but have also Been explored as delivery vehicles for gene-editing tools like CRISPR-Cas9 and base Editors. Research has investigated LNP-mediated delivery of CRISPR-Cas9 or base Editors targeting the BCL11A gene to treat β-thalassemia and sickle cell disease in Humans. These studies demonstrated that long-term deletion of harmful alleles in Hematopoietic stem cells can increase fetal hemoglobin levels, thereby reducing Vaso-occlusive episodes. Overall, LNPs show significant potential for delivering Gene therapies and gene-editing systems, with promising preclinical results and Applications across a range of diseases.

2.Polymeric Drug Delivery Systems (DSSs) :- Polymer-based nanoparticles used in drug delivery are composed of Repeating polymer units and have been extensively studied for medical applications In recent years. Common examples include PEG, chitosan, poly-(lactic-co-glycolic acid) (PLGA), and polylactic acid (PLA), with PEG, PLGA, and PLA being the most Widely researched. Chitosan is gaining attention due to its biocompatibility, low Immunogenicity, and minimal toxicity. Several PEGylated drugs have received FDA Approval for clinical use, making PEG the most commercially utilized polymer in Drug delivery systems. However, PLGA and PLA often exhibit an initial burst release of the encapsulated drug within the first 24 hours, regardless of the drug's location, which can lead to drug accumulation at unintended sites and reduce therapeutic effectiveness.Certain polymer-based drug delivery systems (DSSs) are engineered to respond to subtle changes in pH or reactive oxygen species (ROS) levels within the body. Since tissues affected by ischemia or tumors often exhibit higher pH or ROS levels compared to healthy tissues, these changes can serve as physiological Signals. Self-assembling, pH-sensitive polyamines have demonstrated adaptable Delivery capabilities. For example, doxorubicin-loaded polyamines coated with Folate and HIV transactivator (TAT) ligands have been effective against multidrug-Resistant cancer cell lines. These polyamines release doxorubicin in acidic Environments, allowing them to selectively target the typically acidic tumor Microenvironment without requiring additional targeting molecules. Similarly, Dextran nanoparticles containing arylboronic esters, which degrade in response to ROS, have been used to deliver ovalbumin to murine

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dendritic cells, enhancing Antigen presentation. Overall, polymer-based DSSs offer versatile and less complex Strategies for targeting the tumor microenvironment due to their responsiveness to Its unique conditions.

3.Peptide Nanoparticle Drug Delivery Systems (DSSs) :- Both linear and cyclic peptides, whether synthesized or derived from Natural Protein fragments, play a significant role in nanoparticle-based DSSs. Peptides are particularly useful for targeting cell surface receptors because many Receptor-binding proteins interact through specific peptide sequences. Their ease of Synthesis and low immunogenicity further enhance their suitability as drug delivery Tools. Peptides have been employed either alone or as surface modifications on Other nanoparticles to improve delivery efficiency. For instance, Kim et al. used a Cationic liposome encapsulating a peptidomimetic of the epidermal growth factor Receptor (EGFR) ligand to inhibit EGFR signaling in lung cancer cells. Somatostatins, Peptide hormones that are highly expressed in various cancer cells, have been Conjugated to anticancer drugs like doxorubicin, methotrexate, and paclitaxel to Facilitate selective cancer cell targeting. Additionally, the RIPL peptide, designed to Bind hepsin—a serine protease overexpressed on hepatoma and prostate cancer Cells—has been conjugated to liposomes. This RIPL-liposome system

Characterization of Nanoparticles

Nanoparticles are generally characterized by their size, morphology and surface charge, using such advanced microscopic techniques as scanning electron microscopy (SEM), transmission electron microscopy (TEM) and atomic force microscopy (AFM). The average particle diameter, their size distribution and charge affect the physical stability and the in vivo distribution of the nanoparticles. Electron microscopy techniques are very useful in ascertaining the overall shape of polymeric nanoparticles, which may determine their toxicity. The surface charge of the nanoparticles affects the physical stability and redispersibility of the polymer dispersion as well as their in vivo performance.

Particle size :- Particle size Particle size distribution and morphology are the most important parameters of characterization of nanoparticles. Morphology and size are measured by electron microscopy. The major application of nanoparticles is in drug release and drug targeting. It has been found that particle size affects the drug release. Smaller particles offer larger surface area.

