REVIEW ARTICLE

# Polymeric Nanoparticles as Promising Novel Carriers for Drug Delivery: An Overview

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## ABSTRACT

Polymeric nanoparticles are particulate dispersions or solid particles with size in the range of 10-1000 nm. They represent a promising drug delivery system of controlled and targeted release. The use of polymeric nanoparticle for drug delivery is a strategy that aims to optimize therapeutic effects while minimizing adverse effects. Due to their small sizes, they exhibit unique physicochemical and biological properties like an enhanced reactive area as well as an ability to cross cell and tissue barriers, that make them a favourable material for biomedical applications. The present review focuses on methods of preparation, characterization and potential therapeutic applications of polymeric nanoparticles.

**Keywords:** Nanoparticles, Biodegradble polymers, Drug delivery, Characterization, Applications.

## INTRODUCTION

Over the past few decades, there has been a considerable research interest in the area of drug delivery using nanoparticles as carriers for small and large molecules. Polymeric nanoparticulate systems from biodegradable and biocompatible polymers are interesting options for controlled drug delivery and drug targeting. Polymeric nanoparticles are particulate dispersions or solid particles with size in the range of 10-1000 nm. The drug is dissolved, entrapped, encapsulated or attached to a nanoparticle matrix. They have been used *in vivo* to protect the drug entity in the systemic circulation, restrict access of the drug to the chosen sites and to deliver the drug at a controlled and sustained rate to the site of action. Various polymers have been used in delivery research as they can effectively deliver the drug to a target site and thus increase the therapeutic benefit, while minimizing side effects. [1] Polymer-based nanoparticles effectively carry drugs, proteins, and DNA to target cells and organs. Their nanometer-size promotes effective permeation through cell membranes and stability in the blood stream.

Depending upon the method of preparation nanoparticles, nanospheres or nanocapsules can be obtained. Nanospheres have a monolithic-type structure (matrix) in which drugs are dispersed or adsorbed onto their surfaces or encapsulated within the particles. Nanocapsules are the vesicular system in which the drug is confined to a cavity consisting of an inner liquid core surrounded by a polymeric membrane. In this case the active substance is usually dissolved in the inner core, but may also be adsorbed to the capsule surface [Figure 1]. [2]

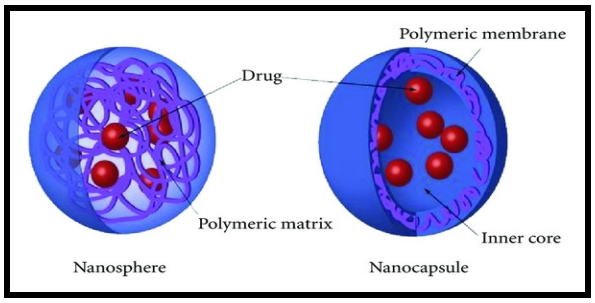


**Figure 1:** Types of polymeric nanoparticles

### Advantages

The advantages of using nanoparticles as a drug delivery system are as follows: [3]

1. Ease of manipulation of the particle size and surface characteristics of nanoparticles so as to

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achieve both passive and active drug targeting after parenteral administration.

2. Controlled and sustained 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.
4. 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. Site-specific targeting can be achieved by attaching targeting ligands to surface of particles or use of magnetic guidance.
6. Small sized nanoparticles can penetrate through smaller capillaries, which could allow efficient drug accumulation at the target sites.
7. The system can be used for various routes of administration including oral, nasal, parenteral, intra-ocular etc.

## Limitations

Inspite of these advantages, nanoparticles have some limitations [3]

1. Their 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 particle size results in limited drug loading and burst release.

## Polymers used in the preparation of nanoparticles

The polymers used for preparation of nanoparticles are as follows: [4]

- Natural polymers
- Synthetic polymers

### Natural polymers:

Natural hydrophilic polymers such as proteins (albumin, gelatine, legumin or vicilin) and polysaccharides (alginate, dextran, chitosan, agarose, pullulan) are widely used. But these polymer But these polymers have certain disadvantages such batch-to-batch variation, conditional biodegradability, and antigenicity.

### Synthetic polymers:

These polymers are divided into two groups:

- Pre-polymerized: Poly (ε-caprolactone) (PECL), Poly (lactic acid) (PLA), Poly (lactide-co-glycolide) (PLGA), and Polystyrene.
- Polymerized in process: Poly (isobutylcyanoacrylates) (PICA), Poly (butylcyanoacrylates) (PBCA), Poly methyl (methacrylates) (PMMA), and Polyhexalcyanoacrylate (PHCA), and Copolymer of aminoalkylmethacrylate methyl methacrylate.

