Applications of aerogels in life sciences

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Abstract

In this paper an overview about the applications of Aerogels in the fields of pharmacy, cosmetics, medicine, agriculture and biotechnology is given. The in situ encapsulation of proteins and enzymes into aerogels was shown to be a very promising technique leading to the increase of biocatalytical activity. Furthermore aerogels are used as host matrix for bio-active compounds, which improve or enable their performance. A promising area here is the use of macroporous silica aerogels as biosensors. In the filed of agriculture the application of fine silica aerogel powders for the storage protection of grains was demonstrated. The ability of aerogels to encapsulate chemical species like herbicides, insecticides, pesticides, fertilizers can be further utilized in this area. The use of both inorganic and organic aerogels as carriers for pharmaceutically active compounds was demonstrated by several groups. Aerogels were loaded with pharmaceuticals by many techniques, whereas the adsorption from supercritical solutions seems to be a most promising one. The bioavailability of many pharmaceuticals is significantly improved in this way. Taking into account all research activities in the area of aerogels application in life science a number of promising applications can be expected in future, whereas supercritical extraction and adsorption are the key technologies thereby.

Keywords: Aerogels; Drug carrier; Supercritical CO_2

1. Introduction

Silica aerogels were used in daily life products since 1960s, when Monsanto's aerogels were introduced as additives in cosmetic and toothpaste. At present, an interest has grown in the field of biocompatible aerogels and composite aerogel materials in life science. Biocompatible aerogels can be principally made from any organic compounds, which properties such as toxicity and biodegradation are suitable for a given application [1,2]. In case of aerogel composites the final product consists of an aerogel matrix (mostly silica aerogel is used) and one or more additional phases (of any composition or scale), which influence the properties of the final product. Thus, at least one phase has a physical structure with dimensions in the order of nanometers (the particles and pores of the aerogel). The aerogel composites can be prepared in two different ways: through addition of the target compound during the sol-gel process or by post-treatment of the dried aerogels (for example by vapour phase deposition after supercritical drying or through reactive gas treatment).

Both approaches have been used by several research groups in order to prepare nanocomposites of silica aerogel, which are used for many different applications (see some recent reviews on aerogel applications [2, 3]). This review will be focused on the synthesis of biocompatible aerogels and aerogel composites and the use of aerogels in life science (medicine, pharmacy, agriculture) and related areas.

Aerogels based on biopolymers

Chitosan

Biopolymers are widely used in pharmacy as drug delivery systems. The preparation of biopolymers in form of aerogel could result in a product having high porosity and high surface area, which is favourable for many applications. One of the most abundant organic polymers is chitin, a polyglucosamide, which contains in exoskeletons of insects, cell walls etc. Chitin itself is not applicable for sol-gel processes, but its derivative, chitosan, being obtained by alkaline deacytylation of chitin can be used for this purpose [4, 5]. Although the preparation of pure chitosan aerogel was not successful due to the high shrinkage of the gel, composite aerogel material (silica-chitosan) could be prepared [5]. Chitosan was shown to prevent the shrinking process to some extent. SANS experiments show [4] that the introduction of chitosan leads to a more open aerogel structure and increases the inter-particle correlations. The biocompatibility of the aerogels was proved by cytotoxicity and hemolysis tests, whereas cytotoxicity tests were considered as passed with a very few cell damage [5]. Chelating effect of chitosan was used for incorporation of transition metal iones [4], Au and Pt [6] into chitosan-silica aerogels, since these metal ions can coordinate with the amine group of chitosan. The chelating effect of chitosan was extensively studied and makes it possible to use chitosan containing aerogels in diverse applications such as drug delivery or wastewater treatment.

Cellulose

Another promising type of bioaerogels is an aerogel based on cellulose and its derivatives [7-9]. Cellulose acetate [8] and mixture of cellulose acetate and cellulose acetate butyrate [7] were used as starting materials for preparing gels. All authors report the high impact strength of resulted aerogels (0.85 Nm for cellulose aerogel compared to 0.08 Nm for organic RF aerogels [7,9]). A principle use many kinds of organic Aerogels as biodegradable matrix is claimed by Berg et al [1].

