Abstract

In recent decades, nanoparticles have become an area of intense research due to their unique physicochemical properties suitable for potential applications in various fields, including medicine. Thanks to their properties, they are useful for both diagnostic and therapeutic purposes, e.g. for targeted therapy of cancer or for transfer of genetic information. Havingsuch a broad spectrum of engineered nanoparticles available brings to the need to better understand the fundamental concepts of how nanoparticles interact with biological systems in *in vitro* as well as *in vivo* conditions. One promising group of nanoparticles consists of so-called dendrimers and dendrons – highly branched polymeric nanoparticles with a well-defined structure that can be controlled and tailored during the synthesis process. Despite a long history of research lasting more than 40 years, only a few products have reached clinical practice so far, which may partly be related to efficient and effective nanomedicine delivery requires full control over the nanoparticle transport in the body. However, this level of control has not been achieved yet non-specific interactions during the nanoparticle transport through the circulation and/or after penetration into tissues. In the introductory chapters, we have described the state-of-the-art in the field of dendrimers and dendrons, their physicochemical properties that condition the interactions, and approaches to their modification. We have focused on 1st and 2nd generation of amphiphilic phosphorous dendrons and dendrimers (AFDs and AFDDs), and in the methods section we describe physical approaches to studying their interactions with model membranes, small extracellular vesicles (exosomes), and with whole human blood. These experiments formed the basis for subsequent investigations of the interactions of AFD and AFDD with whole human blood and its components, i.e., *in vitro* biocompatibility testing. To assess the biocompatibility of AFD and AFDD added at different concentrations more comprehensively, we analysed a range of blood and coagulation parameters and, as a novel approach, we have introduced the measurement of rheological i.e. flow properties of whole human blood. Rheometric measurements using constitutive models allowed us to determine viscosity, which depends on intermolecular interactions. Our results demonstrated good blood tolerability of the 1st generation AFD and AFDD. However, the application of higher generations at higher concentrations affected several hematological and coagulation parameters in a clear concentration- and generation-dependent manner, especially for AFD (when compared to AFDD). Based on our results, we hypothesize that an increase in the positive surface charge of AFD (AFDD) reduces the repulsion between blood particles, which may lead to their interaction with plasma coagulation factors and/or platelets and eventually to their activation. This work highlights the need to involve in basic research evaluation ofthe pro-aggregation propensity and impact on blood rheology of all nanoparticles being developed for medical applications already.

Keywords: dendritic nanoparticles, interaction, biological systems, blood compatibility, rheometry