ABSTRACT

Formulation and in-vivo evaluation of a novel drug delivery system containing a chelating agent for the treatment of iron overload

Cindy Anne Bhagwandin

An iron overload model was created in male Sprague Dawley rats by giving iron dextran 100 mg/kg by intraperitoneal injections, three times a week over a four-week period. Urine and faecal samples were collected daily before treatment, following the period of iron loading, during treatment and after treatment. Two control groups, and four treatment groups were used to compare the efficacy of encapsulation of desferrioxamine in small unilamellar vesicles (SUVs), multilamellar vesicles (MLVs), free drug (25 mg/kg) or a combined therapy (free DFO 25 mg/kg and drug entrapped in SUVs). Samples were analyzed using graphite furnace atomic absorption spectrophotometry. Histological specimens (liver, heart and kidney) were stained with Perl's stain for iron in order to assess the efficacy of the drug treatments.

The mean iron removal in the urine during treatment by free DFO (25 mg/kg) and SUVs were comparable, although a much smaller dose was entrapped in the SUVs. Upon comparison of the percentages of the drug

burden removed, the SUVs removed the most iron (4465%), followed by free DFO (1199%).

Following the discontinuation of treatment, all of the groups containing niosomes continued to promote iron excretion, however the group containing free and encapsulated drug removed the highest percentage of the iron burden (433%).

The mean iron excretion in the faeces during treatment was highest with free DFO, and it removed the highest percentage of the iron burden. The mean iron excretion after treatment was similar with SUVs (96%), free drug (92%) and MLVs (74%). The results clearly display an enhanced efficacy of the drug following its encapsulation particularly by SUVs.

Keywords: Cindy Anne Bhagwandin, iron, iron overload, thalassaemia, hemochromatosis, chelator, desferrioxamine mesylate, non-ionic surfactants, niosomes, targeted drug delivery, atomic absorption spectrophotometry.