Asialoglycoprotein receptor mediated hepatocyte targeting – strategies and applications

Anisha A. D'Souza, Padma V. Devarajan

PII: S0168-3659(15)00122-4
DOI: doi: 10.1016/j.jconrel.2015.02.022
Reference: COREL 7571

To appear in: *Journal of Controlled Release*

Received date: 24 November 2014
Revised date: 14 February 2015
Accepted date: 16 February 2015

Please cite this article as: Anisha A. D'Souza, Padma V. Devarajan, Asialoglycoprotein receptor mediated hepatocyte targeting – strategies and applications, *Journal of Controlled Release* (2015), doi: 10.1016/j.jconrel.2015.02.022

ASIALOGLYCOPROTEIN RECEPTOR MEDIATED HEPATOCYTE TARGETING – STRATEGIES AND APPLICATIONS

Anisha A. D'Souza, Padma V. Devarajan

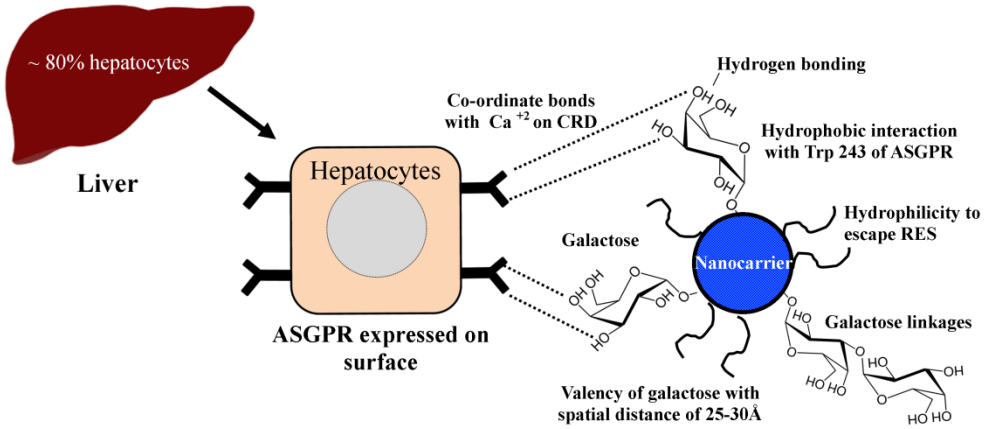
Department of Pharmaceutical Sciences and Technology, Institute of Chemical Technology (Elite status), N. P. Marg, Matunga (East).Mumbai 400019.India.

Email: pvdevrajaran@gmail.com

Contact No: + 91 22 3361 2201 Fax: 912233611020

Abstract

Hepatocyte resident afflictions continue to affect the human population unabated. The asialoglycoprotein receptor (ASGPR) is primarily expressed on hepatocytes and minimally on extra-hepatic cells. This makes it specifically attractive for receptor-mediated drug delivery with minimum concerns of toxicity. ASGPR facilitates internalization by clathrin-mediated endocytosis and exhibits high affinity for carbohydrates specifically galactose, N-acetylgalactosamine and glucose. Isomeric forms of sugar, galactose density and branching, spatial geometry and galactose linkages are key factors influencing ligand-receptor binding. Popular ligands for ASGPR mediated targeting are carbohydrate polymers, arabinogalactan and pullulan. Other ligands include galactose-bearing glycoproteins, glycopeptides and galactose modified polymers and lipids. Drug-ligand conjugates provide a viable strategy; nevertheless ligand-anchored nanocarriers provide an attractive option for ASGPR targeted delivery and are widely explored. The present review details various ligands and nanocarriers exploited for ASGPR mediated delivery of drugs to hepatocytes. Nanocarrier properties affecting ASGPR mediated uptake are discussed at length. The review also highlights the clinical relevance of ASGPR mediated targeting and applications in diagnostics. ASGPR mediated hepatocyte targeting provides great promise for improved therapy of hepatic afflictions.



Nanocarrier anchored with ligand bearing galactose

1. Introduction

Liver, a major reticuloendothelial system (RES) organ actively participates in the body's defense process. Liver diseases are cited as fifth major cause of death and reflect a steady increase. Following drug administration although drugs with molecular weight greater than 300Da accumulate in liver, rapid elimination including P-glycoprotein mediated efflux and non-specific target cell accumulation often result in poor success rates. Hepatocellular carcinoma (HCC) the