## Methods of Preparation of Polymeric Nanoparticles

Nanoparticles can be prepared from a variety of materials such as proteins, polysaccharides and synthetic polymers. The selection of matrix materials is dependent on many factors like:[1]

a) Size of nanoparticles required.
b) Inherent properties of the drug, e.g., aqueous solubility and stability.
c) Surface characteristics such as charge and permeability.
d) Degree of biodegradability, biocompatibility and toxicity.
e) Drug release profile desired.
f) Antigenicity of the final product.

Nanoparticles can be prepared by following methods:

### 1. Solvent Evaporation method

In this method, the polymer is dissolved in an organic solvent such as dichloromethane, chloroform or ethyl acetate, which is also used as the solvent for dissolving the hydrophobic drug. The mixture of polymer and drug solution is then emulsified in an aqueous solution containing a surfactant or emulsifying agent to form oil in water (o/w) emulsion. After the formation of stable emulsion, the organic solvent is evaporated either by reducing the pressure

or by continuous stirring. Particle size was found to be influenced by the type and concentrations of stabilizer, homogenizer speed and polymer concentration. In order to produce small particle size, often a high-speed homogenization or ultrasonication may be employed. [5]

### 2. Spontaneous Emulsification or Solvent Diffusion Method

This is a modified version of solvent evaporation method. In this method, the water miscible solvent along with a small amount of the water immiscible organic solvent is used as an oil phase. Due to the spontaneous diffusion of solvents an interfacial turbulence is created between the two phases leading to the formation of small particles. As the concentration of water miscible solvent increases, a decrease in the size of particle can be achieved. Both solvent evaporation and solvent diffusion methods can be used for hydrophobic or hydrophilic drugs. In the case of hydrophilic drug, a multiple w/o/w emulsion needs to be formed with the drug dissolved in the internal aqueous phase.[6]

### 3. Polymerization Method

In this method, monomers are polymerized to form nanoparticles in an aqueous solution. Drug is incorporated either by being dissolved in the polymerization medium or by adsorption onto the nanoparticles after polymerization completed. The nanoparticle suspension is then purified to remove various stabilizers and surfactants employed for polymerization by ultracentrifugation and re-suspending the particles in an isotonic surfactant-free medium. This technique has been reported for making polybutylcyanoacrylate or poly (alkylcyanoacrylate) nanoparticles. [7,8]

### 4. Coacervation or Ionic gelation method

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 polyanion sodium tripolyphosphate. In this method, positively charged amino group of chitosan interacts with negative charged tripolyphosphate to form coacervates 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. [9]

### 5. Salting out method

In this method acetone is chosen as the water miscible organic solvent because of its pharmaceutical acceptance with regard to toxicity. The method consists of addition of water soluble polyvinyl alcohol (PVA) in a highly concentrated salt solution in water (aqueous phase) to a polymer solution in acetone (organic phase). Although acetone is miscible with pure water in all ratios, the high salt concentration of the aqueous phase prevents mixing of the phase. After emulsification, addition of pure water in a sufficient quantity causes acetone to diffuse into the aqueous phase, resulting in the formation of nanoparticles. [10]

### 6. Nanoprecipitation method

Typically, this method is used for hydrophobic drug entrapment, but it has been adapted for hydrophilic drugs as well. Polymers and drugs are dissolved in a polar, water-miscible solvent such as acetone, acetonitrile, ethanol, or methanol. The solution is then poured in a controlled manner (i.e. drop-by-drop addition) into an aqueous solution with surfactant. Nanoparticles are formed instantaneously by rapid solvent diffusion. Finally, the solvent is removed under reduced pressure.[11]

### 7. Spray drying method

In this method, chitosan is first dissolved in acetic acid; the drug is dissolved or dispersed in the solution and then a suitable cross-linking agent is added; this solution or dispersion is then atomised in a stream of hot air. Atomisation leads to the formation of small droplets, from which the solvent evaporates, leading to the formation of free-flowing powders. Particle size depends upon size of the nozzle, spray flow rate, atomisation pressure and inlet air temperature, and extent of cross-linking.[12]

### 8. Supercritical Fluid Technology

Conventional methods such as solvent extraction-evaporation, solvent diffusion and organic phase separation methods require the use of organic solvents which are hazardous to the environment as well as to physiological systems. Therefore, the supercritical fluid technology has been investigated as an alternative to prepare biodegradable micro- and nanoparticles because supercritical fluids are environmentally safe. [13]

A supercritical fluid can be generally defined as a solvent at a temperature above its critical temperature, at which the fluid remains a single phase regardless of pressure. [13] Supercritical $CO_2$ (SC $CO_2$) is the most widely used supercritical fluid because of its mild critical conditions (Tc = 31.1 °C, Pc = 73.8 bars), nontoxicity, non-flammability, and low price. The most common processing techniques involving supercritical fluids are supercritical anti-solvent (SAS) and rapid expansion of supercritical solution (RESS).

