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難吸収性薬物の経肺吸収性に及ぼす polyamidoamine (PAMAM) dendrimer の影響
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The absorption enhancing effects of polyamidoamine (PAMAM) dendrimer with various generations on the pulmonary absorption of insulin and fluorescein isothiocyanate-labeled dextrans (FDs) with various average molecular weights (4,000-70,000) were studied in rats. For improving the pulmonary absorption of insulin and FDs, the absorption enhancing effect of PAMAM dendrimers was generation dependent. The rank order of absorption enhancement was G3>G2>G1>G0. And for the same generation of PAMAM dendrimers, the absorption enhancing effect of PAMAM dendrimers was concentration dependent. At the same time, when the molecular weight of model drugs increased, the absorption enhancing effect of PAMAM dendrimers increased. As for the pulmonary membrane toxicity of PAMAM dendrimer, there was no significant difference in the release of protein and lactate dehydrogenase (LDH) with or without PAMAM dendrimer with various generations in bronchoalveolar lavage fluid (BALF), indicating that PAMAM dendrimers did not cause any membrane damage to the lung tissues. The zeta potential of insulin solution added PAMAM dendrimers changed to positive, and the degree was linearly correlated with the generation of PAMAM dendrimer. This changing can trigger the absorption enhancing effect of PAMAM dendrimer on the pulmonary absorption of insulin, as the first step of mechanism.