

Harnessing Drug-Based Polymeric Nanoparticles as a Versatile Delivery System in Biomedical Applications: Shaping the Future Market Trends

¹Rakesh Singha, ¹Kartikesh Sahu, ²Samson K Wilson, ^{1*}Prasanthi Boddu

1. Department of Pharmaceutics, GITAM School of Pharmacy, GITAM (Deemed to be University), Rushikonda, Visakhapatnam-530045, Andhra Pradesh, India.

2. Department of Pharmacology, GITAM School of Pharmacy, GITAM (Deemed to be University), Rushikonda, Visakhapatnam-530045, Andhra Pradesh, India.

Corresponding email: pboddu5@gitam.edu; Tel. +91-9848235287

ABSTRACT: Polymeric nanoparticles (PNPs) have gained considerable attention for their beneficial properties and effectiveness. They can enhance cancer treatments by reducing cytotoxic side effects and show strong therapeutic potential. Additionally, PNPs enable photoacoustic amplification by chemically modifying semiconducting polymers. Developed through nanotechnology, they improve drug delivery and other biomedical applications. The application of PNPs in many domains through various polymer types and strategies to achieve successful outcomes was reviewed. In addition, the therapeutic area and its scope of application are outlined next to it. Considering the analysis of several literature review approaches, an overview of the numerous aspects involved in synthesizing PNPs was discussed. Solvent evaporation and nanoprecipitation are the methods most commonly employed for preparing PNPs. The most notable finding was the review of various polymeric nanoparticle (PNP) types with diverse applications. Over recent decades, functionalized PNPs have significantly advanced as innovative delivery systems. They are used in treating brain disorders, liver issues, diabetic wounds, cancer, gene therapy, Alzheimer's, respiratory conditions, and colon cancer. Technological progress has also enabled PNPs to perform both bioimaging and therapeutic diagnostics.

KEYWORDS: Biodegradable, bioimaging, cancer, controlled release, nanoparticles, polymer

INTRODUCTION

A polymer is a material made up of molecules, or macromolecules, that are distinguished by the repeated occurrence of one or more atom species or groups of related atoms. Jons Jacob Berzelius, in the

year 1833, coined the term "polymer," which derived from the Greek words "poly" (meaning many) and "mer" (meaning part). The process of converting a monomer into a polymer is known as polymerization. The atoms in polymers are joined to one another

by covalent bonds. Natural polymers occur naturally in plants and animals, whereas synthetic polymers are those humans synthesize. Semi-synthetic polymers are formulated by further modifying naturally occurring polymers through chemical means. Polymers can be classified as either biodegradable or non-biodegradable based on how microorganisms like bacteria aid in the decomposition or decay (1).

Nanoparticles (NPs) are solid particles or particulate dispersions ranging from 10-100 nm. The area of nanotechnology that deals with atomic, molecular, or macromolecular scale research and development is called NPs. The field of nanoparticle technology is developing quickly and offers new, efficient treatments for several illnesses, like Parkinson's, Alzheimer's, and neurodegenerative disorders. The preparation technique can result in several nanoforms, such as NPs, nanospheres, nanocapsules, etc. The actives are solubilized, encapsulated, entangled, or linked to a nanoparticle matrix of NPs. Surface characteristics, particle size control, and release of pharmacologically active agents are critical parameters for a nanoparticle design, thus aiming to deliver the site-specific activity of the drug at a therapeutically ideal rate and dosage schedule. The three preferred approaches that give high-yield NPs are ionic gelation

or coacervation of hydrophilic polymers, polymerization of monomers, and dispersion of preformed polymers.

PNPs in the size range of 10 to 1000nm are produced based on biocompatible and biodegradable polymers. PNPs are a rapidly developing discipline with numerous applications, including biotechnology, conducting materials, electronics, environmental technologies, medicine, photonics, and sensors. As a promising drug delivery vehicle, PNPs can be easily manipulated to prepare carriers to deliver the pharmaceuticals to a specific target. PNPs are noticed to be used in various applications such as anti-counterfeiting inks, bio-imaging, biomarkers, magnetism, protective layer, antigen detection, etc. (Figure 1). This benefit increases the safety of the drugs. Target cells and organs efficiently deliver medicines, proteins, and DNA via polymer-based NPs. Because of their small size and distinctive characteristics, PNPs have gathered much attention in recent years. Cells often absorb NPs through endocytosis, which is primarily characterized by the particle size, as well as surface properties. Another benefit is that they are entirely removed from the body by the body's normal metabolic processes. Although natural polymers are often biocompatible and biodegradable, their application is limited

because of the variations in the properties from batch to batch (2).

Polymers have applications in various industries because of their site-specific targeting, different routes of administration, control, and sustained release, easy elimination of organic solvents, encapsulation of different actives, and higher stability than lipid-based ones. Different factors are responsible for the formulation of NPs in industries because of the difficulty of their scale-up, including the aggregation of toxic monomers, particle-particle aggregation, and toxic degradation.

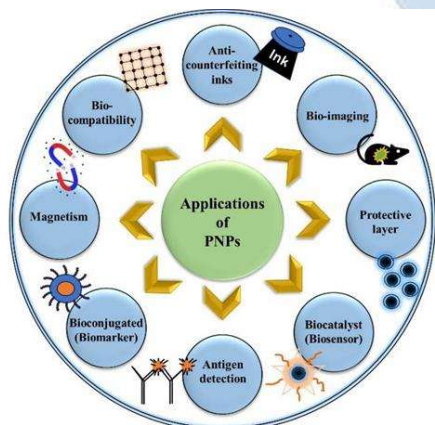


Figure 1. APPLICATIONS OF PNPs

CLASSIFICATION OF POLYMERS USED IN PNPs

BASED ON THEIR SOURCE OF ORIGIN:

i. Natural polymers:

Natural polymers are appealing for pharmaceutical applications because they are affordable, easily obtainable, and non-toxic. They can undergo chemical changes,

potentially be biodegradable, and, with rare exceptions, are biocompatible. There are two kinds of these: Examples of materials derived from plants include agar, cellulose, gum acacia, gum tragacanth, hemicellulose, inulin, karaya gum, pectin, starch, glucomannan, and aloe vera gel. Animal-derived substances comprise xanthan gum, chitin, alginates, carrageenans, and psyllium, as shown in Figure 2. Natural polymers have provoked much interest as they have been thoroughly investigated as encapsulation and delivery vehicles for pharmaceuticals and other bioactive compounds. Natural polymers and their derivatives are already used in many industries, such as textiles and paper goods, food additives, the biomedical field (e.g., drug delivery and cosmeceutical therapy), functional foods, and nutraceutical formulations.

ii. Synthetic polymers:

Polymers developed artificially in labs are referred to as synthetic polymers. Another moniker for them is artificial polymers. As well as epoxy, polyamides, polystyrene (PS), polyethylene (PE), poly (vinyl chloride) (PVC), synthetic rubber, and a few additional types are examples of artificial polymers (Figure 2). There are various synthetic polymers, but some of the most commonly used are plastics, elastomers, and fibers. Synthetic polymer

materials are made from long chains of repeating chemical units, which are categorized into six main categories, i.e., thermoplastics, thermosets, elastomers, fibers, plastic, and adhesives. Synthetic fibers have strength, are lightweight, and have moisture resistance advantages. Additionally, they are typically less costly than natural fibers. Synthetic polymers have several drawbacks, including the potential for toxicity, contamination, and non-biodegradability (30).

iii. Semisynthetic polymers:

Naturally recovering fibers are the source of semi-synthetic fibers, which are then typically treated with formed synthetic materials. Polymers that do not occur naturally can be chemically converted in a lab to form synthetic fibers without sacrificing their fiber characteristics. Thus, semi-synthetic therapeutic agents combine natural and synthetic sources (Figure 2). Semi-synthetic therapeutic agents are often made by converting natural source starting materials into final products through chemical processes. With a high strength-to-weight ratio and process-application adaptability, composite materials are this century's most hopeful and well-known materials. Right now, fiber-reinforced composites made of semi-synthetic and synthetic materials are important because of the many industries they may be used in:

construction, mechanical, textile, military, biomedical, aviation, and many more.