Dynamic light scattering (DLS) :- Currently, the fastest and most popular method of determining particle size is photon-correlation spectroscopy (PCS) or dynamic light scattering (DLS). DLS is widely used to determine the size of Brownian nanoparticles in colloidal suspensions in the nano and ubmicron ranges.It Is possible to extract the size distribution and give a description of the particle's motion in the medium, measuring the diffusion coefficient of the particle and using the autocorrelation function. The photon correlation spectroscopy (PCS) represent the most frequently used technique for accurate estimation of the particle size and size distribution based on DLS.

Scanning Electron microscopy :- Scanning electron microscopy (SEM) is giving morphological examination with direct visualization. The techniques based on electron microscopy offer several advantages in morphological and sizing analysis; however, they provide limited information about the size distribution and true population average. For SEM characterization, nanoparticles solution should be first converted into a dry powder, which is then mounted on a sample holder followed by coating with a conductive metal, such as gold, using a sputter coater. The sample is then scanned with a focused fine beam of electrons.36 The surface characteristics of the sample are obtained from the secondary electrons emitted from the sample surface. The nanoparticles must be able to withstand vacuum, and the electron beam can damage the polymer. The mean size obtained by SEM is comparable with results obtained by dynamic light scattering. Moreover, these techniques are time consuming, costly and frequently need complementary information about sizing distribution.

Transmission electron microscope :- TEM operates on different principle than SEM, yet it often brings same type of data. The sample preparation for TEM is complex and time consuming because of its requirement to be ultra thin for the electron transmittance.The nanoparticles dispersion is deposited onto support grids or films . To make nanoparticles withstand the instrument vacuum and facilitate handling they are fixed using either a negative staining material, such as phosphotungstic acid or derivatives.The surface characteristics of the sample are obtained when a beam of electrons is transmitted through an ultra thin sample, interacting with the sample as it passes through Atomic force microscopy Atomic force microscopy (AFM) offers ultra-high resolution in particle size measurement and is based on a physical scanning of samples at sub-micron level using a probe tip of atomic scale.

Surface Charge :- The nature and intensity of the surface charge of nanoparticles is very important as it determines their interaction with the biological environment as well as their electrostatic interaction with bioactive compounds. The colloidal stability is analyzed through zeta potential of nanoparticles. This potential is an indirect measure of the surface charge. It corresponds to potential difference between the outer Helmholtz plane and the surface of shear. The measurement of the zeta potential allows for predictions about the storage stability of colloidal dispersion. The extent of surface hydrophobicity can then be predicted from the values of zeta potential. The zeta potential can also provide information regarding the nature of material encapsulated within the nanocapsules or coated onto the surface.

Limitation In spite of these advantages nanoparticles do have limitations like,

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1. Altered physical properties which lead to particle-particle aggregation, making physical handling of nanoparticles difficult in liquid and dry forms due to smaller size and larger surface area.
2.Smaller the particles size greater the surface area and this property makes nanoparticles very reactive in the cellular environment.
3. Small particles size results in limited drug loading and burst release. These practical problems have to be sorted out before nanoparticles can be used clinically or made commercially available.

Therapeutic Applications of Nanoparticles
Nanoparticles with diverse compositions and properties have been explored for a wide Range of therapeutic purposes, including
1.Serving as carriers for drugs and biological molecules
2. Delivering genes and DNA
3. Acting as carriers for antigens and vaccines
4.Enabling controlled and targeted drug delivery
5. Transporting diagnostic agents
6. Serving as carriers for MRI contrast materials

CONCLUSION
Nanoparticles represents promising drug carrier for various drug delivery systems Nanotechnology is breakthrough technology pervading all fields newer applications of this field are being explored worldwide. Nanoparticles represent a technology to overcome solubilities and bioavailability problems of drugs which can be generally applied to all poorly soluble drugs. Nanoparticles present a highly attractive platform for a diverse array of biological applications. Nanoparticles provide efficient treatment by enabling targeted and controlled release thus in feature nanoparticulate drug-delivery system seem to be a viable and promising stratergy for the biopharmaceutical industry.

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