Polysaccharides

A lot of efforts was done in the last years towards the synthesis of Aerogels based on polysacchrides. Those materials as starch, alginates carrageenans were used [31,32].

Aerogels as host matrix for biomaterials

The possibility to incorporate different materials into aerogels during sol-gel process resulted into idea to use them as

support matrix for different biological objects, as it was done for other sol-gel materials (xerogels).

Encapsulation of enzymes in silica aerogels

One of the mostly intensive studied topics is the use of aerogels as a support material for enzymatic biocatalysts [11]. Sol-gel support materials for enzymes were known earlier, so the main idea of the encapsulation technique was adopted to aerogels. One of the well studied enzymatic catalysts, lipase, was incorporated into silica and aluminosilicate gels during sol-gel process. It was proved that neither the gelation nor the following supercritical drying damages the lipase, so that aerogels loaded with an intact lipase could be prepared [11]. In all cases, the lipase immobilized in aerogels showed very high catalytic activity, in most cases much higher compared to that of free lipase. This fact was proved also for the other esterification reactions in supercritical fluids (CO2 and propane) [12]. A good catalytical activity of lipase is closely related to its ability to change the conformation. It can be easily provided in case of aerogels because the gel shrinkage during drying is mostly avoided by use of supercritical conditions, so that lipase stays flexible inside the pores. Further the influence of the aerogel structure and hydrophobic-hydrophilic balance on the enzyme performance in different solvent was studied in detail [11,13,16]. By controlling the aerogel hydrophobicity, the transport of the solvents of different polarity inside the aerogel matrix can be controlled. Basso et al [14] reports that the catalytical activity of the enzymes PGA, thermolysin and chymotrypsin - adsorbed on aerogels by their soaking in the enzyme suspension- is rather low. It might be due to the fact that the enzymes are not really integrated into the aerogel structure, so that the aggregation can not be avoided. Moreover, some adsorption sites of the enzyme can be blocked by the interaction with the aerogel surface. This research reveals the possibility to produce aerogels supported enzymatic catalysts which are tailored for the certain reaction conditions.

Encapsulation of proteins in silica aerogels

Encapsulation of proteins in sol-gel materials (gels and xerogels) is a well know procedure. Recently it was shown, that proteins (cytochrom c) can also be stabilized in an aerogel matrix using the so called “nanogluing” [15], which implies the formation of a stable protein superstructure around gold nanoparticles. The presence of the colloid gold allows to preserve the most part of proteins from being damaged by solvent exchange and supercritical drying steps. This example shows the principle possibility to design different complex biofunctionality within an artificial matrix [17].

Lipid membranes on silica aerogels

First efforts were done to prove the applicability of an aerogel matrix for membrane support. Planar phospholipids bilayers were deposited on silica aerogel surfaces and their lateral mobility and homogeneity were studied [18]. It is

expected, that the permeable nature of the porous materials, like aerogels, provide new advantages for supported lipid bilayer systems, like a better accommodation of proteins.

Aerogels as bio- and chemical sensors

The above discussed possibility to stabilize a variety of materials in the transparent porous aerogels matrix leads to an idea that chemical or biological sensors can be prepared on the basis of aerogel composites. The pioneering idea in this area was to create an aerogel based sensor for molecular oxygen [19,20]. Ayers and Hunt [20] utilizes an energized reducing gas (NH3 or H2) to form a thin layer of oxygen-deficient silica (SiOx) on the interior surface of silica aerogels. The techniques used in this case are similar to standard plasma methods. However, the nanoscale pore structure of silica aerogels prohibits the formation of plasma within the aerogel. The process is relatively gentle, and does not alter the physical shape or optical transparency of the original aerogel. As with other reduced silica materials, this aerogels absorb light in the UV region (300-360 nm) and emit visible light (400-600 nm). Defected centers distributed throughout the SiO2 lattice work act as fluorophores. The operation of the optical oxygen sensor is based on the collisional quenching of an excited fluorophore by O2. Further this idea was extended by dopping the aerogel with different samples, which show fluorescence or phosphorescence at certain conditions [21]. Furthermore Erythrosin B shows potential as an oxygen sensor, because oxygen quenches its phosphorescence intensity [22]. Aerogels doped with colloidal metals (Au, Pt) were used for sensing of dyes due to spectral change of the dye environment.

