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Dual Role of Polymeric Nanoparticles in Drug Delivery and Diagnosis

Bezzam Hemanth*, Devarapalli Jijendra Babu, Chandu Babu Rao.
Priyadarshini Institute of Pharmaceutical Education and Research 5th Mile, Pulladigunta, Guntur-522017. Andhra Pradesh, India

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***Corresponding Author**
Bezzam Hemanth

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Abstract

Polymeric nanoparticles (PNPs) have emerged as a crucial tool in the development and optimization of drug-delivery systems, particularly for diseases with significant morbidity, reduced quality of life, or high mortality. PNPs, as a subset of nanomedicine, are characterized by their size, surface properties, drug-loading capacity, targeting potential, and compatibility with diagnostic agents. These characteristics enable the formation of multifunctional nano devices for therapeutic applications. PNPs offer several advantages, including high reproducibility, homogeneity, and control over their properties, which are essential for scaling up from laboratory to industrial production. They are commonly used as drug carriers due to their biodegradability, biocompatibility, and high drug-loading capacity. PNPs can encapsulate a wide range of therapeutic agents, including proteins, peptides, growth factors, DNAs, mRNA, and drugs. They can be administered through various routes, such as nasal, oral, intravenous, topical, and ocular, and have the potential to target specific cells or tissues, thereby increasing local drug concentration, reducing toxicity and side effects, and preventing nonspecific interactions. This review also addresses the challenges associated with nanoparticle stability under physiological conditions and the difficulties in scaling up production while maintaining quality. It highlights the need for high productivity systems that can synthesize PNPs in an easy, fast, and controlled manner.

Introduction

A drug-delivery system (DDS) is a formulation or device that allows the introduction of active ingredients into the body to improve their efficacy and safety by controlling the drug's dosage, duration, and release at the site of action, as well as navigating biologic membranes to reach the therapeutic target. Due to the severity of the condition or the inherent toxicity of the medicine, it may occasionally be necessary to administer it directly to the affected organ. Drug delivery systems are becoming more sophisticated with an emphasis on better controlled release, preserving therapeutic efficacy, and the active ingredient targeting to the specific site of action in order to lessen the risks and disadvantages of conventional administration routes [1].

Various polymers their characteristics, advantages disadvantages and role in drug delivery system are [14]:

a) Collagen:
It is thermally unstable and has high viscosity in the aqueous phase, but it is low immunogenic, biocompatible, biodegradable, and has a good safety profile. It is an ideal material for drug delivery, including growth factor genes and controlled drug release for therapeutic action.

b) Gelatin:
Gelatin has good mechanical properties, is tasteless, odourless, and mainly composed of water and protein. It is biodegradable, biocompatible, and used in food, pharmaceuticals, and cosmeceuticals, particularly in microparticles, bio adhesives, micro patches, and controlled drug carrier systems.

c) Cellulose:
Cellulose is insoluble in water but soluble in some organic solvents, with high tensile strength, non-toxic, biodegradable, and biocompatible. It can be chemically

modified for bio adhesive polymers. It is abundant, low-cost, and used in DNA delivery and controlled drug release.

d) Poly amino carbonate:

This hydrophobic polymer is easily chemically modulated, biodegradable, pH-sensitive, and good for localized and targeted drug delivery, enhancing anti- tumour activity and pharmacokinetics.

e) Polyvinyl alcohol (PVA):

It's a water-soluble, biodegradable synthetic polymer mimicking natural ones, used in medical, industrial, and food sectors to enhance mechanical properties and reduce nanoparticle size for drug delivery [2].

Types of polymeric nano particles

Dendrimers

Dendrimers are spherical with multiple layers over their centre core, each representing their amphiphilic nature and structure allowing laid multiple drugs or genes with site-specific delivery [3].

Polymeric micelle

These are multifunctional nanoparticles in the nanocarrier field which can later the release kinetic of integrated pharmacological drugs. The polymeric micelle improves their permeability and retention, with minimal toxicity

Nanospheres

The nanospheres have broad applications in imaging, sensing, catalysis, diagnostic, and alteration of the optical properties, improving the chemical and biological properties enhance the catalytic properties [4].