BASED ON BIODEGRADABILITY:

i) Biodegradable polymers:

Biodegradable polymers are characterized as polymers originating from diverse renewable resources, particularly those components that are amenable to enzymatic breakdown by microorganisms. In numerous medicinal applications, it has been shown that the instability of the polymers that cause biodegradation is crucial. Biodegradable polymers have many fascinating applications that could benefit from their use, including drug administration, implant coatings, tissue engineering, gene therapy, regenerative medicine, temporary implants, and tissue engineering. A polymer's mechanical characteristics and degradation rate should match the application's requirements; non-toxic degradation products, processability, shelf life/stability, affordability, and biocompatibility are other important considerations. Surgical implants made from biodegradable biomaterials can be a short-term framework to help tissue grow back. Doctors and researchers use biodegradable polymers as a temporary structure in tissue engineering projects, such as growing cells and tissues *in vitro* or for tissue regeneration *in vivo*, which has emerged as a significant area of research and development that expands the

applications of biodegradable polymers beyond their conventional uses (Figure 2) (4).

ii) Non-biodegradable polymers:

It is made up of long chains of hydrogen and carbon atoms. These compounds form an adamant interatomic link, making it difficult for bacteria to break the bonds and digest the molecules. Non-biodegradable polymers, like PVC, Bakelite, and Polythene, take a long time to break down. It takes a long time to break them down as a result. Considering biodegradable polymers are environmentally beneficial and may be recycled or reused, they are the most excellent alternative for managing non-biodegradable plastic waste (Figure 2).

TYPES OF PNPS

FLUORESCENT POLYMERIC NANOPARTICLES:

Materials like poly (methyl methacrylate) and PSMA- poly (styrene-co-maleic acid) are used to prepare fluorescent PNPs. They are employed in security label fabrication, data storage, and rewritable printing. Fluorescent PNPs prepared with methyl methacrylate polymer by mixing followed by the nanoprecipitation method give a promising result for chemosensing applications of pH value variation and the effect of CO₂ in aqueous media. Triple-bond Raman signals are more potent in the

high-class security associated with the anti-counterfeiting field for inkjet printing, which uses polydimethylsiloxane for formulating PNPs by adopting the emulsion polymerization method. Reactive oxygen species (ROS)-loaded platinum nanozyme (PtNP) is used to create NPs containing poly (vinyl alcohol) and camptothecin polymer for the chemo-photodynamic therapy against colon cancer. These PNPs enhance photodynamic therapy as well as photoacoustic imaging and fluorescence imaging.

Pdots were prepared by a combination of orange emitting polymer (CN-PPV) and NIR-II fluorescence-packed NPs, demonstrating quick accumulation and longer retention in bone. It offers encouraging results for treating bone-related diseases and imaging the bones. With the aid of photochromic and fluorescent labeling, which uses a photochromic compound called spiropyran, photoswitchable fluorescent polymer NPs were produced using methyl methacrylate and butyl acrylate by the mini-emulsion polymerization method. These NPs are used as inks in various stamps for security documents such as money, certificates, and passport printing. Near-infrared fluorescence NPs show the unambiguous visualization of tumors with γ -scintigraphy and optical imaging, with a prolonged

blood circulation time, which uses PEG polymer to diagnose cancer (5).

MAGNETITE POLYMERIC NANOPARTICLES

Norfloxacin magnetite NPs prepared by copolymerization method followed by cross-linking with polymer chitosan with Fe₃O₄ as magnetic core to formulate drug-loaded magnetic composite adsorbent, i.e., NOR-Fe₃O₄/CS-P(AM-SSS) for the effective adsorption of norfloxacin against the pH and humic acid for a better release. Green magnetite NPs containing cactus extract and Fe₃O₄ as a core magnetite material coated with chitosan polymer used for drilling fluids have improved potential by reducing the filtration volume and the thickness of mud cake compared to base drilling, which is used in the gas and petroleum industries for drilling operations. Curcumin magnetic polymeric NPs were prepared using the solvent evaporation method, using Fe₃O₄ as a magnetic core. They are coated with sodium alginate polymer for slower drug release and to improve the antibacterial efficiency of the preparation of antibiotics. To effectively treat burns and diabetic wound care, graphene oxide magnetite-coated nanofibers containing polyvinyl alcohol were prepared using ionic gelation and coprecipitation. This method prevents the

drug's burst release while also allowing for a slower release of the drug (6).

Magnetite NPs prepared with polyvinyl alcohol as a polymeric material give promising results regarding the improved heating performance of NPs with high SLP to treat hyperthermia applications in biomedical sectors effectively. In order to treat glioblastoma cell hyperthermia, GRGDS conjugated curcumin-loaded magnetic PNPs are produced by the solvent evaporation method with radio frequency induced superparamagnetic iron oxide NPs (SPIONs) from iron-oleate complex coated with PEG and PLGA polymer. Furthermore, the cytotoxicity in glioblastoma cells was reduced. By selectively attaching to cell receptors, GRGDS-conjugated reduces the therapeutic dose of curcumin and increases the NPs' uptake into cells, increasing curcumin's bioavailability (7).

As Fe₃O₄ has been used as the magnetic core material in the coprecipitation method to form magnetite NPs with SiO₂ and oleic acid coating, the results are satisfactory regarding the coating's lower cytotoxicity compared to the other coating. Likewise, the material's ability to form bonds with biological molecules makes it appropriate for drug delivery. Magnetite NPs coated with PEG and tween-80 by adopting the coprecipitation method give the promising result of lowering the cytotoxicity and

hemolysis than the bare magnetite NPs, which is a biocompatible compound and environment friendly. The novel heterogeneous catalytic system was formulated using magnetite material Fe_3O_4 and palladium via *the in situ* method and coated with PVP polymer to increase the catalytic performance with the high yield capacity (8).

Multifunctional magnetite NPs produced by the co-precipitation method for the effective treatment of microbial activity of the drug ciprofloxacin coated with chitosan polymer induced Fe_3O_4 magnetite materials, which also use the Cu ions fabricated magnetite NPs that were influenced to show the potential antibacterial activity with constant release kinetics. Encapsulation of doxorubicin in magnetic PNPs was prepared by co-precipitation followed by double emulsion evaporation methods, along with the coating material Eudragit E-100 and water-soluble magnetite Fe_3O_4 for the treatment of hyperthermia, by site-specific drug targeting with better release. Using the nanoprecipitation process, docetaxel-encapsulated hydrophobic SPION PNPs constructed with PLGA and PEG polymer covering drug for the management of prostate cancer that is resistant to castration, which provides improved MRI capability with increased contrast and controlled drug release (9). When sorafenib–zinc or

aluminum layered double hydroxide coating and SPION coated with PEG polymer are synthesized using the co-precipitation method and then chemically modified, the results are adequate in terms of cancer treatment that is more biocompatible and bioavailable on 3T3 cells. Quercetin-loaded magnetic micelles prepared by the co-precipitation method followed by dialysis with Fe_3O_4 serve as the magnetite core in targeted drug delivery systems to provide regulated drug release and biocompatibility.

