BIODEGRADABLE POLYMERIC NANOPARTICLE FOR THEAPEUTICE CANCER

Inderpal Singh[1]*, Prabhjot Singh[2], Dewak Kumar[3], Taranpreet Kaur[4], Tamanna[5], Prof Gaurav dhiman[6]

[1,2,3,4,5,6]Shivalik college of pharmacy Naya Nangal

[*]***Corresponding author***
email Id: longijatt@gmail.com

Abstract

Biodegradable polymeric nanoparticles have emerged as an advanced and promising platform in cancer therapeutics.These nanoparticles are capable of encapsulating anticancer drugs and delivering them selectively to tumour sites.They help to improve bioavailability, reduce systemic toxicity, and enhance therapeutic index.Polymers such as PLGA, PLA, PCL, and chitosan are commonly used due to their biocompatibility and controlled degradation nature.By modifying particle size and surface properties, nanoparticles achieve enhanced permeability and retention (EPR) effect for passive tumour targeting.Surface functionalization with ligands, antibodies, or peptides further allows active targeting of specific cancer cell receptors.This improves cellular uptake and reduces drug loss during circulation.Biodegradable polymeric nanoparticles also offer sustained and controlled drug release, decreasing frequent dosing requirements. Many anticancer drugs like doxorubicin, paclitaxel, and cisplatin have been successfully loaded in such polymeric systems.Nanoparticle-based therapy can overcome issues of drug resistance and poor solubility of hydrophobic anticancer agents.These carriers also protect drugs from enzymatic degradation before reaching the tumour.Preclinical studies have demonstrated significant tumour growth inhibition and reduced side effects.Advanced nanocarriers can also co-deliver multiple drugs for combination cancer therapy.This helps in synergistic action and improved treatment response.Biodegradable nature ensures safe metabolite formation and minimal residue accumulation in tissues.Overall, polymeric nanoparticles represent a safe, effective, and targeted platform for cancer management.Future research is focused on clinical translation, scalability, and regulatory acceptance.Personalized nanomedicine and precision drug delivery can be achieved through these systems.Therefore, biodegradable polymeric nanoparticles hold great potential for next-generation therapeutic cancer treatment.They are a transformative approach in modern oncology and nanotechnology-based drug delivery.

1. Introduction

Nanotechnology is revolutionizing cancer drug delivery by using nanoscale particles to deliver therapeutic agents directly to tumor cells, improving efficacy and reducing side effects. These nano carriers, such as liposomes, dendrimers, and polymeric micelles, are engineered to target tumors via passive and active mechanisms accumulate preferentially at tumor sites, and release drugs in a controlled manner This targeted delivery system overcomes challenges in conventional chemotherapy, such as poor solubility, drug resistance, and off-target toxicity paving the way for more precise and successful cancer treatment

Type of nano particles in theragnostics

1)GOLD NANOPARTICLE

Gold nano particle have emerged as a promising tool in theagnostics due to their versatility and num -erous potential biological application .Their high surface to volume ratio and unique optical feature -make them valuable for noninvasive imaging [1]

2)IRON OXIDE NANOPARTICLE

A mutation or cellular aberration that favours tumor formulation in humans in the initial step in a com plex chain reaction that culminates in cancer. The presence of distinct sets of cellular receptors in nor - mal and cancer cells opens the possibility of imaging probes targeting specific receptors [2]

3)SILICA NANOPARTICLE

Silica has earned a positive reputation for being completely safe due to its historical use as a surgical implant .Moreover the ability to precisely control the size and shape of silica nano particle during manu facturing is well-documented.[3]

4)CARBON NANOTUBES

Biomedical researchers are interested in the distinctive characteristics of carbon nanotubes , such as their stable nanoscale size , vast surface area [4],The unique optical characteristics of CNT make them valuable in photoacoustic imaging [5]