Polymeric vesicles

Polymeric vesicles are bi-layered, nano- to micrometer-sized polymeric capsules. These vesicles could be used for medication delivery, in vivo imaging, and nanomedicine.

Polymeric hydrogel

Hydrogels have been used extensively in a variety of biomedical applications, tissue engineering, wound healing ,celltransporters, and drug delivery

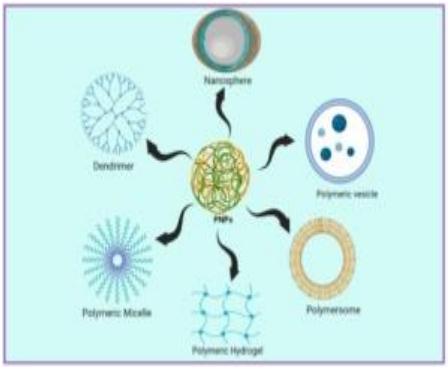

Fig 1. Types of PNPs include dendrites, polymeric micelle, nanospheres, polymeric vesicles and polymeric hydrogel

Production polymeric nano particle

Drugs in PNPs can be trapped, encapsulated, or bonded to NP polymers, including nanospheres, nano capsules, and drug conjugates [15].

Emulsification-solvent evaporation

Emulsification is a process that involves emulsifying an insoluble solvent in water with an aqueous solution at high shear pressures. The solvent is then evaporated, resulting in the formation of the PNPs [5].

Emulsification/Solvent diffusion

This approach involves the formation of an o/wemulsion between a partially water- soluble solvent containing the polymer and drug and an aqueous solution containing the surfactant. This method is highly efficient and only applicable to lipophilic medicines.

Emulsification/reverse salting-out

Compared to emulsification/solvent diffusion method the salting-out method is based on separating the hydro miscible solvent from the aqueous solution through a salting-out effect, which can form nanospheres.

Nanoprecipitation

This technique, referred to as solvent transfer, requires the use of two miscible solvents. After dissolving the polymer in an organic solvent that is miscible with water, the solvent is diffused into an aqueous medium in the presence of a surfactant, resulting in a suspension [6].

Polymeric nano particles in various drug delivery and diagnosis

Polymeric nanoparticles in cancer diagnosis and imaging

According to the WHO, cancer is the world's second biggest cause of death, accounting for an estimated 9.6 million deaths in 2018. Polymeric NPs have thus arisen as an option to limit typical contrast chemicals due totheir surface modification abilities and their capacity to regulate solubility of the embedding agents in order to increase imaging of malignant cells.

Gold-based polymeric nanoparticles used in cancer diagnosis

Gold metallic nanoparticles (AuNPs) and their derivatives can improve diagnostic and imaging procedures. Because of their versatility, they can be utilised in a variety of imaging modalities, resulting in great resolution with minimal or no toxicity.

Gadolinium polymeric nanoparticles (gdnps)used in cancer diagnosis

Gadolinium-based materials are the most commonlyutilised, and are mostly generated by the chelated metal. Gadolinium-chelated complexes are easily removed from the organism by the kidneys due to their low molecular weight (<11 nm). This has become one of the most effective ways in clinical cancer diagnosis[7].

Perfluorocarbonspolymeric nanoparticlesused in cancer diagnosis

Perfluorocarbons (PFCs) are molecules with a structure comparable to typical chemical

Polymeric nanocarriers for ocular drugdelivery

In 2019, the World Health Organisation (WHO) estimated that at least 2.2 billion individuals had vision impairment

or blindness, with at least one billion instances being preventable with effective treatment [16].

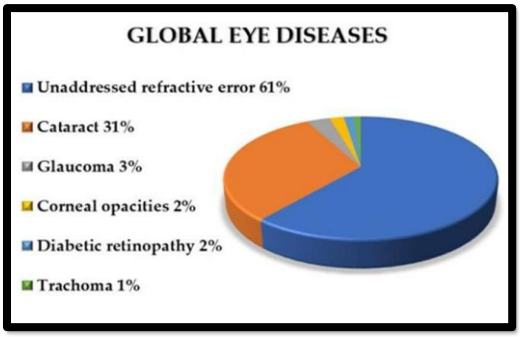

Fig.2 The WHO 2019 reports on the incidence rate of the most common eye illnesses.

