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"In vitro prescreening study of the hemoreactivity of polymeric nanocarriers designed for the delivery of biopharmaceutical drugs"

Christian Grandfils, Chantal Sevrin, Natalia Kutznetsova and Bernardino Cerda

Interfacultary Research Center of Biomaterials, University of Liège, Institute of Chemistry, Building B6C. Sart-Tilman (Liège), Liège (ZIP code 4000), Belgium. C.Grandfils@ulg.ac.be, Phone : + 32 (0) 4 3663506, Fax : + 32 (0) 4 3663623

Abstract

The optimization of nanoparticles (NPs) for drug delivery, in particular to target the blood brain barrier (BBB), imposes to verify their hemocompatibility both for toxicology and targeting efficiency perspectives. The large surface area of the NPs that can be exposed to the biological environment promotes their interaction with various biochemicals, in particular proteins which, following adsorption, can elicit the activation of biological cascades responsible either for NPs clearance or/and harmful body reactions (inflammatory / coagulation).
In the framework of the European Integrated Project : "Nanobiopharmaceutics", we had the opportunity to compare in vitro the hemoreactivity of about 145 different NP samples differing in core and surface chemistry and classified according to their expected difference in hydrophobicity based on the nature of their core materials. According to this classification, poly(lactide-co-glycolide) (PLGA) nanoparticles, polyglycidol-polyethyethylene oxide nanoparticles, polyglycidol thyolated or polyacrylamide nanogels, and polyelectrolyte complexes either based on polyamidoamine or poly(N,N-dimethylamino-2-ethylmethacrylate) have been evaluated within a concentration range of 0.3 to 1000 µg/mL. The in vitro tests have been performed for screening purposes adopting normal human bloods and according to Iso 10993.
The results of this extensive study clearly highlighted that most of the polymeric nanoparticles evaluated give rise to some alterations of the blood components. In particular the platelets, the intrinsic pathway of coagulation and the complement activation were found to be the most reactive biological parameters in the presence of these nanostuctures.
Although not strictly related to their surface chemistry, the classification of the NPs allowed us to derive some clear correlations between the nanomaterial properties and their hemoreactivity.
Within the class of polyelectrolyte complexes, the modification of the surface chemistry was found to drastically improve their hemoreactivity.

Keywords

Nanoparticles, blood brain barrier, biopharmaceutical drugs, hemocompatibility, hemoreactivity, complement activation.

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