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Nitric oxide delivery from radiation-crosslinked hyperbranched polyglycerol hydrogels

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After two decades of study dendritic and hyperbranched polymers are becoming commercially viable raw materials for pharmaceutical industry. Structurally hyperbranched polymers are quite different from the conventional branched or linear polymers applications having a "globular" topology. This 3-dimensional shape leads to unique structure/property relationships and new opportunities for design of drugs. Some of the attractive features of dendritic polymers for medicinal applications include low viscosity at a given molecular weight and high-end group functionality concentration. The aim of this work was the synthesis and characterization of radiation crosslinked nitrated hyperbranched polyglycerol hydrogels (PGLD-NO) and the usefulness of this material for medicine applications such as wound dressings. Nitric oxide is an important cytotoxic agent for host defense that also regulates gene expression, signal transduction, and vasodilation. In normal wounds, nitric oxide synthesis and metabolism are significantly increased during inflammation and tissue remodeling. However, nitric oxide production is suppressed in wounds where healing is impaired by diabetes or steroid-treatment. The delivery of nitric oxide in therapeutic amounts may alleviate this deficiency and thereby enhance wound repair. Consequently, we developed a nitrated hyperbranched polyglycerol (PGLD-NO) radiation crosslinked a nonsoluble, nontoxic hydrogel as a new class of compounds that spontaneously release nitric oxide in a controlled fashion in aqueous media. The PGLD-NO was synthesized from glycerol to provide an extended nitric oxide release. PGLD-NO generation 5 was irradiated with gamma ray radiation from ^{60}Co at 25 °C and different doses (0-100 kGy). Irradiation of PGLD-NO in aqueous solutions at 30 wt% resulted in the formation of gels. Gel content was found to increase with increase of radiation dose and decrease of PGLD-NO concentration within the range studied. PGLD-NO gels swelled by absorbing more than 1,500 g of water per gram of dry gel at a low applied dose, characterizing a superabsorbent gel. Under physiological conditions, NO was produced by the PGLD-NO hydrogels over periods ranging from hours to months, depending upon the PGLD-NO formulation. The rate of wound healing in mouse treated with PGLD-NO hydrogels was elevated. The results showed that a nonsoluble, dendritic PGLD-NO could provide nitric oxide delivery to wounds in a controlled manner, which an enhanced wound healing.

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