MAD-Nano16
MADEIRA INTERNATIONAL CONFERENCE
Emerging Trends and Future of Nanomaterials for Human Health
17-20 November 2016 | Madeira Island | PORTUGAL

Design and applications of Phosphorus Dendrimers in Nanomedicine

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Beside polymeric, solid-lipid, ceramic, magnetic and metal based nanoparticles, and polymeric micelles, dendrimer nanostructures represent outstanding nano-carriers in medicine, Dendrimers are highly branched, uniformly distributed structures, having defined molecular weight, shape, size, host-guest entrapment properties, and diameters in the 2 to 10 nm range size. In addition, 3D multi-functional groups on the dendrimer outer shell – generally doubling with each additional generation – allow to covalently linking different moieties such as drugs to the surface of dendrimers (conjugate approach). The well-defined molecular weight and monodispersity of dendrimers induce reproducible pharmacokinetics unlike polymers. Indeed, dendrimers belong to the nanoworld, but they are constituted of soft matter in marked contrast with classical hard nanoparticles.

Among the different types of dendrimers reported up to now phosphorus dendrimers that are dendrimers having one phosphorus atom at each branching point plays more and more an important role because of their intrinsic properties: easy regioselective functionalization of the core, within the structure and at the surface with the grafting of 2, 3, and even 4 different terminal groups on the outer shell, possibility to play with the hydrophilicity/hydrophobicity of the surface and of the core, the interior being hydrophobic, high thermal stability etc. Such properties allowed the use of these dendrimers in different fields ranging from biology, material science to catalysis. Regarding biology and medicinal chemistry water soluble phosphorus dendrimers display interesting behaviors. Ammonium-ended phosphorus dendrimers are efficient transfection agents, have a high antiprion activity, interact with amyloid monomers and consequently fibril formation is prevented, or affect Alzheimer's($A\beta_{1\text{-}28}$) peptide and MAP-Tau protein aggregation. Polycationic phosphorus dendrimers having an optimized two-photon absorption chromophore as core allowed the imaging of the vascular network in the dorsal part of the rat olfactory bulb or was used for intra-cardiac injection in a living Xenopus tadpole allowing imaging of the blood vessels of the tail: no toxicity was detected for all these experiments.

On the other hand polyanionic phosphorus dendrimers display also fascinating properties,as well as neutral phosphorus dendrimers active *per se*.

After a brief illustration of the diversity of synthesis of phosphorus dendrimers, the lecture will be focused on different applications of cationic, anionic or neutral phosphorus dendrimers in nanomedicine: anti-inflammatory properties, anti-aging, imaging, diagnosis etc.. thus illustrating their fascinating properties.