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Review on Novel Promising Drug Carrier: Polymeric Nanoparticles

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ABSTRACT

One of the most researched methods for drug encapsulation in contemporary medicine is polymeric nanoparticles. The formulation that can deliver the medication in a regulated manner and to a specific spot is what the researchers are primarily interested in. Colloidal assemblies of polymeric nanoparticles are composed of synthetic, semi-synthetic, and natural polymers. Nanoparticles have special physical and chemical properties due to their enormous surface area and nanoscale size. Their unique dimensions, forms, and structures have an impact on their optical properties, reactivity, durability, and other qualities. They have special physicochemical and biological characteristics that are due to their small sizes, such as an improved reactive area and the capacity to pass cell and tissue barriers, which make them an advantageous material for biomedical applications. The present review focuses on methods of preparation, characterization and polymers used for the preparations of polymeric nanoparticles.

INTRODUCTION:

In recent years, innovative drug delivery systems based on nanotechnology have demonstrated promising outcomes. These systems include nanocrystals, polymeric nanoparticles, lipid nanoparticles, liposomes, nanoemulsions, microemulsions, nanofibers, and dendrimers. They have several benefits, including enhanced solubility and stability of the drug, versatility in controlling drug release, enhanced membrane permeability of the drug, adjustable surface properties, potential for drug targeting, and flexibility in administering drugs via intravenous, intramuscular, subcutaneous, and oral routes[1]. Polymeric nanoparticle-based nanomedicine raises drugs' therapeutic index, specificity, and efficacy. It is now common practice to use new medicine--- administration techniques that increase therapeutic efficacy while minimising side effects. Applications for research in nanoscience and nanotechnology have increased significantly in recent years. The possibility of a global revolution brought about by nanotechnology is growing[2–3]. Nanoparticles constructed of polymers are known as polymeric nanoparticles. Depending on the production process, either nanospheres or nanocapsules can be produced once the medication has been dissolved, trapped, and encapsulated into nanoparticles. In vesicular systems called nanocapsules, the medication is housed in a hollow surrounded by a polymer membrane. Nanospheres are matrix structures in which the drug is physically and uniformly distributed [4].

Advantages of Polymeric NPs

- Controlled release
- The capacity to defend pharmaceuticals and other biologically active substances from the environment.
- Improve their bioavailability and therapeutic index[5]

Limitations

- Physical handling of nanoparticles in liquid and dry forms can be challenging due to particle-particle agglomeration caused by their small size and vast surface area.
- Small particle size results in limited drug loading and burst release [6].

Polymers Used In the Preparation of Nanoparticles

The polymers used for preparation of nanoparticles are as follows:

1. 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 Butthese polymers have certain disadvantages such as batch-to-batch variation, conditional biodegradability, and antigenicity.

2. Synthetic polymers:

These polymers are divided into two groups:

- Pre-polymerized: Poly (ε-caprolactone) (PECL), Poly (lactic acid) (PLA), Poly (lactide-coglycolide) (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[7].

Methods for Production of Polymeric Nanoparticles:

Different techniques can be employed to create the particles depending on the kind of drug that needs to be placed into the polymeric NPs and how it needs to be administered.

Table No 1: Different methods for the production of polymeric nanoparticles

Polymeric Nanoparticles	**Production Methods**
Nanospheres	Solvent Evaporation
	Emulsification/Solvent diffusion
	Nanoprecipitation
	Emulsification/Reverse salting-out
Nanocapsules	Nanoprecipitation

1. Solvent Evaporation

Organic solvents, such as dichloromethane, chloroform, or ethyl acetate, which are also employed to dissolve the active component, are utilised to dissolve polymers. The medicine that has been dissolved or dispersed in a polymer solution is then emulsified with an

appropriate surfactant or emulsifying agent in an aqueous solution to create an o/w emulsion. Following that, the organic solvent is evaporated either by lowering the pressure or by constant stirring. It is possible to use an ultrasonicator or a high-speed homogenizer[8].