In the supercritical antisolvent method, both the drug and the polymer are dissolved in a suitable organic solvent and are atomized through a nozzle into supercritical $CO_2$. The dispersed organic solvent phase and the antisolvent $CO_2$ phase diffuse into each other and since $CO_2$ is miscible only with the solvent, the solvent gets extracted causing the supercritical fluid–insoluble solid to precipitate as nanoparticles. [14] In the rapid expansion of supercritical solutions technique, the solute is dissolved in supercritical $CO_2$ and this solution is atomized through a nozzle into a collection chamber at atmospheric conditions. When expanded, $CO_2$ immediately evaporates and the solute precipitates as a coprecipitate of the drug embedded in the polymer matrix. [15]

Supercritical fluid technology technology technique, although environment friendly and suitable for mass production, require specially designed equipments and is more expensive.

## 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 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. As a result, most of the drug loaded onto them will be exposed to the particle surface leading to fast drug release. On the contrary, drugs slowly diffuse inside larger particles. As a drawback, smaller particles tend to aggregate during storage and transportation of nanoparticle dispersion. Hence, there is a compromise between a small size and maximum stability of nanoparticles. [16]

There are a several tools for determining nanoparticle size as discussed below:

### 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 submicron ranges .Shining monochromatic light (laser) onto a solution of spherical particles in Brownian motion causes a Doppler shift when the light hits the moving particle, changing the

wavelength of the incoming light. This change is related to the size of the particle. 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 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. [17]

### Scanning electron microscopy

Scanning electron microscopy (SEM) is giving morphological examination with direct visualisation. 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. [18] 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 the 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, uranyl acetate, etc, or by plastic embedding. Alternate method is to expose the sample to liquid nitrogen temperatures after embedding in vitreous ice. 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. [19]

### 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. [20] Instruments provides a topographical map of sample based on forces between the tip and the sample surface. Samples are usually scanned in contact or noncontact mode depending on their properties. In contract mode, the topographical map is generated by tapping the probe on to the surface across the sample and probe hovers over the conducting surface in non-conduct mode. The prime advantage of AFM is its ability to image non-conducting samples without any specific treatment, thus allowing imaging of delicate biological and polymeric nano and microstructures. [21] AFM provides the most accurate description of size and size distribution and requires no mathematical treatment.

### 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 the 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. High zeta potential values, either positive or negative, should be achieved in order to ensure stability and avoid aggregation of the particles. 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. [22]

### Surface Hydrophobicity

Surface hydrophobicity can be determined by several techniques such as hydrophobic interaction chromatography, biphasic partitioning, adsorption of probes, contact angle measurements etc. Recently, several sophisticated analytical techniques are reported in literature for surface analysis of nanoparticles. X-Ray photon correlation spectroscopy permits the identification of specific chemical groups on the surface of nanoparticles. [23]

### Drug Loading

Ideally, a successful nanoparticle system should have a high drug-loading capacity thereby reduce the quantity of matrix materials for administration. Drug loading can be done by two methods:

- Incorporating at the time of nanoparticle production (incorporation method)
- Absorbing the drug after formation of nanoparticles by incubating the carrier with a concentrated dug solution (adsorption/absorption technique).

Drug loading and entrapment efficiency very much depend on the solid-state drug solubility in matrix material or polymer (solid dissolution or dispersion), which is related to the polymer composition, the molecular weight, the drug polymer interaction and the presence of end functional groups (ester or carboxy). [11]

### Drug Release

Drug release from the carrier-based particulate system depends upon the cross-linking, morphology, size, density of the particulate system and the physiochemical properties of the drug, as well as presence of adjuvant. *In vitro* drug release also depends upon pH, polarity and presence of enzymes in the dissolution medium.

The release of drug from the particulate system depends upon three different mechanisms: [24]

- Release from the surface of particles.
- Diffusion through the swollen rubbery matrix.
- Release due to erosion.

Various methods, which can be used to study the *in vitro* release of drug, are as follows:

- Side-by-side diffusion cells with an artificial or biological membrane.
- Dialysis bag diffusion technique.
- Reverse dialysis bag technique.
- Ultracentrifugation.
- Centrifugal ultrafiltration.

