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Chitosan Based Nanostructures

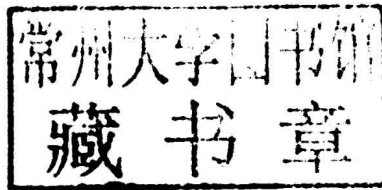
Drug delivery shuttles able to cross biological barriers

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Preface

A new era of science and technology has evolved in pharmaceutical research focused at development of different novel drug delivery systems. The evolution of an existing drug from its traditional form to a novel delivery system may considerably improve its performance in aspects of efficacy, safety and patient compliance. So the method of administering a drug can also have significant effect in its efficacy. In recent years the considerable advances in drug delivery systems have enabled more effective routes of administration.

A number of nanocarriers have been developed intended to transport and deliver drugs across mucosal barriers. These nanocarriers are particularly important in the case of drugs that are very unstable in biological fluids and can not cross epithelial barriers. Biotech compounds such as peptides, proteins, and nucleic acid based-drugs enter within this category of drug. In fact, despite the great potential of these macromolecules their clinical application has been greatly restricted by their extremely short action and the necessity of being administered by injection.

As a basic material for the formation of these nanocarriers we chose the polysaccharide chitosan. Two different types of structures are considered: (a) Chitosan nanocapsules, consisting of an oily core surrounded by a chitosan wall and (b) chitosan nanoparticles, which are nanomatrices of cross-linked chitosan alone or in association with other hydrophilic polymers.

Chitosan, a natural cationic polysaccharide, is prepared industrially by the hydrolysis of the amino acetyl groups of chitin, a naturally available marine polymer. Chitosan is a non-toxic, biocompatible and biodegradable polymer and has attracted considerable interest in a wide

range of biomedical and pharmaceutical applications including drug delivery, cosmetics, and tissue engineering. The primary hydroxyl and amine groups located on the backbone of chitosan are responsible for the reactivity of the polymer and also act as sites for chemical modification. However, chitosan has certain limitations for use in controlled drug delivery and tissue engineering. These limitations can be overcome by chemical modification. On suitable chemical modification, these polymers can provide better materials for drug delivery systems. Nanostructured drug carriers allow the delivery of not only small-molecule drugs but also of nucleic acids and proteins. Chitosan nanoparticles have gained more attention as drug delivery carriers because of their better stability, low toxicity, simple and mild preparation method, and providing versatile routes of administration. Their sub-micron size not only suitable for parenteral application, but also applicable for mucosal routes of administration, i.e., oral, nasal, and ocular mucosa, which are non-invasive routes. Furthermore, chitosan nanoparticles also showed to be a good adjuvant for vaccines. Therefore, the objectives of this book are to summarize the available preparation techniques involved chitosan nanoparticles, the recent applications of chitosan Nano/micro particles in oral and/or buccal delivery, the mechanism of cell entry, stomach-specific drug delivery, intestinal delivery, colon-specific drug delivery, and gene delivery, giving special emphasis to oral drug delivery and the application as targeted drug carriers of different types of drugs to overcome different biological barriers.

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1. Introduction

Nanotechnology is said to have brought a new era with unlimited applications, opening doors to new branches of academia and research today. Although many Nano applications are still promises, many of them could potentially change the way we live our lives.

Among the most prominent areas of medical research today is the design of drug delivery at the specific location and at the right dosage to reduce side effects.

Many drugs have problems of poor stability, water insolubility, low selectivity, high toxicity, side effects, and so on. Good drug carriers play a significant role in resolving these problems. Chitosan nanoparticles are drug carriers with wide development potential and have the advantage of slow/controlled drug release, which improves drug solubility and stability, enhances efficacy, and reduces toxicity. Because of their small size, they are capable of passing through biological barriers in vivo (such as the blood–brain barrier) and delivering drugs to the lesion site to enhance efficacy.

Modified nanoparticles also have other properties such as improved drug targeting. Under the action of enzymes in vivo, biodegradable nanoparticles can produce water and carbon dioxide without adverse effects, and have thus become the focus of increasing research.

