

# Enzyme Nanocapsulation in Silica Gel-based Nanoparticles Towards Development of Novel Nanocarriers for Enzyme-Mediated Therapeutics

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Nanoencapsulation of bioactive molecules is expected to have an increasing number of applications in drug delivery, where sub-micron carriers can provide long-term blood circulation while protecting sensitive biomolecules, such as enzymes or more generally proteins, from the attack of the immune system *in vivo*<sup>1, 2</sup>. More specifically, nanoencapsulated enzymes may exploit the accumulation of biocompatible nanocarriers in tumoral masses as a mean to perform there chemical transformations of inert pro-drugs into corresponding active chemotherapeutics.

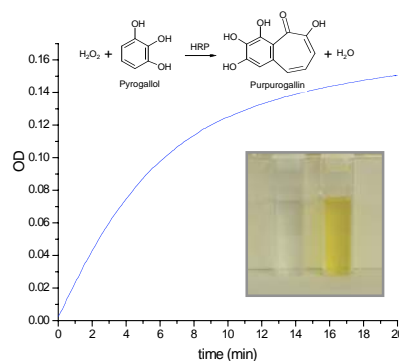
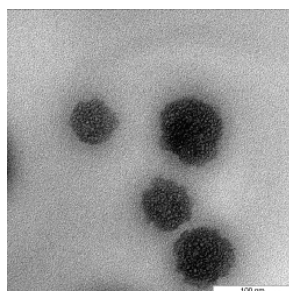
For this scope, silica gel-based nanoparticles have been synthesized and used as nanocarriers for enzyme encapsulation. Silica gel has indeed a number of interesting characteristics, namely its high biocompatibility *in vivo*, excellent physical and chemical stability, and, last but not least, it can be produced under very mild conditions (sol-gel process) that can retain the functionality of the entrapped protein<sup>3, 4</sup>. In the present work we have focused on two targets: a) the improvement of existing sol-gel processes for a milder encapsulation of active biomolecules in silica-based colloids, b) the functionalization of silica nanoparticles with organic polymers to provide “stealth” character to the carriers.

**Nanoencapsulation:** The classical sol-gel synthesis of silica gels has been adapted to a W/O microemulsion process under conditions that minimize denaturation of encapsulated enzymes and any tendencies to colloidal instability during the purification steps<sup>2</sup>.

**Functionalization:** the anionic surface of colloidal silica has been functionalized by the adsorption of a synthetic polycation which contains initiators of Atom Transfer Radical Polymerization (ATRP)<sup>5</sup>. The initiators offer the possibility to decorate the nanoparticles with polymer layers composed of e.g. poly(ethylene glycol) (PEG) or poly(2-hydroxyethyl methacrylate) (poly(HEMA)), which could respectively provide stealth character and chemical functionality to the nanocarriers<sup>3</sup>. Encapsulation of enzymes such as horseradish peroxidase (HRP) and glucoxidase (GOx) has shown that the process has preserved the enzyme activity.

**Left:** Transmission Electron Microscopy image of coated SiO<sub>2</sub> NPs

**Right:** Spectrophotometric analysis of the activity of Horse Radish Peroxidase encapsulated in coated SiO<sub>2</sub> NPs. Pyrogallol is converted in the yellow purpurogallin by enzymatic oxidation



## References

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