Investigate the Nanoparticle Mediated Antiretroviral Therapy in Prostate Cancer

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Abstract
In the process of integrating inorganic materials with polymers and in the process of merging various classes of polymers together in nanoparticle form, more practical design advancements have been obtained. These enhancements have been realised. It is now feasible to design and build a broad range of unique shapes of polymer particles as a consequence of recent breakthroughs in chemistry, processing techniques, and analytical equipment. These developments have made it possible to design and manufacture these novel forms. For example, we currently have particles that are hollow, multiplied, conductive, thermo responsive, magnetic, functionalized with reactive groups on the surface, and pH responsive. These particles fulfil all of these characteristics. These particles have the potential to be employed in a wide range of applications, such as floating carrier, multiparticulate drug delivery, dual core or multiple layering medicines, and a number of other applications. Polymeric nanoparticles have been made since the 1970s with the intention of combining them into a broad variety of high-performance materials. These materials include high impact-resistant polymers and specialised coatings that have been designed expressly for these purposes.
Keywords: Polymeric, Nanocarriers

I.   INTRODUCTION

Through the development of a better knowledge of disease processes, new chances to prevent and cure illnesses are becoming available. By using delivery vehicles that have been rationally developed, it is possible to circumvent the inherent restrictions that are associated with therapeutic bio-macromolecules like proteins and nucleic acids. Considering the fact that more powerful and targeted medications are being produced, the distribution of pharmaceuticals is becoming an increasingly significant component of the medical industry. This discipline is no longer dependent on small-molecule medications; rather, it now involves not only the extension of the duration of drug release but also the concentration on individualised systems that are meant to provide unique spatial and temporal control. The introduction of nanotechnology into so-called smart drug-delivery systems allows for the integration of bio-sensing functions. These features provide unassisted in vivo feedback control, which is one of the aspects that contribute to the new name "nanomedicine."

For this purpose, a wide variety of biomaterials, especially those based on polymers or lipids, may be utilised. These biomaterials provide a wide range of chemical compositions and the possibility of further modification through the utilisation of nanoparticles. The nanoparticles have a surface area that is exceptionally vast, which provides a wide variety of chances for the placement of functional groups on the surface. In order to conduct quick ex-vivo medical diagnostic tests, particles can be generated by rapidly expanding or contracting in response to changes in temperature or pH. Additionally, particles can interact with anti-bodies in a variety of unique ways.

More practical design enhancements have been achieved in the process of integrating inorganic materials with polymers and in the process of combining diverse classes of polymers together in nanoparticle form. As a result of recent developments in chemistry, processing techniques, and analytical instruments, it is now possible to design and create a wide variety of novel forms of polymer particles. For instance, we now have particles that are hollow, multilobed, conductive, thermoresponsive, magnetic, functionalized with reactive groups on the surface, and pH responsive. These particles have the potential to be utilised in a variety of applications, including floating carrier, multiparticulate drug delivery, dual core or multiple layering pharmaceuticals, and more.

Since the 1970s, polymeric nanoparticles have been manufactured with the goal of incorporating them into a wide range of high-performance materials, including high impact-resistant polymers and specialised coatings designed specifically for these applications. The ability to assess structure and design control methods

for the production of structured particles is made possible by the application of sophisticated analytical techniques and computer simulations of the processes that take place during the generation of particles. In order to establish new levels of product performance in the targeted drug delivery system, our capability to build new control process techniques, such as modifying the shape of the carrier, the chemical composition, the internal structure, and the morphology of the nanoparticles, is essential.

OBJECTIVE OF THE STUDY
1.   Prepare 12 formulations of PCL microspheres
2.   To analyse the effects of different PCL molecular weights on product yield.
3.   To investigate the factors that influence different release profiles.

