

A REVIEW ARTICLE ON PULMONARY DRUG DELIVERY USING POLYMERIC NANOPARTICLES IN TREATMENT OF LUNG CANCERNaushad Ahmad^a, Komal Pathania^{*b} and Dr. Bhartendu Sharma^c^a Student, School of Pharmacy and Emerging Sciences, Baddi University, Baddi, District-Solan, H.P., India.^b Assistant Professor, School of Pharmacy and Emerging Sciences, Baddi University, Baddi, District- Solan, H.P., India.^c Associate Professor, School of Pharmacy and Emerging Sciences, Baddi University, Baddi, District-Solan, H.P., India.***Corresponding Author: Komal Pathania**

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ABSTRACT

Lung cancer accounts for a sizable portion of all cancer incidences, it poses a serious threat to world health. Chemotherapy is one of the conventional treatments that has negative effects. The use of nanoparticles in colloidal medication delivery has received a lot of attention lately. When properly constructed, nanoparticles can improve drug release and retention in the lungs and provide a variety of administration routes. Tobacco smoke and other toxins are the main causes of lung cancer, innovative therapeutic approaches are required. When used with traditional medications, nanoparticles reduce adverse effects and improve the effectiveness of treatment. With an emphasis on polymer-based nanoparticles and their advantages over other carriers, the research explores the various types of nanoparticles and their relationship to lung cancer. With a focus on inorganic, lipid-based, and polymeric nanoparticles, we explore the many kinds of nanoparticles utilized in the treatment of lung cancer in this thorough discussion. Gold-based magnetic nanoparticles exhibit special qualities for cancer detection and targeted treatment. Drug delivery relies heavily on liposomes due to their biocompatibility, while solid lipid nanoparticles provide a different colloidal system that is also highly biocompatible. The safety and effectiveness of polymeric nanoparticles, particularly those derived from biodegradable polymers, have led to their increased popularity. Additional options for cutting- edge cancer treatment are offered by hydrogels, nanocapsules, and nanospheres. Notwithstanding the enormous obstacles that lung cancer presents, developments in nanotechnology, especially with regard to polymer-based nanoparticles, present encouraging opportunities for better patient outcomes, decreased toxicity, and improved medication delivery. This paper offers a glimpse into the future of individualized and successful cancer treatments by shedding light on the changing field of nanoparticle-based therapeutics for lung cancer.

KEYWORDS: AcDex—acetylated dextran; F108—poly(ethylene oxide)-blockpoly(propylene Oxide)-block-poly(ethylene oxide); NCs—nanocapsules; NPs—nanoparticles; PCL— poly(ecaprolactone); PEG—poly(ethylene glycol); PLA—poly(lactic acid); PLGA— poly(lactide-coglycolide) NPs -Nanoparticles.

1. INTRODUCTION

One of the most deadly forms of cancer in humans is lung cancer. Chemotherapy is primarily used as a surgical adjuvant. Chemotherapeutic drugs do, however, have certain adverse effects. Therefore, colloidal drug delivery—particularly using nanoparticles—is gaining a lot of attention these days. There are several ways to give nanoparticles, including parenteral, oral, intraocular, transdermal, and pulmonary inhalation.^[1] Delivery of nanoparticles to the lungs is generally a wonderful idea since, if big porous nanoparticles are employed, this can result in both a prolonged drug release and particle retention in the lungs.^[2] One kind of cancer where carcinogens are the main cause is lung cancer. It accounts for 14% of newly reported cases and is the second most frequent cancer globally. There are two categories for it:

(1) non-small cell lung cancer (85%) (2) Lung small cell.^[3] The physical alterations in the body that cause lung cancer are referred to as the pathophysiology of lung cancer. Tobacco smoke exposure is the main cause of lung cancer. Additional potential causes include exposure to excessive amounts of arsenic in drinking water, radiation, asbestos, radon gas, and air pollution. Lung cancer risk may be increased by inherited or acquired gene mutations. A chronic cough with bloody sputum, chest pain, appetite loss, breathing difficulties, and jaundice are some of the signs and indicators.^[2]

