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Types of Nanocarriers – Formulation Method and Applications

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Abstract

Colloidal nanocarriers have provided a plethora of opportunities in terms of advancing the drug delivery field based on their immense biocompatibility, size, target-specific delivery and increased efficacy. The current passage entails an in-depth discussion regarding the varied types of nanocarriers such as dendrimers, polymeric micelles, solid-lipid nanoparticles along with their conventional formulation strategies and their specific applications. These nanoparticles have been extensively researched, till date, for their different diagnostic as well as therapeutic uses and their recent developments have been covered in this short review.

Introduction

Nanocarriers, when presented in the colloidal form, have afforded utmost advantages over conventional delivery systems. These possibilities are not devoid of challenges, but by and large, various research activities, till date, have been undertaken to circumvent these challenges. This research has embodied an in-depth discussion about their formulation, types and their site-specific delivery strategies. Some of the general nanotechnological delivery systems encompass quantum dots, dendrimers and integrins have been specifically utilized for targeted delivery of either therapeutic or diagnostic or even some theranostic agents. Delivery of the payload to the active target site precisely, over a period of time, without ushering in the toxic potential of these potent drugs remains the ultimate yardstick of drug delivery [1]. The risk to benefit ratio needs to be at minimal levels at all costs, for the safe and effective delivery of these highly hydrophobic drugs. Nanocarriers have traditionally been used to improve upon the existing pharmacokinetics and bio-distribution potential of various poorly water-soluble drugs, thus minimizing their toxicity potential [2]. They bring about a lot of improvement in their water solubility, and also increase the stability of a number of therapeutic agents like peptides [3]. These nanocarriers enable the drugs to remain in circulation for longer period of times bypassing the endosome-lysosome processing [4]. Generally, when these nanoparticles come into contact with cells or tissues, they provide good compatibility [4] as most of these agents are GRAS (Generally Recognized as Safe) excipients.

Formulation Techniques and Applications

Production of nanoparticles generally encompasses two basic approaches: top-down or bottom-up techniques of the components [2]. The top-down approach involves the breaking down of larger particles into smaller nano-sized particles through processes such as milling, grinding or by the use of laser. The bottom-up approach involves the engineering build-up of nano-sized particles on an atom scale arrangement, usually regulated by thermodynamic controls [5]. Bottom-up techniques are known to create huge aggregates or cluster of masses with common techniques such as precipitation, anti-solvent techniques and so forth. One of the other techniques such as co-precipitation involves a complex coacervation method thus aiding the preparation of nanoscale core-shell particles, which provides good dispersion stability to highly insoluble drugs [6]. One of the classic examples is the preparation of Ibuprofen nanoparticles, which are stabilized by Diethyl Amino Ethyl Cellulose (DEAE) dextran. This process involves precipitation of Ibuprofen in a highly supersaturated solution, followed by the deposition of DEAE Dextran through electrostatic interactions [7]. Solid-Lipid Nanoparticles (SLN) are one such types of nanocarriers which were developed, as an alternative delivery system to the existing traditional carriers such as emulsions, liposomes and polymeric nanoparticles. Physiological lipids can be used in their synthesis, thus fulfilling the requirements of an optimal delivery system, which can incorporate both hydrophilic and hydrophobic drugs. The basic advantages of SLN can be summarized by the avoidance of organic solvents, use of physiologically biocompatible lipids and additionally, improved bioavailability and enhanced controlled release characteristics when incorporated into appropriate solid-lipid matrices [8]. Lipid-Drug Conjugates are another set of promising nanoparticles which can overcome some of the disadvantages of SLN such as low capacities to load hydrophilic drugs due to partitioning effects. An insoluble drug-lipid conjugate is synthesized either by salt formation (with fatty acid) or by covalent linking (to ester). Then this conjugate is subjected to processing by any surfactant solution, which then yields a nano-formulation using high pressure homogenization. These particles may have wide-spread applications in brain targeting of these drugs in protozoal infections [9]. Polymeric micelles are another set of nanocarriers which are core-shell structures created by spontaneous self-assembly of amphiphilic di/tri-block copolymers at a concentration above a known specific concentration, which is also called as the Critical Micellar Concentration (CMC) [10]. These micelles can be afforded extra robustness by various techniques such as core or shell cross-linking [11]. Chemotherapeutic agents, when administered alone, possess many unfavourable characteristics such as limited solubility and dose-limiting toxicity. These attributes can be substantially overcome by either covalently conjugating them to polymeric micelles or encapsulating these drugs in either the core or shell of these polymeric micelles. Dendrimers are another set of nanocarriers, which are highly monodispersed, branched with prolific drug entrapment properties. They possess multi-dimensional properties such as the presence of a hydrophobic core and hydrophilic surface thus providing a better loading platform for both hydrophobic and hydrophilic drugs. They can be easily conjugated with imaging as well as targeting agents owing to

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their multi-branched structures [1]. Because of these favourable binding characteristics, they serve as excellent carriers for chemotherapeutic agents. Partially Acetylated Polyamidoamine (PAMAM) dendrimers, when conjugated to a targeting molecule like biotin coupled with another imaging molecule, can be used for cancer therapy as well as diagnosis [12]. Solubility profiles of various drugs like ketoprofen can be enhanced multi-fold due to their unique solubilization properties [13]. PAMA dendrimers coupled with Polyethylene Glycol (PEG) have been reported to increase the loading capacity and more so, the circulation times of chemotherapeutic agents such as 5-Fluorouracil [14].

Conclusion

These nanocarriers thus possess some unique advantages, both as therapeutic and diagnostic agents. Through optimal and judicious use of these nanocarriers, facile delivery of proteins and peptides, targeted cancer therapy along with a simultaneous improvement in the efficacy and safety of these extremely potent drugs can be easily achieved.

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