THE NANOPARTICLES FOR BIOMEDICAL

The challenge in the coming decades in the life sciences will perform analysis in-situ and in vivo at the micro level, identifying the link between biological molecules and their function and act upon them for the improvement of human health. Since the nanoparticles may come to have very close in size to those of biomolecules (see fig. 1), their use can be very important to win this challenge. There is a vast field of their application in medicine and biotechnology, diagnostics of diseases, the release of medicines, repair genes, gene therapy, etc. .

In recent years, nanoparticles of core-shell type biocompatible have had considerable development and attracted interest from the international scientific community working in analytical chemistry, as part of a multidisciplinary collaboration between researchers working in nanotechnology, chemistry, materials and biotechnology.

The core-shell nanoparticles can be used in analytical biochemistry, in the separation of biomolecules and to perform bio pictures.

1. Configuration of core-shell nanoparticles

These nanoparticles have a size between 1 and 100 nanometers and consist of an inner part functionalized inside an outer structure (shell) editable and of biomolecules on the outer surface to make the biocompatible particles (see Fig. 2). All three partners play a crucial role assigned to the nano particle function.

The inner part of the nano particle (heart) can be prepared with different materials, thermal, luminescent, electronic, magnetic, etc., So that the functionality that the particles can play spans a wide range of biomedical applications. For example, the nanoparticles having inside of the fluorescent dyes can be used to identify by means of the technique of fluorescence numerous biomolecules and tissues. Nanoparticles having in the heart of semiconductors such as CdSe, also called quantum dots, are used for sensors thanks to the fact that the quantum dots can emit signals in a very narrow band of luminescence as a function of the size of their size. If the heart of the nanoparticles is magnetite $FeO.Fe_2OR_3$ nanoparticles can be used for the separation and enrichment of biological molecules to be analyzed, finally placing a medicinal product within the heart is possible to transport such encapsulated in external structure medicinal product until the tissue where it must be the administration, obviously with great curative efficiency .

With regard to the external structure (shell) it may be formed from inorganic material, organic (polymers). The most widely used inorganic material is silicon oxide. If is compared with a biological organic material, liposomes, it has superior characteristics in that it is not subject to microbial attack, is resistant to salts present in the bile and the present lipase in the gastrointestinal tract and can withstand autoclaving. In addition, the silicon oxide is chemically inert and therefore compromises with oxidation-reduction reactions that may occur on the surface. Which organic shell is often used chitosan, the material constituting the outer part of the crustaceans, in so far as it is soluble in water, very stable and biocompatible.

The biocompatibility of the nanoparticles, adapted to ensure the functionality, is entrusted to molecules that are adsorbed on the surface of the external structure. In particular biomolecules modified

They can play an important role in biological applications. In this sense they can be used proteins which include antibodies or antigens, enzymes, DNA or RNA. The function that has the mail all'esterna substance of the nano particle is the recognition is the traceability of the fabric with which the nano particle comes into contact. Some examples of core-shell nanoparticles with a magnetic core are shown in Table 1.

2. Synthesis of core-shell nanoparticles biocompatible

The nanoparticles will have a size between 1 and 100 nm and a narrow particle size distribution. The production takes place in three phases:

1. Generation nucleation of nanoparticles present in the heart
2. Training of the shell coating
3. Modification of the biological surface

As you know there are many techniques to produce **nanoparticellle, which will form the core** of the core-shell nanoparticles: from gas, liquid phase, by sol-gel, etc. . The technique is most suitable in this case that of inverse emulsion or microemulsion. The droplets of the nanoparticles, dispersed in an organic system in which they are immiscible, contain within the material to produce the nanoparticles of the heart (see Fig. 3) and work as a nano reactor which subsequently results in the formation of the external structure. The size of the droplets, as determined by an appropriate system for the formation of emulsions, controls the size and the particle size distribution of the produced nanoparticles. Through this technique are obtained very uniform particle size and shape, in fact this technique is adopted to produce nanoparticles with quantum dots the heart, magnetic material, medicinal, etc. .