## Applications of Nanoparticles

### 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 (CNS). [25] The BBB is characterized by relatively impermeable endothelial cells 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 consequently only permits selective transport of molecules that are essential for brain function. [26]

Strategies for nanoparticle targeting to the brain rely on nanoparticle's interaction with the 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 melanotransferrin have been shown to be capable of delivery of a self non transportable drug into

the brain via the chimeric construct that can undergo receptor-mediated transcytosis. [28-30] It has been reported that poly(butylcyanoacrylate) (PBCA) nanoparticles were able to deliver hexapeptide dalargin, doxorubicin and other agents into the brain which is significant because of the great difficulty for drugs to cross the BBB. [29] Despite some reported success with polysorbate 80 coated nanoparticles, this system does have many shortcomings including desorption of polysorbate coating, rapid nanoparticle

degradation and toxicity caused by presence of high concentration of polysorbate 80. [31] OX26 MAbs (anti-transferrin receptor MAbs), the most studied BBB targeting antibody, have been used to enhance the BBB penetration of lipsosomes. [32]

Another study by Kreuter et al. demonstrates the delivery of several drugs successfully through the blood brain barrier using polysorbate 80 coated PACA nanoparticles. [33] It is thought that after administration of the polysorbate 80-coated particles, apolipoprotein E (ApoE) adsorbs onto the surface. The ApoE protein mimics low density lipoprotein (LDL) causing the particles to be transported across the blood brain barrier via the LDL receptors. The effects of polysorbate-80 on

transport through the blood brain barrier were confirmed by Sun et al. with PLA nanoparticles. [34] Nanoparticles were also functionalized with thiamine surface ligands. These particles, with an average diameter of 67 nm, were able to associate with the blood brain barrier thiamine transporters and thereby increase the unidirectional transfer coefficient for the particles into the brain. [35]

### Nanoparticles for vaccine/gene delivery

Polynucleotide vaccines/DNA vaccines/plasmid 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. [36] 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/DNA vaccines are set to supersede many conventional vaccines particularly for immunotherapy. However, there are several issues related to the delivery of polynucleotides which limit their application. These issues include efficient delivery of the polynucleotide to the target cell population, its localization to the nucleus of these cells, and ensuring that the integrity of the polynucleotides is maintained during delivery to the target site. Nanoparticles loaded with plasmid DNA could also serve as an efficient sustained release gene delivery system due to their rapid escape from the degradative endo-lysosomal compartment to the cytoplasmic compartment. [37] Hedley et al. [38] reported that following their intracellular uptake and endolysosomal escape, nanoparticles could release DNA at a sustained rate resulting in continuous gene expression. This gene delivery strategy could be applied to facilitate bone healing by using PLGA nanoparticles containing therapeutic genes such as bone morphogenic protein.

### Tumor Targeting

The rationale of using nanoparticles for tumor targeting is based on

1. Nanoparticles ability to deliver the requisite dose load of drug in the vicinity of the tumor due to the enhanced permeability and retention effect or active targeting by ligands on the surface of nanoparticles.
2. Nanoparticles ability to reduce the drug exposure to healthy tissues by limiting drug distribution to the target organ.

Active tumor targeting of nanoparticles may be achieved with either direct targeting or the pretargeting method. In direct targeting method, nanoparticles are covalently coupled with the

ligands. The ligand coupled nanoparticles are received by the tumor cells expressing a homologous receptor on their surfaces. The specific ligand-receptor binding ensures that the nanoparticles carrying drugs will get attached specifically to the tumor cells. This will facilitate delivery of drugs only to the cells (tumor cells) expressing receptor and not the normal healthy cells. In the pretargeting approach, the therapeutic molecule is not coupled with the ligand and is

administered after an appropriate delay time following the administration of the targeting ligand.

Nobs et al. explored both-approaches to target PLA nanoparticles to tumor cells. In the direct approach, nanoparticles with MAbs exposed on their surface were incubated with the two tumor cells, while in the pretargeting protocol, tumor cells were pretargeted with biotinylated MAbs prior to the administration of avidin-labelled nanoparticles. [39]

Verdun et al. in an elegant experiment demonstrated positive effects of using poly- isohexylcyanoacrylate-nanospheres in the delivery of doxorubicin in mice. The doxorubicin incorporated into poly (isohexylcyanoacrylate) nanopsheres and delivered in mice showed higher concentrations of doxorubicin in the liver, spleen and the lungs than in mice treated with only free doxorubicin. [40]

