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Assessing toxicity of dendrimers by neuronal signaling functions

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Polyamidoamine (PAMAM) dendrimers have great potential in biomedical applications, including gene transfer and drug delivery to the brain, as a result of their surface properties which enable their internalization. However, little is known about their neurotoxicity. We examined the effect of PAMAM dendrimers with different surface groups on the function and viability of neural cells. Changes in the electrophysiological parameters of neuronal activity of rat hippocampal slices have been compared during and after a 15-minute dendrimer application. Cell viability was determined by imaging propidium iodide staining after one hour of incubation in the dendrimeric solution. Polycationic generation 5 PAMAM dendrimer (G5-NH2) depolarized and inactivated most of the neurons, and increased the number of dead cells in hippocampal slices, showing this dendrimer clearly toxic within the range of 1–0.01 mg/ml concentration. β-D-glucopyranose conjugation of G5-NH2 decreased the toxic effects of smaller concentrations (0.1–0.01 mg/ml). By comparison, polyanionic generation 4.5 dendrimer, containing surface carboxylate groups affected the membrane potential much less, and did not affect cell viability. Results can be explained by molecular modeling simulation of interactions between cationic and anionic PAMAM monomers and the membrane or membrane-protein potassium channel. β-D-glucopyranose conjugation of G5-NH2 may moderate the risk of dendrimer mediated neuronal gene/drug delivery.

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