There **external configuration (the shell)** It is carried out by coating over the particles previously obtained to increase the chemical stability, improve the biocompatibility and mechanical strength of the particles present in the heart. You can use inorganic and organic materials. A typical example are the particles that have a biocompatible silicon oxide coating. The technique consists, in this case, in dealing with the emulsified droplets with tetraetossidosilano (TEOS) which is hydrolyzed on the surface of the same droplets, in the presence of ammonia as a hydrolysis catalyst (see fig. 4). In nanoreattore constituted by microemulsioante droplets it is also possible to lay the TEOS molecules functionalized with vinyl terminals, amine or other type of particles for use in biomedicine. In fig. 5 shows the image of the particles produced with this technology. For example, the silicon oxide nanoparticles modified with the amino group can be synthesized directly using essre sicrona hydrolysis of TEOS and AEAPS N- (β- ammonoetile- γ- aminopropyltriethoxysilane) in the emulsified oil droplets If you have a magnetic heart you can take the following steps:

1) is made to occur between the precipitation of iron chloride and sodium sulfite, in the presence of ammonia, obtaining iron hydroxide, $Fe(OH)_3$;
2) the water is evaporated and the oxide hydrate is obtained and for heating its anhydrous form;
3) calcining at 1400 ° C is obtained magnetite $FeO.Fe_2OR_3$;
4) the particles thus obtained are placed in a stirred aqueous solution containing 3% of sodium silicate 3%, thereby obtaining the precipitation of the silicon oxide on the magnetite particles;

5) the nanoparticles may be placed in a stove to dry.

There **Biological modification of nanoparticles** it is essential to bind the nanoparticles to biological molecules that are part of the cells to be analyzed or identified. For example, quantum dots modified can give evidence of the particles to which they bind with a change of color or diffraction of light and thus can be used as biosensors. But the quantum dots have low biocompatibility and must be modified to reduce their cytotoxicity in vitro and in vivo.

For biologically modify the nanoparticles are three methods:
The modification can be carried out in situ during the synthesis operation. As described above for the silicon oxide, the simultaneous synthesis of TEOS and AEAPS which involves a heart with a coating of silicon oxide modified with an amino group.
The second method consists in making a biomelocola adsorb on the surface of the nano particle, establishing a bond of physical type. This technique, however, can lead to separation of the biomolecule from the nano particle surface.

The most widely used method is to define a chemical bond between the functional group type already fixed on nano particle to a biomolecule. In fig. 6 shows various reaction leading to bind a biological molecule that has a terminal capable of reacting with a terminal present on the outer surface of the nanoparticles, said binder. The pairs of the most common ligand-receptor are: biotin-avidin, antibody-antigen, etc.

3. Applications of the core-shell nanoparticles

Applications can be the most diverse in the field of biomedicine. The most frequent are in the analytical field, but there are also applications which release of a medicinal product, in the latter case, however, the composite particle often has an organic material external configuration, typically chitosan.

In the analytical field, one of the most common applications is that concerning the analytical method based on fluorescence. There are chemicals that attach fluorescence inside or outside of cells with which they bind, failing to provide important information for early diagnosis. Unfortunately, these products have limitations both as they can undergo a partial elimination of their quality by reducing the intensity of the fluorescence, both because in significant quantities can be toxic. The nanoparticles with quantum dots provide much higher fluorescence intensity (see Fig. 7). For example, nanoparticles of CdSe coated with ZnS present compared to rhodamine dye a luminescence 20 times higher and a 100 times higher stability with respect to agents that reduce the fluorescence. The nanoparticles placed in the body detect and bind to the cells to be identified through their ligands (see fig. 8).

Table 1: Examples of core-shell particles with magnetic heart

the shell material	surface Modification	Application
SiO2	DNA	DNA separation
Chitosan	Enzymes	Purification of enzyme
polylactic acid	Medicinal antinoplastico	Detection of cancer cells

