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Radiation Synthesis of Nanosized Drug Delivery Devices

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The radiation chemistry of polymer aqueous solutions is a successful synthetic methodology for large scale production of nanosized drug delivery systems. That is particularly true for nanogel drug carriers. Nanogels are fascinating nanoparticles that, for their tunable chemical structure and swelling ability by water molecules, can be designed to be biocompatible, to offer conformable cavities to incorporate bulky therapeutic proteins, but also small hydrophobic pockets to host barely polar molecules, which is the case of most medical drugs. They can display reactive groups to conjugate targeting ligands, such as monoclonal antibodies, peptides and oligonucleotides. These nanoparticles can be used to target specific cells and cellular microenvironments with high specificity and affinity. They can also incorporate chelating agents that bind radioactive ions, either for bio-imaging or therapeutic purposes. The possibility of producing nanogels as aqueous dispersions, without going through a drying step for purification since no recourse to organic solvents and surfactants is made, is the best guarantee for preserving their size, hence functionality.

Water radiolysis provides a means of generating initiating radicals at the desired rate. These radicals can either recombine or react with the polymer solute, transforming the otherwise chemically inert macromolecule into multi-radical species. Radicals formed on the polymer can either react with molecular species present or formed in solution, or combine with other macroradicals. Intramolecular combination creates permanent loops and crosslinking points within the same chain, transforming the linear or branched polymer chain into a nanoscalar network. Intermolecular combination, binding polymer chains together, contributes to increase the nanogel size and molecular weight. By tuning the irradiation conditions we expect to be able to tailor both particle size and chemical composition.

In order to establish relevant process–structure–property relationships, irradiations are performed with pulsed electron beams varying the irradiation conditions and system composition. The efficiency of the polymer in scavenging the initiating radicals is estimated. The produced nanogels are characterised for their composition and particle size.

The possibility of generating nanogels with controlled hydrodynamic diameter in the range from 20 to 200 nm and relatively narrow particle size distributions (PDI<0.3) is demonstrated.

Irradiation conditions that favour intra-molecular crosslinking are identified, the most important parameter to control being the polymer molar concentration. Functional groups are generated on the polymer by the reaction of some macroradicals with molecules that may be produced in situ by irradiation (e.g. H2O2, O2) or purposely added to the system (unsaturated monomers). These groups are used to bind therapeutic biomolecules, that can be protected by the nanogel from degradation when in solution and be exposed to their receptors when the nanoparticles experience a change in their microenvironment (e.g. at the cell membrane).

The easy of manufacture and purification of the base nanogels, the possibility to use them as substrates for different therapeutic strategies by attaching specific ligands and drugs, and their properties when evaluated in relevant cellular and animal models represent today a very promising prospect for translation into clinic.

Country/Organization invited to participate

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