

MRI-contrasting system based on water-soluble fullerene/Gd-metallofullerene mixture

Grushko Yu.S., Kozlov V.S., Sedov V.P., Kolesnik S.G.,
Lebedev V.T., Shilin V.A., Loginov Yu.E., Kukorenko V.V., Tsyrlina E.V.¹,
Krzhevitsky P.I.¹, Khodorkovsky M.A.², Artamonova T.O.², Shakhmin A.L.²,
Shamanin V.V.³, Melenevskaya E.Yu.³, Konnikov S.G.⁴, Zamorianskaya M.V.⁴

St. Petersburg Nuclear Physics Institute RAS, 188300 Gatchina, Russia

¹*N.N. Petrov Institute of Oncology, 197758 Pesochnyi, St. Petersburg, Russia*

²*Russian Scientific Centre "Applied Chemistry", 197198 St. Petersburg, Russia*

³*Institute of Macromolecular Compounds RAS, 199004 St. Petersburg, Russia*

⁴*Ioffe Physical-Technical Institute RAS, 194021 St. Petersburg, Russia*

The last decade intensive studies of Gd-metallofullerenes as MRI contrasting agents demonstrated their much stronger relaxivity compared to conventional agents ("Gadovist", "Magnevist" et al.) and their nontoxicity because of encapsulation of Gd ion in chemically stable carbon cage. In our report we present the results of proton relaxivity study the water-soluble mixtures of empty and Gd-metallofullerenes. We reveal that it is possible to prepare such mixtures highly enriched with Gd@C₈₂ (up to ca. 90%) by selective liquid extraction avoiding complicated and low productive preparative HPLC what makes them tens times less expensive than pure water-soluble Gd@C₈₂. A detailed study of hydroxylation of gadofullerenes has shown that hydrogen peroxide oxidation of solid intermediates is easiest method to produce and isolate the contrasting product. We examined the catalytic action of transition metals Fe, Co, Ni on the yield of metallofullerene in electric arc synthesis, and found that Co metal is the most effective one to increase the yield. It is well known that in water solution hydroxofullerenes undergo an aggregation enhancing their relaxivity in times. We performed SANS (small angle neutron scattering) study of agglomeration process depending on acidity and salinity of solution. These results are presented elsewhere (V.T. Lebedev et al., this conference). The MRI-contrasting properties of the preparations were studied in-vivo on rats by full scale MR-tomography. The relaxivity was compared with the standard preparations "Gadovist" and "Magnevist".

It was shown that referred to equal molar dose the prepared contrasting agent is 15-30 times more effective than standard ones depending on the targeted tissue.

This work is performed in the framework of Russian State Contract № 02.513.11.3210.