TOXICITY OF GOLD NANOPARTICLES STABILIZED BY CATIONIC CARBOSILANE DENDRONS

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To deliver drug to the desired site in the body is the main aim of biomedical research today. Nanotechnology based drug delivery approaches have proven some exciting results in this perspective. Nanoparticles (NPs) are a class of highly tunable nanoscale objects with wide range of applications. NPs usually exhibit size related characteristics that differ significantly from those observed in bulk materials [1]. Gold nanoparticles (AuNPs) [2] have been among the most extensively studied nanomaterials, because of their properties that include large surface-to-volume ratio, stability, excellent biocompatibility, low toxicity and ease to functionalize [3-5]. Their utilization in different applications is limited due to the aggregation processes occuring frequently in the colloidal systems of metal or semiconductor NPs. Thus, in order to prevent or slow down the aggregation, NPs are usually functionalized with a thin shell of monomeric stabilizers (thiols, carboxylates, phosphates or sulfates), synthetic and natural polymers (dextran, polyethylene glycol (PEG), polyvinylpyrrolidone, polyethylene oxide or chitosan), inorganic materials (silica), liposomes and another class of emerging molecules such as dendrimers and dendrons [1]. We are interested in possible biomedical applications of carbosilane dendritic molecules, where the scaffold is built with very apolar C-C and Si-C bonds. Since this framework is highly hydrophobic, the presence of cationic moieties on the periphery of carbosilane dendrimers makes them more water soluble. However, the duality in hydrophobicity/hydrophilicity of these systems seems to be important, because ammonium carbosilane dendrimers not only have been proved successful as non-viral vectors for gene therapy [6-8], but can cross the blood-brain barrier [9, 10]. In view of these attractive properties of carbosilane dendrimers, we have investigated the way to translate them to other macromolecular systems. Owing to the presence of a large num-

ber of terminal groups and the metal surface, drug molecules can be attached by covalent bonds or electrostatic interactions, making them suitable for gene delivery through electrostatic interactions. Nevertheless, interactions with cell compounds and compartments are non-selective, with the risk of causing cyto- and hemo-toxicity mainly due to their surface charge. Thus, we focused on 3 kinds of dendronizedAuNPs and their capping dendrons (first, second and third generation) by assessing the effects on erythrocytes (hemolytic activity), platelets (aggregation) and peripheral blood mononuclear cells (PBMCs; lymphocyte proliferation) to clarify their potential use in drug and gene delivery systems.

Table 1. Selected data of AuNPs: a) Obtained by TEM; b) DLS; c) Obtained by TGA and elemental analysis; d) Number of -NMe3+ groups by NP; e) Z potential.

Nanoparticles	D (nm)[a]	D (nm)[b]	Av. MW ($gmol^{-1}$)[c]	N[d]	ZP[e] (mV)
AuNP(SG_1(S-NMe_3^+)$_2$)	1.8	4.9	64761.64	118	+50.0
AuNP(SG_2(S-NMe_3^+)$_4$)	2.2	15.7	201105.70	528	+63.7
AuNP(SG_3(S-NMe_3^+)$_8$)	2.0	21.0	307482.90	984	+59.6

Hemolysis of human erythrocytes was determined by measuring the free hemoglobin content after incubation with dendronsHSGn(S-NMe3+)m and corresponding dendronized systems AuNP(SGn(S-NMe3+)m) at 0.05, 0.5, 1, 5, 10 and 20 μM for 2 different times: 2 h and 24 h. The concentrations of AuNPs refer to dendron concentration in AuNPs and, hence, data can be used to correlate behavior of free dendrons with those attached to nanoparticle surfaces. To investigate the effect of human serum albumin (HSA) on hemolysis caused by nanoparticles studied at 5 and 10 μM, 2 mg/ml HSA were added to the solutions prior to the treatment of red blood cells. The parameters of platelet aggregation induced by thrombin were measured for dendronsand their corresponding AuNPsat 10 μM. Peripheral blood mononuclear cells (PBMCs) were challenged with dendronsHSGn(S-NMe3+)m and nanoparticles AuNP (SGn(S-NMe3+)m) at 0.05, 0.5, 1, 5, 10 and 20 μM to see the level of induction of lymphocyte proliferation or its inhibition due to mitogen–PHA-M.

The effects of dendronizedAuNPs and their dendrons on erythrocytes, platelets and peripheral blood mononuclear cells PBMCs have confirmed that the surface charges for dendrons have a significant effect on their toxicity, presenting first generation dendron with very low hemolytic values. However, the poorest values for dendronizedAuNPs were clearly found for the second generation derivative AuNP(SG2(S-NMe3+)4). However, in the presence of

human serum albumin (HSA), the toxicity of all the systems falls below 10 % (after 2 h of treatment). Regarding platelet aggregation, only third generation dendrons produced a marked negative effect. After AuNPsdendronization, the 3 systems gave higher aggregation than thrombin. Finally, cell proliferation measurement in peripheral blood mononuclear cells (PBMCs) indicated that none of the dendrons and AuNPs stimulated lymphocyte proliferation. The data indicate the influence of cell size, type of interaction between dendrons or AuNPs with cell membrane, and topology of the systems employed. Regarding the hemolysis and proliferation profiles of studied nanosystems (dendron and dendronizedAuNPs) it can be concluded that they are suitable candidates for drug and gene delivery.

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RESEARCH OF ZINC OXIDE NANORODS APPLICATION AS A PLATFORM FOR IMMUNE BIOSENSORS DEVELOPMENT

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Zinc oxide (ZnO) is an important wide band gap semiconductor material having a great potential of application in catalysis, sensing and nanodevices development based on its unique physical properties. Nanostructured ZnO not only possesses high surface area, good biocompatibility and chemical stability being non-toxic, but it also shows biomimetic and high electron communication features important for potential applications in biosensing [1]. However, applications of ZnO in biological or clinical testing schemes have remained largely unexplored, so far even though many biological assay systems rely on optical detection techniques. Many efforts have been recently made to construct ZnO-based biosensors with high performance [2, 3]. Aim of our work