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REVIEW ON POLYMERIC NANOPARTICLES FOR TRANSDERMAL DRUG DELIVERY SYSTEM

Akash Ajith*, Sheikh Sofiur Rahman and Chinmoy Bhuyan

Department of Pharmaceutics, Girijananda Chowdhury Institute of Pharmaceutical Science, Hathkhowapara, Azara, Guwahati, Assam, 781017.

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***Corresponding Author**
Akash Ajith
Department of Pharmaceutics, Girijananda Chowdhury Institute of Pharmaceutical Science, Hathkhowapara, Azara, Guwahati, Assam, 781017.

ABSTRACT

Nanoparticles are the best shape of systems with sizes withinside the nm range. In precept any series of atoms bonded collectively with a structural radius of less than 100 nm may be taken into consideration a nanoparticle. In the existing time nanoparticles are extensively used in lots of dosage shape because of their exact solubility, much less length and higher penetrability. Applications of nanoparticles in micro wiring are mobileular specific, internalization, vaccine transport and gene transport. Nanoparticles are used withinside the subject of drugs additionally for the remedy of most cancers or for the orthopaedic implants. Nanoparticles suggests excessive solubility and speedy penetration that's why they may be utilized in nearly components now a days.

KEYWORDS: Nanoparticles, Gold nanoparticles (AuNPs), Poly lactic co- glycolic acid (PLGA).

INTRODUCTION[1,2]

Nanotechnology is a new option for addressing therapeutic limitations such as high toxicity, limited absorption, and effectiveness. Several nanostructured drug delivery systems have been created, opening up new avenues for more precise and less harmful therapies. Polymeric nanoparticles have distinct and useful physicochemical and biological features. Because of their tiny size, large surface area, superficial charge, and capacity to attach moieties to the surface of nanoparticles, these systems are new drug carriers, allowing for better drug transport and penetration into tissues and cell.

Nanotechnology is getting evolved at numerous degrees consisting of substances, structures and devices. At found in industrial programs and medical information, the maximum modern stage is nanomaterials. In nanotechnology, a minor item that acts as a whole unit in phrases of its houses and shipping is called a particle. It may be classified in step with sizes as satisfactory particle and ultrafine particle. In phrases of diameter, satisfactory debris are sized among one hundred and 2500 nanometers, whilst ultrafine debris cowl a variety among 1 and one hundred nanometers. Nanoparticles also are sized among 1 and one hundred nanometers just like the ultrafine debris. Nanoparticles might also additionally or might not exhibit length associated houses that change knowingly from the ones found in bulk substances and satisfactory debris. Thus, nanoparticles are sized much less than some 100 nm. This discount in length brings approximately big adjustments of their bodily houses with recognize to the ones found in bulk substances. They may be mineral, metallic, polymer-primarily based totally or a mixture of substances. Due to a huge type of capacity programs in optical, digital fields and biomedical, Nanoparticle studies is presently a place of extreme medical interest. The purpose at the back of nanoparticles is appealing is primarily based totally on their precise and crucial features, consisting of their floor to mass ratio, that's lots large than that of different debris and substances, their capacity to adsorb and convey different compounds consisting of drugs, probes and proteins in addition to allowing the catalytic merchandising of reactions.

Advantages[3,4]

- To achieve both passive and active drug targeting particle size and surface properties after parenteral delivery nanoparticles are simple to modify.
- To attain a high level of medication therapeutic effectiveness and with fewer side effects, during the transportation. the drug's release, as well as the location of localization, resulting in a shift in the distribution of the medication, as well as the subsequent clearance of the drug.
- By affixing targeted ligands to the surface of particles or the use of magnetic guiding Site-specific targeting is possible.
- Including oral, intra-ocular, parenteral the system can be used for a variety of purposes, including nasal Administration routes.
- Drug delivery to small cells within the body regions that can be improved by nanoparticles.