5)QUANTUM DOTS

Quantum dots provide a wide surface area for drug conjugation due to their inflexible structure. The two most common function group used for medicine binding are carboxylic acid groups and free amine groups[6]

6)LIPOSOMES

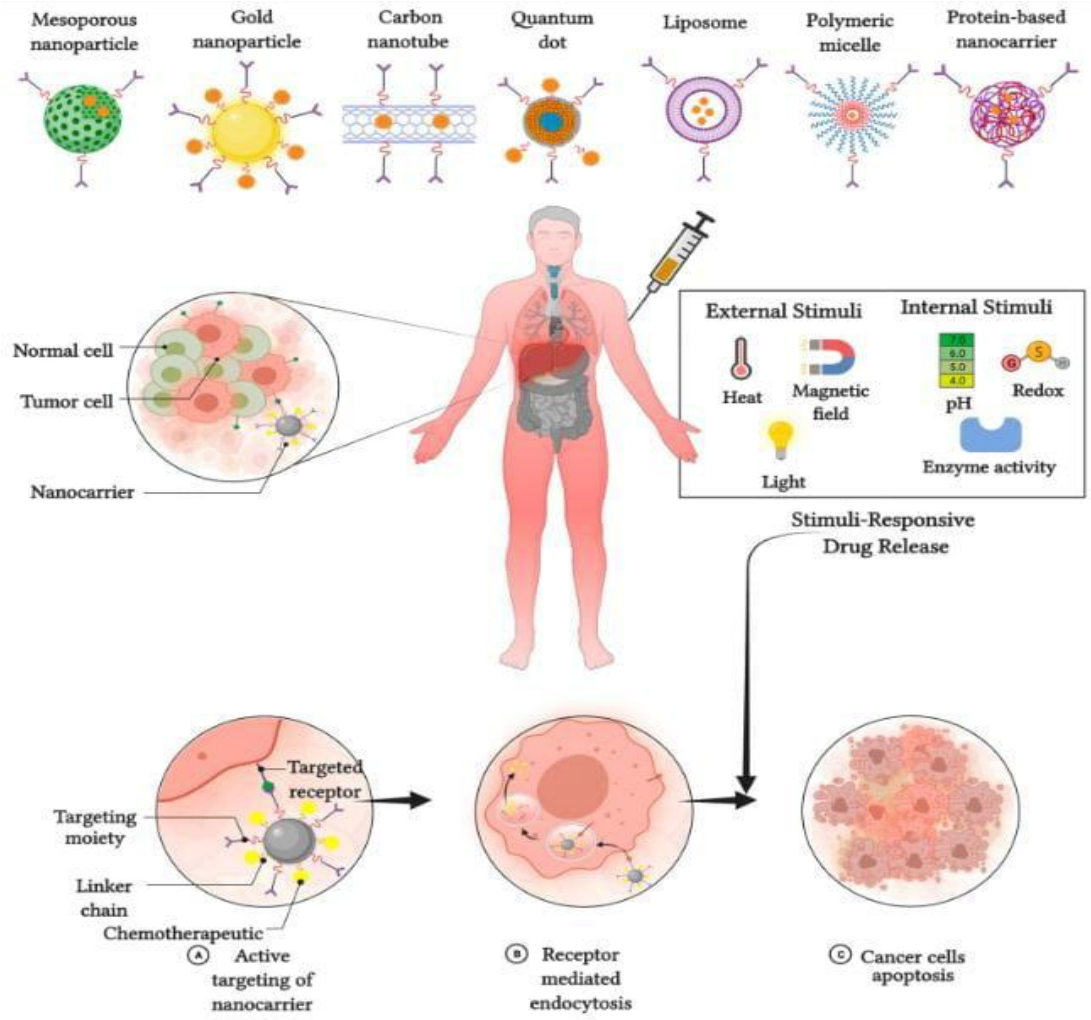
The distinctive round shape of liposomes allows them to encapsulate hydrophilic chemical in the central aqueous compartment and hydrophobic compounds in the lipid bilayers ,shielding them from destruc -tion [7]