Polymeric nanoparticles

The medication is dissolved, entrapped, encapsulated, or linked to a nanoparticle matrix in order to create polymeric nanoparticles (PNPs), which are made from biocompatible and biodegradable polymers and range in size from 10 to 1000 nanometers. In the process of creating nanoparticles, it is possible to create nanospheres or nanocapsules, each of which is distinct from the other. In nanocapsules, the drug is contained within a hollow that is enclosed by a one-of-a-kind polymer membrane. On the other hand, nanospheres are matrix systems in which the drug is physically and evenly spread throughout the matrix. The field of polymer nanoparticles, also known as PNPs, is rapidly increasing and playing an essential role in a broad variety of fields, including but not limited to electronics, photonics, conducting materials, sensors, medicine, biotechnology, pollution control, and environmental technology. PNPs are potential vehicles for drug delivery because they are simple to manipulate and may be used to build carriers with the intention of delivering pharmaceuticals to particular targets. This advantage contributes to an improvement in the safety of the drug. Nanoparticles made of polymers are capable of transporting medicines, proteins, and DNA to the cells and organs that they are intended to reach. Because of their nanoscale size, they are able to effectively pass through cell membranes and maintain their stability in the central nervous system. In the process of manufacturing innumerable and diverse molecular patterns, polymers are extremely practical materials. These designs may be integrated into one-of-a-kind nanoparticle constructions, which have the potential to be used in a wide variety of medicinal applications.
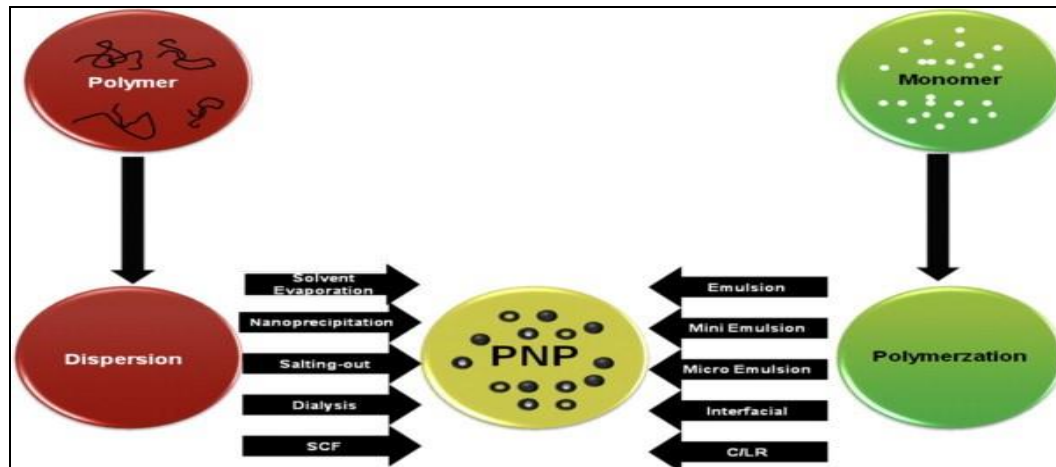

Figure 1   Schematic representation of various techniques for the preparation of polymer nanoparticles

The preparation of PNPs may be accomplished in a convenient manner by either employing premade polymers or by directly polymerizing monomers through the use of polyreactions or conventional polymerization mechanisms. The creation of polymer nanoparticles (PNP) from premade polymers can be accomplished by the use of techniques such as solvent evaporation, salting-out, dialysis, and supercritical fluid technology. These techniques involve the fast expansion of a supercritical solution or the quick expansion of a supercritical solution into liquid solvent. PNPs, on the other hand, can be directly synthesised by the polymerization of monomers through the use of a variety of polymerization processes, including micro-emulsion, mini-emulsion, surfactant-free emulsion, and interfacial polymerization. A variety of methods for preparing PNP are depicted in Figure 1, which provides an example of these methods. The selection of the preparation technique is determined by a variety of parameters, including the kind of polymeric system, the region of application, the size requirement, and other considerations.

SOLID-LIPID NANOPARTICLES

Solid lipid nanoparticles, also known as SLN, are particles that are formed from solid lipids and have mean diameters that range from 50 to 1000 nanometers. These particles offer an alternative to polymeric particulate carriers. When it comes to medication administration, the most significant benefit that lipid carriers provide is the utilisation of physiological lipids or lipid molecules that have a track record of being safe for use in human medicine. This can help reduce the risk of both acute and chronic exposure to hazardous substances. The absorption of lipid particulate materials through Peyer's patches is the primary method of lipid particulate materials translocation throughout the gut. There is sufficient data available for the use of drug-loaded lipid nano and micro-particles for oral administration.

The findings of a study indicate that stearic acid and phosphatidylcholine-containing SLN were found in the lymph and blood of rats following duodenal administration. The tiny diameters of SLN may make it easier for the lymphatic system to absorb these substances. A limited number of approaches for the preparation of SLN have been documented in the published literature up till the present day. These techniques include high pressure hot homogenization and cold homogenization techniques, microemulsion-based preparation, and the solvent emulsification/evaporation treatment method. In particular, the emulsification/evaporation approach is used for the creation of nanoparticle dispersions from O/W emulsions. This method involves dissolving the lipophilic material in a water-immiscible organic solvent, which is then emulsified in an aqueous phase.