Micelle nanocarriers for ocular delivery

The most often used polymer for producing micelles as DDSs is poly (lactic-co-glycolic acid) (PLGA), which is both biocompatible and biodegradable. This polymer has good muco adhesion and penetration capabilities, making it appropriate for medication delivery in the mucosa and ocular regions.

Dendrimeric nanocarriers for ocular delivery

The potential of dendrimers made from a PEGylated polyamidoamine and modified with cyclic arginine-glycine-aspartate hexapeptide and penetratin as drug carriers [9].

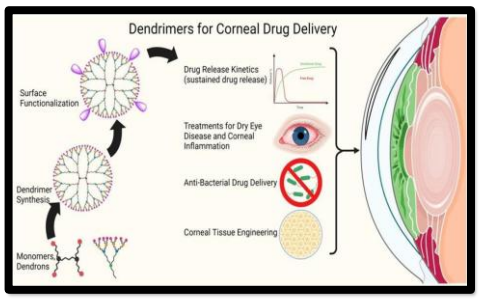

Fig.3 Applications of dendrimers for corneal drug delivery

Polymeric nanoparticles in oncologic treatment

Nanomedicine, defined as the use of nanometric-scale materials in medicine, provides a more specialised option. Its primary goal in oncology is to preferentially deliver the medicine to cancer cells, hence improving efficacy and reducing toxicity [17].

Challenges associated with nanoparticulate drug-delivery systems

The limited shape, chemistry, wide size distribution agglomeration state, and electromagnetic properties of these substances can cause poor oral bioavailability, circulation instability, and inadequate tissue distribution

The enhanced permeability and retention (EPR) effect

The EPR effect is a particular paradox that occurs only in solid tumours, and it is directly related to their pathophysiological and anatomic characteristics, which differ from normal tissues. In order to intensify the EPR effect, blood pressure can be elevated, or NO- releasing and CO-releasing agents can be administered.

Active targeting

This method, based on molecular recognition processes, consists of modifying the NPs surface with one or more required moieties to achieve their fictionalization and, in consequence, raising the drug concentration in tumour tissues.

Stimuli-responsive and triggered release systems

The objective of these systems is the controlled release of antineoplastic drugs provoked by stimuli that develop a change in the nanocarrier. Both internal (changes in pH, redox, ionic strength) and external stimuli (temperature, magnetic fields or light) can trigger the release of drugs [18].

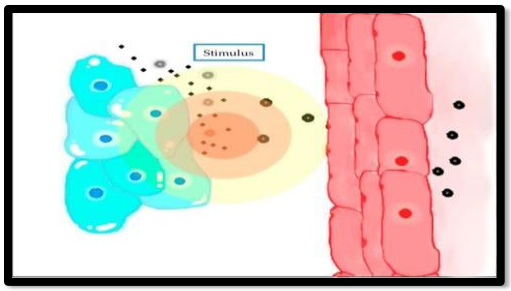

Fig.4. The exposure to a stimulus triggers congregated nanoparticles drug release

Advantages of nanotechnological drug-delivery systems

Nanomedicines have been shown to improve solubility of low soluble drugs and to reduce toxicity by dissolving them in their hydrophobic or hydrophilic compartment. Studies also report they have prolonged plasma half-life and a different biodistribution profile compared to conventional chemotherapy [10].

Polymeric nano particles in nutraceuticals.

Nutraceuticals, often known as pharma-foods, are a potent toolbox that may be utilised as a dietary supplement and prior to pharmacological prescriptions to improve health and prevent or treat pathologic conditions [11].