GOLD-BASED POLYMERIC NANOPARTICLES

Gold NPs made by the citrate reduction method monitor fish spoilage by measuring the total volatile elemental nitrogen with the least antibacterial activity, which is appropriate for monitoring fish refrigerated at 50 degrees Celsius. The biodegradable, non-toxic, and environmentally friendly polymer sodium alginate is used in this process (10). Hamelia plant extract, along with the gold NPs, are mixed to form the optoelectronic sensor for the energy storage device, which uses the polymer PVP and PVA by adopting the method ablation technique and solution casting method, which reduces the free areas within the host matrix that tends to decrease the interatomic distances and increase in refractive index with enhanced optical properties. Cyclic voltammetry is used to

construct a molecularly imprinted polymer membrane with NPs for the electrochemical sensor that will be used to detect norfloxacin in pharmaceutical and aquaculture samples by dictating the antibiotic resistance of bacteria (11).

Since AuNC-loaded polymer NPs implement the nanoprecipitation technique to encapsulate gold nanoclusters in small polymer NPs, thereby minimizing autofluorescence and scattering in the second near-infrared window (NIR-II), they are desirable prospects for enhanced *in vivo* imaging. This results in a significant improvement in detection sensitivity and resolution. Gold NPs are prepared by coprecipitation method by taking the active polymer of organic lasers, i.e., MEH-PPV nanocomposites, which emits intensive fluorescence from conjugated polymer for imaging and photothermal killing of cancer cells due to the carbodiimide reaction. Utilizing chitosan as the polymeric material, self-assembled polymeric gold NPs produced through the nanoprecipitation approach hold considerable potential for use in developing immunosensors and other biological devices that aim to detect carcinogenic embryonic antigens with extreme sensitivity (12).

By halting the autophagic flux that causes an excessive loss of vital proteins and cellular organelles and eventually affects

cell death, AuNP produced by the dialysis method entrenched with polymer material PEG forms an encapsulated pH-sensitive polymeric micelle to kill cancer cells. Gold nanoshells containing doxorubicin as core material and PLGA as a polymer for the development of NPs for the effective treatment of tumoral cells and for imaging by the fluorescent near-infrared (NIR) conjugated to the protein human serum albumin (HSA) by electrostatic and hydrophobic interactions. AuNP made from the cationic polymer, PDDA prepared using the citrate reduction technique for recognizing thrombin in human serum, has excellent potential for diagnosis (13).

GADOLINIUM POLYMERIC NANOPARTICLES:

Gadolinium PNPs were prepared successfully with the combination polymer of PVP to form encapsulated NPs for the magnetic resonance of multifunctional contrast agents for imaging applications for diagnostic purposes in MRI and CT scans. Anti-EGFR monoclonal antibody-gated gadolinium boron NPs were made using the solvent evaporation technique with the polymeric chain F127-COOH for the effective treatment of eradication of head and neck tumors by killing the cancer stem cells, in which gadolinium has a much larger killing zone, and boron can eradicate cancer cells in outlying tumor tissues. o

treat oral squamous cell carcinoma, gadolinium-grafted triblock amphiphilic copolymer (F127-DTPA-Gd) was applied as a magnetic resonance imaging (MRI) contrast agent. The nanocarrier was prepared using the nanoprecipitation method and PCPDTBT as a polymer. PLGA-based NPs encapsulated gadolinium compound and rolipram were prepared using solvent evaporation to target the microglial cells to treat neuroinflammation disorder and for bioimaging by magnetic resonance imaging by targeting the specific site. Gadolinium oxide and europium-encapsulated polymeric NPs were prepared by the emulsion polymerization method using PMAA as an encapsulating polymeric material and doxorubicin as an anticancer drug, which exhibit slow release in neutral environments but rapid release in acidic environments or at elevated temperatures. Their exceptional photoluminescent qualities enable them to function well in both *in vitro* and *in vivo* optical imaging (14).

PEGylated polypyrrole NPs conjugating gadolinium, synthesized through aqueous dispersion, exhibit excellent NIR absorbance, superior physiological stability, and a high magnetization effect, making them ideal for use in cancer therapy and detection, also recognizing the tumor site as well that external laser irradiation can be directed there for photothermal

ablation of malignancies without killing nearby healthy tissues. Gadolinium-conjugated polymeric folate-PEG NPs were prepared successfully with the potential of tumor-targeting MRI contrast-agent and increased PDI by improving their biocompatibility. Inducing solvent diffusion was a successful way to manufacture gadolinium-based PEG-gated polymeric NPs for liver cancer treatment, enabling early detection of hepatocellular carcinoma. Compared to commonly used contrast agents in clinical MRI for dual-modality imaging, gadolinium oxide polymeric NPs made by polyol followed by a hydrolysis-condensation technique using polymer polysiloxane and PEG enhance the positive contrast of MR images (15). Gadolinium NPs prepared using the microemulsion method are coated with PEG and folate ligand because gadolinium has the potential for neutron capture therapy (NCT) of tumors. However, folate-coated NPs significantly enhanced cell uptake and tumor retention in tumor therapy.

Gadolinium-based NPs were prepared using the emulsion-droplet coalescence method, which was coated with chitosan polymer for adequate retention time in tumor tissue, by which suppression of tumor growth will occur due to high tumor-killing effects. Gadolinium NPs are prepared by using MAA polymer by

emulsion polymerization method, which targets endothelial $\alpha_v\beta_3$ receptors via the LM609 monoclonal antibody, to show the practical result of outstanding visualization of the vasculature, particularly arterial flow, as well as used to diagnose structural irregularities and diseases (16).

PERFLUOROCARBON POLYMERIC NANOPARTICLES

Fluorinated NPs are prepared using the aqueous dispersion method and are used as diagnostic and therapeutic tools. It also gives the practical outcomes of the drug release pattern of antileprotic clofazimine and tracers in preclinical fluorine-19 resonance imaging. PFC-loaded NPs were prepared by adopting solvent evaporation, using PLGA as a polymeric agent with fluorinated carbon for *in-vivo* ^{19}F MRI with perfluoro-15-crown-5 ether-loaded NPs and theranostic agent for cancer and stroke therapy as well as act as oxygen carrier. Wireless drug infusion catheters with ultrasound activation are prepared by the solvent evaporation method using the polymer PEG and PLGA along with the perfluorobutane to give a satisfactory result for efficacious, non-invasive, and localized ultrasonic drug uncaging for myriad targets in the brain and body. Perfluoro-15-crown-5-ether loaded NPs are prepared by miniemulsion using polymer PLGA, which gives the potential result about the *in vivo*

cell tracking and enhanced ultrasound contrast imaging for enduring *in vivo* multimodal imaging, also used to label therapeutic dendritic cells in melanoma patients. PFC NPs are prepared with PLGA polymer as a coating agent by inducing solvent evaporation for diagnostic imaging and improving stability. PFC NPs are prepared with PLGA polymer as a coating agent by inducing solvent evaporation for diagnostic imaging and improving stability (17).

