Studies on the Preparation and Evaluation of Chitosan Nanoparticles containing Cytarabine

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ABSTRACT: The activity of cytarabine was decreased by its rapid deamination to the biologically inactive metabolite uracil arabinoside. This rapid deamination is the reason for the ongoing research for effective formulation of cytarabine that can not be deaminated and exhibit better pharmacokinetic parameters. Protection of cytarabine from fast degradation and elimination was investigated by encapsulating the drug into chitosan nanoparticles. Cytarabine loaded nanoparticles prepared by ionotropic gelation were characterized by SEM and was found to in the range of 200 nm. The mechanism by which drug is being released is non-Fickian (anomalous) solute diffusion mechanism. It is evident from the result that initial burst release was retarded or delayed due to adsorption of coating material. The in vivo biodistribution study results showed that the nanoparticles were having better distribution of drug compared to free drug in different organs like spleen, lungs, kidney etc.

KEY WORDS: Cytarabine; Deamination; Chitosan; Nanoparticles

Introduction

The colloidal drug delivery systems are capable of carrying high drug load and of controlling the drug release in a predictable manner and provide site specific and targeted drug delivery (Yong Hua et al., 2008). Injectable, colloidal drug delivery systems especially the nanoparticles have gained much interest during last few years as they improve the distribution of drugs in the body because of their enhanced efficiency against tumors and reduced toxicity. The submicron size of nanoparticles offers numerous advantages over microparticles. Nanoparticles have relatively higher intracellular uptake compared to microparticles. In the last decade, significant effort has been made to develop nanoparticles for drug delivery. Considerable research has been directed towards developing safe and efficient chitosan based particulate drug delivery systems such as nanoparticles. Various polymeric nanoparticles have been studied for intracellular delivery of different classes of therapeutic agents. Nanoparticles are thought to enter cells via an endocytic pathway through either specific or nonspecific interaction with cell membrane. The possibility of improving the plasma half life of the drug polymer conjugate with maximum accumulation in the tumor, can be achieved through encapsulation of the drug in a long circulating carrier such as nanoparticles. By maintaining the optimum size of these nanoparticle carriers, it can accumulate in the tumor tissue through enhanced permeability and retention effect (Lowman A.M et al., 2002)

Biodegradable and biocompatible polymers are suitable for human use and can be prepared into particles of various sizes. Chitosan is a positively charged natural biodegradable and biocompatible polymer. It is a linear polysaccharide consisting of h-1,4 linked monomers of glucosamine and N-acetylglucosamine. There are numerous reports highlighting the low toxicity and biocompatibility of chitosan. In recent years, interest in the use of chitosan in the medical field, especially in biomedical and pharmaceutical applications, has been increasing. Chitosan nanoparticles (CS-NPs) can be obtained by a very mild ionotropic gelation procedure, and have been reported with an excellent capacity for the association of proteins (Anavil et al., 2003, Yang-Chuang Chang et al., 2004)