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Review Article

Polymeric Nanoparticles as Potential Carrier for Cancer Diagnostic and Treatment

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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. A number of polymeric NPs are in the preclinical phase for the delivery of cancer therapeutics owing to the unlimited potential for targeted delivery. Recently, there has been significant interest in employing synthetic polymers like polyethyleneglycol (PEG), polylactide (PLA), and poly(D,L-lactide–co-glycolide) (PLGA) . Delivery of genes into neurons can be achieved by optimization the size of nanoparticles, as well as the conformation of their surface. Another advantage of their using is the possibility to obtain vaccines for oral administration. Polymeric nanoparticles can deliver drugs in the optimum dosage over time, thus increasing the efficacy of the drug, maximizing patient compliance and enhancing the ability to use highly toxic, poorly soluble, or relatively unstable drugs. These systems can also be used to co-deliver two or more drugs for combination therapy. YM155 (Sepantronium Bromide) is a potent survivin inhibitor that is the subject of clinical trials for multiple types of cancer including melanoma, lypmphoma, lung cancer, prostate and breast cancer. YM155 is a therapeutic candidate for the treatment of glioblastoma (GBM), however, its rapid plasma clearance and minimal blood-brain barrier penetration are obstacles to clinical translation. So nanoparticle plays a important role in pharmacy.

Key words: Polymeric nanoparticles, YM155, glioblastoma, survivin, polyethyleneglycol.

INTRODUCTION

Nanotechnology-enabled drug delivery systems (DDS) over the next five years are forecast to dramatically reshape the way existing drugs are delivered. The growing range of nanotechnology enabled drug delivery methods is poised to change the way new compounds are formulated, and to extend the life cycle of existing compounds.[1] Advancement in the field of nanotechnology and its applications to the field of medicines and pharmaceuticals has revolutionized the twentieth century. Nanotechnology is the study of extremely small structures.[2] The prefix "nano" is a Greek word which means "dwarf ". The word "nano" means very small or miniature size .[3] There is a great interest globally in the field of drug delivery (DDSs), cell delivery (CDSs) and gene delivery systems (GDSs). The increased interest in this field is because of the easy to engineer the carriers and monitoring the drugs for tumour specific delivery. There are some

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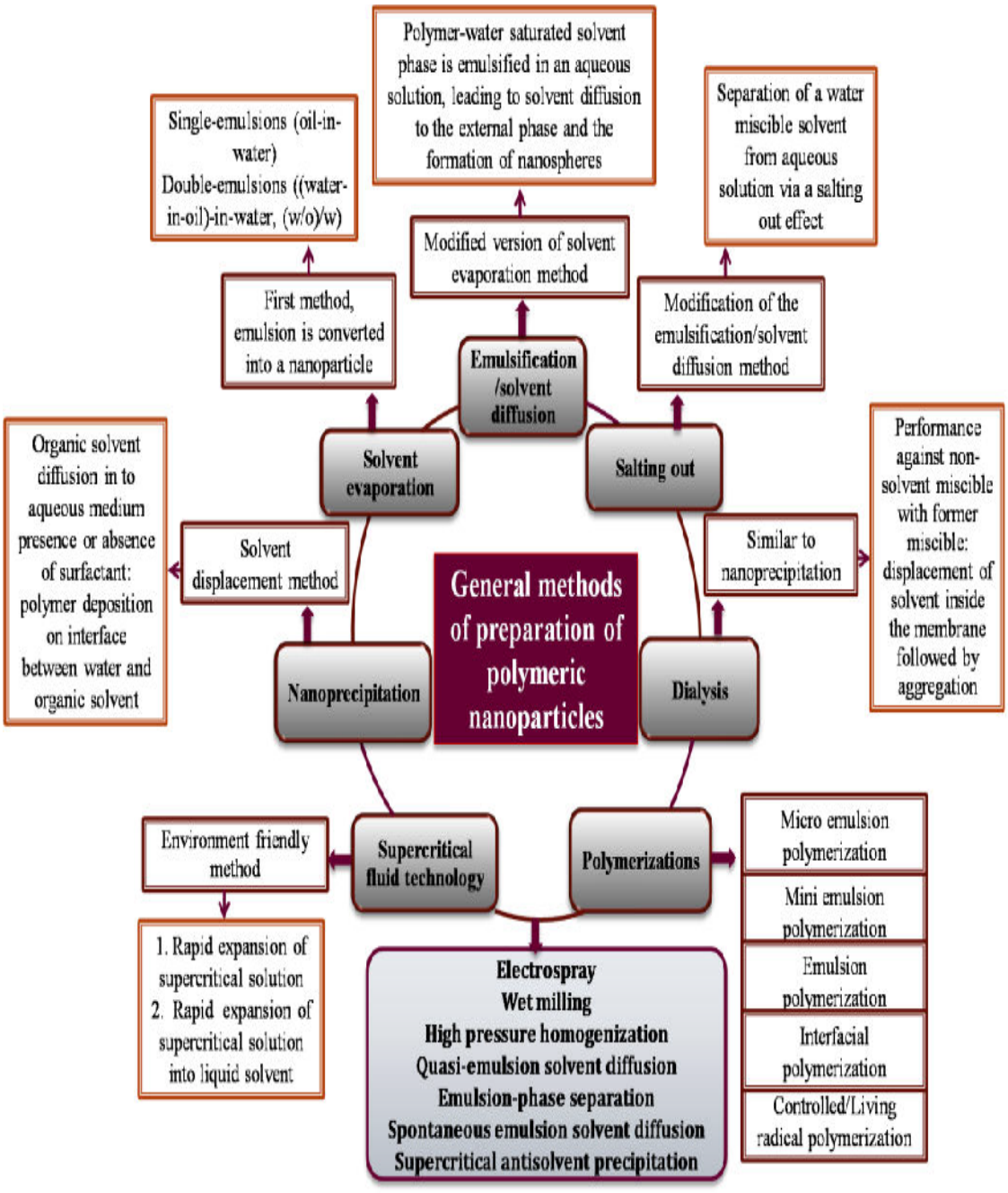