Power et al [23] showed the potential of aerogels as biological sensor for immobilization of large biological materials (bacteria). A difficulty of the small size of aerogel pores, which are generally to small for the cell immobilization was overcame by using pre-gelled silica matrices containing water-soluble organic polymers, which allows to produce macroporous aerogels (10 -100 μm) [23 and ref. therein]. Such aerogels can be doped with high bio-affinity receptor drugs to facilitate the detection of biological organisms (viren, bacteria etc.) within the environment

From these results it can be concluded that selective biosensors can be produces based on silica aerogels doped with bacteria having specific biological functions. One of the examples is the detection influenza virus by aerogels doped with sialic acid [24].

Aerogels as host matrix for drugs (drug carrier)

Several principle ideas for the use of aerogels in pharmaceutical applications already exist. It has been reported [DE 19653758 A1] that aerogel powder can be used as a free flow agent. Since aerogels have an extremely large surface area, it is expected that the drug dispersed or adsorbed in the aerogel can get improved dissolution characteristics. Schwertfeger et al [25] loaded both

hydrophobic and hydrophilic silica aerogels with pharmaceuticals by means of adsorption from corresponding liquid solutions. The resulting powder was dried and could be used as a drug delivery system (DDS). However, adsorption of drugs from liquid solutions leads to the partial collapse of aerogel structure, especially for hydrophilic aerogels. Lee and Gould (26) have loaded organic aerogels with drugs like methadone, naltrexone by co-gelling method before supercritical drying. The resulting aerogel powder was proposed to be used as a part of aerosol for inhalation since the low density of the product allows the particles to be carried by the aerosol stream when applying. Our group has studied adsorption of different drugs on silica aerogels from supercritical solutions [27-30]. The drug adsorption depends on one hand on the solubility of drugs in supercritical CO2 and on the other hand on the affinity of the specific drug to a given aerogel surface. The structural properties of aerogels like density, pore size and surface area influence the adsorption process and thus the maximal loading as well. High density aerogels having higher surface areas adsorb more drugs as low density samples [27]. As proved by the X-ray diffraction no crystallites of the drug are present in drug-aerogel formulations and therefore no long-range order is established upon adsorption of the drugs on silica aerogels, leading to the conclusion that intact drug molecules adsorb as a thin layer on the surface of silica aerogel.

The release of drugs can be drastically affected by adsorption on aerogels. The use of hydrophilic aerogels as a carrier promotes very fast release of the drugs, as shown for drugs ketoprofen and griseofulvin [27]. In case of griseofulvin the release is even much faster as the dissolution of griseofulvin nanoparticles [28]. This effect can be explained by both an increase of specific surface area of the drug adsorbed on the aerogel and its non-crystalline structure in this state [30]. Furthermore, the possibility to use polysaccharide-based Aerogels as drug carrier was evaluated in our group.

Conclusions

The discussed applications show a big potential of aerogel based materials in the field of life science. Not only the unique properties of the existing aerogels, but especially the flexibility of the sol-gel chemistry plays here an important role. In accordance to the suggestion of Kistler, aerogels can be produced from virtually any organic and inorganic gels, and almost every year we observe that new types of aerogels and aerogel composites coming out. Taking into account all research activities in the area of aerogels a number of promising applications can be expected in future.

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