1.1 Nanoparticles (NPs)

Synthetic particles with a diameter of less than 100 nm are called nanoparticles (NPs), and they are typically made of metals like gold, lipids, or polymers. From

cancer treatment to detection, NPs have shown exceptional use in a variety of medicinal applications.^[4] These NPs are strikingly close in size to the majority of biological molecules and structures. As a result, they offer useful characteristics for cancer research conducted *in vitro* as well as *in vivo*.^[5] To achieve concentrated local medication delivery with prolonged release potential, these NPs can be safely loaded with medicinal chemicals when accompanied by biodegradable carriers.^[6] These characteristics allow them to access bodily cavities and the bloodstream for therapeutic purposes with reduced invasion and enhanced bioavailability.^[7] Additionally, compared to micro- and macro-sized particles, NPs have a larger surface volume ratio, which allows them to be coated with multiple ligands simultaneously, increasing drug loading and possibly facilitating interaction with various molecules, including receptors on target cell surfaces.^[8] In order to increase the cell permeability and efficacy of traditional medications or active components, as well as to lessen the side effects and morbidity of advanced cancer therapies, nanoparticles are typically used in combination with them rather than directly as anticancer medications.^[9]

1.2 Few facts about lung cancer

Lung cancer is more common in people over 45 and accounts for the greatest number of cancer-related deaths in both men and women. In addition to being essential for the exchange of gases between the blood and the air, the lungs are frequently the site of metastases from malignancies that started in other areas of the body. The epithelial cells lining the main airways entering the lungs, such as the bronchi and bronchioles, are thought to be the source of 90–95% of lung cancer cases.^[11]

- NSCLC is a more prevalent lung kind. Bronchogenic carcinomas, another name for lung cancer, are divided into four main types according to their histological appearance: small cell lung cancer, non-small cell lung cancer (NSCLC), and (SCLC).^[11]
- NSCLC is far more prevalent and has several subtypes, including large cell carcinoma, adenocarcinoma, and squamous cell carcinoma.^[11]
- Under a microscope, SLC, often referred to as oat-cell cancer, resembles oats. Beginning in the innermost layer of the bronchial wall, this cancer grows and swiftly spreads to other areas of the body. Lung cancer of this kind is not very prevalent.^[11]
- Compared to SLC, NSCLC is a more prevalent form of lung cancer and often grows more slowly.^[8]

1.3 Types of nanoparticles used in lung cancer

- In general, nanoparticles come in three varieties: Inorganic nanoparticles include gold, magnetic, and other types.
- Liposomes, solid lipid nanoparticles, phospholipid micelles, and nano emulsions are examples of lipid-based nanocarriers.
- Polymeric nanoparticles, which include inorganic

nanoparticles such as nanospheres, nanocapsules, dendrimers, micelles, and nanogels.

1.3.1 Magnetic nanoparticles (MNPs)

One particular kind of inorganic nanoparticle utilized to treat lung cancer is the magnetic nanoparticle. The surface of MNPs binds to biological units, transforming them into a possible vector for delivering medications or anti-cancer agents to the precise cells where they are expected to exhibit their intended function. Their action within the patient's body can be externally regulated by a magnetic field because of their intrinsic magnetic characteristics. Without concurrently reducing the therapeutic efficacy of the medicine placed into MNPs, they readily penetrate deeply injured tissues.^[12] Super paramagnetic substance with an average size of above 25 nm makes up MNPs.^[13] Likewise, when MNPs are exposed to alternating current, sub-lethal heat is produced, which exacerbates tissue damage. MNPs are made up of a magnetic core and a functional coating around it. Its magnetic properties come from the elements that make up its innermost core, which include iron (Fe), cobalt (Co), gold (Au), and nickel (Ni). In contrast, the surface coat limits magnetic core contact with other particles and prevents aggregation.^[14–15]

1.3.2 Gold Nanoparticles

Often utilized inorganic nanoparticles for drug delivery and cancer diagnosis include gold nanoparticles (GNPs).^[16] They also exhibit strong antibacterial activity. The interaction of gold ions with S-H bonds is another possible mode of action of microorganism's biological proteins, causing their deactivation. It is thought that the main way that GNPs prevent bacterial replication is by binding to DNA, which causes the DNA molecules to condense and lose their capacity to replicate.^[17]

