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Selective aggregation of PAMAM dendrimer nanocarriers and PAMAM/ZnPc nanodrugs on human atheromatous carotid tissues: a photodynamic therapy for atherosclerosis

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Abstract

© 2015, Spyropoulos-Antonakakis et al.; licensee Springer. Photodynamic therapy (PDT) involves the action of photons on photosensitive molecules, where atomic oxygen or OH^- molecular species are locally released on pathogenic human cells, which are mainly carcinogenic, thus causing cell necrosis. The efficacy of PDT depends on the local nanothermodynamic conditions near the cell/nanodrug system that control both the level of intracellular translocation of nanoparticles in the pathogenic cell and their agglomeration on the cell membrane. Dendrimers are considered one of the most effective and promising drug carriers because of their relatively low toxicity and negligible activation of complementary reactions. Polyamidoamine (PAMAM) dendrite delivery of PDT agents has been investigated in the last few years for tumour selectivity, retention, pharmacokinetics and water solubility. Nevertheless, their use as drug carriers of photosensitizing molecules in PDT for cardiovascular disease, targeting the selective necrosis of macrophage cells responsible for atheromatous plaque growth, has never been investigated. Furthermore, the level of aggregation, translocation and nanodrug delivery efficacy of PAMAM dendrimers or PAMAM/zinc phthalocyanine (ZnPc) conjugates on human atheromatous tissue and endothelial cells is still unknown. In this work, the aggregation of PAMAM zero generation dendrimers (G0) acting as drug delivery carriers, as well as conjugated G0 PAMAM dendrimers with a ZnPc photosensitizer, to symptomatic and asymptomatic human carotid tissues was investigated by using atomic force microscopy (AFM). For the evaluation of the texture characteristics of the AFM images, statistical surface morphological and fractal analytical methodologies and Minkowski functionals were used. All statistical quantities showed that the deposition of nanodrug carriers on healthy tissue has an inverse impact when comparing to the deposition on atheromatous tissue with different aggregation features between G0 and G0/ZnPc nanoparticles and with considerably larger G0/ZnPc aggregations on the atheromatous plaque. The results highlight the importance of using PAMAM dendrimer carriers as a novel and promising PDT platform for atherosclerosis therapies.

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Keywords

AFM, Atheromatous plaque, Biosurfaces, Cardiovascular, Dendrimers, Fractal analysis, Nanodrugs, Nanoparticle aggregation, Photodynamic therapy, Surface roughness parameters