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Review Paper

Review on Nanoparticle

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ABSTRACT

Nanotechnology is an emerging field that deals with materials at the nanoscale (1–100 nm) and has gained significant attention in drug delivery and biomedical applications. Nanoparticles, as fundamental building blocks of nanotechnology, exhibit unique physical and chemical properties compared to bulk materials, making them highly suitable for advanced therapeutic applications. In drug delivery systems, nanoparticles provide improved control over particle size, surface characteristics, and drug release, enabling targeted and sustained delivery of therapeutic agents. Various types of nanoparticles, including silver, gold, alloy, and magnetic nanoparticles, have been widely explored due to their distinct properties and biomedical relevance. Several preparation techniques such as solvent evaporation, polymerization, nanoprecipitation, dialysis, supercritical fluid technology, and emulsion diffusion methods are commonly used for nanoparticle synthesis. Evaluation parameters like particle size, zeta potential, drug entrapment efficiency, in-vitro release, and stability studies are essential for assessing nanoparticle performance. Overall, nanoparticles offer significant advantages in improving bioavailability, therapeutic efficacy, and patient compliance, making them a promising tool in modern nanomedicine, particularly in targeted drug delivery and disease diagnosis.

INTRODUCTION

Nanotechnology is the study of materials at a very small scale, usually between 1 and 100 nanometers (nm). One nanometer is equal to (10^{-9}) meters. It involves understanding and controlling matter at the atomic and molecular level.Nanoparticles are the basic building blocks of nanotechnology. They are smaller than everyday objects but larger than single atoms or molecules. Because of their small size, nanoparticles show unique physical and chemical properties that are different from bulk materials.Nanotechnology has gained great importance in recent years. In 2000, the United States started the National Nanotechnology Initiative (NNI) to support research and

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development in this field. Soon after, many government departments and agencies began working on nanotechnology projects.[1]

The main goals of designing nanoparticles as a drug delivery system are to control their particle size, surface properties, and drug release. This helps in delivering the drug directly to the target site at the right rate and proper dose for better therapeutic effect.Liposomes have been widely used as drug carriers because they can protect drugs from degradation, target specific sites, and reduce toxicity and side effects. However, they have some limitations such as low drug loading capacity, quick leakage of water-soluble drugs in the bloodstream, and poor storage stability.In comparison, polymeric nanoparticles offer several advantages over liposomes. They improve the stability of drugs and proteins and provide better control over drug release, making them more effective for drug delivery applications.[2,3]

In general, nanoparticles have a size between 1 and 100 nanometers (nm). Metallic nanoparticles show different physical and chemical properties compared to bulk metals. For example, they may have lower melting points, larger surface area, unique optical properties, improved mechanical strength, and special magnetic behavior.These unique properties make nanoparticles useful in many industrial applications. However, the definition and importance of a nanoparticle can vary depending on its specific application.

- **Types of Nanoparticles:-**

1. Silver Nanoparticles:-Silver nanoparticles are widely used because of their strong antimicrobial properties. They are effective against bacteria, viruses, and other microorganisms.[4,5] Due to these properties, they are used in medical applications, textile industries, water treatment, and sunscreen products. [6,7]Silver nanoparticles can also be produced using plants such as Azadirachta indica,[8]Capsicum annuum, [9,10]and Carica papaya[11].

2. Gold Nanoparticles:-Gold nanoparticles are commonly used in biomedical research. They help in studying protein interactions and are used in DNA fingerprinting to detect DNA in samples. They are also useful in detecting certain antibiotics like streptomycin, gentamycin, and neomycin. Gold nanorods are used in cancer detection and in identifying different types of bacteria.[12,13]

3. Alloy Nanoparticles:-Alloy nanoparticles are made from a combination of two or more metals. [14]They show different properties compared to pure metals. For example, silver-based alloys have high electrical conductivity.Bimetallic nanoparticles combine the properties of both metals, often giving better performance than single-metal nanoparticles.[15]

4. Magnetic Nanoparticles:-Magnetic nanoparticles, such as Fe_3O_4 (magnetite) and Fe_2O_3 (maghemite), are biocompatible and widely used in medical applications. They are used in targeted cancer treatment (magnetic hyperthermia), stem cell separation, drug delivery, gene therapy, DNA analysis, and MRI (magnetic resonance imaging).[16]