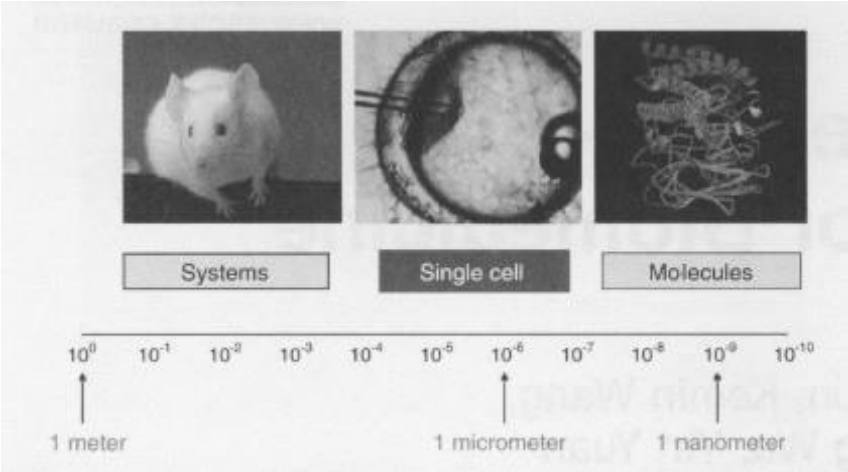


Figure 1 Dimensions of several items to consider in biomedicine

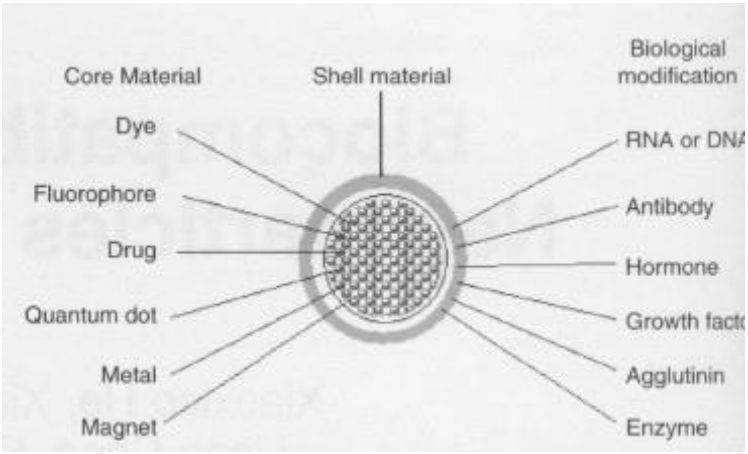


Figure 2 Core-shell nanoparticles and their use

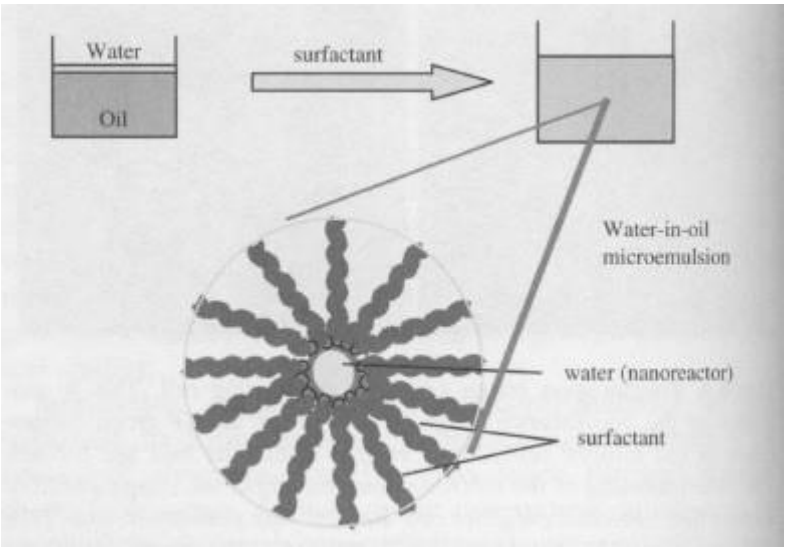


