Synthesis of paramagnetic dendrimers for the detection of atherosclerosis plaque

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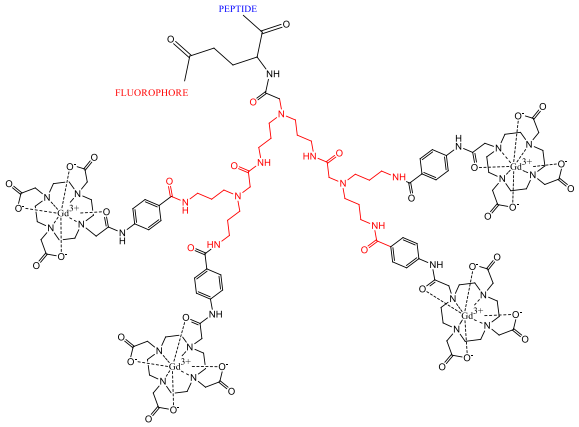
Atherosclerosis and its cardiovascular complications are one of the leading causes of death in developed countries and constitute a major public healthcare problem. It consists in formation of plaques at the wall of the arteries. These plaques are composed of lipid deposits rich in cholesterol (atheroma) enveloped in a fibrous gangue (sclerosis) [1]. It is therefore very important to have protocols for the identification and the analyse of atherosclerotic plaques and their evolution. For this purpose, we develop the synthesis of an organic platform carrying four Gd complexes that will constitute MRI probes, fluorophores for optical imaging along with a bio-vector for specific targeting.

The synthesis of the dendrimer is carried out in 6 steps by a divergent method. The interest of the dendrimer is that it has 4 primary amino functions on its periphery, so it can support up to 4 macrocyclic ligands. In a second time, the DO3A ligands [2] will be prepared and them complexed with Gd^{3+} ions to form the MRI probe. Then fluorophore for optical imaging and peptide for targeting will be added on the platform. Till now the DO3A ligands have been grafted, this reaction was carried out with an excess of macrocyclic derivatives in the presence of a base to deprotonate the quaternary amines of the dendrimer (G1). Each synthesis step is characterized by NMR or mass spectrometry.

Relaxometry measurements on the Gd complexes are performed. A NMRD profile confirms the efficacy of the paramagnetic dendrimer.



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