Amino-Coated Metallofullerene Nanoparticles for Glioblastoma Mutiforme Tumor Detection

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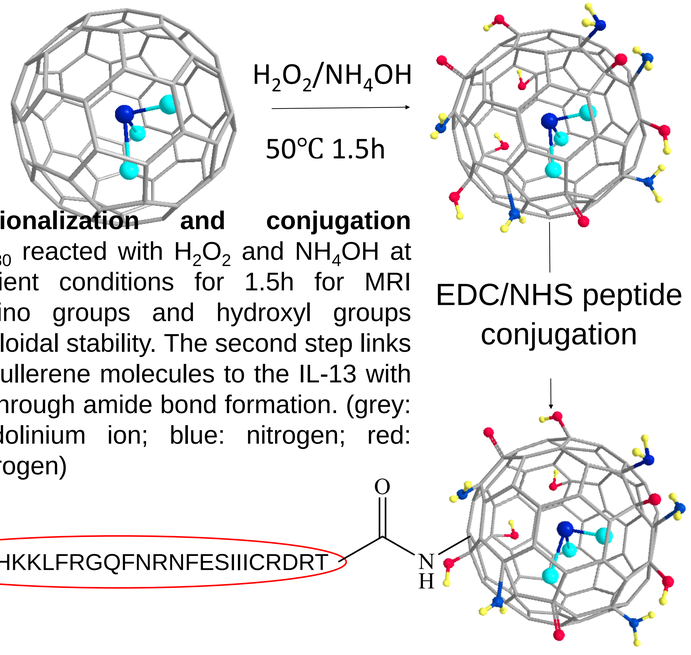
Introduction

Water-soluble derivatives of gadolinium-containing metallofullerenes have been synthesized and tested as excellent candidates for magnetic resonance imaging (MRI) contrast agents because of their high relaxivity and safety. In this poster, we report the preparation of a new functionalized trimetallic nitride endohedral metallofullerene, $Gd_3N@C_{80}(OH)_x(NH_2)_y$ with a cage surface consisting of positively charged amino groups ($-NH_3^+$), which is expected to bind more efficiently to negatively charged cell phospholipid bi-layer cellular surfaces and will more readily undergo endocytosis. We now report that this Gd-nanoplatform when subsequently conjugated with an IL-13 peptide, (IL-13-$Gd_3N@C_{80}(OH)_x(NH_2)_y$) exhibits enhanced targeting of U-251 GBM cell lines.

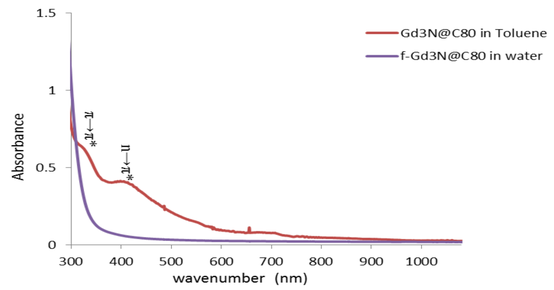
Methods



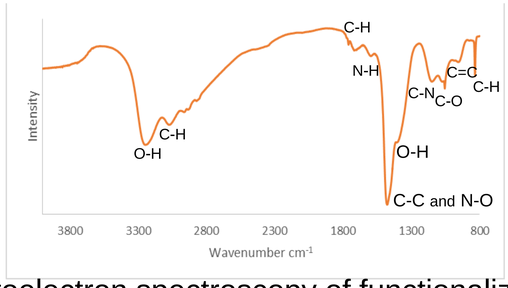
$Gd_3N@C_{80}$ functionalization and conjugation process. $Gd_3N@C_{80}$ reacted with H_2O_2 and NH_4OH at 50 ℃ under ambient conditions for 1.5h for MRI contrast, both amino groups and hydroxyl groups provide aqueous colloidal stability. The second step links functionalized gadofullerene molecules to the IL-13 with fluorescent tagged through amide bond formation. (grey: carbon; aqua: gadolinium ion; blue: nitrogen; red: oxygen; yellow: hydrogen)

Results

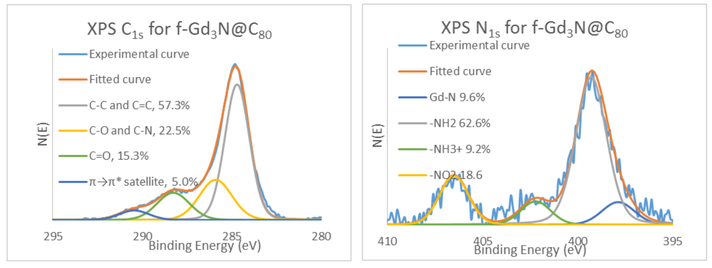
Electronic Absorption Spectroscopy



Infrared spectrum of functionalized $Gd_3N@C_{80}$



x-ray photoelectron spectroscopy of functionalized $Gd_3N@C_{80}$

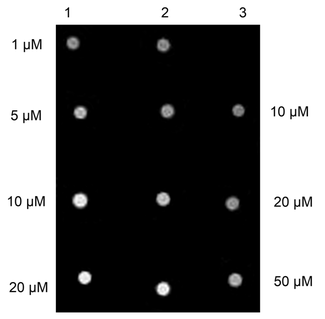


$Gd_3N@C_{80}0_{12}(OH)_{10}(NH_2)_8(NO_2)_2$

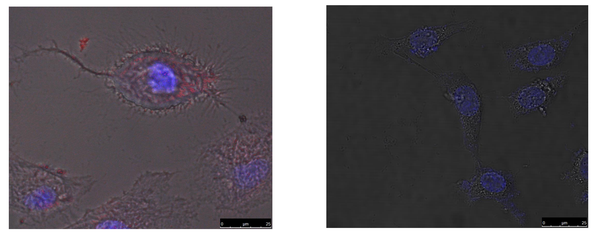
Relaxivities of functionalized $Gd_3N@C_{80}$ (in units of $mM^{-1}s^{-1}$ per mM of Gadofullerene Molecules) and r_2/r_1 ratios in pure water, at 0.47, 1.4 and 9.4 T, 25℃

0.47 T (20 MHz)			1.4 T (60 MHz)			9.4 T (400 MHz)		
r_1	r_2	r_2/r_1	r_1	r_2	r_2/r_1	r_1	r_2	r_2/r_1
88.1	102	1.2	101.4	131.1	1.3	30.5	96.1	3.2

T_1- weighted MR imaging on 3 T instrument (123 MHz) with functionalized Gd as contrast agent. 1 is carboxylated $Gd_3N@C_{80}$, 2 is amino-$Gd_3N@C_{80}$, 3 is Magnevist® commercial contrast agent.



The confocal microscopy image showing the nanoparticles efficiently bind to the U251 tumor cells （Left: U251 Right:Hela）



Conclusion

The results of this study demonstrate that conjugated IL-13 with amino-coated gadolinium metallofullerene can work as a new platform to deliver diagnostic agents to glioblastoma multiforme brain tumors cells with excellent contrast and targeting ability.

References

1. Zheng .et al, *Carbon*, 65, 175–180, (2013)
2. Fillmore, H.L, et al, *Nanomedicine*. 6, 449-458. (2011)

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