## Nanoparticles for oral delivery of peptides and proteins

Significant advances in biotechnology and biochemistry have led to the discovery of a large number of bioactive molecules and vaccines based on peptides and proteins. Development of suitable carriers remains a challenge due to the fact that bioavailability of these molecules is limited by the epithelial barriers of the gastrointestinal tract and their susceptibility to gastrointestinal degradation by digestive enzymes. Polymeric nanoparticles allow encapsulation of bioactive molecules and protect them against enzymatic and hydrolytic degradation. For instance, it has been found that insulin-loaded nanoparticles have preserved insulin activity and produced blood glucose reduction in diabetic rats for up to 14 days following the oral administration. [41] The surface area of human mucosa extends to 200 times that of skin. The gastrointestinal tract provides a variety of physiological and morphological barriers against protein or peptide delivery, for example: proteolytic enzymes in the gut lumen like pepsin, trypsin and chymotrypsin; proteolytic enzymes at the brush border membrane (endopeptidases); bacterial gut flora; and mucus layer and epithelial cell lining itself. [42] The histological architecture of the mucosa is designed to efficiently prevent uptake of particulate matter from the environment. One important strategy to overcome the gastrointestinal barrier is to deliver the drug in a colloidal carrier system, such as nanoparticles, which is capable of enhancing the interaction mechanisms of the drug delivery system and the epithelia cells in the GI tract.

## Nanoparticles for Ocular delivery

Topical ophthalmic drugs have generally poor absorption in the eye due to the cornea's low permeability to drugs and noncorneal factors such as rapid tear turnover, nasolacrimal drainage, and systemic absorption. One of the major problems in ocular delivery is providing and maintaining an adequate concentration of the therapeutic agent in the precorneal area. Topical drop administration of ophthalmic drugs in aqueous solutions results in extensive drug loss due to tear fluid and eyelid dynamics. Most non-invasive approaches for enhancing ocular drug absorption involve the use of prodrugs, the use of viscosity agents designed to prolong the drug residence time, and colloidal systems.[43] Polymeric nanoparticles are attractive colloidal systems because they demonstrate increased stability and have a longer elimination half-life in tear fluid (up to 20 min), than do conventional drugs applied topically to the eye, which have half-lives of just one to three minutes. Nanoparticulate drug delivery systems have been evaluated for ocular applications to enhance absorption of therapeutic drugs, improve bioavailability, reduce systemic side effects, and sustain intraocular drug levels. [44] Qaddoumi et al. have studied the characteristics and mechanism of uptake of poly(lactic-co-glycolic acid) (PLGA) based nanoparticles for ophthalmic application.[45] They suggested that PLGA-based nanoparticles could be used for the enhancement of drug absorption in the eye and the controlled release of proteins and drugs. Salgueiro et al. demonstrated ophthalmic application of cyclophosphamide loaded polybutylcyanoacrylate (PBCA) nanosphere as an

immunosuppressive agent. The morphometrical properties such as average particle size and polydisparity index of these drug delivery systems are adequate for ophthalmic application without induced corneal or conjunctival irritation. [46]

### Nanoparticles for Pulmonary Treatment

Nanostructured drug delivery and targeting systems are tools to overcome the limitations of lung delivery by stabilizing and protecting the release in the bronchi and make lung therapy through inhalation possible and effective. Insulin-loaded PBCA nanoparticles were studied by Zhang et al., they demonstrated that the pulmonary administration of these nanoparticles could significantly prolong the hypoglycemic effect of insulin. [47] An interesting study was reported by Liu et al. incorporating estradiol and colloidal gold nanoparticles in PLGA nanoparticles to be used as a model for the pulmonary drug delivery systems. [48] Vila et al. have shown that polyethylene glycol (PEG) coating of the PLA nanoparticles increased the absorption of drug in nasal mucosa. [49] Pandey et al. demonstrated the application of nanoparticulate drug delivery systems for the treatment of experimental tuberculosis using poly(d,l-lactide-co-glycolide) as a polymer. They used an inhalable system using the nanoparticles and three anti-tubercular drugs Rifampicin, Isoniazid, and Pyrazinamide. [50]

## CONCLUSION

In the past few decades, researchers have studied alternative delivery systems to improve the efficacy of different medicines. Nanotechnology is an exciting novel field with hopes for improvements in wide variety of uses in drug delivery in pharmaceutical research. Polymeric nanoparticles offer a new avenue to achieve drug delivery and drug targeting with newly discovered disease site-specific drugs and existing poorly soluble drugs. Overcoming the obstacles in conventional drug delivery systems, polymeric nanoparticles are anticipated for better application and effective drug delivery, and would ultimately enhance treatment and patient compliance.

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