RADIOACTIVE POLYMERIC NANOPARTICLES

PEGylation polymeric NPs were prepared by the nanoprecipitation method incorporating Lu-177, a radioactive drug for the effective treatment of *in-vivo* anticancer by inhibiting cancer cell growth by enhancing cellular uptake and having them with long-time tumor retention. With excellent chelation efficiency and stability, ^{68}Ga embedded polymeric NP has been effectively produced using polymer PEG, offering a promising outcome for diagnosing lymph node metastases in cancer patients and sensitive PET probes for lymph node imaging. Strong radio labeling stability and exceptional singlet oxygen generation capabilities are further demonstrated by rSPNs produced via solvent evaporation with polymer PEG and radioactive material iodine-131 for

multimodal cancer theranostic fluorescence imaging. These NPs also improve antitumor efficacy by inhibiting tumor growth. Radium dichloride [^{223}Ra] RaCl_2 co-loaded with radioactive gold [^{198}Au] Au NPs gives the effective result in the reduction of cell cytotoxicity as well as reduction of radiation in the surrounding tissues for the Osteosarcoma therapy. Additionally, it provides a notable boost in the killing of tumor cells when alpha and beta therapy are used together (18).

SERP NPs were prepared using a complex coacervation technique using PLGA polymer. They have the potential for *in vitro* and *in vivo* observation in the presence of strong acid enzymes released by macrophages. They are also used to monitor the degradation of radiolabelled TMC. A novel semiconducting polymer nanoparticle (SPN)-based radiopharmaceutical was made using the technique of nanoprecipitation by the use of radioactive material astatine-211 for the highly accurate and effective management and treatment of cancer since GIPR-specific binding sites occur in GIPR-positive tumors. Palladium(0)-catalyzed Suzuki coupling reaction was used to formulate PEGylated HSP NPs, which use a variety of radionuclides for cancer imaging and therapeutic therapy, such as technetium-99m, iodine-131, and iodine-125. Whereas ^{131}I -labeled HSP-PEG NPs

had excellent tumor growth suppression, ^{125}I -labeled HSP-PEG SPECT imaging suggests that the body could slowly eliminate NPs. At the same time, $^{99\text{m}}\text{Tc}$ -labeled PEGylated HSP NPs deploy high accumulation in two distinct tumor models (19).

PNPs are prepared by incorporating the polymer chitosan and radioactive material iodine-125 for the biodistribution of novel particles. Additionally, the *in vitro* investigations in saline and human blood have shown that ^{125}I remains coupled to particles long enough to allow further *in vivo* application, which has implications for regulated drug administration and targeting. Endothelial targeting of polymeric NPs was prepared by incorporating the iodine-124 as radioactive material for tracking lung tissue distribution using micro PET imaging with the polymeric coating material PVPh by inducing solvent diffusion method. LLA-based polymeric NPs prepared by solvent evaporation method gave promising results in radionuclide intra-tumoral therapy using radioactive material such as dirhenium decacarbonyl for novel drug therapy as anticancer therapy. Polymeric gold nanoparticles prepared by physical mixing of polymer PEG-4000 and the radioactive gold substance Au-198 for organ-specific distribution and imaging-based *in vivo* monitoring employing antibodies on the surface of gold NPs, which may be helpful

for concurrent organ detection and aberrant cell death (21).

BIOMIMETIC POLYMERIC NANOPARTICLES

High-performance E-skin based on a polymer nanoparticle-coated hydrogel system was achieved by a simple yet reliable *in situ* interfacial precipitation polymerization with an embedded sensor for effective performance by preventing water loss, tactile sensing capability, and a resistive sensor toward temperature and pressure sensing. The dialysis method prepared doxorubicin encapsulating polymeric NPs by incorporating the PLGA polymeric material and phospholipid-modified ICG molecules as a biomimetic therapy for OSCC, whereby chemo/photothermal therapy. Both demonstrate notable anticancer properties when exposed to near-infrared light and initiate intrinsic mitochondria-mediated apoptosis using the p53 signaling pathway. The nanoprecipitation method prepared the semiconducting polymer nanoparticle, which uses DSPE-PEG2000 polymer and camouflages a photothermal agent that targets explicitly disrupted vasculature by enhancing tumor vascular disruption for complete tumor eradication and efficient metastasis inhibition. PLGA PNPs were prepared using the solvent evaporation method, which was then coated with an

RBC membrane for the effective target of breast cancer cells, effectively delivering doxorubicin with an extended-release profile and also for visualization (22).

GCT@CM NP-mediated chemotherapy, which is formed by the nanoprecipitation method, can significantly boost tumor immunotherapy to prevent tumor recurrence and metastasis effectively. This is because GCT increases the bioavailability of the NPs, and camouflage can make the NPs homologously targeted to the tumor. Targeted tumor MR imaging can also be performed using GCT@CM NP. Biomimetic polymer magnetic nanocarrier was prepared by solvent evaporation method by coating with PLGA polymer with a combination of Fe₃O₄ NPs and R837 nanocarrier, which gives the potentiating immunotherapy of breast cancer through selectively targeting and polarizing TAMs. Bufalin NPs were prepared from chitosan oligosaccharide-poly (lactic-co-glycolic acid) copolymer by the nanoprecipitation method, which was then coated with platelet membrane for effective tumor growth inhibition as well as platelet membrane coating leads to particles with pH-dependent sustained release of the drug. PLGA-PEG NPs coated with AXT050 peptide potentially target and disrupt both cancer cells and endothelial cells, increasing accumulation in the tumor and

lowering accumulation in the liver. Precipitation polymerization reaction was used to create molecularly imprinted polymer NPs, which had a much quicker start of action and more insulin release. Biomimetic MIPs NPs attached to insulin-bound islets demonstrated a significantly greater affinity for insulin, exhibiting prompt adsorption kinetics. Erythrocyte membrane-camouflaged polymeric nanoparticles were prepared using the solvent dispersion method, providing effective delivery for protein identifications, purifications, and conjugations by bypassing the labor-intensive processes and long-circulating properties. The polymeric NPs were made up with the solvent evaporation method, followed by the miniemulsion technique, which gives a satisfactory result about the biomimetic mineralization of calcium phosphate, enhancing bone growth to treat bone defects and supporting wound healing.

BIOFILM RESPONSIVE POLYMERIC NANOPARTICLES

In order to prevent biofilm bacterial infection, doxycycline-loaded polymeric NPs coated with hyaluronic acid and chitosan have been successfully prepared. The NPs' HA and CS coatings allowed a pH-regulated and bacterial hyaluronidase-controlled response. The core of the

doxycycline-loaded NPs was responsive to bacterial gelatinases. Guanidine-embedded biofilm-responsive polymeric NPs promote the deep penetration and accumulation of bacterial biofilm, and photothermal removal of bacterial biofilm is accomplished upon exposure to NIR laser irradiation, which tends to protect against antibiotic inhibition and bacterial immune attacks. MRSA novel NPs were prepared successfully with having the antibacterial resistance capacity of drug-resistant infections. In *vitro*, cytotoxicity tests also exhibited that FTP NPs have lower toxicity and good potential to treat MRSA biofilm-associated wound infections.

Thonzonium bromide-loaded polymeric NPs are prepared using the nanoprecipitation method, which is again coated with saliva for hydroxyapatite biofilm assays and shows the potential effect of oral disease by reducing bacterial infection. Single-chain polymeric NPs were prepared using copolymer oligo ethylene glycol to prevent complexation with proteins in a biological medium, which showed a high MIC and is helpful for inhibiting gram bacteria. By using the nanoprecipitation process, pH-responsive polymeric NPs were produced. These NPs improve micelle disintegration, drug release at acidic pH levels, and micelle drug loading and targeting to negatively charged tooth surfaces for bacterial infections (1).