Fig. 1 : General Method for Prepration of Polymeric Nanoparticles

potential materials for DDSs, CDSs, and GDSs such as nanoparticles .[4]

New opportunities to prevent and to treat diseases are by emerging the understanding of disease pathways. Drug delivery is becoming an increasingly important aspect for medicine field, as more potent and specific drugs are being developed. The use of nanotechnology for drug

delivery systems is an actual subject today. A lot of research is taking place at different universities in the world in order to find new formulations capable of delivering drugs to specific areas of the body.(5) Nanotechnology refers to the interactions of cellular and molecular components and engineered materials—typically, clusters of atoms, molecules, and molecular fragments into incredibly small particles.(6)The use of nanotechnology in medicine and more specifically drug delivery is set to spread rapidly. Currently many substances are under investigation for drug delivery and more specifically for cancer therapy. (7)

Nanoparticles can be divided into three groups:

• Inorganic nanoparticles

• Solid lipid nanoparticles

• Polymer nanoparticles

Polymer nanoparticles involve various natural or biocompatible synthetic polymers.(8) Polymeric nanoparticles have been synthesized using various methods according to needs of its application and type of drugs to be encapsulated.(9) Cancer in its myriad forms affects millions of people worldwide and is growing at an alarming rate to become the world's deadliest disease of all time . The most common methods of cancer treatment are the use of chemotherapy or invasive surgical procedures. (10)

2. General Method For Preparation of Polymeric Nanoparticles(11) Fig. 1.

3. Mechanism of Drug Release from Polymeric Nanoparticle (12)

The drug release mechanisms are equally important as the drug polymer formulation because of the proposed application in sustained drug delivery. For manipulation of the rate and the timing of the drug release from nanoparticles, a good understanding of the mechanisms of drug release is needed. There are five possible methods for drug release:

1. Desorption of drug bound to the surface,
2. Diffusion through the nanoparticle matrix
3. Diffusion through the polymer wall of nanocapsules,
4. Nanoparticle matrixerosion,
5. A combined erosion–diffusion process.

4. Advantages of Polymeric Nanoparticles

1. Increases the stability of any volatile pharm--aceutical agents, easily and cheaply fabricated in large quantities by a multitude of methods.

2. Delivers a higher concentration of pharmaceutical agent to a desired location.

3. The choice of polymer and the ability to modify drug release from polymeric nanoparticles have made them ideal candidates for cancer therapy, delivery of vaccines, contraceptives and delivery of targeted antibiotics. (13)

4. They offer a significant improvement over traditional oral and intravenous methods of administration in terms of efficiency and effectiveness.