- Engineering empowers scientists to Exercising on this scale precisely and formerly possessing control over the biomaterials considering the physical properties of polymers.
- Nanoparticles facilitate drug distribution to many regions of the body overcoming the opposition provided by physiological obstacles in the body that must be overcome, particle size has a direct impact.
- Nanoparticles can help with medicinal efficacy distribution by increased aqueous solubility of poorly soluble medicines, as well as a rise in bioavailability for planned release of medicinal compounds, and precise drug targeting.
- The surface is ideal for focused medication delivery. The characteristics of nanoparticles can be modified. for proteins, small molecules, peptides, and other biomolecules Nanoparticles containing nucleic acids are not used. Immune system recognition and targeting to specific tissue types effectively.
- By focusing on nano drug carriers, Toxicity can be decreased and efficiency improved. Drug distribution is possible. Throughout the numerous anatomic extremes of such as the blood-brain barrier (BBB) Nanocarriers have the capacity to deliver biotech drugs.

Transdermal Drug Delivery Systems

Innovations in drug delivery are occurring at a much faster rate than in the previous two decades. Improved patient compliance and efficacy are inextricably linked to new drug delivery systems. Optimal therapeutic outcomes necessitate not only appropriate drug selection but also effective drug delivery. Developing controlled drug delivery systems has become increasingly important in the pharmaceutical industry over the last three decades. The pharmacological response of a drug, both the desired therapeutic effect and the undesired adverse effect, is determined by the concentration of the drug at the site of action, which is determined by the dosage form and the extent of absorption of the drug at the site of action. While tablets and injections have traditionally been the preferred methods of administration, new options are becoming increasingly popular. Transdermal delivery is a highly effective alternative delivery method. An average adult's skin covers a surface area of approximately $2cm^2$ and receives approximately one-third of the blood circulating throughout the body. It is necessary to understand the skin in order to deliver a drug into the body through the transdermal layer of skin. The human skin is a drug-delivery surface that is easily accessible. Transdermal drug delivery system (TDDS) is a type of controlled drug delivery system in which the drug is delivered through the skin at a predetermined and controlled rate. TDDS are defined as self-contained, discrete dosage forms, also known as 'patches', because when patches are applied to intact skin, the drug is delivered to the systemic circulation at a controlled rate through the skin. The primary goal of TDDS is to deliver drugs into the systemic circulation via the skin at a predetermined rate with minimal inter and intra patient variation. Transdermal drug delivery is currently one of the most promising drug delivery methods.

Advantages

- Transdermal drug delivery enables the avoidance of gastrointestinal absorption with its associated pitfalls of enzymes and pH associated deactivation.
- Avoidance of first pass metabolism.
- Similar to intravenous infusion, it also achieves consistent plasma levels, but non-invasive in nature.
- Avoidance of gastro intestinal incompatibility.
- Provide suitability for self-administration
- It is of great advantages in patients who are nauseated or unconscious.

Disadvantages

- Many drugs especially drugs with hydrophilic structures permeate the skin too slowly may not achieve therapeutic level.
- Transdermal drug delivery system cannot deliver ionic drugs.
- It cannot develop for drugs of large molecular size.
- Possibility of local irritation at site of application.
- May cause allergic reaction.
- It cannot achieve high drug levels in blood.

Types of nanoparticles

Silver

These have been shown to be the most effective due to their high antibacterial activity against bacteria, viruses, and other eukaryotic organisms. microorganisms. Of all nanomaterials they are most often employed as antibacterial agents for use in sunscreen creams, water treatment, and textiles industry, and so on. By using the plants, such as *Capsicum annuum*, *Azadirachta indica*, and *Carica papaya* silver biosynthesis is a success.[5,6,7,8,9,10,11]

Gold

In immunochemical research, gold nanoparticles (AuNPs) are employed to identify protein interactions. They are employed as a lab tracer in DNA fingerprinting to identify the presence of DNA in a sample. These nanoparticles may also detect aminoglycoside drugs such as streptomycin, gentamycin, and neomycin. Using Gold nano rods, researchers were able to detect cancer stem cells, diagnose cancer, and identify several groups of germs.[12,13]

Alloy

The structural characteristics of alloy nanoparticles differ from bulk samples. Silver flakes are the most often utilized metal filler due to their maximum electrical conductivity among other metal fillers; their oxides are also comparatively more conductive. Bimetallic alloy nanoparticles characteristics are impacted by both metals and above regular metallic NPs, resulting in greater benefits.[14,15,16]