The formation of nanoparticle dispersion occurs as a result of the precipitation of the lipid in the aqueous medium after the solvent has been evaporated. There is an obvious downside to this process, which is the use of organic solvents, whose toxicity cannot always be ignored. However, extremely tiny particle sizes may be achieved, ranging from 30 to 100 nanometers, depending on the composition and the concentration of the lipid in the organic phase. An emulsification–diffusion approach was created not too long ago. This technique makes use of non-toxic and physiologically suitable solvents, as well as monoglycerides or waxes, as components of the dispersion phase of oil-in-water emulsions that are formed at a temperature of fifty degrees Celsius. The solvent-in-water emulsion–diffusion approach was previously reported in the literature, mostly for the purpose of obtaining polymeric micro- and nanoparticles. However, only a few writers claimed that it may also be utilised in the manufacture of SLN.

Physiological system specific nano-delivery

Nano-scale drug delivery systems are currently being developed with the purpose of regulating the sustained release of drugs, particularly in the areas of pharmacokinetics, pharmacodynamics, solubility, immunocompatibility, cellular uptake, and biodistribution. Additionally, these systems aim to minimise toxic side effects, thereby enhancing the therapeutic impact of conventional pharmaceutical applications. There is a possibility that nanoparticle-mediated drug delivery might make a contribution to the improvement of the drug development process, which has traditionally depended on conventional formulation tactics that are frequently insufficient. The establishment of a connection between the in vitro potency, physicochemical properties, absorption, distribution, metabolism, excretion, and toxicity characteristics of a drug candidate is a fundamental concept in the process of drug development. This is a factor that is frequently cited as a major contributing factor in the failure of drug functionalization. In the meanwhile, the continuous release of medications that is mediated by nanoparticles has a clear therapeutic benefit. In order to limit the release of therapies at non-specific areas and to guard against any undesired side effects, it is necessary to distribute medications in the body in a targeted manner. Examples of nanodelivery medications that have been evaluated by researchers in physiological systems are included in Table 1. which may be found below this paragraph.

TABLE 1. Physiological system with specific example of nano-delivery drug

Physiological systems	Examples of nanodelivery drugs
Central nervous system (CNS)	Amitriptyline, polybutyl-cyanoacrylate nanoparticles coated with polysorbate-80, dalagrin, kytorphin, neuromuscular blocking agent tubocurarine, GLUT1 transporter, choline transporter, insulin, transferrin, beta-endorphin peptides, OX26, Doxorubicin, Transferrin-liposomes, folates, Doxorubicin-loaded folic acid-PEG-PLGA micelles, Paclitaxelloaded PCL/MPEG micelles decorated with folic acid, Cationized bovin serum albumin (CBSA), Polysorbate 80-coated atovaquone-loaded SLN, dipalmitoylated apoE-derived peptides, camphotericin, dalargin, diminazene diaceturate, paclitaxel
Pulmonary system	Beclomethasone dipropionate loaded polymeric micelles, liposomes, synthetic lung surfactant Alveofact®, Liposomal aerosols, non-phospholipid vesicles loaded with beclomethasone dipropionate, Levonorgestrel encapsulated liposomes, Liposomes modified with cell-penetrating peptides, antennapedia, the HIV-1 transcriptional activator, and octaarginine, Liposomes of EYPC-

	cholesterol (CHOL) incorporating dexamethasone palmitate (DEXP), prednisolone, diazepam, camptotecin, rifampicin, isoniazid, pyrazinamide, low molecular weight heparin (LMWH)–dendrimer complex, pegylated dendrimers (mPEG–dendrimer), Pulmospheres™, 9nitrocamptothecin (9NC) encapsulated into DLPC liposomes, Lectins, Mucoadhesive nanoparticles coated with mucoadhesive polymers, Poly-lactide-co-glycolide (PLGA), alginate and solid lipid nanoparticles
Cardiovascular systems (CVS)	Resveratrol-loaded nanoparticles micelles with a clotbinding peptide, cysteine-arginineglutamic acid-lysine-alanine (CREKA), magnetofluorescent nanoparticles, paramagnetic liquid perfluorocarbon nanoparticles incorporated a peptidomimetic victronectin antagonist, modified chitosan nanoparticles with a peptide targeting ligand

