Chapter 5

BIOMIMETIC APPROACH TO DRUG DELIVERY AND OPTIMIZATION OF NANOCARRIER SYSTEMS

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Abstract: In biomimetic approach, nanoparticulate surfaces can be covered with phospholipid bilayer(s) to obtain biological surfaces similar to cell membranes. This approach not only increases biocompatibility of drug carriers, but also provides a lipophilic medium for insertion of amphiphilic proteins which have higher affinity for target cells and channel proteins for controlling solute transfer through phospholipid layer. This chapter explains recent developments in biomimetic approach to drug delivery.

Key words: Nanoparticles, Cell membranes, Phospholipid coating, Encapsulation efficiency, Surface modification.

1. INTRODUCTION

Covering the surfaces of nanocarriers with phospholipid molecules increases the stability and biocompatibility of the carrier-drug systems. Biovector biomimetic synthetic delivery system, a virus-like particle made of an inner core of polysaccharide hydrogel surrounded by a lipid bilayer, is a recent example for this new family of nanoparticulate drug carriers. It is possible to increase the encapsulation efficiency by modification of nanoparticle preparation conditions. Among these modifications are the covalent attachments of amphiphilic polymers to proteins to be encapsulated, thereby increasing the interaction between the hydrophobic polymer phase in suspension, decreasing the protein solubility by adjusting the pH of the water.
phase of emulsion to the protein’s isoelectric point, or by increasing polymer-drug interaction by using oppositely charged polymers. Great efforts have been made in recent years to obtain nanoparticles with reduced reticuloendothelial uptake and prolonged circulation time. The modification of the surfaces of particles intended for intravenous injection, by a polymer, in order to provide a hydrophilic and steric barrier would minimize coating by plasma proteins, opsonization and recognition phenomena. In order to provide longer circulation time, the nanoparticles have been modified by surface coating with hydrophilic polymers (polyethylene oxide, poloxamer)/surfactants (lauryl ethers, polysorbate) and by synthesis of biodegradable copolymers with hydrophilic segments (diblock poly(ethylene oxide)-poly(lactic acid)). Conjugation of heparin to poly (3-hydroxybutyrate-co-3-hydroxyvalerate) nanocapsules was reported to increase \textit{in vivo} half-life and eliminating the immunogenicity of encapsulated anti-leukaemic asparaginase.

2. APPLICATION OF CELL MEMBRANE RESEARCH TO DRUG DELIVERY

The emerging aim of controlled and targeted drug delivery is to obtain effective drug dose at the disease site and prevent side effects. Cell biology related bioevents triggered by extracellular regulators such as controlled secretion of hormones by secretory cells and a better understanding of material exchange across the cell membrane combined with the recent achievements in membrane protein science are providing important insights to researchers who try to design more biological friendly drug carriers.

Red Blood Cells (RBC) have become a useful model for pharmaceutical scientists due to possessing a surface inert to serum protein adsorption and reticuloendothelial cells. It has already been shown by several investigators that RBC can be used as carrier for drugs, such as anti-leukaemic enzyme L-asparaginase (ASNase), with a long half-life, almost as long as the native RBC half-life in human circulation \cite{1, 2}. In addition, this surface inertness of RBC can be harnessed for prolonging intravascular particle circulation by anchoring the nanoparticles to the surface of RBCs \cite{3}.

The delivery of drugs to distant targets inside circulatory system can be possible at RBC cell membrane level as well. This kind of drug delivery system involves the transient ‘loading’ of RBC with a lipophilic ‘hook’ macromolecule which has enough affinity for the RBC plasma membrane to anchor. But given the opportunity, the macromolecule can exit its position and transfer to another (target) cell membrane for which it has a greater affinity. Binding of antimicrobial peptide, derivative of antimalarial dermaceptin S4, K-S4 (1–13)a to the plasma membrane 4 of RBC was assessed \textit{in vitro} and \textit{in vivo} and found to be rapid, spontaneous and receptor