Multifunctional Coordination Polymer Particles for Bio-medical application

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The development of different techniques to achieve nanomaterials with unusual and enhanced properties compared to traditional materials have afford new systems with interesting applications in areas such as electronics, catalysis, sensing or biomedicine. The coordination polymers are a fascinating family of materials created from supramolecular assembly of metal ions or clusters and organic ligands that act as building blocks to generate a superstructure with genuine and highly tailorable properties. The results obtained in the last years have shown that these systems can be interesting alternative materials for technological uses. The easy of tuning and modification of their properties based on chemical-structural changes allow control rationally their physicochemical properties.

Our principal efford within our research group is to develop an specific kind of coordination polymers particles synthesized at the nanoscale with application in Biomedicine.[1] In this research area there is an special interest in achieve multifunctional platforms that can provide different properties with interest in biomedicine.[2] A posible ideal system would consist in a nano-platform with optimun size and shape to penetrate in different tisues but also to avoid the immunological system, that is be able to encapsulate different active substances, with biosensing properties and active as bioimaging agent. Moreover, the posibility of building these systems containing the active specie as building-block open a new approximation to achieve a platform with smart activity and added value.

With this aim, our research group has developed the synthesis of nanoscale polymeric coordination particles (CPPs)¹ able to encapsulate a wide variety of substances and materials for biomedical application.[3,4] The last experimental results have afford the synthesis and characterization of smart responsive CCPs able to tune such release upon external stimuli.[5] We will also show our most recent advances for their use not only for delivery but also for bioimaging purposes as well as the possiblity to functionalize them to improve their cell internalization processes, biocompatibility, and targeting directionality for especific recognition.[6] The good physicochemical properties of these nanoplatforms joint to the extremelly low toxicity, make them an interesting alternative to the current systems.

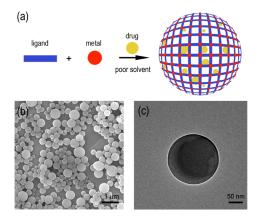


Fig.1 a) Scheme of CPPs synthesis, b) SEM images of the resulting nanoparticles, and c) TEM image of a drug loaded nanoparticles.

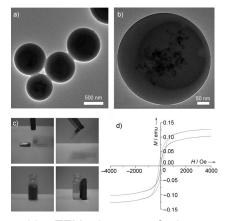


Fig.2 a-b) TEM image of iron oxide nanoparticles, c) interaction of the loaded nanoparticles with a magneto, and d) hysteresis loop of encapsulated magnetic nanoparticles.

Here we report the synthesis and characterization of CPPs with controllable dimensions (between $40nm-2\mu m$) bearing reactive groups (-COOH, -NH₂, etc.) at the surface. Their crystallinity and morphology can be controlled systematically by the proper combination of ligands and metal ions and reaction conditions. Using carbodiimide assisted coupling reactions different active molecules and biomolecules have been attached to the nanoparticles surface confering them a given specific property. In that manner we have been able to graft CPPs with dyes or poly-ethylene glycol derivates, among others. These ligands confer new interesting properties such as fluorescene to follow the cellular internalization of the CPPs or robustness against opsonization processes.

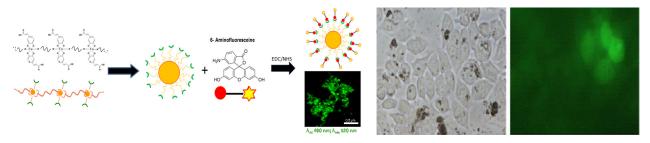


Fig.3 Scheme of fluorescein functionalized CCPs by carbodiimine assisted coupling reaction

Fig.4 Optical and fluorescence images of the fluorescent nanoparticles internalization

As complementary studies, we have achieved the robust immobilization of these functionalized systems in gold surfaces. This approximation provides interesting platforms to be used in integrate systems with potential uses in biosensing and in clinical diagnosis.

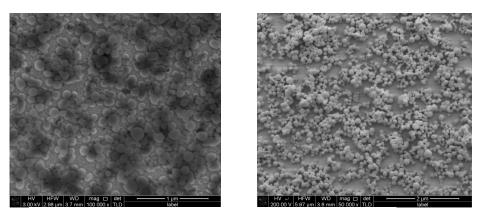


Fig.5 HR-SEM images of CPPs attached to gold surface

All these preliminary results joint to the cytotoxicity experiments that shown a very good biocompatibility of the resulting functional capsules even for the case of using cobalt metal ions, open new venues for CPPs to be used as multifunctional platforms at biological level.

References

- [1] F. Novio, J. Simmchen, N. Vazquez, L. Amorín, D. Ruiz-Molina, *Coord. Chem. Rev.* submitted invited paper.
- [2] M. De, P. S. Ghosh, V. M. Rotello Adv. Mater. 20, (2008), 4225.
- [3] I. Imaz, J. Hernando, D. Ruiz-Molina, D. Maspoch, Angew. Chem. Int. Ed. 48, (2009), 2325.
- [4] I. Imaz, M. Rubio-Martínez, L. García-Fernández, F. García, D. Ruiz-Molina, J. Hernando, V. Puntes, D. Maspoch, *Chem. Commun.*, 46, (2010), 4737.
- [5] F. Novio, J. Simmchen, J. Ruiz, V. Rodriguez, N. Cutillas, J. Lorenzo, D. Ruiz-Molina, *paper in preparation*
- [6] F. Novio, P. González-Monje, J. Lorenzo, D. Ruiz-Molina, Angew. Chem. Int. Ed. Engl. submitted