1.3.3 Organic/lipids- based nanoparticles

Liposomes, which are spherical phospholipid structures, are frequently employed as nanocarriers because of their special qualities, which include low toxicity, biocompatibility, biodegradability, and lack of immune system activation. Because of these characteristics, liposomes are a great option for delivering hydrophilic and lipophilic medications to various target locations.^[20] In order to prevent tumor growth, BLP25 uses a liposomal carrier that selectively targets the tumor-associated antigen MUC1. A human MUC1 transgenic lung cancer mouse model (hMUC1.Tg) was used in a preclinical investigation. It was shown that the number of tumor foci was considerably decreased by pretreatment with a low dosage of cyclophosphamide and two cycles of liposome BLP25 therapy. Notably, liposome BLP25 is presently the subject of phase III clinical trials.^[23] In various phases of clinical trials, about 12 liposome-based drugs have been approved for use in medicine.^[24]

1.3.4 Solid lipid nanoparticles (SLNs)

An alternative to the conventional colloidal delivery system, SLNs are a new medication delivery technique.

The combination of liposomes and polymeric nanoparticles in SLNs offers a number of therapeutic benefits.^[26] Since the core's solid hydrophobic environment permits long-term circulation, SLNPs are frequently used as colloidal carriers for hydrophobic chemotherapeutic medicines and genes in the bloodstream. The primary cause of endobronchial cancer is apoptosis, or programmed cell death, resulting from a mutation and subsequent loss of the p53 tumor suppressor gene's ability to induce growth arrest.^[27] Transferring the wild type p53 gene to the faulty and deficient tumors in the lower respiratory airways could therefore treat the condition.^[26] Cationic SLNPs engage with negatively charged DNA plasmids to form a stable complex. They are amphiphilic because they contain hydrophilic amino groups with a linker and hydrophobic fatty acid side chains. The efficient transmission of genes to cells is facilitated by this complex. Thus, either aerosol inhalation or intra-tracheal instillation (direct delivery via an airway catheter) can be used to deliver the p53/cationic SLNPs complex to the afflicted areas.^[28]

1.3.5 Polymeric nanoparticles

Polymers are big molecules composed of repeating subunits that can form microscopic particles called polymeric nanoparticles. These nanoparticles are becoming more and more well-liked in the medical industry because of their special qualities.^[29] The biodegradability of polymeric nanoparticles is one of its main benefits. These nanoparticles are frequently made from biodegradable polymers, including poly (lactic acid) (PLA), poly(lactic-co-glycolic) acid (PLGA), gelatin, albumin, chitosan, polycaprolactone, and poly-alkyl-cyanoacrylates.^[30] Nanoparticles of polymers are biocompatible. These drugs' distribution to tumor tissues can be enhanced by encapsulating them in nanoparticles, which will increase patient survival and local tumor control.^[30] Abraxane is one instance of a successful treatment based on polymeric nanoparticles. These nanoparticles may be used in cancer treatment in the future, as evidenced by their entry into phase I clinical trials.^[29]

1.3.6 Dendrimers

These artificial polymers have a variety of cationic, neutral, and anionic terminal functions on their surface. They are made up of repeatedly branching units that radiate from a central point. As a result, either hydrophilic or hydrophobic chemicals are present. These nanometric molecules are homogeneous, monodisperse, globular in form, and radial symmetric.^[31] They are also suitable as medication delivery devices because of their internal chambers and features. Dendrimers are useful ligands that help move medication molecules between various biological compartments and into tumor tissues.^[32]

1.3.7 Micelles

Micelles are 100 nm-diameter spherical self-assemblies of amphiphilic copolymers in water. Hydrophobic

medicines can be encapsulated by the hydrophobic groups on the inner surface of the micelles.^[33] Conversely, the micelles' outer shell is made up of hydrophilic polymers that can interact with a variety of bioactive substances, such as DNA/siRNA and targeting moieties. Micelles' controlled release and tissue-penetrating properties make them excellent candidates for gene delivery systems.^[34]