Table no 1.0 SELECTED CLINICAL TRIALS OF BIO DEGRADABLE POLYMERIC NANO PARTICLE CANCER DRUG DELIVERY SYSTEM

NAME	*COMPANY*	*MATERIAL*	*CARGO*	*PHASE*	*CANCER*	*RESULT*	*REFERNCE*
CALAA-01	Calando pharmaceuticals	PEG-Cyclodextrin	sirna	1	Solid tumors	Significant toxicity was not observed	[8]
BIND-014	Bind therapeutic	PLGA with PSMA targeting ligand	Docetaxel	1	Prostate	Significant toxicity was not observed,12%overall response rate	[9]
NC-6004	Nano carrier	PEG-POLY block co-polymer	cisplatin	1	Pancreatic,head,and,neck	Significant toxicity was not observed	[10]
CRLX101	Newlink genetics corsporation	PEG-Cyclodextrin	camptothecin	2	Lungs,ovarian ,solid,tumors	Significant toxicity was not odserved,16%overall response rate	[11,12]
NK105	Nippon kayaku co.	PEG-polyaspartate	paclitaxel	2	Breast,gastric	Significant toxicity was not observed,25% overall response rate.	[13,14]

TARGETED DRUG DELIVERY TO TUMOR CELLS

Targeted drug delivery to tumor cells using nanoparticles or ligands that specifically bind to cancer cell surface markers .releasing therapeutic agent directly at the tumor site and Graphical explain the targeted drug delivery to tumor cells show in figure [1.1][15]



The nano partical or drug conjugates release therapeutic agent in controlled manner maintaining effective drug concentration at the tumor site

NCs used for drug delivery in cancer therapy

NCs offers several advantages over the direct administration of refined chemotherapeutic drugs and reduction of side effect that improves therapeutic efficacy[17.31.32] here firsty we discuss the main Type of NCs that have been used delivery systems in the treatment of cancer

TABLE NO [1.1] INORGANIC DRUG DELIVERY NCs IN CANCER THERAPY

MATERIAL	***DESCRIPTION OF CARRIER***	***MATERIAL ADVANTAGE***	***SEPCIFICITY***	***REFERENCE***
CNT	Anti p glycoprotein antibody functionalized CNT doxorubicin	Defeats multidrug resistance	Leukemia cells	[18]
CNT	Multi walled CNT decorated with guanidinylated dendritic molecular transport	Efficient dox delivery	Prostate cancer cells	19
CNT	PEG-CNT complex	Mitochondrial targeting	Lungs cancer cells	20
Layered double hydroxide NPs	Co delivery of 5-fluorouracil and sirnas	Prevent drug resistance	Various cancer cells	21
Layered double hydroxide NPs	Raloxifene intercalated into the interlayer gallery of ldm host	Improve therapeutic efficacy	Solid tumor	22
Iron oxide NPs	Phospholipid PEG coated superparamagnetic	Chemotherapy and hyperthermia treatment	Solid tumor	23
Magnetic NPs	Pluronic F127 anchored iron oxide NPs	Active and passive delivery of hydrophobic drug	Folate positive cancer cells	24
Magnetic NPs	Chitosan coated superparamagnetic iron oxide NPs	Doxorubicin delivery	Ovarian cancer cells	25