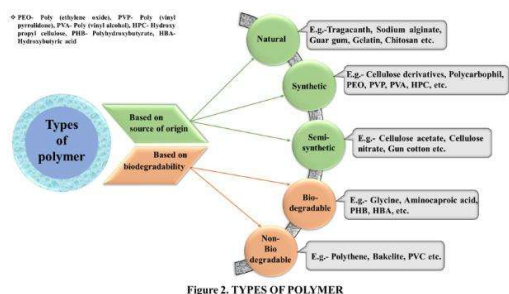


Figure 2. TYPES OF POLYMER

METHODS OF PREPARATION OF PNPS

Many techniques are used to manufacture PNPs to obtain the desired stabilized NPs, categorized into two groups, mainly physical and chemical, as depicted in Figure 3.

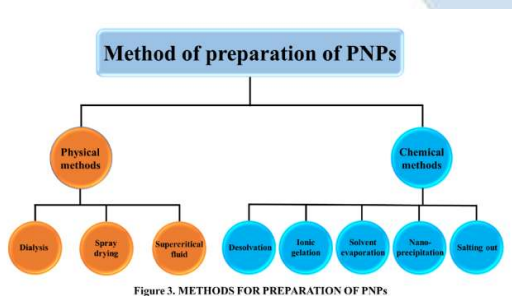


Figure 3. METHODS FOR PREPARATION OF PNPs

PHYSICAL METHODS:

i) Dialysis:

Dialysis is a simple yet successful approach for making small PNPs; it has been used to make PNPs with a restricted distribution of proportions. In short, the drug and polymers are dissolved in organic solvents that are miscible with water, and the combination is then put into a dialysis membrane bag after the proper molecular weight is removed. The dialysis membrane bag diffuses the organic phase by lowering the interfacial tension between the organic and aqueous phases. The solvent is then

moved inside the membrane to create a consistent suspension of NPs, and the polymer gradually loses its solubility. A fine powder of NPs is obtained by freeze-drying the resulting nanosuspension, with 5% mannitol as a cryoprotectant as shown in Figure 4.

ii) Spray drying:

A one-step manufacturing method called spray drying transforms a dry particle from a liquid feed into a dry particle. Using a hot drying gas to evaporate the solvent and atomizing the liquid input into small droplets are the two main principles of the process. The method involves four steps: Generating the particles by evaporative mass transfer of the liquid from the droplet into the drying gas; atomizing the liquid feedstock through a nozzle and into contact with the hot drying gas; and, finally, separating the dried product from the gas. Industries employ pressure nozzles and rotary atomizers in spray dryers to generate fine droplets of dried NPs, as shown in Figure 4. After implementing a surfactant, dissolve the drug and polymer in ultrapure water and then filter through a 0.45 μm syringe filter before spray drying to avoid clogging. After that, the resultant solution is spray-dried at the conditions mentioned, with an exit temperature range of 30 to 55°C. Millions of perfectly sized droplets are created when the ultrasonic frequency

(60 KHz)-driven piezoelectric actuator causes the mesh to vibrate upward and downward. The tiny powder is efficiently collected using a new electrostatic particle collector that consists of a cylindrical particle collecting electrode (anode) and a grounded star electrode (cathode).

iii) Supercritical fluid:

Supercritical fluids can display both liquid and gaseous properties because they have temperatures beyond their critical and critical pressures. Since SCFs are highly compressible at temperatures close to their critical point, substantial pressure shifts can alter the density of the fluid and mass-transport characteristics, affecting its solvent power. Nevertheless, it uses safe solvents for the environment and can create highly pure PNPs without organic solvents. In short, an aperture or capillary nozzle is a way to quickly release medicinal products and polymer solutions into the surrounding air once they have been dissolved in a supercritical fluid. When high supersaturation and rapid expansion pressure diminish, homogenous nucleation and uniformly sized NPs are produced, which are dispersed equally after passing through the filter shown in Figure 4.

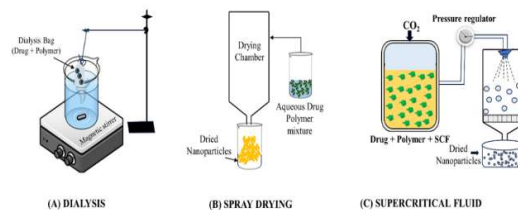


Figure 4. PHYSICAL METHODS OF PREPARATION OF PNPs

CHEMICAL METHODS:

i) Desolvation:

The most popular technique for creating protein-based NPs is desolvation. By adding desolvating chemicals, like acetone and ethanol, to protein solutions containing medicines, the desolvation approach facilitates the creation of NPs, as shown in Figure 5. Protein precipitation in the form of protein NPs is caused by desolvating chemicals, altering the structure of proteins, and decreasing their solubility. The process of particle production is wherein the number of particles of the same size gradually grows, and the particle size increases to a specific point. Following their formation, NPs are joined together by bridging agents like glutaraldehyde. The particle size of protein NPs produced using desolvation can be altered based on the circumstances. The desolvation method is a self-assembly process that concentrates protein by decreasing solubility through a desolvating chemical. Nevertheless, it does not directly contribute to the production of NPs. The technique is frequently applied while creating albumin-based NPs.

ii) Ionic gelation:

The manufacture of microparticles, or NPs, via this process, is based on the electrostatic interaction of opposite charge types, including a minimum of one polymer while being stirred mechanically. Ionotropic gelation typically happens between molecules with opposing charges. Negatively charged divalent or multivalent ions react with positively charged polymer chains. Microstructured particles with interconnected nano-fibrillar networks are produced due to the electrostatic response. To summarize, the drug and polymer are dissolved in water, or a weakly acidic medium based on their solubility, and the resultant mixture is progressively added to the solution that contains stabilizer and counter ions while continuously agitated. When opposite charged species complex, gelation, and precipitation occur, forming spherical-shaped particles. The particle size is lowered to the nanometric range by subjecting the resulting solution to sonication. To create a fine powder of NPs, which is shown in Figure 5, the subsequent nanosuspension is freeze-dried with 5% mannitol added as a cryoprotectant.

iii) Solvent evaporation:

One of the most popular methods when producing polymeric particles is the solvent evaporation technique (SET). This adaptable method ensures appropriate

release profiles and allows for the inclusion of multiple active medicinal components in polymeric matrices. Solvent evaporation involves emulsifying a polymer in an aqueous phase and then dispersing it in a volatile solvent, such as dichloromethane, chloroform, or ethyl acetate. After that, the solvent is constantly swirled, heated to a high temperature, or vacuum-evaporated, as shown in Figure 5. Here, the drug is dissolved or disseminated into an organic solvent that has dissolved the polymer. In order to create an emulsion, the final solution is subsequently added under high homogenization to the aqueous phase that contains surfactant/emulsifier such as polyvinyl alcohol, polysorbate 80, poloxamer 188, etc. The organic solvent is evaporated or eliminated when a stable emulsion forms. This can be done by swirling continuously or raising the temperature while applying less pressure. Using 5% mannitol as a cryoprotectant, after freeze-drying the resultant nanosuspension, a fine powder of NPs can be obtained.

iv) Nanoprecipitation:

Fessi was the first to introduce nanoprecipitation technology to create PNPs. Particle formation results from semi-polar solvents being withdrawn from a lipophilic solution that is miscible with water, precipitating the polymers and

solidifying them due to their interfacial deposition. The drug and polymer are blended with an aqueous phase that contains a stabilizer after being liquefied in a water-miscible organic solvent. Reduced interfacial tension between the organic and aqueous phases causes rapid organic solvent diffusion into the aqueous phase. Disruption is created quickly at the interface between the organic solvent and the aqueous phase by surface tension, diffusion, and the emergence of tiny nanoparticle droplets with a specific size and narrow distribution. Using 5% mannitol as a cryoprotectant, the resulting nanosuspension is freeze-dried to generate a fine powder of NPs, as shown in Figure 5.

v) Salting out:

The salting-out technique reduces the unfolding or inactivation of protein upon encapsulation. When salts like calcium or magnesium chloride are added to the aqueous solution in this approach, the water-miscible solvent containing the polymer and protein dissolves. Under continuous stirring, an organic solvent that is water miscible is used to solubilize the drug and polymer together, and an aqueous solution consisting of the stabilizer and salting-out agent is combined with the resultant solution, as shown in Figure 5. The three salting-out agents most frequently utilized are magnesium acetate, calcium chloride, and magnesium chloride.

An emulsion is formed when these salting-out agents inhibit organic solvent miscibility in the aqueous phase. NPs are created when a reverse salting out reaction caused by diluting the emulsion with too much water precipitates the polymer and wraps the drug in the polymer matrix. The residual solvent and salting out agents are removed using the cross-flow filtration procedure (24).

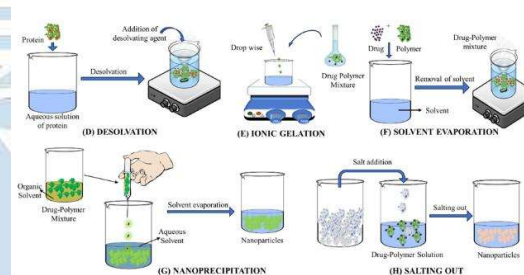


Figure 5. CHEMICAL METHODS OF PREPARATION OF PNPs

CHARACTERIZATION OF PNPS

PARTICLE SIZE (PS), POLYDISPERSITY INDEX (PDI), AND ZETA POTENTIAL (ZP):

A zeta sizer (Malvern, zeta sizer) examined the PS and PDI of the NP formulation. The sample's PS, PDI, and ZP were quantified after it had been diluted with distilled water and placed into a cuvette. Each formulation's zeta potential, polydispersity index, and mean particle size were measured and maintained at 25°C. The polydispersity index will gauge the distribution of nanoparticle sizes.

PERCENTAGE YIELD:

Accurate measurements and collection of NPs were made. After that, the yield percentage (%) was determined using the following formula.

$$\% \text{ yield} = \frac{\text{Mass of nanoparticles obtained}}{\text{Total weight of drug and polymer}} \times 100$$

ENCAPSULATION EFFICIENCY:

By centrifuging the drug-loaded NPs from the liquid-containing free drug, the amount of drug entrapped in the NPs was ascertained. After centrifuging the suspension created by solvent evaporation, an ultraviolet (UV) spectrophotometer operating at a specific wavelength determined the amount of free activity in the supernatant. The difference between the amount of drug employed in the formulation and the amount in the supernatant was used to calculate the amount of drug entrapped into NPs. Using

the following formula, the percentage of entrapment efficiency was determined.

$$\% \text{ EE} = \frac{\text{Total amount of drug added} - \text{Nonbound drug}}{\text{Total amount of drug}} \times 100$$

SURFACE MORPHOLOGY:

Scanning electron microscopy (SEM) is used to examine the surface morphology and particle size. The instrument-mounted sputter coater was used to coat the metal stubs with conductive gold after the NPs were placed on them. Using a scanning electron microscope with appropriate magnification, the photos were captured.

STABILITY STUDIES:

To test the drug content's stability, stability tests of NPs were conducted by storing the formulation in a stability chamber at various temperatures for a specified period.

Table 1. Types of polymeric nanoparticles and their therapeutic usage

Therapeutic Class / Payload	Polymer(s) Used	Application / Target Use	Key Outcome / Benefit
Fluorescent polymeric NPs	PMMA, PPV, PEG, methacrylates	Optical imaging, security printing, chemosensing	High sensitivity, rewritable interface, diagnostic value
ROS / platinum-loaded NPs	PVA, camptothecin polymer	Photodynamic and photoacoustic imaging	Enhanced therapy + dual imaging capability

Bone-targeting fluorescent polymer	CN-PPV	Bone diagnosis and disease detection	Strong imaging potential for bone disorders
Magnetite drug-loaded nanocomposites (e.g., norfloxacin, curcumin)	Chitosan, alginate, PEG, PLGA	Wound healing, infection clearance, drug delivery	Targeted response, reduced dose, better antibacterial effect
Magnetite thermotherapy systems	PEG, PVA	Hyperthermia, cancer support therapy	Improved heating & cellular uptake, lower toxicity
Gold-based polymeric NPs	Alginate, PVP, PLGA, PEG	Biosensing, anti-counterfeiting, cancer cell imaging	High sensitivity, antimicrobial detection, photothermal killing
Gadolinium-polymer NPs	PEG, PLGA, MAA, polysiloxane	MRI, dual modality tumor imaging	Strong contrast enhancement & tumor-targeting efficiency
Perfluorocarbon polymer NPs	PEG, PLGA	Multimodal imaging, ultrasound, oxygen delivery	Theranostic capacity, controlled drug infusion
Radioactive polymeric NPs	PEG, PLGA, chitosan	PET/SPECT imaging, targeted cancer therapy	Precise biodistribution, multimodal tracking, controlled toxicity
Biomimetic / Biofilm-responsive polymer NPs	PLGA, HPMA, PAA, chitosan	Tumor immunotherapy, MRSA biofilm eradication, drug delivery	Superior targeting, immune evasion, strong antibiofilm action

Table 2. Clinical trial status of polymeric NPs (Year 2015 to 2024)

Therapeutic agent	Polymer used	Clinical trial phase	Indications	NCT No.
Cetuximab	Ethyl cellulose	Phase-1	Colon cancer	NCT03774680
Quercetin	PLGA, PEG	Phase-2	Oral carcinoma	NCT05456022
Ciprofloxacin HCl	PLGA	Completed	E.faecalis infections in endodontics	NCT05475444
Chitosan and sodium hypochlorite	Chitosan	Phase-3	E. faecalis in infected root canal	NCT03719261
Anti-bacterial agent	Chitosan	Completed	Semi-facial respirator	NCT04490200

BTS International
Advanced
Pharmaceutical
Sciences Journal

RECENT ADVANCEMENT OF PNPS IN CANCER TREATMENT

TARGETTTED DRUG DELIVERY:

Polymeric nanoparticles are effective carriers for targeted drug delivery for cancer treatment because of their biodegradability, biocompatibility, non-toxic, and prolonged drug circulation. The formulation of anticancer drugs is interesting in absorbed, encapsulation, or conjugated form because the drug-loaded PNPs are sustained release and site-specific for anticancer therapy. The researchers are interested in the polymeric nanoparticles conjugated with a compound with a targeting ligand for better results with low cytotoxicity. Additionally, stealth nanoparticles with particular tumor-homing ligands like antibodies, antibody fragments, polysaccharides, saccharides, peptides, aptamers, folic acid, and so on show the potential effect for active tumor targeting. Because of the benefits of liposomes and polymers, such as their superior biomimicking ability, structural stiffness, and personalized targeting, a hybrid approach guarantees that different chemotherapeutics will exert their effects on tumor locations while enhancing overall curative efficacy.