1.3.8 Hydrogels

Hydrogels can be categorized as either chemical or physical and can be made in a variety of ways according to their method of cross-linking. For the creation of hydrogels with regulated drug release and a range of strengths, chemical-based techniques such pH-responsive, self-assembling hydrogel, and thermoresponsive methods are advised. Hydrogels are in solution form at room temperature, but they gel when they get to body temperature. By creating a drug depot through which the medication progressively diffuses, this gel form is employed to treat cancer.^[36]

1.3.9 Nanospheres and capsules

A polymeric coating that controls the medication's release surrounds the oily core of the nanocapsule, where the drug is normally dissolved. Conversely, the drug can either be adsorbed onto the surface of nanospheres or kept within due to their continuous polymeric structure. These two types of nanoparticles made of polymers are described as a reservoir shown in (fig1).

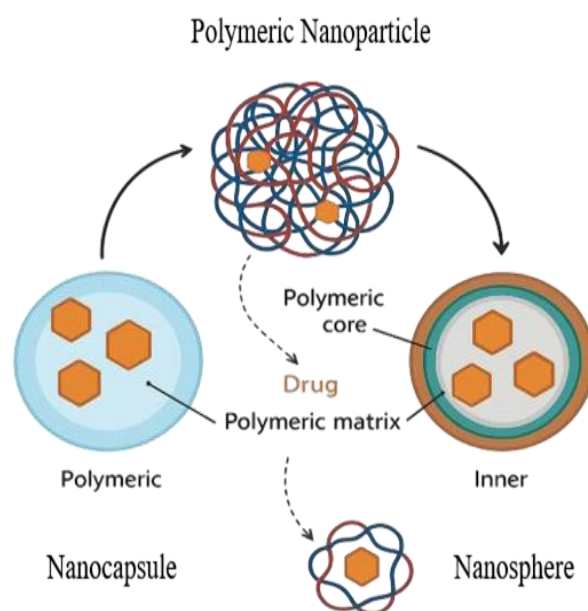


Figure 1: Structure of Nanocapsules And Nanospheres.

2. The following justifies the preference for polymeric nanoparticles over alternative carriers

We will now talk about the rationale behind the preference for polymeric nanoparticles as the best delivery system for lung cancer treatment. The advantages

of polymeric nanoparticles over alternative carriers are as follows:

- Both synthetic and natural polymers can be used to create polymeric nanoparticles (NPs). In addition to their exceptional stability, biodegradability, and good biocompatibility, they also have the added virtue of being inexpensive to produce.
- In some cases, the presence of heavy metals or other chemicals makes inorganic nanoparticles somewhat harmful, while polymeric nanoparticles are less toxic. These carriers use biodegradable polymers.
- Polymeric nanoparticles offer controlled release and a high loading capacity.
- Because polymeric nanoparticles can promote regulated release, protect drugs and other biologically active molecules from environmental influences, increase their bioavailability, and improve their therapeutic index, they may prove to be efficient drug carriers.^[37]

3. Techniques for making polymeric nanoparticles

Generally speaking, there are four ways to create polymeric nanoparticles:

- Solvent evaporation
- Emulsification/solvent diffusion

- Salting out
- Nanoprecipitation

3.1 Solvent evaporation

Solvent evaporation from an existing polymer was the first method created for creating polymeric NPs. In order to produce nanospheres, an oil-in-water (o/w) emulsion must first be made.^[38] First, the polymer is dissolved in a polar organic solvent to generate an organic phase, and then the active ingredient (such a medication) is added by dissolution or dispersion. It's also common practice to prepare an aqueous phase that contains a surfactant, like polyvinyl acetate (PVA). A dispersion of nanodroplets is produced by processing the organic solution using high-speed homogenization or ultrasonication after it has been emulsified in the aqueous phase with a surfactant.^[39] The solvent for the polymer evaporates. Centrifugation can be used to wash and gather the formed nanoparticles once the solvent has evaporated.