5. Polymeric nanoparticles can be easily incorporated into other activities related to drug delivery, such as tissue engineering. (14)

5. Disadvantage of Polymeric Nanoparticles

1. Small size and large surface area of nanoparticle based drug delivery systems can cause some physical stability problems like aggregation

2. Low drug loading capacity and low loading efficiency are the other limitations of developing a nanoparticle drug delivery system (15)

6. Evaluation Parameter of Polymeric Nanoparticle

1. **Shape and surface morphology** (16)

Shape and surface morphology of nanoparticles was visualized by scanning electron microscopy. Samples were prepared by lightly sprinkling nanoparticles on a double adhesive tape, on an aluminum stub. The stubs were then coated with gold to a thickness of 200 to 500 A^0 under an argon atmosphere using gold sputter module in a high vacuum evaporator. The samples were then randomly scanned and photomicrographs taken at different magnifications with SEM.

2. Yield of Nanoparticles (17)

The yield of nanoparticles was determined by comparing the whole weight of nanoparticles formed against the combined weight of the copolymer and drug.

$$\%\text{yield} = \frac{\text{Amount of Nanoparticle}}{\text{Amount of drug + polymer}} \times 100$$

3. Loading Efficiency (18)

Drug content in the prepration was determined by extracting the drug from the nanoparticle with 0.1m hydrochloric acid. In this method , the nanoparticle were stirred in 50 ml of 0.1 m hydrochloric acid until dissolved ,it was filtered through a milipore filter and the drug content was determined after suitable dilution by uv spectrometery the loading efficiency (L) of the nanoparticle was calculated according to equation.

$$L\,(\%) = (Qn/Wh) \times 100$$

Where Wh is the weight of the nanoparticle and Qn is the amount of drug present in the nanoparticle (148)

4. **Drug Entrapment Efficiency** (19)

The entrapment efficiency is also known as Association Efficiency. The drug loaded nanoparticles were centrifuged at a high speed of 3500-4000 rpm for 30 min and the supernatant is assayed for non-bound drug concentration by UV spectrophotometer. The percentage Drug

Entrapment Efficiency (DEE) was calculated as follows:

$$DEE\% = \frac{\text{Amount of drug actually present}}{\text{Theoretical drug load expected}} \times 100$$

5. Particle size, Particle size distribution and Zeta potential (20)

The particle size and particle size distribution of the formulation was determined by photo correlation spectroscopy with the (Malvern instrument) Equipped with the Malvern PCS software.

6. Drug Content (21)

The drug content in each formulation was determined by weighing nanoparticles equivalent to 30mg of drug and dissolving in 100 ml of phosphate buffer, followed by stirring. The solution was filtered through a 0.45µ membrane filter, diluted suitably and the absorbance of resultant solution was measured spectrophotometrically using phosphate buffer as blank. The drug content of the prepared nanoparticles was determined by the formula:

$$\text{Drug content (\%)} = \frac{\text{Weight of drug in nanoparticles}}{\text{Weight of nanoparticles}} \times 100$$

7. In vitro permeation studies (22)

In vitro permeation study was conducted usingKeshary-Chien (K-C) cell with an effective diffusion area of 2.0 cm^2 and a cell volume of 25 mL. The diffusion cells were thermoregulated with a water jacket at 37±2 ºC. Excised goat nasal mucosa was used for the evaluation of formulation permeation which was obtained from local slaughter house within 15 minutes of goat sacrifice. After skin removal, the nose was stored on ice cold phosphate buffer and nasal mucosa was carefully removed using forceps and surgical scissors. The mucosal tissues were immediately immersed in Ringer's solution. The freshly excised nasal mucosa was mounted on the diffusion cell and 10 mL of aqueous drug loaded nanoparticulate suspension (containing drug equivalent to 10 mg) was kept on it. The receptor chamber was filled with fresh saline (phosphate buffer). 1ml of sample aliquots were withdrawn at predetermined time intervals and subsequently replenished with an equal amount of phosphate buffer. The samples were filtered and diluted appropriately. The samples were analyzed using spectrophotometrically.

6. Use of Nanoparticles for Cancer Diagnosis and Treatment

The delivery of an anticancer drug to the target tissue can be achieved by NPs primarily in two ways: passive and ligand-based targeting.

