Abstract

This PhD thesis is entitled "*Supramolecular and hetero-supramolecular chemistry in controlled release and molecular recognition processes*" and it is focused on two of the most important and recent subjects of supramolecular chemistry: **molecular recognition** and **controlled delivery processes**.

In particular the first part of this thesis is focused on the design and synthesis of suitable organic compounds as chemosensors for anionic and neutral species. The selected sensing paradigm was the *chemodosimeter* approach. This presents some advantages with respect to the other two paradigms (*displacement* and *binding site-signaling subunit*); among others the possibility of operating in aqueous solution. In particular two selective probes were synthesized one for fluoride anion (F^-) and another for glutathione (GSH). The selective chemodosimeter for F^- is a phenolic azo-dye functionalized, on the phenolic –OH, with a silylether. This sensor displays an intense absorption band centered at 350 nm and, upon treatment with F^-, underwent a significant hypochromic and a slight bathochromic shift (of ca. 10 nm), while a new band appeared at ca. 470 nm, resulting in a change from colorless to orange red. In the case of the selective sensing of GSH a pyrylium based chemodosimeter was prepared. This compound was later dissolved in a CTAB/water solution that resulted in an intense blue color. In this case GSH was able to induce a remarkable hypochromic effect in the absorption bands with the subsequent bleaching of the initial blue solution. Moreover, addition of GSH induced the appearance of strong emission band centered at 485 nm (upon irradiation at 350 nm).

The second part of this PhD thesis deals with the design and synthesis of organic-inorganic nanoscopic hybrid systems for controlled delivery of bioactive molecules into intracellular environments. These hybrid materials are composed of two main units: an inorganic silica based mesoporous scaffold, able to store organic molecules (dyes or drugs) and an organic compound anchored on the external surface of the inorganic mesoporous support than acts as *molecular gate*. The application of an external stimulus can modify the steric hindrance of the capping organic compound (molecular gate) enabling or disabling the diffusion of the stored molecules from the inner to the outer of the pores. The first synthesized and studied system was composed of an inorganic mesoporous nanoscopic matrix (MCM-41), loaded with the dye $Ru(bipy)_3^{2+}$ and functionalized with an oligoethylene moiety anchored to the silica surface through an ester group. The addition of a esterase enzyme induced the selective hydrolysis of the ester moiety, the subsequent reduction of the steric hindrance of the molecular gate and the release of the entrapped dye. A second delivery system consisted of a MCM-41 matrix and the dye $Ru(bipy)_3^{2+}$, but in this case the outer surface was functionalized with a photocleavable molecule. The irradiation on the molecular gate's absorbance maximum determined the photodegradation of the capping molecule and the consequent delivery of the cargo. A third example contained a gate characterized by the presence of two different enzymatically hydrolizable groups: urea and amide moieties. The final hybrid material, consisting of a mesoporous MCM-41 characterized inorganic matrix, loaded with $Ru(bipy)_3^{2+}$, was able to specifically release certain amount of dye, depending on the enzyme used. Thus a rapid but less intense delivery or a slower but more intense delivery could be induced, by simply selecting the appropriate enzyme. Finally a MCM-41 based hybrid material, loaded with rhodamine-B and functionalized with galactooligosaccharides on the outer surface was

synthesized. This material was able to deliver the entrapped dye selectively in senescent cells due to the presence in theses cells of overexpressed β-galactosidase enzyme, which is able to selectively hydrolyze the galactooligosaccharides groups.