BIOTECHNOLOGICAL DENDRIMERS WITH A PROTOPORPHYRINIC CORE: A MOLECULAR DYNAMICS STUDY

Maurizio Fermeglia, Marco Ferrone and Sabrina Pricl

Department of Chemical Engineering, University of Trieste, Piazzale Europa 1, 34127 Trieste, Italy

The exigencies of the modern society are leading research towards the design of synthetic molecular systems, which may be employed, with success, in complex biomedical procedures. The vast majority of the natural processes involve time scale, which are too long to obtain the required biological products, thus making the production of artificial molecules, able to mimic the physiological function of interest, vital.

Blood is an extremely complex assembly of substances, whose primary function is oxygen transport and delivery to tissue. Nonetheless, the main features of blood are such that we can envisage some alternative compounds, which can mimic its primary function. Within red cells, oxygen is carried by hemoglobin, a proteic ensemble of four mioglobin molecules, whose prosthetic group is the heme group. This, in turn, is made up by a protoporphyrinic ring, which chelates a bivalent iron ion. An hypothetical artificial blood, than, should at least possess similar characteristics to be able to exhibit a similar biological activity.

In this work we have inserted the ion-heme group characterizing human blood in a class of synthetic, dendrimeric macromolecules, with the purpose of evaluating a series of properties – both structural and physico-chemical – which may, in turn, provide an indication of the possible biological activity of these polymers. To this purpose, we have performed a complete series of investigations of up to 5 dendrimer generations both *in vitro* and in a water environment. To mimic oxygen binding, we have studied also the same molecules in which the protoporphyrinic core contained a Fe^{2+} ion, bounded to O_2 and a HYS residue. Finally, we have performed a detailed investigation of the possibility of including, in the protoporphyrinic core, different metal ions.

The main results of this study have leaded us to conclude that all dendrimer generations can bind oxygen stably, the fifth generation being the most affine to the mioglobin molecule, the natural carrier of blood oxygen. Further, the series of tests performed on the molecules containing different metal atoms within the protoporphyrinic core has revealed a trend which is harmony with the biological evidence, has highlighted the

possibility of binding ions useful, for instance, in nuclear medicine and, finally, the poor affinity of this dendrimers for toxic metal ions.