COMBINATION THERAPY:

Combination therapy using multiple drug-loaded polymeric nanocarriers has the potential to treat cancer, along with adopting a co-delivery system, which is a feasible treatment for cancer therapy. Using multiple small-molecule chemotherapeutic drugs and genes improves the effectiveness by optimizing efficacy and synergistic effects. This innovative approach enhances the therapeutic outcomes and minimizes side effects associated with conventional treatments.

NPS MEDIATED TUMOR IMAGING:

Polymeric nanoparticles have been employed for tumor imaging and targeted delivery, which tends to lower adverse effects and drug dosage and expense. For several illnesses, such as cancer, heart disease, and infectious diseases, diagnostic techniques include positron emission tomography (PET), optical imaging, magnetic resonance imaging (MRI), single photon emission computed tomography (SPECT), and X-ray computed tomography (CT) (25).

IMPROVED PHARMACOKINETICS AND BIOAVAILABILITY:

For the improvement of pharmacokinetics and bioavailability, the adoption of stealth nanocarriers can be a promising strategy for delivering the drug to the targeted site by minimizing the collateral damage to healthy tissue by evading the immune system. The polymers used for the pharmaceutical formulation of nanoparticles are biodegradable and biocompatible, where drugs are encapsulated within the polymer matrix. Following the drug's release from the encapsulation, the polymer matrix breaks down into innocuous molecules like water, nitrogen, and hydrogen and is eliminated from the body.

Cell surface indicators like CD44 can be used to detect the existence of cancer stem cells, and they may help select or create polymer therapies that are particularly targeted for individualized care. Individualized care is increasingly important in oncology, as it allows for treatments tailored to the unique characteristics of a patient's tumor.

PERSONALIZED CANCER THERAPY:

Table 3. Recent studies conducted on PNPs in cancer therapy:

Drug used	Polymer used	Result
Tamoxifen citrate	Chitosan	Tamoxifen citrate loaded chitosan-soluplus nanoparticles were prepared. Shows high entrapment efficiency and high cellular uptake. Successfully targeted to cancer cell.
Docetaxel and lificiquat	PEG	A stable nanostructure was formed by combining two polymer prodrug conjugates leads to a synergistic effect on solid tumors.
Camptothecin	poly(1,4- butadiene)-b-poly(ethylene oxide)	Polymeric micelles were successfully prepared, with LMs showing lower mucosal

		barrier penetration, while WLMs had higher retention and movement in mucus.
5 fluorouracil	Chitosan	5-fluorouracil was successfully prepared, showing high entrapment efficiency and prolonged drug release.
Paclitaxel	Leucine based-poly(ester amide)	Leucine-based-pol(ester amide) with paclitaxel was successfully prepared, showing great potential for drug loading and cancer treatment.
Doxorubicin	Photo switchable smart polymer (spiropyran acrylate and amino-acid)	Sustained drug delivery was achieved in an acidic tumor-like environment. The light-responsive cationic polymer is useful for diagnosing and treating TNBC.
Tamoxifen citrate	Pluronic 123 or pluronic 84	Tamoxifen citrate-loaded folic acid-pluronic micelles were successfully prepared, showing effective anti-tumor activity by reducing tumor size.
Doxorubicin	PEG	The polymeric drug carrier of doxorubicin was successfully prepared having enhance tumor suppression.
Silibinin	Chitosan	Folic acid-linked silibinin nanoparticles were successfully developed for targeted delivery to the lungs in the treatment of lung cancer.
Gemcitabine	Chitosan	A gemcitabine-loaded nano-microencapsulation system was developed, demonstrating enhanced cytotoxicity against lung cancer cells.
Curcumin	PEG	By the use of polymer PEG curcumin-loaded SLNPs were prepared for the effective treatment of cancer.
Enzalutamide	PLGA	Enzalutamide-loaded PLGA nanoparticles were successfully made for safe and effective drug delivery.

Capecitabine, Thymoquinone	PLGA, Eudragit	Capecitabine and thymoquinone were successfully combined in galactosylated PLGA nanoparticles coated with Eudragit polymer.
Silybin	PLGA	Silybin-loaded PLGA NPs were developed with modified aptamers for cancer diagnosis and treatment.
Curcumin and salicylic acid	PEG, Chitosan	A drug combination was successfully prepared using PEG as a copolymer and chitosan as a stabilizer for effective colon cancer treatment.
Camptothecin	PEG, polydopamine	Camptothecin-loaded liposomes were prepared with polymer coatings of either PEG or polydopamine for localized treatment of colorectal cancer.
Cisplatin	PLGA	Cisplatin-loaded PLGA NPs coated with anti-HER2 CAR-T-cell membrane were prepared, reducing tumor growth and ensuring sustained drug release.
Curcumin	PLGA, PCL	Curcumin-loaded PLGA-PCL nanobeads were successfully prepared as a biocompatible drug delivery system for lung cancer treatment.
5-fluorouracil	PAA, PVP	5-fluorouracil was loaded with hydrogel to enhance the retention time and targeting to the cancer cells.
Ceftazidime and usnic acid	Chitosan	The formulation showed in vitro antibacterial activity against E. coli and inhibited both biofilm formation and bacterial growth in the biofilm.
5-fluorouracil and shikonin	Chitosan	The formulation demonstrated that the blended nanoparticles achieved higher drug loading efficiency for targeted delivery.

CHALLENGES AND FUTURE PERSPECTIVES OF PNPS

PNPs can look into new conductive materials for use in NPs and scaffolds for heart regeneration, alongside natural polymers as safer substitutes for synthetic components (26,27,28). Their future trajectory can enhance the loading capacity and targeting abilities of NPs. Scaling up the quality of NPs is hampered by factors

such as the 3D conformation of NPs, green nanotechnology, *in vivo* environments, and the reproducibility of nanotechnology surfaces. The need for more efficient drug delivery methods and the rising incidence of chronic illnesses fuel the pharmaceutical industry's need for polymeric NPs. Due to polymeric NPs' adaptability, their use has expanded in numerous industries, such as food packaging, cosmetics, and agriculture, fueling market expansion (29,30).

Table 4. FDA-approved drug for marketed availability

Generic name	Polymer used	Indication	Year of approved
Pegademase bovine	PEG	Severe combined immunodeficiency disease	1990
Certolizumab pegol	PEG	Psoriatic arthritis	2013
Certolizumab pegol	PEG	Ankylosing spondylitis	2013
Leuprolide acetate and polymer	PLGA	Prostate cancer	2002
Pegvisomant	PEG	Acromegaly	2003
Zilretta	PLGA	Osteoarthritis	2017
Rebinyn	PRG	Hemophilia B	2018

CONCLUSIONS

Polymeric NPs comprise an oily core, into which the drug is often dissolved, and a distinct polymeric shell that regulates the drug's release profile from the core. NPs offer a promising means of preventing nonspecific contact, reducing toxicity and adverse effects, and raising local drug concentration. Only by combining many

analytical approaches is it possible to characterize these drug carriers physicochemically. Because of their promising results, polymeric NPs have found extensive application in medical and other fields due to their extraordinary versatility. Various techniques are used to create more stable polymeric NP formulations that can be used in various

fields, such as bioimaging, inkjet printing, thrombin detection, fluorescence imaging for cancer diagnosis, and petroleum drilling operations. For most of that stage, PNPs are made using solvent evaporation and nanoprecipitation methods with polymers like PAA, PLGA, MAA, and PEG. Owing to their adaptability, polymeric NPs may be the best option for meeting every need for a drug delivery system.

