SIZE DOES NOT MATTER … BUT SOMETIMES IT DOES: SMART NANOHYDROGELS

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Since the early twentieth century science advanced greatly to the point of being able to modify the structure of a large number of molecules, polymers among them, which nowadays are everyday materials and have great industrial and technological importance. Thanks to these advances, current polymer research is centered not from the perspective of inert materials, but in developing materials for applications that are beyond its typical use.

In the last decade, nanoscience has taken a growing interest because of the wide range of potential applications that can bring in areas such as biomedicine, agriculture, the cosmetics industry, polymer science, etc. [1]. Undoubtedly, the complexity of nanotechnology involves the use of new techniques for structuring and chemical functionalization exploiting the most of the properties of nanoparticles to enable its use on a selective or specific manner [2]. In this regard, the science of polymers makes it possible to obtain macromolecules with new chemical structures and physical-chemical properties with extraordinary because the polymers are complex materials that have a wide variety of properties that may change before, during and after their synthesis [3].

The so-called stimulus-response smart nanogels have emerged as a promising new class of materials with pharmaceutical applications. In these systems, small changes in some environmental variable such as temperature, pH, ionic strength, leads to a reversible phase transition in the structure of the gel. The poly(N-isopropylacrylamide) hydrogel presents a well-defined LCST in water near 32°C, above this temperature the gel structure collapses resulting in a sharp deswelling, which is reversible if the system temperature returns to below 32ºC. Furthermore, when these materials have ionizing functional groups are sensitive to changes in pH. The pH affects these systems similarly to temperature, so that a given change in pH of the medium makes the nanogel to swell, leading to an increased pore size of the polymer network, this facilitate molecules migration toward outside of the nanogel. This process is known as "release" and is the principle governing the current drug dispensing systems. Within the drug dosing systems we can find two basic types, which are the starting point for designing new mechanisms of transport and drug delivery, these are called "controlled release" and "targeted release".

The hydrogels are polymers that have similar characteristics to those of a living tissue. This feature has allowed them to be the focus of the biomedicine [4]. The combination of nanoscience, biomedicine and polymer science has become the main topic of research in recent years because it is a new discipline that exploits the potential of nanoparticles for use in biomedical applications [5]. Undoubtedly, the complexity of the nanoscience implies the use of new chemical structuration and functionalization techniques that exploit

the properties of nanoparticles that let express them in selective manner specific qualities. In this regard, the polymer science is the nearest to allow selective chemical structure due to the polymers are complex materials that have a wide variety of properties that can be changed before, during and after their issuance.

Here is reported the chemical functionalization of smart nanogels by incorporating pH-sensitive functional groups and folic acid as a tumor targeting ligand into the same initial polymer network. One of the most promising strategies in anticancer therapies is the targeted delivery through malignancy-associated cellular markers. Recently, Katime and coworkers [6] have designed new synthetic devices with enhanced stimuli-responsive sensitivity and targeting ligands that can be a promising field for the development of cancer-specific delivery systems. The new devices would lead to a reduction in the minimum effective dose of the drug required for each target [7]. The over-expression of folate receptors on many cancers identifies them as a potential target for a variety of ligand receptor-based cancer therapeutics. In fact, folate receptors are qualified as a tumor-specific target. Furthermore, folic acid molecules have numerous advantages in comparison with other ligands, such as their small size, availability, simple chemical conjugation, and no inmumogenicity. Due to these unique characteristics folic acid is actually presented as an ideal ligand for targeted delivery into tumors. Katime have developed new synthetic molecules based on microemulsions systems that can offer an interesting and potentially quite powerful alternative carrier system for drug delivery because of their high solubilization capacity, transparency, thermodynamic stability, ease of preparation, and high diffusion and absorption rates when compared to solvent without the surfactant system [8]. The microemulsión polymerization process is one of the most versatile methods to obtain smart nanocarriers ranged between 10-100 nm with a very homogeneous particle size distribution (≈ 1.1).

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