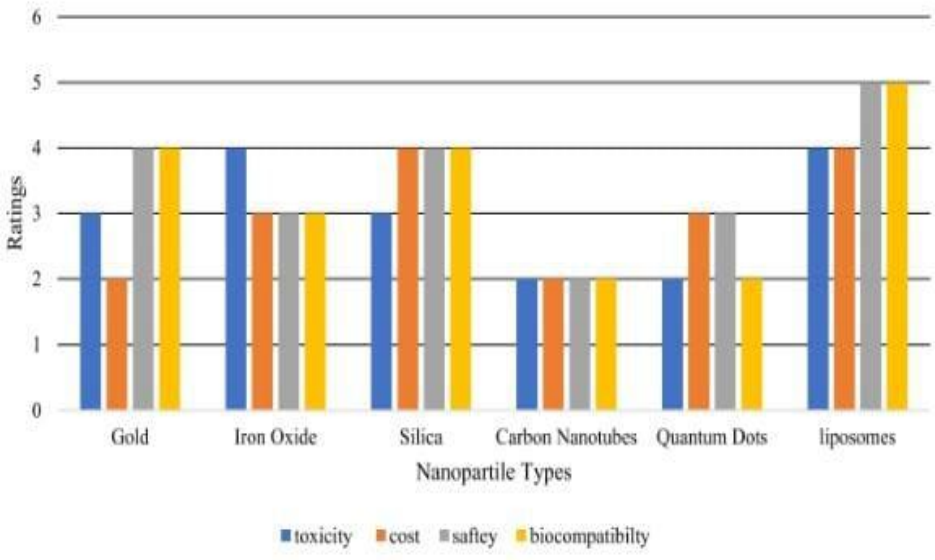
Mesoporours silica NPs	Azobenzene modified mesoporous silica for NIR triggered anticancer drug delivery	Drug release rate can be controlled by varing the intenstiy	Solid tumor	26
Mesoporours silica NPs	Hyaluronic acid capped mesoporous silica NPs	Site selective controlled release delivery	M DA-MB-231 AND NIH3T3 CELLS	27
QDs	Riboflavin targeting grapheme quantum dots-PEG-benzofuran	High potency	LARYNGEAL	28
QDs	Hyaluronic acid\ferrocene anchored FC-GQD-HA	Selrctive binding to cd44 receptors	DIVERS RANGE OF CANCER	29
QDs	Hederagenin anchored black phosphorus QDS encapsulated with platetet membrane	Mono dispersive capacity	IN VIVO APPLICATION	30

2D-MATERIALS NCs

2D materials have excessive light photodynamic and heat conversion profciency, therefore they retain various benefts in biomedical applications. Tese characteristics provide them high potentials in medicine felds, including imaging [33], sensing [34] and therapy [36, 37].In the meantime, 2D materials exhibited a challenging capability in drug delivery with various advantages. One of the exclusive crucial features of 2D materials is the lamella organization, that ofers the huge surface space for high drug loading efciency [38]. Yu et al. synthesized a reduced GO nanocomposite modifed with a polydopamine (PDA). Tey coated the dopamine-modifed rGO surface with antiarrhythmic peptide 10 which limit tumor development about more than 95% while used with radiotherapy [39]. Tis innovative drugs possesses several abilities, such as large surface area, excellent biocompatibility, and a high drug loading capacity. Moreover, these NCs confrmed subsequent pH responsiveness and drug release. As stated by Xing et al. injectable hydrogel made of black phosphorous nanosheets and cellulose exhibits noteworthy antitumor activity in contrast to PTT. Interestingly, these nanoscale hydrogel platform is non-toxic and 100% biocompatible as confirmed by both in vitro and vivo studies [35]

COMPARISON OF NANOPARTICAL BASED ON TOXICITY COST,SAFTEY,AND BIOCOMPATIBILITY

Comparative analysis of nanoparticles: based on toxicity, cost, safety, and biocompatibility The inherent compatibility of nanoparticles with the body and their degradability over time is a fundamental advantage when employing them in MRI [40]show in figure[2.0] Researchers are currently exploring advanced techniques in MRIbased imaging through the use of nanoparticles, like magnetic resonance spectroscopy (MRS) and magnetic resonance angiography (MRA)[41]