For long-term storage, freeze-drying comes next. Nanospheres can be produced using this technique.^[38]

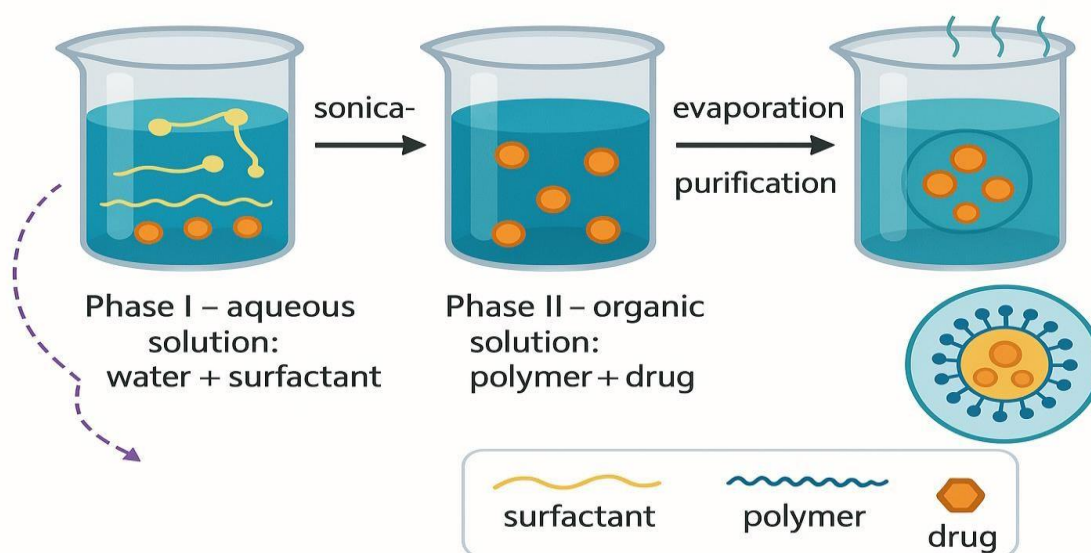


Figure 2: representation of solvent evaporation method.

3.2 Emulsification/ Solvent Diffusion

A somewhat water-miscible solvent containing the medication and polymer is combined with an aqueous solution containing a surfactant to create an o/w emulsion.^[40] A somewhat hydro-miscible organic solvent, such as benzyl alcohol or ethyl acetate, that has been saturated with water to maintain the thermodynamic balance of both phases at room temperature makes up the emulsion's internal phase. The size of the resultant NPs might vary from 80 to 900 nm. despite the danger of the hydrophilic drug diffusing into the aqueous phase and the

requirement for a large volume of the aqueous phase, which must be extracted from the colloidal dispersion.^[41]

3.3 Salting out method

The process of salting-out involves removing a water-soluble solvent from an aqueous solution, which causes the salting-out effect to generate nanospheres. The main distinction is found in the emulsion's composition, which is made up of a gel, a salting-out agent, a colloidal stabilizer in the aqueous phase, and a water-miscible polymer solvent such as ethanol or acetone.^[42] Salting-

out agents can be non-electrolytes like sucrose or electrolytes like magnesium chloride (MgCl₂), calcium chloride (CaCl₂), or magnesium acetate [Mg(CH₃COO)₂]. Although total miscibility between the organic solvent and water is not essential, it makes the process easier to carry out. The nanospheres created with this technique range in size from 170 to 900 nm and by changing the volume of the exterior phase or the concentration of polymers in the internal phase, the average size can be changed to values between 200 and 500 nm.^[43]

3.4 Nanoprecipitation

Two miscible solvents are used in the solvent displacement process, sometimes referred to as nanoprecipitation. A polymer dissolved in an organic solvent that is miscible, like acetone or acetonitrile, makes up the internal phase. They are easily eliminated by evaporation because they are immiscible in water. The method depends on the displacement of the organic solvent from a lipophilic solution to the aqueous phase, followed by the interfacial deposition of a polymer.^[44] After dissolving the polymer in an intermediately polar water-miscible solvent, the solution is gradually added to an aqueous solution while being stirred or at a controlled addition rate.^[45] The rapid spontaneous diffusion of the polymer solution into the aqueous phase, which aims to evade the water molecules, causes the nanoparticles to form instantly. The resulting nanoparticles are often superior than those made by the emulsification solvent-evaporation process because they have a restricted size dispersion and a well-defined size.^[44]