Magnetic

Magnetic nanoparticles, such as maghemite and magnetite, are known to be biocompatible. A guided drug is a medication that is used in magnetic resonance imaging (MRI). delivery, cancer therapy (magnetic) gene therapy, stem cell sorting, and heat They have been used for DNA analysis and modification. actively contemplated.[17]

Preparation of Nanoparticles

Emulsion-Solvent Evaporation Method

This approach is used to create the majority of nanoparticles. This approach consists mostly of two phases. Emulsification of the aqueous phase in the first stage, a polymer solution is required. When you're in the second stage, polymer evaporation the formation of nanospheres is caused by the formation of a solution causing polymer precipitation assemblage of ultracentrifugation is used to separate nanoparticles. free drug or residue removed, rinsed with distilled water These are lyophilized for storage after being immersed in water. Solvent evaporation and high-pressure emulsification are another name for this process. The procedure entails homogenization under high pressure and overall stirring to eliminate organic solvent. The viscosity of the fluid may be changed by varying the stirring rate. Temperature, type, organic and aqueous phases the size can be determined by the quantity of dispersion agent used. However, to lipid soluble drugs, this technique can be applied and by the scale up issue limitation are imposed. Polymers used are PLA, Poly (β-hydroxybutyrate)(PHB),Poly(caprolactone) (PCL), PLGA, cellulose acetate phthalate, and EC in this method.[18,19,20,21,22,23,24,25,26]

Double Emulsion and Evaporation Method

The fundamental disadvantage of this approach is the poor trapping of hydrophilic drugs. As a result, the double emulsion approach is used to encapsulate hydrophilic drugs, in which aqueous drug solutions are added to organic polymer solutions while vigorously swirling to generate w/o emulsions. This w/o emulsion is put into another aqueous phase while being continuously stirred to generate a mixed emulsion (w/o/w). The solvent is then removed by evaporation, and nano particles can be separated by high-speed centrifugation. The produced nanoparticles must be washed before lyophilization. The variables employed in this procedure are the amount of hydrophilic drug integrated, the amount of polymer, the volume of aqueous phase, and the stabilizer concentration. These characteristics also have an impact on the characterization of nanoparticles.[27,28]

Salting Out Method

This process separates the water-miscible solvent by salting-out from aqueous solution. Polymer and drug are first dissolved in a solvent, which is then emulsified with the salting out agent (electrolytes such as calcium chloride and magnesium chloride, or sucrose as a non-electrolyte) and polyvinylpyrrolidone (PVP) or hydroxyethyl cellulose as a colloidal stabilizer into an aqueous gel. This oil-in-water emulsion is diluted with water or an aqueous phase to improve solvent diffusion, indicating the generation of nanospheres. Several factors, including electrolyte concentration, polymer content in the organic phase, stabilizer type, stirring rate, and internal/external phase ratio, can be changed. In the synthesis of Ethyl cellulose, PLA, and Poly(methacrylic) acid nanospheres, this process yields great efficiency and is readily scaled up. Because salting out does not need a rise in temperature, it may be advantageous for heat sensitive compounds. The limitations of this approach include its restricted applicability to lipophilic drugs and the long nanoparticles cleaning processes.[29,30,31]

Emulsions Diffusion Method

Another approach that is often used to prepare nanoparticles is the emulsions diffusion method. The encapsulating polymer is dissolved in a solvent that is somewhat miscible with water, such as propylene carbonate or benzyl alcohol, and the initial thermodynamic equilibrium of both saturated liquids is ensured. Following that, the polymer-water saturated solvent phase is emulsified in an aqueous solution containing a stabilizer, resulting in solvent diffusion to the exterior phase and the formation of nanospheres or nano capsules based on the oil-to polymer ratio. Finally, the solvent is removed via evaporation or filtering based on its boiling point. This approach has various advantages, including good repeatability (batch-to-batch), minimal need for homogenization, high encapsulation efficiency (usually 70%), simplicity, narrow size distribution, and ease of scaling-up. However, there are significant downsides to this approach, including the large amounts of water that must be removed from the suspension and the lower encapsulation effectiveness during emulsification due to water-soluble drug leakage in the saturated-aqueous exterior phase. Some drug-laden nanoparticles generated by this technology include cyclosporine (cy-A-); loaded sodium glycolate nanoparticles, mesotetra (hydroxyphenyl) porphyrin-loaded PLGA (p-THPP) nanoparticles, and doxorubicin-loaded PLGA nanoparticles.[32,33,34,35]