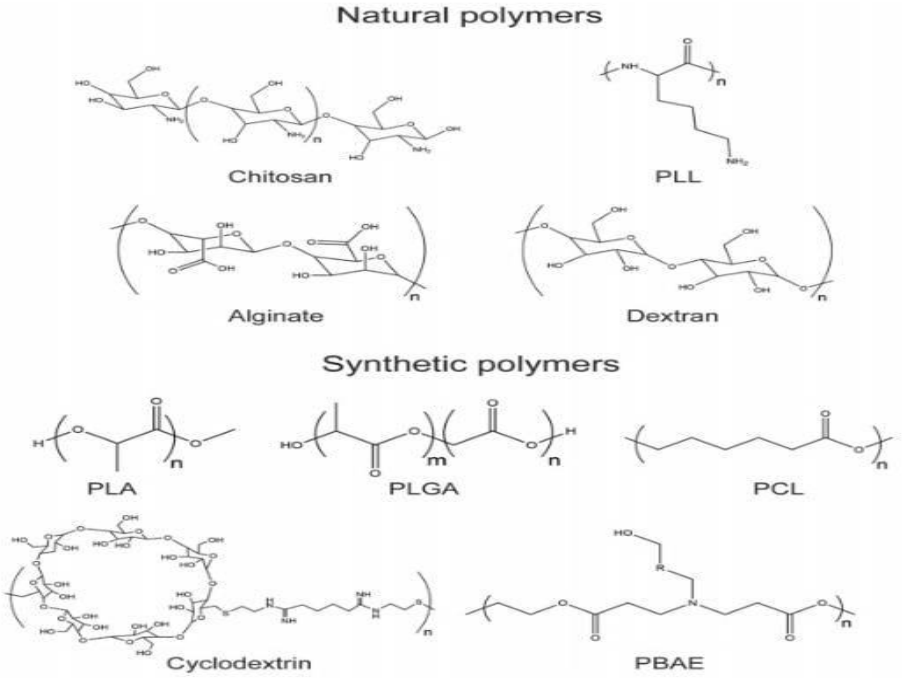


NATURAL POLYMERS

Naturally derived polysaccharide and protein-based polymers (Figure 2.1) have already been approved for diverse food, cosmetic, and medical applications (42). They show excellent biocompatibility since they are broken down by enzymatic degradation into easily metabolized peptides or polysaccharides in the body, and this degradation rate can be tuned for a desired release profile (43). However, these polymers are more variable batch-to-batch, often require chemical modification to act as efficient nanocarriers, and must be extensively purified to avoid immunogenicity.

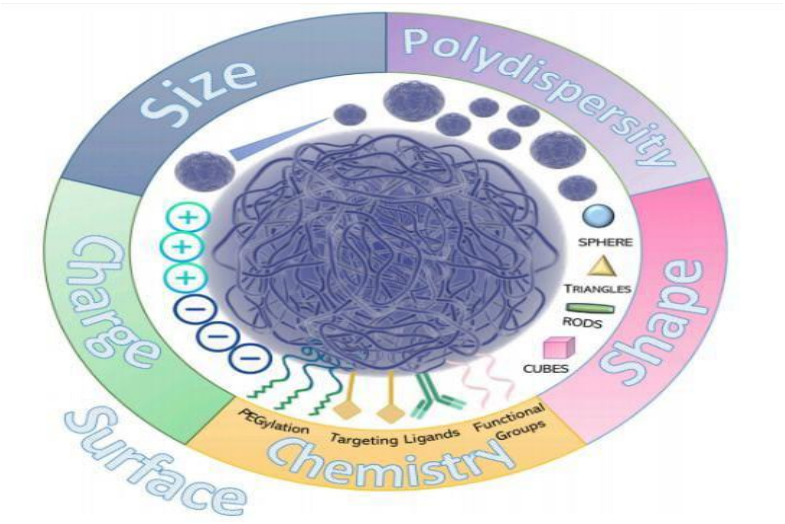
SYNTHETIC POLYMERS

Synthetic polymers[44] (Figure 2.1) are engineered with desirable properties such as charge, hydrophobicity, and degradation profile, which are optimized for particular cargos, delivery routes, and disease targets. Synthesis is controlled for low batch-to-batch variability, and production is typically scalable for large scale manufacturing. However, unintended degradation products or metabolites can cause synthetic polymers to be cytotoxic or immunogenic.



