

Polymer nano materials as drug delivery system for renal disease: A short commentary

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Abstract

Particularly in the field of smart drug delivery, polymer played a significant role because it can deliver therapeutic agents directly into the intended site of action, with superior efficacy. The perfect requirements for designing nano-particulate delivery system are to effectively be controlled particle size, surface character; enhance permeation, flexibility, solubility and release of therapeutically active agents in order to attain the target and specific activity at a predetermined rate and time. The smart drug delivery systems have been successfully made by the advances in polymer science in the bio-nanotechnology field. Recently, these advances have been found in various medical applications for nano-scale structures in smart drug delivery. The smart drug delivery systems should possess some important feature such as pre-scheduled rate, self controlled, targeted, predetermined time and monitor the delivery. This article comments on the important efficacy of polymer nanoparticles for drug delivery which has enormous benefits to medical science and polymer industry.

Drug targeting

In the field of smart delivery of drug into human system polymer nano particles have been playing significant role in medical field. In order to treat the effected area. Drug-targeting aims at reducing the obstacles caused by extra-target effects, the narrow therapeutic index and the inactivation of the drug before reaching its target. Unfortunately, most of the pharmaceuticals used nowadays lack a selective delivery into their target tissues. The selective delivery or selective activation in the targeted tissue minimizes toxic side effects [1]. The improvement of the pharmacokinetic profile should be accomplished by drug targeting strategies [2,3]. However, diverse drug-targeting concepts have been pinpointed in order to fulfill those principles [4,5].

A variety of drug delivery systems carriers such as viral vectors [6], colloidal particles or macromolecular carriers (such as liposomes [7], nanoparticles [8], microspheres [9], lipid particles and polymeric micelles [10-12], modified-plasma proteins, polysaccharides [13], biodegradable carriers [14], dendrimers [15], antibodies [16], and peptide carriers have been developed [17].

A huge diversity of drug delivery systems has been developed to boost the therapeutic effect in the target tissue. The exclusive transfer of a drug to the targeted site of action that has been accomplished with minimal toxic side effects, and the usage of a pharmacologically inactive vector are main features of an ideal carrier for drug-targeting delivery system [18]. A specifically targeting drug delivery system can serve not only as a therapeutic vehicle but also as a research tool. Generally, the drug-targeting approach depends on the drug to be delivered, the target tissue, and of course the proper delivery system [17].

Carriers might be classified into three major types; the particle-type, the soluble and the cellular carriers. Liposomes, nanoparticles, microspheres, lipid particles, and polymeric micelles are all included in the particle-type carriers. Whereas peptides, modified-plasma proteins, polysaccharides, and biodegradable carriers are classified under soluble carriers. However, viral vectors belong to the cellular carriers.

Despite the advantages provided by the cellular carriers depending upon their natural biocompatibility and their possibility to cause an immunological response is still a obstacle [18].

In recent decades, polymers are widely used as biomaterials due to their favorable properties such as good biocompatibility, easy design and preparation, a variety of structures and interesting bio-mimetic character. Particularly in the field of smart drug delivery, polymer played a significant role since it can deliver therapeutic agents directly into the intended site of action, with superior efficacy. The ideal requirements for designing nano-particulate delivery system are to effectively be controlled particle size, surface character; enhance permeation, flexibility, solubility and release of therapeutically active agents in order to attain the target and specific activity at a predetermined rate and time [18]. The smart drug delivery systems have been profitably made by the advances in polymer science in the bio-nanotechnology field. Recently, these advances have been found in various medical applications for nano-scale structures in smart drug delivery.

Polymers can be classified according to their natural or synthetic origin, stability (whether biodegradable or not), backbone, and upon their chemical nature (vinyl and acrylic polymers, polyethylene glycol (PEG), polysaccharides, polyamino acids, etc.) [19]. The natural polymer carriers comprises several polysaccharides (dextran, inulin, or chitosan), proteins (albumin) or glycoproteins (transferrin), as well as cationic polymeric carriers such as PLL (poly-L-lysine) backbones [20-25].

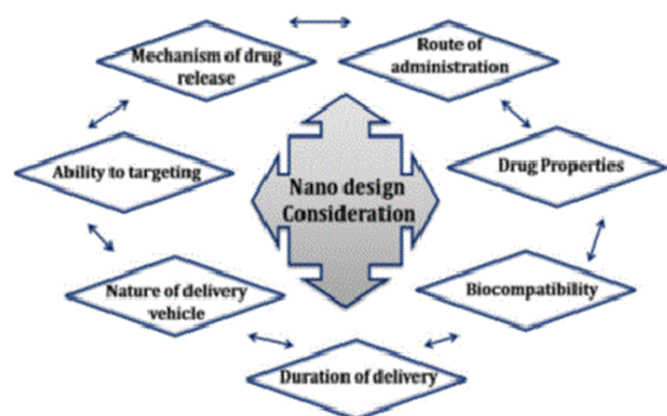
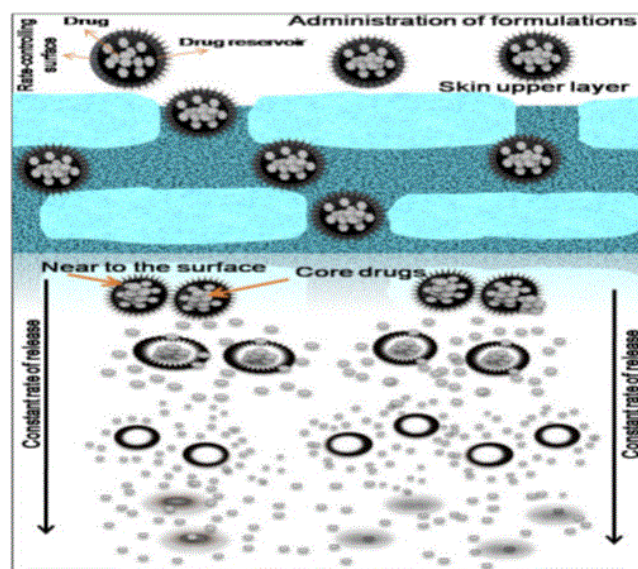
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Key words: Polymer nano particles, drug delivery, applications

Received: August 21, 2017; **Accepted:** September 25, 2017; **Published:** September 28, 2017

Table 1. Examples of various nanoparticles with different functionalization and therapeutic uses based on the targetPolymer Nanoparticles for Smart Drug Delivery [5].