Solvent Displacement/Precipitation method

Solvent displacement comprises the precipitation of a preformed polymer from an organic solution and the diffusion of the organic solvent in the presence or absence of a surfactant in the aqueous medium. Polymers, drugs, and lipophilic surfactants are dissolved in a semi-polar water miscible solvent such as acetone or ethanol. The solution is then poured or injected into an aqueous solution-containing stabilizer utilizing magnetic stirring. Nano particles are produced as a result of fast solvent diffusion. The solvent is then withdrawn from the suspension at decreased pressure. The rate of addition of the organic phase into the aqueous phase also influences particle size. It was discovered that increasing the pace

of mixing reduces particle size and drug entrapment. The nano precipitation approach is highly suited for the majority of poorly soluble medicines. Nanosphere size and drug release may be efficiently regulated by altering preparation conditions. While altering the polymer concentration results in a decent yield of smaller sized nanospheres.[36,37]

Polymerization method

In this process, monomers are polymerized in an aqueous solution following the completion of polymerization, the medication is integrated either by adsorption onto the nanoparticles or by being dissolved in the polymerization solution. By ultra-centrifugation, the nanoparticle suspension is purified and re-suspended in an isotonic surfactant-free medium to remove different stabilizers and surfactants used for polymerization. This process has been published for producing polybutyl cyanoacrylate or poly(alkylcyanoacrylate) nanoparticles. The concentration of surfactants and stabilizers utilized influences the formation of nano capsules and their particle size.[7,38]

Coacervation or ionic gelation method

Much study has been conducted on the creation of nanoparticles utilizing biodegradable hydrophilic polymers such as chitosan, sodium alginate, and gelatin. Calvo and colleagues devised an ionic gelation technique for producing hydrophilic chitosan nanoparticles. The approach includes two aqueous phases, one containing the polymer chitosan and the other containing a polyanion, sodium tripolyphosphate. In this approach, the positively charged amino group of chitosan interacts with the negatively charged tri polyphosphate to generate coacervates with a nanometer size range. The development of coacervates arises from electrostatic contact between two aqueous phases, whereas ionic interaction conditions at ambient temperature result in the transition from liquid to gel owing to ionic gelation.[39,40]

Application of Nanoparticles

Nanomedicine offers enormous potential for improving human illness detection and therapy. The utilization of microorganisms in the creation of nanoparticles is an ecologically friendly method. Nanotechnology has the potential to change a wide range of biotechnological instruments, making them more affordable, tailored, safer, portable, and easier to administer.

Cell specificity

Enhancement of cell specificity by conjugating antibodies to carbon nanotubes with fluorescent or radiolabeling. [41]

Internalization

Internalization within mammalian cells can be achieved by surface- functionalized carbon nanotubes.

Vaccine delivery

Conjugation with peptides may be used as vaccine delivery structures.

Gene silencing

Highly selective therapy is required for cancer therapy where tumor cells will be selectively modulated. In this case with small interfering RNA gene silencing has been done. By targeting functionalized single walled carbon nanotubes with siRNA this can be achieved in the targeted cell to silence targeted gene expression.[42]

In diagnostics

Compounds attached to nanotubes have been shown to improve the effectiveness of diagnostic procedures. This functionalization feature, as well as the high length to diameter aspect ratio (which produces a high surface to volume ratio), aids in the construction of extremely efficient biosensors. Carbon nanotubes provide a number of benefits over existing medication delivery and diagnostic methods due to their intriguing physicochemical features. High thermal conductivity, organized structure with high aspect ratio, ultra-light weight, metallic, high electrical conductivity, high mechanical strength, or semi metallic behavior are the physicochemical features.[43,44]