4. Polymeric nanoparticles characterisation

Physical characteristics such as composition, concentration, size, form, surface characteristics, crystallinity, and dispersion state vary among polymeric nanoparticles. To obtain a thorough characterization of the nanoparticles, these characteristics are usually assessed using a variety of techniques.^[46] Electron microscopy, dynamic light scattering (DLS) or photon correlation spectroscopy (PCS), near-infrared spectroscopy, electrophoresis, and chromatography are a few of the most commonly used methods.^[56] In addition to their practical uses, the characterisation of polymeric nanoparticles is essential for resolving issues with nanotoxicology and workplace exposure assessment. These evaluations are crucial for identifying the risks to health and safety posed by these nanoparticles as well as for controlling production procedures.^[46]

4.1 Morphology

Scanning and transmission electron microscopy (SEM and TEM) can be used to determine the size and form of polymeric nanoparticles. These approaches are frequently used in conjunction with cryofracture techniques to examine the morphology of NPs. TEM is especially helpful for differentiating between nanospheres and nanocapsules and figuring out how thick the wall of a nanocapsule. While nanocapsules have an oily core

surrounded by a thin (about 5 nm) polymeric coating, nanospheres are spherical and have a solid polymeric structure.^[46]

4.2 Distribution of particle sizes

The mean diameter of polymeric nanoparticles produced using different techniques usually ranges from 100 to 300 nm. It is crucial that the size distribution be unimodal and that the polydispersity be as low as feasible, ideally close to zero. Particles as tiny as 50 nm or even 60-70nm in diameter can be produced. The size measuring technique can have an impact on the outcomes; for example, DLS can be used to determine the hydrodynamic radius of suspended particles, whereas electron microscopy can provide an image of the isolated particle. Additionally, DLS may be used to measure bigger sizes and provide details about the state of aggregation of nanoparticles in solution. A number of variables, including the type and amount of materials utilized, might affect the size of polymeric nanoparticles.^[57]

4.3 Chemical composition and crystal structure

The combination of atomic elements and compounds, including any produced or native functional groups, makes up a nanoparticle's chemical composition. The chemical composition can be measured using a variety of techniques, including single-particle or ensemble analysis. Atomic absorption spectroscopy is a popular ensemble technique that depends on the energy absorbed by atoms' ground state electrons when they are stimulated by light of a certain wavelength. The amount of energy absorbed, which is correlated with the kind and quantity of atoms in the light path, can be used to calculate the sample mass concentration by comparing the signal with calibration standards of known concentrations.^[58]

4.4 Molar mass distribution

A useful insight into the impact of formulation components on the polymerization process can be obtained by evaluating the polymer mass distribution following preparation. In addition to the degradation of the polymer, the medication and polymer undergo chemical reactions. SEC, or size-exclusion chromatography, is the most commonly used technique for determining the polymer molar mass.^[57]

4.5 Surface area and chemistry

One of the most important factors in determining surface area is determining their ligand interactions and reactivity. Various techniques are used to quantify various features of the surface region. Adsorption of gas (e.g., N₂) at varying pressure conditions to form a monolayer of gas coverage is necessary for a direct measurement of surface area. The "total surface area" is calculated using the number of gas molecules needed to create a monolayer and the cross-sectional area of the adsorbate gas molecule. Because the gas adheres to internal holes and crevices,

this technique is especially helpful for assessing the morphology of porous materials.^[57]

4.6 Zeta potential

Variations in the contact with the dispersing media might have an impact on the particles' surface charge, which is indicated by the zeta potential (C). These alterations may be brought about by the solvation effect, the adsorption of ionic species in the aqueous dispersion medium, or the dissociation of functional groups on the particle's surface. This parameter is found by measuring the particle velocity as a function of voltage using Doppler techniques. The electrophoretic mobility of the particles in the solvent is then used to compute the zeta potential. The main constituents of polymeric NPs include

phospholipids, poloxamers, and polymers, which, when included in formulations, can affect the zeta potential. For the colloidal solution to remain physicochemically stable, a comparatively high zeta potential value—typically about ± 30 mV—is essential. This is because to the powerful repulsive forces that a high zeta potential reduce collisions between neighboring nanoparticles to aid in the avoidance of agglomeration.^[58]

5. Individual polymers and drugs loaded in polymeric nanoparticles as examples

A promising medication delivery method that can increase drug bioavailability and target particular delivery sites is drug-loaded polymeric nanoparticles (table 1).