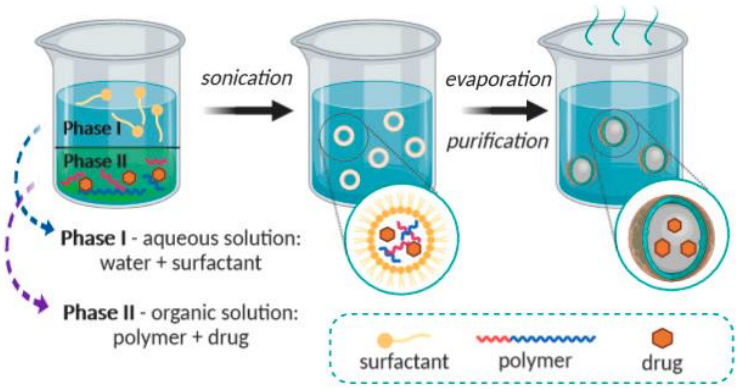

Figure No 1: Schematic representation of the solvent evaporation method [9]

2. Emulsification/Solvent diffusion:

The emulsification diffusion method is an additional technique for creating nanoparticles. The process makes use of a solvent that is only partially water-soluble, such as acetone or propylene carbonate. The drug and polymer are dissolved in the solvent, and then they are emulsified in the stabilizer-containing aqueous phase. By adsorbing to the surface of the droplets, the stabilizer's function is to stop the aggregation of emulsion droplets. When water is added to the emulsion, the solvent might diffuse into the water. The particles are precipitated at the nanoscale as a result of stirring the solution. Additionally, it can be collected by centrifugation, or dialysis can successfully remove the solvent. The fundamental issue with this technology is that during the diffusion steps, the water-soluble medicines have a tendency to seep out of the polymer phase. Therefore, medium chain triglycerides were used as the dispersion medium instead of aqueous media, and a little amount of surfactant was also added. Centrifugation is used to separate the nanpoarticles from the oily solution [10].

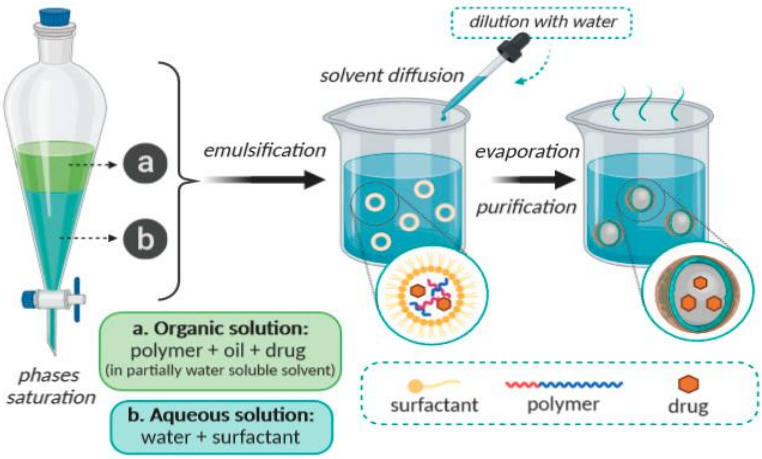

Figure No 2: Schematic representation of the emulsification/solvent diffusion method [9]

3. Nanoprecipitation:

The Fessi et al. team invented the solvent displacement method, often known as the nanoprecipitation method. The basic idea behind this system is that a semi-polar solvent that is water soluble is removed from a lipophilic solution, followed by the interfacial deposition of a polymer. The following fundamental elements make up the nanoprecipitation system: As a polymer solvent, one selects an organic solvent that is miscible in water and is easily eliminated by evaporation, such as ethanol, acetone, hexane, chloride, or dioxane. Acetone is the most often used polymer-solvent in this process as a result of this[11].