Nanotechnology in Medicine

Drug Delivery

One use of nanoparticles in medicine is currently being investigated, which includes delivering drugs, heat, light, or other components to certain types of cells (such as cancer cells) in the form of nanoparticles. Nanoparticles are designed to be attracted to disease cells, allowing for direct therapy of specific cells. This technology will not only reduce harm to healthy cells in the body, but it will also allow for early illness identification. Another method for treating cancer cells is to provide chemotherapeutic medications to the cells while also providing heat to the cells. Researchers link gold nanorods to DNA strands, which operate as a scaffold, keeping the nanorod and the delivered medication together.[45,46]

Diagnostic Techniques

Researchers are working on a nanoparticle that will aid in the early identification of cancer tumors. When the adhesive to cancer tumors is recognized, the nanoparticles release "biomarkers" molecules, which are known as peptides. The concept is that even in the early stages of cancer, each nanoparticle contains many peptides, resulting in a high concentration of these biomarkers, allowing for early identification of the illness. When proteins aggregate on the nanorods, the color changes. The test is intended to be performed quickly and cheaply in order to discover an issue as soon as possible.[9]

Anti-Microbial Techniques

Staph infections can be treated with a nanoparticle cream containing nitric oxide gas, which is known to destroy germs. Using a nanoparticle cream to produce nitric oxide gas at the site of staph abscesses decreased the infection considerably in mouse studies. If an infection is caused by hazardous bacteria producing antibiotics, a burn dressing coated with antibiotic-containing nano capsules will open. Treatment of an infection is completed more quickly, reducing the number of times a dressing must be changed.[47]

Use of silver nanoparticles as antibacterial agent

Ultrasonography creates images using sound waves for a variety of reasons. These sound waves travel through the body, bounce against tissue, and return to a receiver. This receiver detects the time it takes for a sound wave to reflect and return to its source, which is perceived as a distance, and converts it into an electrical signal, which is subsequently turned into an image by the computer.

CONCLUSION

Nanoparticles have become important in many fields in recent years due to their incredible properties, including energy, healthcare, the environment, and agriculture. Nanoparticle technologies have enormous potential because they can transform poorly soluble, poorly absorbed, and labile biologically active substances into promising deliverable substances.

Characterization of nanoparticles

1. Particle Size, Zeta Potential and Polydispersity Index (PdI)

The nanoparticles will be characterized by measuring Z and PDI using a dynamic light-scattering system. The samples will be diluted 20 times with distilled water prior to Z and PDI analyses.[48]

2. X-Ray Diffraction (XRD) Analysis

The XRD analysis will be carried out by x ray diffractometer.[48]

3. Fourier Transmission Infrared (FT-IR) Spectroscopy

The surface chemistry and physical interaction between the polymers and drug can be determined from FTIR spectra. The samples for FT-IR spectrometry will be mixed with KBr and compressed into transparent tablets prior to the analysis over the 4000-400 cm-1 range using a Jasco 6700 FT-IR spectrometer.

4. Encapsulation Efficiency and drug loading

The values of encapsulation efficiency and drug loading capacity of NPs can be determined using HPLC. The nanosuspension (2 mL) will be loaded into a Millipore UFC801008 Amicon® filter (Amicon Ultra, Millipore, USA) with a molecular weight cut-off of 10 kDa and centrifuged at 3000 × g for 30 min (Hermle, Germany). Unbound drug, which will move across the filter membrane to the bottom compartment, will be assayed, and the drug encapsulation efficiency (EE) and the drug loading capacity (LC) will then be calculated using the following equation.[49,50]

$$\text{EE (\%)} = \frac{(Wt\ of\ initial\ drug - Wt\ of\ unbound\ drug)}{Wt\ of\ initial\ drug} X\ 100$$

$$\text{LC (\%)} = \frac{(Wt\ of\ initial\ drug - Wt\ of\ unbound\ drug)}{Wt\ of\ nanoparticles} X\ 100$$

5. Stability Studies

The stability studies of nanoparticles can be done by storing the nanoparticles in 4°C for 28 days and on particle size, zeta potential and PDI will be checked on specific intervals.

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