Table 1: Types of polymers and drug loaded.

Types of polymers	Drug loaded	Reference
PCL,PLA,PLGA	Coumarin (C-6)	[59]
PLGA	Repamycin	[60]
AcDex	Hyperforin	[61]
Biopolymer of PCL	Amphotericin B	[62]
PEG	Pegademase bovine	[63]
Anionic copolymers based on methacrylic acid and methyl methacrylate	Fenofibrate	[64]
PCL-PEG-PCL	Paclitaxel	[65]
PCL	Paclitaxel	[66]
PCL	Cyambopogon martini (Palmarosa oil)	[67]
Poly lactide	Essential oils	[68]
F 108: PEG-PPG-PEG	Curcumin	[69]
PCL	Geraniol	[70]

Abbreviations: AcDex—acetylated dextran; F108—poly(ethylene oxide)- blockpoly(propylene Oxide)-block-poly(ethylene oxide); NCs—nanocapsules; NPs— nanoparticles; PCL—poly(ecaprolactone); PEG—poly(ethylene glycol); PLA—poly(lactic acid); PLGA— poly(lactide-coglycolide).

6. APPLICATIONS OF POLYMERIC NANOPARTICLES

6.1 Polymeric nanoparticles in imaging and cancer diagnosis

The World Health Organization (WHO) estimates that 9.6 million people died from cancer in 2018, making it the second most common cause of death worldwide. These figures demonstrate the substantial influence that cancer has on current rates of morbidity and mortality. Finding efficient methods for early cancer detection, diagnosis, and therapy has been a top priority in the development of nanomaterials as drug delivery systems (DDSs).^[71–72] Tumors must normally be at least one centimeter in size to be detected by conventional imaging and diagnostic methods, which limits their capacity to identify them early.^[73] As a result, scientists are now working to create tiny composites that can recognize cancerous cells linked to cancer processes. The goal of this development is to give healthcare providers the essential data they need to create effective treatment plans. Because polymeric nanoparticles (NPs) may alter surfaces and control the solubility of embedding agents, they have become a possible substitute for traditional contrast agents in

improving the imaging of malignant cells. Recent studies in this area have looked at both therapeutic and diagnostic goals, using what are commonly known as "theranostic agents." Although diagnostic and imaging outcomes are the main emphasis of this review, some treatment aspects are also briefly mentioned.^[74]

6.2 Polymeric nanoparticles based on gold for the diagnosis of cancer

In order to create new composites that can improve imaging and diagnosis methods, research into gold metallic nanoparticles (AuNPs) and their derivatives is essential. Because of their adaptability, they can be used in a variety of imaging techniques, offering minimal toxicity and great resolution. Because of its affordability, excellent imaging resolution, and suitability for all patient types, computed tomography (CT) is a commonly utilized diagnostic method in cancer imaging. This method of soft tissue scanning necessitates the use of contrast agents that absorb X-ray energy. Due to their non-toxicity and up to three times greater X-ray absorption efficiency than the existing iodine-based CT contrast agents, AuNPs have attracted a lot of interest as

contrast agents. Furthermore, AuNPs provide the opportunity to design and alter their surface, size, and form.^[73] When near-infrared (NIR) light strikes a tissue and is absorbed by the target, thermoelastic expansion causes wideband ultrasonic waves (PA waves) to be produced. PAI is a trustworthy method that is connected to widely used clinical diagnostic methods. After being created, the gold nanospheres were coated with silica, fluorinated, and added to a previously created.^[76] Perfluorocarbons (6.3) The usage of polymeric nanoparticles (PFCNPs) in the diagnosis of cancer: Perfluorocarbons, or PFCs, are chemicals that resemble common organic substances such as alkanes. However, the substitution of fluorine (19F), the most electronegative element in the Periodic Table, for each hydrogen atom distinguishes PFCs from ordinary organic compounds.^[75] This substitution produces special and desirable qualities that may be used in medical settings.