Nanoparticles	Functionalization	Drug	Use	Reference
Human serum	albumin Amino/acid group	Doxorubicin	Antineoplastic	260
Trimyristin	Sterically stabilized	Paclitaxel	Ovarian, lung, breastcancer	261
PLLA-b-PEG	Folate targeted	Doxorubicin	Solid tumors	262
PEG-PE	Lipid conjugated	Paclitaxel	Various cancers	263
PEG	Lipid conjugated	Tamoxifen	Lung carcinoma	264
Polymer-lipid hybrid	Lipid conjugated	Doxorubicin	Solid cancer	265
PCL-b-trimethylene carbonate-PEG	Serum protein	Ellipticin	Anticancer	266
PAMAM	dendrimers	Folic acid ethotrexate	Epithelial cancer	267
PEG	Albumin bound	Doxorubicin	Various cancers	268
Micelles	Biotin-antibodyconjugated	Daunomycin	Brain tumor	269
Poly(DEAP-Lys)-b-PEG -b-PLLA)	Poly(lysine	Doxorubicin	pH sensitive tumor	271
PLGA-b-PEG-COOH	PSMA	Anti cancer	Prostate Cancer	272
PEG or PE particles	Transferrin	Oligonucleotide	Brain- gene	273
PLLA-PEG	Biotin	Anti cancer	Cancer therapy	274
Polystyrol	Sc-TNF	Anti cancer	Cancer therapy	275
PLA	Aptamer	Anti cancer	Prostate cancer	276
PE	RGD peptides	siRNA	Vasculature cancer	277
mPEG/PLGA	Peptidomimetics	Anti cancer	Brain cells cancer	278
PLA	Galactose	Retinoic acid	Hepatocytes	279
PLGA	MP lipid A	Anti cancer	Dentritic cells	280


Figure 1. Requirements of several factors for simultaneous consideration to design a polymeric nanoparticle for the smart drug delivery system [5].

Figure 2. Schematic diagrams represent the rate controlled drug delivery systems of topical applications.

Nanoparticles and microspheres can be assign either to the soluble or to the particle type carriers. The major backbone of these carriers is based on range of polymers such as dextran, ficoll, sepharose, or PLL. Nowadays, poly(D,L-lactic-co-glycolic-acid) (PLGA) microspheres have been expansively studied to gain a wide acceptance for application as nanoparticles and microspheres following to their approval for use in humans by the American Food and Drug Administration (FDA) [26]. Parenteral application of microspheres and nanoparticles for the cell selective delivery of drugs is not the only administration route since they have been studied more recently for their application in oral and pulmonary delivery of peptides and peptidomimetics [20].

Antibodies are aimed at targeting tumor-associated antigens with the aim of over-expressed by tumor cells. Therefore, the birth of innovative techniques such as recombinant DNA and protein engineering has led to the development of optimal tailored-antibodies [22]. The stretch of amino acids or peptides, contained by a biomolecule which is responsible for specific receptor binding, is called the homing-ligand. Their covalent attachment to a carrier backbone can result in targeted DDS [23]. Polymeric micelles are small (10-100nm) in size and they have a core-shell structure. In contrast to their hydrophobic core, the shell represents their hydrophilic part. Micelles provide a penetration property within the tissue for targeted DDS. Usually, their efficacy is still demanding since they disintegrate rapidly *in vivo* [23-26]. Usually, the application of peptide carriers requires an over-expressed receptor and adequate *in vivo* stability. Additionally, the conjugated drug should not hamper with the binding region of the peptide. Peptides were developed in different ways, for example for targeted transport using carrier peptides for tumor and tissue targeting [25-26].

Conclusions

Kidney diseases require, usually, long-term administration of therapeutics; therefore, they are always accompanied with systemic toxicities and adverse side effects. The uses of bio-nanotechnology in therapeutics a number of unexpected inventions have been done recently on polymer based nano meters, which have great attention in the field of smart drug delivery applications. Several attempts have been performed aiming to target the kidneys, and the majority of kidney-specific delivery systems targets the proximal tubular cells and may

contribute to the treatment of renal diseases. Additionally, the overall charge of the carrier seems to play a key role in kidney-specific drug delivery. The biomaterials including protein based nano polymers, polysaccharide based polymers, natural or synthetic or semi-synthetic nano polymers, various biomaterials and combination of polymer have utilized to prepare various kinds of nano-formulations towards the smart drug delivery applications. Such strategies involve LMWPs, PVP, PVD, LMWC, G3-C12 peptide, ϵ PLL derivatives and the carrier peptide (KKEEE)3K. The specific uptake by renal proximal tubular cells is confirmed in many cases to be megalin-mediated endocytosis. Several nanoparticle based drug delivery systems have been approved in clinical trials, some of them in under pre-clinical trial levels.

Acknowledgement

The authors acknowledge management of University of Namibia for encouragement in research.

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