Passive targeting

This targeting approach exploits the pathophysiological conditions, such as leaky

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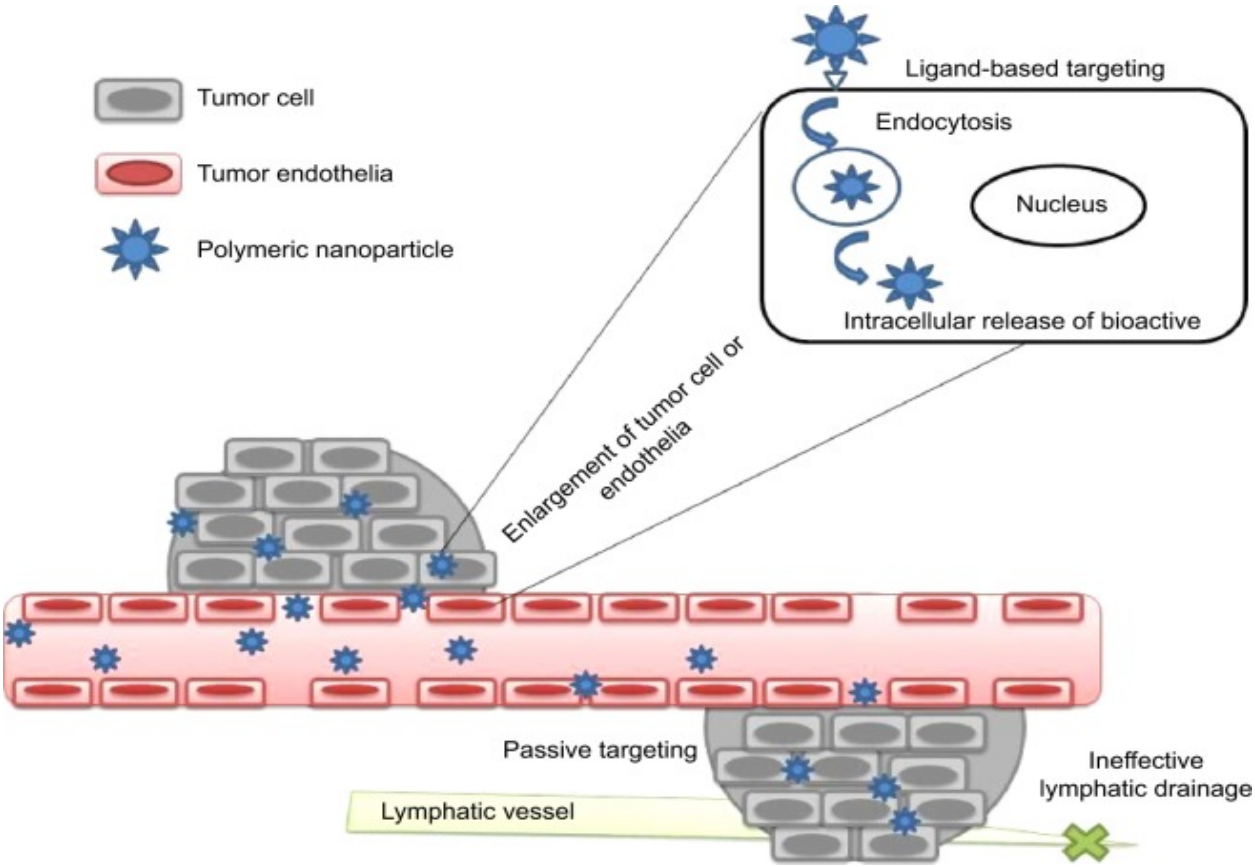

Fig. 2: targeting approaches of polymeric nanoparticles in cancer.

vasculature, pH, temperature, and surface charge surrounding the tumor for specific delivery of NPs.

Ligand-based targeting

In ligand-based targeting, ligands are conjugated at the periphery of the nanoparticulate system to bind with appropriate receptors at the target tumor site. The targeting ligands can be categorized as proteins (antibody and its fragments), nucleic acids (aptamers), or other ligands (peptides, vitamins, and carbohydrates), which generally bind to the receptor uniquely over expressed by tumor cells or vasculature.[23]

Conclusion

Nano materials have increased surface area and nano scale effects, hence used as a promising tool for the advancement of drug and gene delivery, biomedical imaging and diagnostic biosensors. Nano materials have unique physicochemical and biological properties as compared to their larger counterparts. Nanoparticulate drug delivery systems seem to be a viable and promising strategy for the biopharmaceutical industry. They have advantages over conventional drug delivery systems. They can increase the bioavailability, solubility and permeability

of many potent drugs which are otherwise difficult to deliver orally. Nanodelivery systems such as nanosuspensions, polymeric nanoparticles, and solid-lipid nanoparticles, provide a broad range of techniques.

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