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RESEARCH ARTICLE

Exploiting 4-sulphate *N*-acetyl galactosamine decorated gelatin nanoparticles for effective targeting to professional phagocytes *in vitro* and *in vivo*

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Abstract

The present study was focused on the development of surface modified gelatin nanoparticles (SGNPs) using novel ligand 4-sulfated *N*-acetyl galactosamine (4-SO_4GalNAc) for specific targeting to macrophages. The gelatin has been modified with the potential targeting moiety 4-SO_4GalNAc, which was further used for the preparation of modified nanoparticles. The nanoparticles have been prepared by two step desolvation method. The SGNPs and unmodified gelatin nanoparticles (GNPs) were loaded with doxorubicin (DxR) and its targeting potential was compared. Developed DxR-loaded SGNPs (DxR-SGNPs) were found to have negative zeta potential (−19.8 ± 0.22 mV) whereas DxR-loaded GNPs (DxR-GNPs) have the positive zeta potential of around +12.2 ± 0.36 mV. The mean particle size of DxR-SGNPs and DxR-GNPs was found to be 283 ± 7 and 134 ± 5 nm, respectively. Flow cytometric data confirmed the enhanced uptake of DxR-SGNPs in J774A.1 and PBMC when compared with DxR-GNPs. Intracellular localization studies indicate that the fluorescence intensity of DxR-SGNPs was significantly higher when compared to DxR-GNPs. DxR-SGNPs rendered significantly higher localization of DxR in liver and spleen as compared to DxR-GNPs after i.v. administration. The study stipulates that 4-SO_4GalNAc assures for targeting resident macrophages.

Keywords: 4-sulfated *N*-acetyl galactosamine, gelatin nanoparticles, mannose receptors, macrophages

Introduction

There are number of colloidal formulations such as polymeric nanoparticles that have attracted interest as drug carriers for achieving site specific drug delivery which offers an intelligent delivery system (Mitra et al., 2001). The colloidal formulation built up with excipients like gelatin has promising features, for instance they are biodegradable, non-antigenic and though they are often easy to prepare according to the required size distribution (Weber et al., 2000). The major advantage which can be executed through these colloidal drug carrier systems is the drug targeting to a particular site and enhancing the cellular uptake of a number of pharmaceutical active agents (Hans & Lowman, 2002, Shukla et al., 2010). The GNPs have a higher molecular weight, which enables them to get opsonised immediately after application (Owens & Peppas, 2006). Gelatin, in addition to its biodegradable properties, its primary structure offers room for chemical modification, which may be exploited to achieve enhanced stability and circulation time *in vivo* (Marty et al., 1978; Jahanshahi et al., 2008; Jameela & Jayakrishnan, 1995; Weber et al., 2000). GNPs, when surface modified with site-specific ligands, further facilitates uptake by receptor-mediated endocytosis (Chellat et al., 2005). Surface modification of these materials can be done by covalent coupling or by topography changes which imparts desirable properties to these particles which plays an important role during cell adhesion. GNPs have been successfully modified by poly ethylene glycol (PEG), mannose, pegylated mannose for intracellular

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