6.3 Polymeric nanoparticles in oncologic treatment

As was already said, one of the main causes of death in developed countries is cancer. Over the next 20 years, experts estimate that the incidence of this disease will increase by almost 70%. The traditional treatment for cancer consists of radiotherapy, chemotherapy, and surgery. Chemotherapy is the recommended treatment for the majority of tumors, but because it affects both malignant and healthy cells, it can be extremely hazardous.^[78] A more focused option is provided by nanomedicine, which uses materials at the nanometric size in medical treatment. In oncology, its main goal is to deliver medications to cancer cells specifically, increasing their effectiveness and decreasing their toxicity. Additionally, nanomedicine may offer combination medicines that can enhance therapy effectiveness and prognosis, as well as early cancer detection technologies.^[74]

6.4 Polymeric nanoparticles in vaccine delivery

Encapsulated in polymer-based nanoparticles, vaccination antigens administered via the mucosal channel provide a barrier against deterioration. This guarantees the release of the encapsulated antigen at the targeted location of action efficiently eliciting immunological reactions. Furthermore, using polymer-based nanoparticles has demonstrated great potential for improving vaccine immunogenicity and developing the field of nanovaccines.^[75]

6.5 Agricultural application

Polymeric nanoparticles have been proposed as a way to administer pesticides, including insecticides, herbicides, and fungicides, for crop growth and protection, as well as plant growth boosters. Polymeric nanocarriers may also be used to deliver antibiotics to animals and aquaculture.^[77] When compared to the unencapsulated active components, nano-formulations have been reported to show comparable to greater efficacy in boosting plant growth and reducing weeds, pests, and diseases. The focused or better delivery made possible by the

nanoparticles may be the cause of the increased efficiency.^[78]

6.6 Polymeric nanoparticles in the delivery of drugs to the eyes

Because of the eye's distinct architecture and physiology, drug administration to this organ poses substantial hurdles. The anterior segment and the posterior segment are two separate regions. The aqueous humor, conjunctiva, cornea, iris, ciliary body, and lens are some of the parts that make up the anterior segment, which is situated in front of the eye. Because of the ease of access to this area, eyedrops are the most common way to administer medications. However, it is challenging to achieve adequate drug bioavailability at the site of action in the posterior segment, which comprises the choroid, neural retina, optic nerve, retinal pigment epithelium, sclera, and vitreous humor.^[77] Lacrimation, reflex blinking, tear-film turnover, and nasolacrimal duct drainage are some of the factors that help the body quickly get rid of eyedrops that contain drugs. Biodegradable polymer-based nanotechnological solutions have drawn a lot of interest in eye therapy as a means of overcoming these obstacles. These systems are intended to increase formulation solubility, boost bioavailability, facilitate targeted distribution, and offer prolonged drug release. Polymeric nanoparticulate materials including micelles, dendrimers, cyclodextrins, and polymeric vesicles are examples of recent studies in this area.^[78]

7. CONCLUSION

Because of their enormously varied and distinctive structure, polymeric nanoparticles have the potential to completely transform the materials industry. The fabrication process is crucial to getting the required qualities. The addition of polymeric nanostructures results in unique properties. When compared to bulk polymers, the nanoparticles' higher surface area encourages stronger interfacial contacts, producing well-blended characteristics. Composite materials with remarkable properties that outperform conventional macro-scale components can be produced by fusing the characteristics of polymeric nanoparticles with those of other materials. These materials are important in many applications, including targeted medicine delivery to tumor cells, because of the special qualities that polymeric nanoparticles offer. Additionally, they are necessary to improve solar applications' efficiency. Gaining insight into the connection between these materials' structure and characteristics could lead to improvements in a variety of applications and further the development of nanotechnology.

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