Stealth silica nanoparticles for theranostic applications

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Silica nanoparticles (SNPs) of controllable size, shape and porosity had shown to be a useful platform for different uses. In recent years our group studied and developed SNP-based systems, functionalizing, loading and embedding SNPs for different purposes.[1]

As far as biomedical applications are concerned, the surface modification of SNPs with molecules for active targeting has turned out to be a desirable step. For this purpose we selected Boletus Edulis Lectin (BEL), since it shows T-antigen recognition capabilities together with antiproliferation activity.[2] Systems composed of silica functionalized with lectin molecules have been already described in literature, for chromatography applications or assay probes. Nonetheless, to the best of our knowledge, no one has ever performed the grafting of lectins onto SNPs obtaining a functional system to be used in nanomedicine.

The aim of our research is the creation of a theranostic system, composed of SNPs suitably tailored with BEL, and carrying contrast agents and/or therapeutic phases. The tethering of PEG molecules on the nanoparticles surface will be performed in order to impart stealth properties, steric stabilization to the system and reduce citotoxicity.

Herein we present the first results of this research. The grafting of BEL has been attempted *via* two bioconjugation routes: the first relies on *in situ* reduction of the Schiff base generated from the reaction between protein's amine groups and aldehydic functionalities on previously modified silica surface. The second protocol is the well-established reaction involving EDC coupling, eventually in presence of NHS[3]. Coomassie Brilliant blue assay was performed to have a qualitative indication of the success of bioconjugation protocols. A surface coverage of 8,72 nmol of lectins per mg of SNPs was estimated from spectrofluorimetric assays recording the emission of protein's tryptophans on modified SNPs, having a diameter of around 150 nm. The permanence of the diameter of the particles after their superficial modification was confirmed by DLS measurements, while ζ-potential analyses showed a slightly negative potential in both values measured before and after modification.

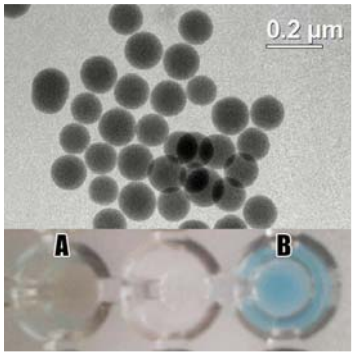

Figure 1. TEM micrograph of SNPs (upper part) and photograph of Coomassie colored wells of nanoparticle before (A) and after (B) lectins surface grafting.

At the same time, PEGylation was successfully performed on pristine SNPs with a co-condensation process, which allowed to obtain fairly monodisperse SNPs covered with a polymer layer, as confirmed by TEM observations, IR spectroscopy and cell viability tests.

Although some issues have been encountered, like the presence of some aggregates during the grafting of lectins and a partial loss of the activity of BEL, we foresee the possibility of combining the two procedures creating an efficient and multi-purpose theranostic nano-carrier.

References

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3. Hermanson G. T., Bioconjugate chemistry **2008**, Elsevier (Academic Press)