



Polyhedral Oligomeric Silsesquioxanes (POSS)s in Medicine

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Abstract

In the last 25 years a new class of nanostructured materials has overwhelmingly made its way into the biomedical field. Polyhedral Oligomeric Silsesquioxanes (POSS)s which, thanks to their hybrid nature (organic-inorganic), are materials with both high mechanical strength and biocompatibility. These characteristics, and others, make them ideal candidates for the most varied applications in medicine. This short review traces the aspects of the main recent applications.

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Introduction

One of the chemists dream is, since several years, to unify in the same products the different characteristics of both inorganic and organic compounds, different from those we can obtain by a simple blend at macroscopic level [1]. Aiming to improve the quality of life, both the academy and industry need to address a number of challenges related to health, through the design and development of new functional materials. Thus, the concept of “hybrid organic-inorganic” composites has had much emphasis since the second half of the 20th century with the development of the soft chemistry [2]. The idea is to take advantage of the best performances of both, inorganic and organic, components and avoid their drawbacks. In this context, a significant advance could be the synthesis of nanomaterials, where the structural order within the product can be controlled on nanometer/submicron scales [3]. Among the interesting class of inorganic/organic hybrid materials of silsesquioxanes (random, ladder, caged or partially caged) we found the Polyhedral Oligomeric Silsesquioxanes (POSSs). These nanoparticles are characterized by the presence of a cage of silicon and oxygen atoms, with linked to organic R groups by covalent bonds. POSSs are well known with the formula $(\text{RSiO}_{1.5})_n$ and have 8 as

the most common value of n, thus presenting a very highly symmetric structure, with a diameter usually falling in the 1.5–3 nm range [4]. Despite POSSs were synthesized first time in 1946 by Scott [5], they acquired, thanks to their excellent thermal, mechanical, optical and electrical properties [6-10], considerable importance just since '80s. Their peculiar characteristics make POSSs suitable for the use in various fields and due to their excellent mechanical properties and biodegradability, provided by Si-O-Si bonds, these molecules have been considered a next generation material in biomedical fields [10-12].

Nomenclature

Polyhedral has been assigned because, despite in many literature reports they are represented like a cube (**Figure 1**), the silicon-oxygen cluster forms a polyhedron (cage) as the silicon-oxygen-silicon and oxygen-silicon-oxygen bonds form angles different than 90°. The prefix -oligo denotes the existence of a small number of units present in the molecule; -meric is derived from the Greek language -μερής which means part; -sil is for silicon; -sesqui because each Si atom is bound to an average of one and a half oxygens; -ane because Si atom bound to one



hydrocarbon group.

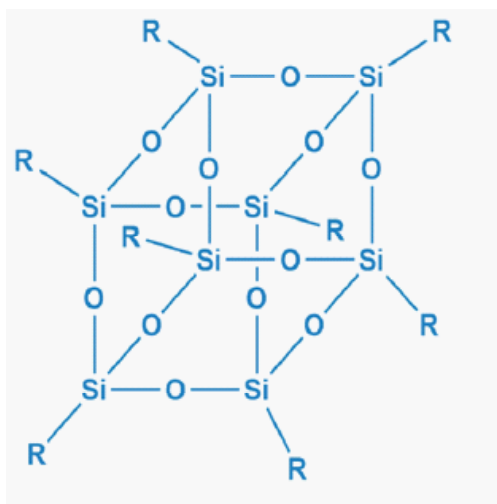


Figure 1: Polyhedral Oligomeric Silsesquioxanes structure

Biomedical Application

Owing to their biocompatibility, cytocompatibility, non-toxicity, low inflammatory response and ability to be easily incorporated into different polymers, in biomedical application, POSSs can be used both as nanoparticles and as POSS-based nanocomposite. The resulting nanostructures have been shown to have potential for various applications in diverse areas such as drug delivery, dental applications, biomedical devices and tissue engineering. BODIPY is a commonly employed fluorescent cellular membrane marker, which can be readily conjugated to various systems to track cellular migration patterns [13]. McCusker et al. demonstrated that amine-functionalized POSS units exhibit very low toxicity and efficient uptake in the cytoplasm of Cos-1 cells [14]. The migration pattern of POSS– BODIPY is drastically different from the non-conjugated control, demonstrating that the POSS unit is directly responsible for this behaviour. Furthermore, dispersion in the cytosol demonstrated that the POSS-BODIPY conjugate entered into a cell via diffusion, and not via endocytosis. The lack of nuclear uptake demonstrated specific localization in the cell, and observations showed that the silicon cages had potential as drug delivery carriers via direct conjugation with drug molecules that were insoluble in water, or exhibited a lower cellular uptake. In 2008, Tanaka et al. found that a POSS core dendrimer can entrap a larger amount of guest molecules, in respect to a pristine dendrimer, without loss of affinity. Consequently, the water solubility of the entrapped guest molecules can be increased. In addition, effective inhibition of fluorescence photobleaching of the entrapped molecules was accomplished, thus suggesting the potential widespread application of POSS-core dendrimers for medicinal science and biotechnology [15].

More recently, Yuan et al. proposed a Poly(l-glutamic acid) dendrimers with a polyhedral oligomeric silsesquioxane (POSS) nanocubic core that are promising vectors for fabricating smart and targeting drug delivery systems, due to its globular morphology and compact structure with multiple peripheral functional groups [16]. In particular, the release rates of doxorubicin at different pH levels were investigated, and the cellular uptake of the biotin modified conjugates was analysed, endorsing this nano-system suitable for drug delivery applications. Cyanoacrylate (CA) based adhesives are good soft tissue adhesives, but their low mechanical properties and lack of hydrolytic stability has made them less interesting in the applications deal with

hard tissues. Fadaie et al. evaluate the effect of incorporation of an acrylate polyhedral oligomeric silsesquioxane nanostructure (APOSS) on the physical and mechanical properties and hydrolytic stability of octyl (CA) adhesives for dental application [17]. In particular, they observed a significantly improve of the flexural strength of CA adhesive by incorporating less than 20 wt.% APOSS, while they observed an increasing trend in the flexural modulus with the nanostructures loading. Furthermore, degradation due to the hydrolysis in water was diminished in the specimens containing APOSS nanostructures. As regards the area of tumour diagnosis, the POSS nanoparticle features, described in the introduction, allow the qualitative/quantitative in vitro detection of tumour cells at the site of interest. Nanoparticles can act either by direct or indirect mechanisms. Taking advantage of tumour vasculature hypermeability can give these nanomaterials the flexibility required for the direct targeting of tumour tissues. However, in an indirect way, these particles can also target the tissue or cells near the tumour, and act as a drug reservoir to fight against the adjacent neoplastic cells [18].

Conclusion

In these years POSSs have proved to be absolutely versatile materials, therefore perfect to perform the tasks that are often required in the biomedical field. Moreover, thanks to the possibility of functionalizing their organic periphery in various ways, Polyhedral Oligomeric Silsesquioxanes can still give a lot to nanomedicine.

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