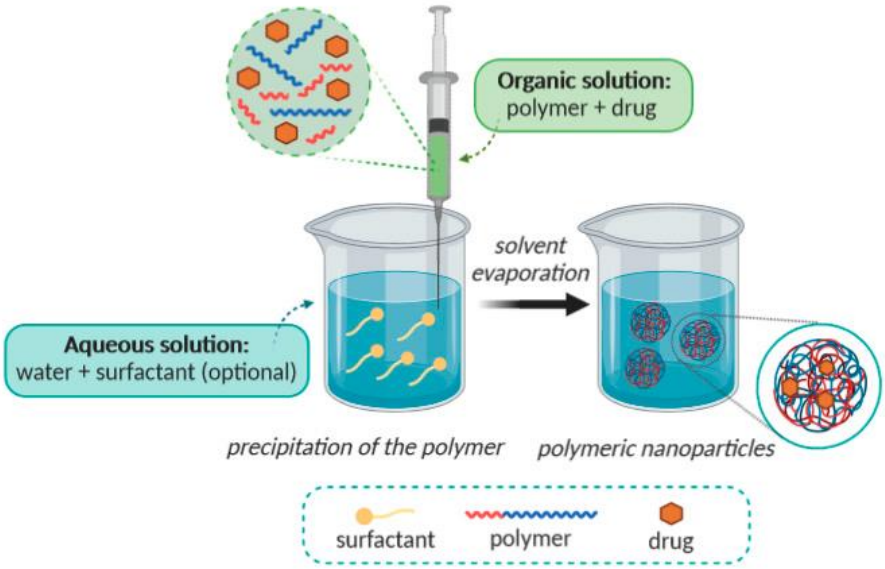

Figure No 3: Schematic illustration of the nanoprecipitation method [9]

4. Emulsification/Reverse salting-out:

Acetone and emulsifying the polymer solution are examples of organic solvents that must be used in the procedures and are normally completely miscible with water. Surfactants and chlorinated solvents are not used in the salting-out process. Without using any high-shear pressures, the emulsion is created by dissolving a high concentration of salt or sucrose that is selected to have a significant salting-out effect in the aqueous phase. Typically, castoff-appropriate electrolytes include magnesium chloride, calcium chloride, and magnesium acetate. As these components melt in the water, the properties of water's miscibility with other strippers are altered[12].

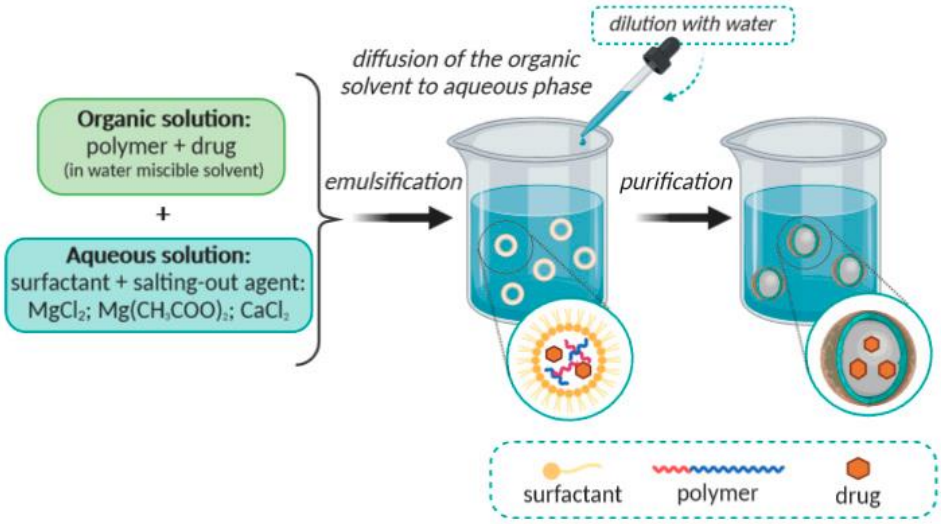

Figure No 4: Schematic representation of the emulsification/reverse salting-out method[9]

Characteristics of Nanoparticles

1. Particle size

The two most crucial factors in the characterisation of nanoparticles are the particle size distribution and shape. Electron microscopy is used to measure size and morphology. Particle size has been discovered to influence medication release. Greater surface area is offered by smaller particles, and particle size can also influence polymer breakdown. For instance, in vitro research revealed that the disintegration rate rose as particle size increased. Different nanoparticles have been measured using DLS (Dynamic light scattering), AFM (Atomic force

microscopy), TEM (Transmission electron microscopy), and SEM (Scanning electron microscopy) [13-15].