DECLARATION OF COMPETING INTERESTS:

There are no conflicts of interest among the authors.

REFERENCES

1. Young, R.J. and P.A. Lovell, *Introduction to polymers*. 2011: CRC press.
2. Jensen, W.B., *The origin of the polymer concept*. Journal of Chemical Education, 2008. 85(5): p. 624.
3. Chandra, R. and R. Rustgi, *Biodegradable polymers*. Progress in polymer science, 1998. 23(7): p. 1273-1335.
4. Gedde, U., *Polymer physics*. 1995: Springer Science & Business Media.
5. Khan, I., K. Saeed, and I. Khan, *Nanoparticles: Properties, applications and toxicities*. Arabian Journal of Chemistry, 2019. 12(7): p. 908-931.
6. Biswas, P. and C.-Y. Wu, *Nanoparticles and the environment*. Journal of the air & waste management association, 2005. 55(6): p. 708-746.
7. Salata, O.V., *Applications of nanoparticles in biology and medicine*. Journal of Nanobiotechnology, 2004. 2(1): p. 3.
8. Crucho, C.I. and M.T. Barros, *Polymeric nanoparticles: A study on the preparation variables and characterization methods*. Materials Science and Engineering: C, 2017. 80: p. 771-784.
9. Nagavarma, B., H.K. Yadav, A. Ayaz, L. Vasudha, and H. Shivakumar, *Different techniques for preparation of polymeric*

SUPPORT:

The authors thank GITAM School of Pharmacy, Visakhapatnam, for the GITAM Research Fellowship provided to Rakesh Singha, Kartikesh Sahu, and Samson K Wilson.

ACKNOWLEDGEMENTS

The authors are thankful to The Dean of GITAM School of Pharmacy (GSP) and Prof. Partha Roy, Research Supervisor of the authors Rakesh Singha and Kartikesh Sahu, GSP, Visakhapatnam, AP, INDIA.

- nanoparticles-a review*. Asian J. Pharm. Clin. Res, 2012. 5(3): p. 16-23.
10. Silva, A.C., A.J. Silvestre, C. Vilela, and C.S. Freire, *Natural polymers-based materials: A contribution to a greener future*. Molecules, 2021. 27(1): p. 94.
 11. Tong, X., W. Pan, T. Su, M. Zhang, W. Dong, and X. Qi, *Recent advances in natural polymer-based drug delivery systems*. Reactive and Functional Polymers, 2020. 148: p. 104501.
 12. Kulkarni Vishakha, S., D. Butte Kishor, and S. Rathod Sudha, *Natural polymers—A comprehensive review*. Int. J. Res. Pharm. Biomed. Sci, 2012. 3(4): p. 1597-1613.
 13. Shrivastava, A., *Introduction to plastics engineering*. 2018: William Andrew.
 14. [Feldman, D. and A. Barbalata, *Synthetic polymers: technology, properties, applications*. 1996: Springer Science & Business Media.
 15. Sulakhe, V.N., *Introduction to Semisynthetic and Synthetic Fiber Based Composites*. Natural and Synthetic Fiber Reinforced Composites: Synthesis, Properties and Applications, 2022: p. 67-79.
 16. Mathur, S. and C. Hoskins, *Drug development: Lessons from nature*. Biomedical reports, 2017. 6(6): p. 612-614.
 17. Doppalapudi, S., A. Jain, W. Khan, and A.J. Domb, *Biodegradable polymers—an overview*. Polymers for Advanced Technologies, 2014. 25(5): p. 427-435.
 18. Chu, C.-C., *Biodegradable polymers: an overview*. Encyclopedia of biomaterials and biomedical engineering. New York: Informa Healthcare USA, Inc, 2008: p. 195-206.
 19. Samir, A., F.H. Ashour, A.A. Hakim, and M. Bassyouni, *Recent advances in biodegradable polymers for sustainable applications*. Npj Materials Degradation, 2022. 6(1): p. 68.
 20. Weng, Y., Y. Hong, J. Deng, S. Cao, and L.-J. Fan, *Preparation and dynamic color-changing study of fluorescent polymer nanoparticles for individualized and customized anti-counterfeiting application*. Journal of Colloid and Interface Science, 2024. 655: p. 622-633.
 21. Babazadeh-Mamaqani, M., S. Alipour-Fakhri, M. Mohammadi-Jorjafki, H. Roghani-Mamaqani, H. Mardani, and A. Babaie, *Design of chemosensors and dynamic anticounterfeiting inks based on colloidal nanoprecipitated polymers*. Journal of Materials Chemistry C, 2024. 12(2): p. 545-555.
 22. Yu, D., Y. Shen, W. Zhu, J.-M. Hu, and A.-G. Shen, *Raman inks based on triple-bond-containing polymeric nanoparticles for security*. Nanoscale, 2022. 14(21): p. 7864-7871.

23. Hao, Y., Y. Chen, X. He, Y. Yu, R. Han, Y. Li, C. Yang, D. Hu, and Z. Qian, *Polymeric nanoparticles with ROS-responsive prodrug and platinum nanozyme for enhanced chemophotodynamic therapy of colon cancer*. *Advanced Science*, 2020. 7(20): p. 2001853.
24. Chen, D., Y. Liu, Z. Zhang, Z. Liu, X. Fang, S. He, and C. Wu, *NIR-II fluorescence imaging reveals bone marrow retention of small polymer nanoparticles*. *Nano Letters*, 2020. 21(1): p. 798-805.
25. Abdollahi, A., H. Alidaei-Sharif, H. Roghani-Mamaqani, and A. Herizchi, *Photoswitchable fluorescent polymer nanoparticles as high-security anticounterfeiting materials for authentication and optical patterning*. *Journal of Materials Chemistry C*, 2020. 8(16): p. 5476-5493.
26. Yang, Z., J. Leon, M. Martin, J.W. Harder, R. Zhang, D. Liang, W. Lu, M. Tian, J.G. Gelovani, and A. Qiao, *Pharmacokinetics and biodistribution of near-infrared fluorescence polymeric nanoparticles*. *Nanotechnology*, 2009. 20(16): p. 165101.
27. Zheng, X., C. Shen, Z. Deng, C. Pan, and Y. Guo, *Application of a novel polymer cross-linked with magnetite for efficient adsorption of norfloxacin at a wide pH range*. *Environmental Research*, 2024: p. 118471.
28. Faisal, R., I. Kamal, N. Salih, and A. Pr  at, *Optimum formulation design and properties of drilling fluids incorporated with green uncoated and polymer-coated magnetite nanoparticles*. *Arabian Journal of Chemistry*, 2024. 17(2): p. 105492.
29. Sadeghi-Ghadi, Z., N. Behjou, P. Ebrahimnejad, M. Mahkam, H.R. Goli, M. Lam, and A. Nokhodchi, *Improving antibacterial efficiency of curcumin in magnetic polymeric nanocomposites*. *Journal of Pharmaceutical Innovation*, 2023. 18(1): p. 13-28.
30. Hosseini, S.M., M. Abdouss, S. Mazinani, A. Soltanabadi, and M. Kalaei, *Modified nanofiber containing chitosan and graphene oxide-magnetite nanoparticles as effective materials for smart wound dressing*. *Composites Part B: Engineering*, 2022. 231: p. 109557.