- **Advantages of Nanoparticles:-**

i. Nanoparticles offer many advantages in drug delivery systems compared to conventional methods. Some of the important advantages are:
ii. Nanoparticles provide better drug delivery than traditional systems.
iii. They allow controlled and sustained release of drugs at the target site.
iv. They improve drug distribution in the body and increase blood circulation time,

bioavailability, and therapeutic effectiveness.[17]

v. They can be administered through different routes such as oral, nasal, parenteral, and intra-ocular routes.
vi. Due to their small size, nanoparticles can easily reach tiny areas in the body and target specific cells or receptors.
vii. They can cross biological barriers like cell membranes, blood vessels, stomach lining, and even the blood–brain barrier.
viii. Nanoparticles improve the solubility of poorly soluble drugs, which enhances their bioavailability.
ix. They reduce drug toxicity and help in more efficient drug distribution.
x. Drug release can be modified using polymers, making them useful for cancer therapy, vaccines, contraceptives, and antibiotics.[18]
xi. Nanoparticles can also be used in the diagnosis of various diseases.
xii. They improve the stability of drugs and increase shelf life.
xiii. They are used in dental treatments, such as filling small cavities.
xiv. They can improve patient acceptance and may reduce manufacturing costs.[19]

- **Preparation Techniques:**

A.Solvent Evaporation Method:-

The solvent evaporation method is one of the first and most commonly used techniques for preparing nanoparticles. In this method, a nanoemulsion is first prepared.[18]A polymer is dissolved in an organic solvent such as dichloromethane, chloroform, or ethyl acetate. The drug is then added and dispersed in this solution. This mixture is then emulsified into an aqueous phase containing surfactants like polysorbates, poloxamers, sodium dodecyl sulfate, polyvinyl alcohol, or gelatin, forming an oil-in-water emulsion. This emulsification is done using mechanical stirring, sonication, or high-pressure homogenization (microfluidization).After the emulsion is formed, the organic solvent is removed by increasing temperature and/or reducing pressure while continuously stirring. This leads to the formation of solid nanoparticles.[17-20]

B. Polymerization Method:-

In the polymerization method, monomers are polymerized in an aqueous solution to form nanoparticles. After polymerization is completed, the drug can be added either by adsorption onto the nanoparticles or by dissolving it in the polymerization medium.[21]To remove stabilizers and surfactants used during the process, the nanoparticle suspension is purified using ultracentrifugation. After purification, the particles are re-suspended in an isotonic solution without surfactants.This method is commonly used for preparing nanoparticles such as polybutyl cyanoacrylate and poly(alkyl cyanoacrylate) nanoparticles. The size and formation of nanocapsules depend on the concentration of surfactants and stabilizers used during preparation.[22]

C. Nanoprecipitation Method:-

Nanoprecipitation, also called the solvent displacement method, is a widely used technique for preparing nanoparticles. It was first described by Fessi and co-workers in 1989. In this method, the polymer and drug are dissolved in an organic solvent, and then this solution is added into an aqueous phase. The organic solvent diffuses into the water, leading to the formation of nanoparticles. This process may occur in the presence or absence of surfactants[.18]For example, in one study, lamivudine-loaded nanoparticles were prepared using this method. First, the drug was dissolved in water, and a co-solvent such as acetone was added to improve

homogeneity. Separately, a polymer solution (ethyl cellulose or Eudragit) with propylene glycol in chloroform was prepared and added to the drug solution.[18-20] This mixture was then slowly added into 70% aqueous ethanol. After mixing for a few minutes, the organic solvent was removed by evaporation at 35°C under normal pressure. Finally, nanoparticles were collected using centrifugation, washed with water, and dried at room temperature.[23]

D. Dialysis:-

is an effective method used for preparing nanoparticles. In this method, the polymer (such as poly(benzyl-L-glutamate)-b-poly(ethylene oxide) or poly(lactide)-b-poly(ethylene oxide)) and the drug are first dissolved in an organic solvent.This solution is then placed inside a dialysis tube and dialyzed against a non-solvent that is miscible with the original solvent. During dialysis, the organic solvent slowly diffuses out through the membrane. As a result, the polymer loses its solubility and gradually aggregates, leading to the formation of a stable and uniform suspension of nanoparticles.The exact mechanism of nanoparticle formation in this method is not completely understood, but it is believed to be similar to the nanoprecipitation process.[18]

E. Supercritical Fluid Technology:-

Supercritical fluid technology is an alternative method for preparing nanoparticles. It is considered environmentally friendly because it does not use harmful organic solvents.A supercritical fluid is a substance that is above its critical temperature and pressure, where it behaves like both a liquid and a gas. Supercritical carbon dioxide (CO_2) is the most commonly used fluid because it has mild critical conditions (Tc = 31.1°C and Pc = 73.8 bar), is non-toxic, non-flammable, and inexpensive.[18]

This technique mainly uses two processes:[24]

1. Supercritical Anti-Solvent (SAS) Method:

In this method, a liquid solvent such as methanol (which is fully miscible with the supercritical fluid) is used. When the supercritical fluid is added, it extracts the solvent, causing the solute to rapidly precipitate. This leads to the formation of nanoparticles.

