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Potential of low molecular mass chitosan as a DNA delivery system: biocompatibility, body distribution and ability to complex and protect DNA

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Abstract

Cationic polymers have the potential for DNA complexation and it is recognised that they may be useful as non-viral vectors for gene delivery. Highly purified chitosan fractions of <5000 Da (N1), 5000â€“10â€ˆ000 Da (N2) and >10â€ˆ000 Daltons (N3) were prepared and characterised in respect of their cytotoxicity, ability to cause haemolysis, ability to complex DNA as well as to protect DNA from nuclease degradation. Also the biodistribution of ^{125}I-labelled chitosans was followed at 5 and 60 min after intravenous injection into male Wistar rats. All chitosan fractions displayed little cytotoxicity against CCRF-CEM and L132 cells (IC_{50}>1 mg/ml), and they were not

haemolytic (<15% lysis after 1 and 5 h). Chitosanâ€¨DNA interaction at a charge ration of 1:1 was much greater than seen for poly(L-lysine) and complexation resulted in inhibition of DNA degradation by DNase II: 99.9Â±0.1, 99.1Â±1.5 and 98.5Â±2.0% for N1, N2 and N3, respectively. After intravenous injection, all the chitosans showed rapid blood clearance, the plasma levels at 1 h being 32.2Â±10.5% of recovered dose for N1 and 2.6Â±0.5% of recovered dose for N3. Liver accumulation was molecular mass dependent, being 26.5Â±4.9% of the recovered dose for N1 and 82.7Â±1.9% of the recovered dose for N3. The observations that the highly purified chitosan fractions used were neither toxic nor haemolytic, that they have the ability to complex DNA and protect against nuclease degradation and that low molecular weight chitosan can be administered intravenously without liver accumulation suggest there is potential to investigate further low molecular weight chitosans as components of a synthetic gene delivery system.

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Keywords

Biocompatibility; Body distribution; Chitosan; Gene delivery

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