Nanoparticle mediated antiretroviral therapy

Acquired Immunodeficiency Syndrome, more often referred to as AIDS, is currently representing one of the most significant worldwide concerns. AIDS is the sickness that manifests itself when therapy is not available. AIDS could not be cured with any of the treatments that were available anywhere in the globe, despite the fact that conventional therapy was reported. The currently available therapeutic medication, which is referred to as "highly active antiretroviral treatment" (HAART), has made a substantial contribution to the reduction of the death rate. However, it is important to highlight that Home-Administered Antiretroviral Therapy (HAART) is not an effective technique of therapy since it has the potential to reintroduce a few adverse effects to the patient. Furthermore, the medicine that is administered has a restriction, such as low drug stability when treated in a gastrointestinal environment. In light of this, nanodelivery medication was developed with the purpose of enhancing drug release and preventing drug restriction. In order to improve the bioavailability of these medications and protect patients from the adverse effects that are associated with them, nanoparticles have the ability to deliver a targeted and sustained release of these medications. The following table provides a summary of several examples of nanoparticle medicines that are utilised for the treatment of AIDS:

TABLE 2 Examples of nanoparticle drugs used for AIDS therapy and its functions in summary

Examples	Functions
Poly (isohexyl cyanate) nanoparticles of zidovudine	for targeting the lymphoid tissue in the gastrointestinal tract
Polyhexylcyanoacrylate nanoparticles	for the delivery of zidovudine thus improving its bioavailability
Zidovudine-loaded poly(isohexyl cyanate) nanoparticles	Accumulated in the cells of the reticuloendothelial system
Poly(epsilon-caprolactone) nanoparticles loaded with saquinavir	for targeting the phagocytic mononuclear system
Stavudine, zidovudine and lamivudine entrapped in polybutylcyanoacrylate (PBCA) and methylmethacrylatesulfopropylmethacrylate (MMA-SPM) nanoparticles	for brain targeting
Dendrimers	deliver antiretroviral drugs
Tuftsinconjugated with poly(propyleneimine) dendrimers loaded efavirenz	for targeted delivery to macrophages and enhanced cellular uptake by mononuclear phagocytic cells
Stavudine loaded into mannosylated and galactosylated liposomes	greater cellular uptake by cells of the mononuclear phagocytic system and greater accumulation in organs of the reticuloendothelial system
PLGA nanoparticles containing ritonavir, lopinavir and efavirenz	increased uptake of the drugs by macrophages
PHCA nanoparticles containing zidovudine	higher drug concentration in the organs of the reticuloendothelial system
PPI dendrimer-based nanocontainers	for targeting of efavirenz macrophages

Cancer is a group of diseases involving abnormal cell growth with the potential to invade or spread to other parts of the body. Cancer can start almost anywhere in the human body, which is made up of trillions of cells. Normally, human cells grow and divide to form new cells as the body needs them. When cells grow old or become damaged, they die, and new cells take their place. When cancer develops, this orderly process breaks down and the cells become more and more abnormal, survive longer and new cells form when they are not needed. These extra cells mutate rapidly without stopping and form growths called tumors.

Prostate cancer is the sixth leading cause of cancer death among men worldwide and is expected to grow to 1.7 million new cases and 4,99,000 new deaths by 2030 simply due to the growth and aging of the global population (J. Ferlay, et al., 2012). This type of cancer is prevalent in men between the ages of 65-79 years old, with 25% of cases are occurring in men younger than 65 years old. Treatments that are currently available for prostate cancer include surgery, hormone therapy, radiation therapy and chemotherapy. These treatment methods are either very invasive or have harsh side effects. Though chemotherapy is successful to some extent, the main drawbacks of chemotherapy is the limited accessibility of drugs to the tumor tissues requiring in high doses, intolerable toxicity, development of multiple drug resistance and their non specific targeting.

II.   CONCLUSIONS

A wide variety of procedures and tactics that can optimise the delivery of medication into the targeted cell are made available by nanodelivery systems. Some examples of these systems are nanosuspensions, polymeric nanoparticles, and solid-lipid nanoparticles. They were highly effective in releasing the medications inside the human body, as well as managing the time to protect the apopotosis cancer cell, increasing the bioavailability of prospective therapy, and ensuring that it was biocompatible with the body. Additionally, the carcinogenicity of the medications may be identified at an early stage, prior to their release to the market, which is very important. In addition, the use of nanodelivery has the potential to improve the physiological and particular location of the cell that is being addressed. As a result, one may draw the conclusion that nanodelivery drugs can be utilised throughout the entirety of the drug development process, beginning with formulations and finishing with therapeutic applications, in order to achieve optimal delivery in clinical trials.

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