2. Rapid Expansion of Supercritical Solution (RESS):

In this method, the solute is first dissolved in a supercritical fluid. This solution is then quickly released through a nozzle into normal air. The sudden drop in pressure causes rapid supersaturation, leading to nucleation and formation of well-dispersed nanoparticles.

F.Emulsion Diffusion Method:-

The emulsion diffusion method is commonly used for preparing nanoparticles. In this method, the polymer is dissolved in a solvent that is partially miscible with water, such as propylene carbonate or benzyl alcohol. Before emulsification, both the solvent and water phases are saturated to maintain equilibrium.The polymer-containing organic phase is then emulsified into an aqueous solution containing a stabilizer. During this process, the solvent diffuses from the internal phase into the external aqueous phase, leading to the formation of nanospheres or nanocapsules depending on the oil-to-polymer ratio. Finally, the solvent is removed by evaporation or filtration based on its boiling point.This method has several advantages, including good reproducibility between batches, no need for high-pressure homogenization, high drug encapsulation efficiency (around 70%), simple procedure, narrow particle size distribution, and easy scalability.However, it also has some limitations. A large amount of water needs to be removed after preparation, and there may be loss of water-soluble drugs into the aqueous phase, which can reduce encapsulation

efficiency.[25]Examples of drugs prepared using this method include cyclosporine-loaded sodium glycolate nanoparticles, meso-tetra (hydroxyphenyl) porphyrin-loaded PLGA nanoparticles, and doxorubicin-loaded PLGA nanoparticles.[26,27]

- **Evaluation Parameters of Nanoparticles:-**

1. Yield of Nanoparticles:-The percentage yield of nanoparticles is calculated by comparing the total weight of nanoparticles obtained with the combined weight of the polymer and drug used in preparation.[29]

2. Drug Content / Drug Entrapment Efficiency:-After centrifugation, the amount of free drug present in the supernatant is measured using UV spectrophotometry. A standard calibration curve is used for analysis. The amount of drug entrapped in nanoparticles is calculated by subtracting the free drug (w) from the total drug used (W). The difference (W − w) gives the entrapped drug, and entrapment efficiency is expressed as a percentage.[28]

3. Particle Size and Zeta Potential:-Particle size and zeta potential of nanoparticles are measured using instruments such as the Malvern Zetasizer. These parameters help in understanding stability and behavior of nanoparticles.[29]

4. Surface Morphology:-The surface structure and shape of nanoparticles are studied using Scanning Electron Microscopy (SEM).[30]

5. Polydispersity Index (PDI):-PDI indicates the uniformity of particle size distribution. It is also determined using the Malvern Zetasizer.[31]

6. In-vitro Drug Release Study:-Drug release is studied using a USP Type II dissolution apparatus at 50 rpm. Nanoparticles are placed in phosphate buffer solution (900 mL) at 37 ± 0.2°C. At specific time intervals, samples are withdrawn and replaced with fresh medium. The drug concentration is analyzed using UV spectrophotometry.[32]

7. Kinetic Study:-To understand the drug release mechanism, data from in-vitro studies are fitted into different models such as zero-order, first-order, and Higuchi models. Regression analysis is used to calculate r^2 values and rate constants.[23]

8. Stability Study:-Stability studies are carried out by storing nanoparticles at 4°C ± 1°C and 30°C ± 2°C for up to 90 days. Samples are analyzed at regular intervals (0, 1, 2, and 3 months) for drug content, release rate, and physical appearance changes according to ICH guidelines.[33]

- **Applications of Nanoparticles:-**

i. Nanomedicine has great potential to improve the diagnosis and treatment of many human diseases.
ii. It allows for more effective and targeted therapies, which can improve patient outcomes.
iii. The use of microorganisms for the biosynthesis of nanoparticles is an environmentally friendly method.
iv. It avoids harmful chemicals and supports green nanotechnology.
v. Nanotechnology can also improve many tools used in biotechnology. It helps make these tools more personalized, portable, cost-effective, safer, and easier to use. Because of these advantages, nanotechnology is expected to play an important role in the future of medicine and healthcare.

CONCLUSION

Nanotechnology offers promising applications in pharmaceutics. Nanoparticles are an advanced drug delivery system that can improve therapeutic

effects, enhance bioavailability, and reduce toxicity. They are widely used in areas such as brain targeting and cancer therapy. Overall, nanoparticles help improve treatment effectiveness and patient complianc.

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