PHYSICO-CHEMICAL PROPERTIES OF POLYMERIC NANOPARTICLES

Depending on the processes used for the preparation of polymeric nanoparicles, these can be either nanospheres or nanocapsules. Nanospheres are matrix systems in which the drug is dispersed throughout the structure or adsorbed onto the surface,whereas nanocapsules are systems in which the drug is contained within the core (aqueous or oily) surrounded by a polymeric shell[45] drug-release profiles and surface characteristics, can all affect their behavior in complex biological environments. At the same time pH and ionic strength of the dispersion medium can influence biodistribution, pharmacological efficacy, and safety of the entrapped drug(s) (Figure 3.0)[46]



PARTICALE SIZE

The size of nanoparticles used as drug delivery systems should be large enough (diameter of ~100 nm) to prevent their rapid escape from blood capillaries and renal filtration, but small enough to avoid mononuclear phagocyte system (MPS) clearance (Yanget al., 2016). Several techniques are used to evaluate the mean diameter and size distribution of nanoparticles which include laser scattering (dynamic or static light scattering, laser diffraction), field flow fractionation (FFF), electron microscopy(EM), centrifugation (analytical ultracentrifugation andcentrifugal particle sedimentation), tunable resistive pulse sensing (TRPS), and particle tracking analysis (PTA) (Caputoet al., 2019). While many of these

are still being perfected(Halamoda-Kenzaoui et al., 2019), dynamic light scattering(DLS) is the most common sizing technique. [47]

PARTICLE SHAPE

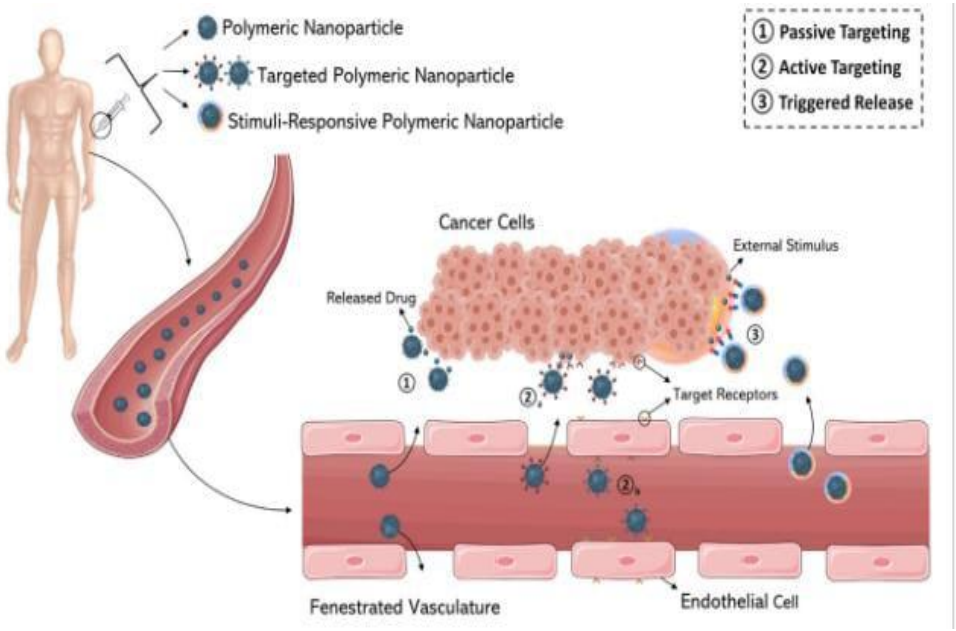
In addition to particle size, the shape of nanoparticles is also an important parameter because it affects their pharmacology and functions (Truong et al., 2015). Whereas spherical nanoparticles are the most desired and versatile types with high surface-tovolume ratio and peculiar optical properties, asymmetrical and non-spherical polymeric nanosystems have also been of interest in tissue engineering, immune-engineering, and for theranostic applications (Banik et al., 2016).[48] Because of isometry, spherical particles have better cellular uptake independently of the way they are presented on the cell surface, but in the case of rod-like systems, the uptake is best when they perpendicularly interact with biological surfaces (Stylianopoulos and Jain, 2015).[49]