Figure 3 Production of core-shell nanoparticles for microemulsion

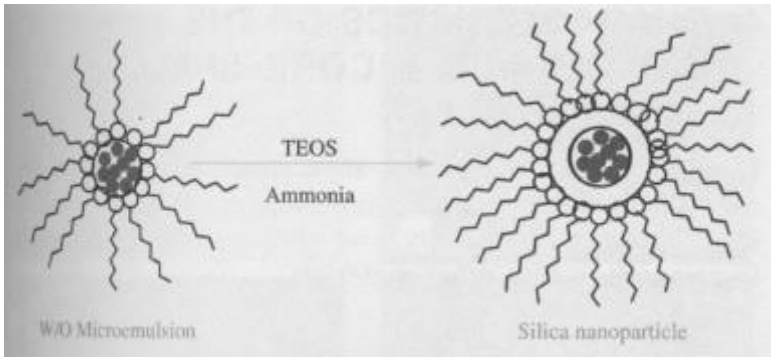


Figure 4 Creation of the shell of the core-shell nanoparticles

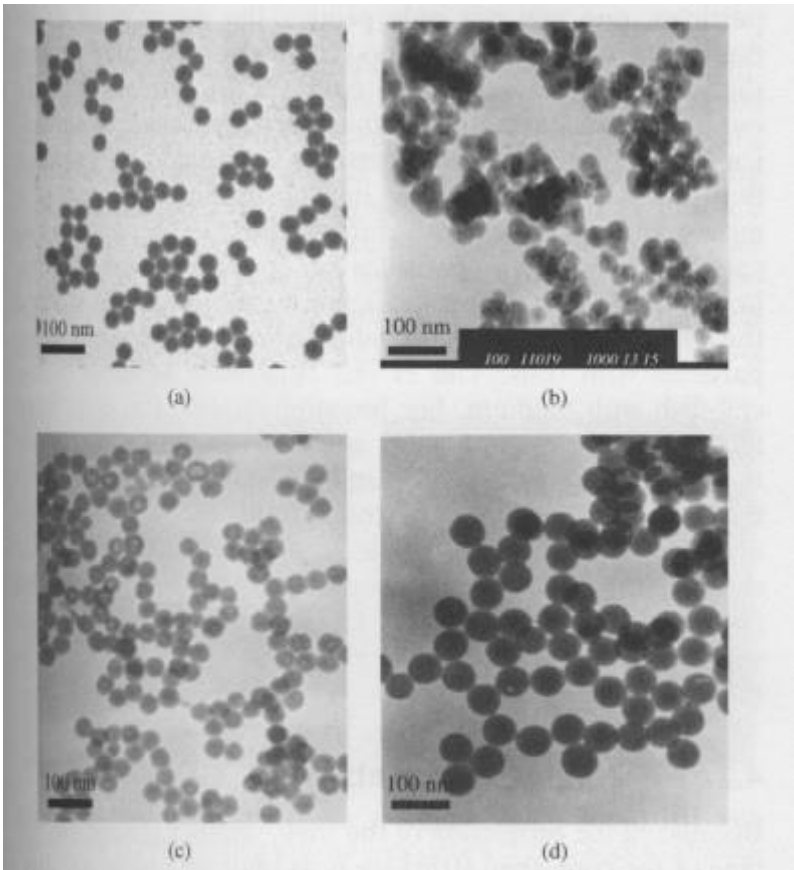
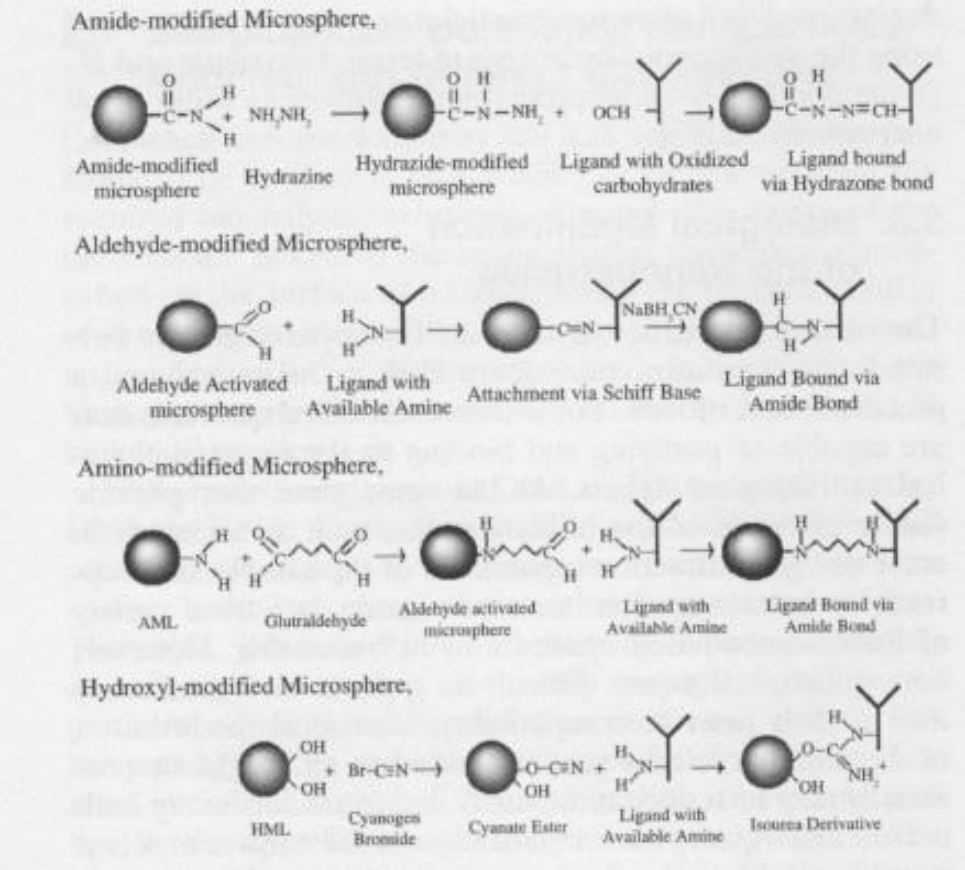


