

The Further Characterisation of Soluble, Linear, Poly(amidoamine)s as Cytoplasmic Delivery Vehicles

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Abstract

Over the last 10 years we have shown that, relative to polycationic DNA delivery systems, poly(amidoamine)s (PAA)s demonstrate, 2-3 orders of magnitude less *in vitro* toxicity. PAA derived delivery systems can avoid rapid liver clearance, target either towards or away from the liver or passively accumulate in solid tumour mass. PAAs have also been shown to change their charge and radius of gyration in response to the pH of their environment, significantly altering the propensity of the PAA to rupture biological membranes, selectively delivering both DNA to the nucleocytosolic compartment. Previously, the delivery of membrane-impervious protein toxins ricin A chain and gelonin by ISA1 and ISA23 has been reported. The PAAs were incubated with the toxins and no attempt was made to conjugate the two entities. Here a sulphur atom has been introduced pendant to the polymer main-chain to provide a conjugation point (via a disulphide bond) with Cys172 of ricin A chain in an attempt to improve the ratio of PAA required to deliver the toxic ricin A chain via the putative endosomolytic activity of the PAAs. Here, two new derivations of the previously characterised PAA families have been tested for toxicity against Vero cells *in vitro*.