

GS01-5 Preparation and Evaluation of PAMAM Dendrimer (G2)/ Glucuronylglucosyl- β -cyclodextrin Conjugate as a Novel Gene Transfer Carrier

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We previously reported that polyamidoamine dendrimer (dendrimer) conjugate with α -cyclodextrin (G2) has significantly higher gene transfer activity than dendrimer (G2) due to its endosomal escaping ability. However, we have not evaluated the effects of spacers between dendrimer and cyclodextrin (CyD), and the cavity size of CyDs on gene transfer activity of the conjugates. In the present study, therefore, we newly prepared the dendrimer (G2) conjugates with 6-*O*- α -(4-*O*- α -D-glucuronyl)-D-glucosyl- β -CyD (GUG- β -CyD) with low hemolytic activity, and evaluated the potential of the conjugate (GUG- β -CDE (G2)) as a novel gene transfer carrier. By mixing with solutions containing GUG- β -CyD and dendrimer (G2) at the various molar ratios, four GUG- β -CDEs (G2) having the different average degrees of substitution (DS) were prepared. Of four conjugates, gene transfer activity of GUG- β -CDE (G2, DS 1.8) was highest, and was higher than that of α -CDE (G2) or β -CDE (G2) in A549 cells and RAW264.7 cells. The cellular uptake of the pDNA complex with GUG- β -CDE (G2, DS 1.8) was almost the same as that with α -CDE (G2, DS 1.2) or β -CDE (G2, DS 1.3) in A549 cells, suggesting the different intracellular behavior of the pDNA complex with GUG- β -CDE (G2, DS 1.8) from that with α -CDE (G2) or β -CDE (G2). Negligible cytotoxicity of pDNA complexes with GUG- β -CDE (G2, DS 1.8) was observed. These results suggest the potential use of GUG- β -CDE (G2, DS 1.8) as a novel gene transfer carrier.