Figure 8. TEM images of silica coated nanoparticles. (a) RuBPY doped silica nanoparticles, (b) silica coated magnetic nanoparticles, (c) TRITC doped silica nanoparticles, (d) RuBPY doped silica nanoparticles.

Figure 5 Images TEM nanparticelle core-shell with the coating of silicon oxide functionalized



Figures 6 Modification of biological nanoparticles

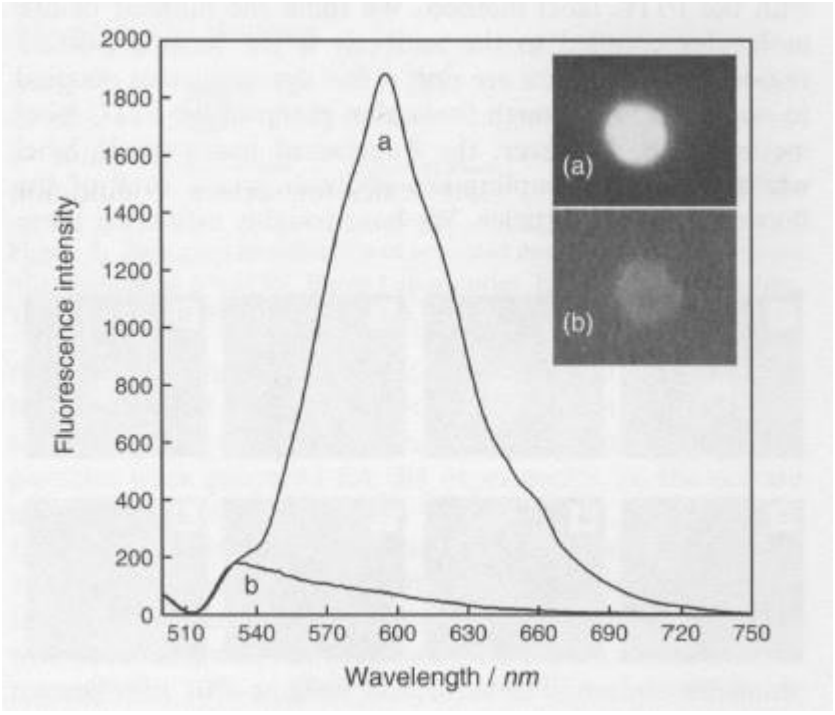


Figure 7 Emission spectrum and images of lymphocytes: a) in the presence of nanoparticles; b) presence of chemicals (FITC)

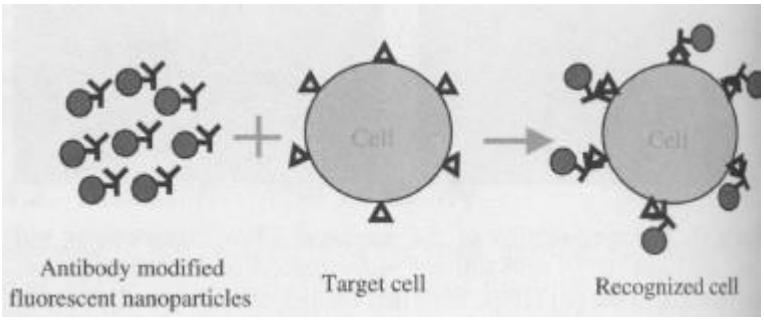


Figure 8: Linkage between nanoparticles and cell to be identified