Researches carried out on nanocarriers have shown that these nanostructures minimize and can prevent drug degradation as well as cellular efflux.[1] Drug release is also of concern when considering a polymer as drug carrier since the time and dosage of drug released are

crucial for the proper functioning of most drugs [2]. Polymeric nanoparticles have shown great promise as potential oral delivery systems especially for vaccines, as they protect encapsulated substances and are able to modify physicochemical characteristics, drug release and biological behavior [3]. The potential success of these particles in the clinic relies on consideration of important parameters such as nanostructure fabrication strategies, their physical properties, drug loading efficiencies, drug release potential, and, most importantly, minimum toxicity of the carrier itself.

Natural and synthetic polymers have been used as a promising tool for nanoscale drug carrier systems, especially in oral administration of poorly absorbed therapeutic drugs [4]. In recent years, great developments have been made in the field of mucoadhesive polymer systems in formulations that increase the residence time of drugs on mucosal membranes and subsequently, enhance the bioavailability of drugs with poor oral absorption [5, 6]. The potential use of polymeric nanoparticles as drug carriers/ drug delivery vehicles has led to the development of many different colloidal delivery vehicles. The main advantages of this kind of systems lie in their capacity to cross biological barriers, to protect macromolecules such as peptides, proteins, oligonucleotides, and genes from degradation in biological media, and to deliver drugs or macromolecules to a target site with following controlled release. Chitosan nanoparticles are good drug carriers because of their good biocompatibility, biodegradability and readily modifiable properties. A good drug carrier can overcome the disadvantages of commonly used drugs such as poor stability, water insolubility, low selectivity and high toxicity. Chitosan nanoparticles are drug carriers with wide development potential and have the advantage of slow/controlled drug release, which

improves drug solubility, stability, enhances efficacy, and reduces toxicity. Because of their small size, they are capable of passing through biological barriers in vivo (such as the blood–brain barrier) and delivering drugs to the lesion site to enhance efficacy [7].

Nanoparticles are solid colloidal particles with diameters ranging from 1-1000 nm. They consist of macromolecular materials and can be used therapeutically as adjuvant in vaccines or drug carriers in which the active ingredient is dissolved, entrapped, encapsulated, adsorbed or chemically attached.

Polymers used to form nanoparticles can be both synthetic and natural polymers. There are two types of nanoparticles depending on the preparation process: nanospheres and nanocapsules. Nanospheres have a monolithic-type structure (matrix) in which drugs are dispersed or adsorbed onto their surfaces. Nanocapsules exhibit a membrane-wall structure and drugs are entrapped in the core or adsorbed onto their exterior. The term “nanoparticles” is adopted because it is often very difficult to unambiguously establish whether these particles are of a matrix or a membrane type.

Nanoparticles not only have potential as drug delivery carriers as they offer non-invasive routes of administration such as oral, nasal and ocular routes, but also show to be good adjuvant for vaccines. Despite these advantages, there is no ideal nanoparticle system available. Most of nanoparticles prepared from water-insoluble polymers are involved heat, organic solvent or high shear force that can be harmful to the drug stability. Moreover, some preparation methods such as emulsion polymerization and solvent evaporation are complex and require a number of preparation steps that are more time and energy consuming.

In contrast, water-soluble polymers offer mild and simple preparation methods without the use of organic solvent and high shear force. Among water-soluble polymers available, chitosan is one of the most extensively studied. This is because chitosan possesses some ideal properties of polymeric carriers for nanoparticles such as biocompatible, biodegradable, nontoxic, and inexpensive. Furthermore, it possesses positively charge and exhibits absorption enhancing effect. These properties render chitosan a very attractive material as a drug delivery carrier. In the last two decades, chitosan nanoparticles (chitosan NP) have been extensively developed and explored for pharmaceutical applications. Thus, this book focuses on the chitosan nanoparticle preparation technology, applications and mechanism of cell entry.