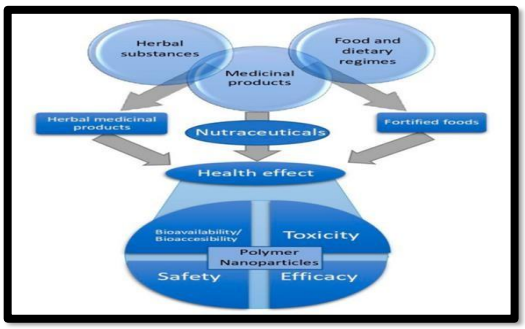

Fig.5. Use of polymeric nanoparticles for nutraceuticals and different bioactive compounds for greater health and medical benefits.

Biodegradation of polymeric nano particles

Introduction to biodegradation

Biodegradation is a crucial environmental process that allows for the natural breakdown of materials into biocompatible or harmless byproducts. Biodegradable polymers are high-

molecular-weight compounds that degrade over time in the presence of physiological fluids. The biodegradation of natural polymers occurs through biological processes such as hydrolysis. Enzymes, which are biological catalysts, are instrumental in facilitating the breakdown of these natural polymers, ensuring that they are efficiently converted into simpler, non-toxic compounds.

Mechanisms of natural polymer degradation

The degradation of natural polymers is predominantly driven by enzymatic hydrolysis. Enzymes, produced by microorganisms, target specific chemical bonds within the polymer structure, leading to its disintegration.

Degradation of synthetic polymers

In contrast to natural polymers, the degradation of synthetic polymers relies heavily on the hydrolysis of ester linkages. The degradation of synthetic polymers can also be influenced by external factors such as radiation, moisture, heat, and mechanical forces.

Factors influencing polymer degradation

The degradation of polymers, whether natural or synthetic, is influenced by a multitude of factors that can induce changes in their composition, molecular weight, and structural properties. Environmental variables such as radiation, moisture, heat, and mechanical forces can trigger different types of degradation mechanisms.

Understanding these factors and their interactions is vital for predicting and controlling the degradation behaviour of polymers in various applications, from medical implants to environmental waste management [12].

Future challenges and limitations for production of PNPs

The ongoing expansion of NP production necessitates market and economic efficiency. One problem is to scale up the production and continuous synthesis of NPs on a big scale. The next issue is to integrate a "one-stop solution" from a piecemeal approach to creating good and safe NPs in a sustainable and large-scale manner.

Mass manufacturing of NPs is still limited to metal and oxide NPs, with some exhibiting persistent toxicity and inflammatory reactions. The next issue is establishing oral administration of PNPs, as these NPs must endure a hostile environment in the GI tract before releasing the medicine to the appropriate target [19].

The oral route will be the primary focus of future PNP development. The limitations are primarily related to NPs, physiological and biological, and instrument differences [20].

The future path of collaborations between theoretical and experimental scientists, as well as the pharmaceutical industry, physicians, and regulatory agencies, will be critical in allowing us to implement laboratory results in the clinic and thus initiate the next generation of clinical therapies [13].

Conclusion

In conclusion, the journey of polymeric nanoparticles (PNPs) in the realm of drug delivery is truly remarkable. These tiny yet powerful particles have emerged as a beacon of hope, addressing the limitations of traditional drug therapies and offering a versatile solution for a wide range of biomedical applications.

Their biocompatibility, biodegradability, and adaptability make them a perfect candidate to revolutionize the way we treat diseases. From targeting cancer cells with precision to delivering therapies to hard-to-reach areas like the brain, PNPs are set to transform the drug delivery landscape.

However, the path to widespread clinical adoption is not without its challenges. Scaling up production to meet the growing demand while ensuring affordability and ease of use is a significant hurdle. Interdisciplinary collaboration is crucial, bringing together experts from diverse fields to tackle the technical, regulatory, and economic barriers. This collective effort will be the driving force behind the successful integration of PNPs into mainstream medical practice, making these innovative therapies accessible to all who need them.

Looking ahead, the future of PNPs is bright. As nanotechnology continues to advance, we can expect PNPs to become even more efficient, cost-effective, and accessible.

Author Contributions

All authors are contributed equally

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Declaration of Competing Interest

The Authors have no Conflicts of Interest to Declare.

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