PARTICALE SURFACE

Surface characteristics contribute to the solubility of particles,aggregation features, ability to bypass biological barriers,biocompatibility, and targeting properties. The majority of nanoparticles used as drug delivery systems have a hydrophilic surface which is able to favorably interact with the aqueous environment of biological systems. Indeed, a common strategy for avoiding the MPS uptake of nanomaterials is to introduce neutral hydrophilic polymers in order to decrease the opsonizationand hence macrophageal phagocytosis. The use of polyethylene glycol (PEG) or poly(ethylene oxide) (PEO) to coat nanoparticles is a prime example of this strategy (Hu et al., 2018). The hydration layer formed by PEG chains around the nanoparticles sterically precludes their interaction with other nanoparticles as well as blood[50]

DEUG TARGETING

An important goal in nanomedicine is to combine the unique properties of nanosystem in order to enhance the characteristics of an entrapped drug. [51]on the particle surface;specific ligand-receptor interaction increase spatial accumulation of nanoparticle in tissues of interest [fig 3.1]



CONCLUSIONS AND PERSPECTIVES

Despite the fact that PNs have been considered promising formulations for cancer therapy, their successful application is limited by various drawbacks (Kumari et al., 2016). In particular,changes in the physico-chemical properties of nanocarriers (size,surface charge, aggregation, appearance of protein corona) promoted by the components of the blood stream and early drug release in addition to the development of multiple drug resistance by cancer cells, all limit their pharmacological efficacy. Moreover, the toxicity of PNs made up of novel materials, including organic polymers or mixed systems with inorganic materials such as gold, silver oxide and silica are issues for clinical application. The particle size, shape,sedimentation, drug encapsulation efficacy, desired drug release profiles, distribution in the body, circulation and cost are some of the parameters used to select suitable formulations for an efficient cancer targeted drug delivery (Biswas et al., 2013).[52]However, although many efforts have been made to develop novel targeted nanocarriers, only a few of them are approved for clinical use by the FDA (Barenholz, 2012). This phenomenon could be due to the lack of knowledge on the distribution and accumulation of targeted nano particles after oral or intravenous administration and/or to the deficiency of regulatory aspects (e.g., study design and approval challenges) (Kumari et al., 2016)[53]. The future of nano medicine, especially by means of PNs, will improve the efficacy of conventional therapies by exploiting the concept of personalized therapy as a consequence of the opportunity of modulating the various parameters of nanosystems as

previously described. For instance, the application of PNs for the combined therapy of tumor (simultaneous delivery of multiple anticancer drugs/combination of conventional chemotherapeutics with other treatment modalities) as well as the delivery of anticancer drugs in association with photosensitizing agents, nucleic acids, antiangiogenic compounds may all better exploit the versatility of the proposed systems and their ability to overcome MDR mechanisms thus increasing the final anticancer effect. The continuous research on PNs in both preclinical and clinical studies will improve the prevention, diagnosis and treatment of cancer.[54] Development of polymeric nanocarriers for cancer therapy has the potential to bring new combinations and multimodal avenues of therapeutic treatments to the forefront, including new anti-angiogenic therapies and immunotherapies.[55]

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