2. Particle shape

The previously useful for evaluation nanosuspension is embodied by SEM; the nanosuspension is lyophilized to produce dense units. Using a sputter coater, platinum alloy is applied to the solid particles[16].

3. Surface charge

The type and strength of a nanoparticle's surface charge affects both how well they interact with their biological surroundings and how they interact electrostatically with bioactive substances. Through a study of nanoparticle zeta potential, colloidal stability is examined. The surface charge can be estimated indirectly using this potential. Colloid dispersion's storage stability can be predicted using the zeta potential measurement. To confirm stability and prevent particle aggregation, high zeta potential values—whether positive or negative—should be attained. Additionally, it generates data about the nature of the material[17-18].

4. Surface hydrophobicity

Numerous methods, including hydrophobic interaction chromatography, biphasic partitioning adsorption of probes, contact angle measurements, etc., can be used to assess the hydrophobicity of a surface. For the surface investigation of nanoparticles, a number of advanced analytical approaches have recently been reported in the literature. The surface of nanoparticles can be identified by certain chemical groups using X-ray photon correlation spectroscopy[19-20].

5. Zeta potential:

The surface charge property of nanoparticles is frequently described using the zeta potential of the nanoparticle. It is affected by the makeup of the particle and the medium in which it is spread and reflects the electrical potential of the particles. When the zeta potential of a nanoparticle is between 10 and +10 mV, it is said to be about neutral, however when it is larger than +30 mV or lower than 30 mV, it is said to be strongly cationic or anionic. The presence of an encapsulated charged active substance or an adsorbate on the surface of a nanocapsule can be determined using the zeta potential. The magnitude of the Zeta Potential

provides information about particle stability, with higher magnitude potentials exhibiting increased electrostatic repulsion and therefore increased stability.

- 0-5 mV: Particles tend to agglomerate or aggregate.
- 5-20 mV: Particles are minimally stable.
- 20-40 mV: Particles are moderately stable.
- 40+ mV: Particles are highly stable.

It is important to consider that the magnitude of the charge on the nanoparticle surface depends on the solution pH.

The Henry equation is then used to calculate the zeta potential, z:

$$\mathbf{Ue = 2\in zf(Ka)/3\eta}$$

Where Ue is the electrophoretic mobility, e is the dielectric constant, η is the absolute zero-shear viscosity of the medium, f(ka) is the Henry function, and ka is a measure of the ratio of the particle radius to the Debye length[21].

6. X-ray diffraction (XRD) analysis:

A common method for figuring out the morphology and structure of crystals is X-ray diffraction. The intensity changes depending on the amount of a constituent. This method is used to determine whether a particle is metallic. It provides information on the size and shape of the unit cell's translational symmetry from peak positions, as well as information on its electron density—specifically, the location of its atoms—from peak intensities. XRD patterns were calculated using X per Rota flex diffraction meter using Cu K radiation and =1.5406 Å. Crystallite size is calculated using Scherrer equation:

$$CS = K / \cos$$

Where CS is the crystallite size Constant [K] = 0.94 is the full width at half maximum [FWHM] in radius.

$$[\beta] = FWHM \times \pi / 180\lambda$$

Cos = Bragg angle. X-ray diffraction analysis with various nanoparticles has been studied by various research workers to find the high crystallinity of the prepared sample[22].

CONCLUSION

The use of therapeutic nanotechnology in the market has led to the development of many drugs. Polymer-based nanoparticles have recently undergone a number of amazing inventions, making them the most effective and practical medication delivery technology with the fewest side effects and toxicity. Comparing polymeric nanoparticles to traditional pharmaceuticals, they have better therapeutic and diagnostic benefits. Controlling the surface's functionalization, which can increase specificity, and physical-chemical qualities are the only factors that affect the nanotherapeutic efficacy. We are confident that targeted polymeric nanoparticles could produce more effective treatments of significant human diseases if used in a well-characterized system that includes: safe, effective, and specific targeting ligands; biocompatible; biodegradable; and bioeliminable materials; as well as the right choice of therapeutics and disease models.

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