ADSORPTION ON AEROGELS: A THERMODYNAMIC STUDY BY SUPERCRITICAL FLUID CHROMATOGRAPHY

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ABSTRACT

Packed column supercritical fluid chromatography (SFC) is used to measure retention of several organic solids on aerogels. Silica and alginate aerogels is prepared in the form of microspheres and used as stationary phases. Supercritical carbon dioxide and its mixtures with methanol are used as mobile phases at different densities. Thermodynamic analysis is applied to determine adsorption thermodynamic quantities. Enthalpy and entropy of the adsorption were calculated from retention factors for given pair solute – aerogel. Some experimental data on adsorptive crystallization in aerogel are discussed in the light of SFC results. In this context the packed SFC is viewed as a powerful tool to quantify aerogel – drug interaction.

INTRODUCTION

Having extremely high specific surface, large pore volume and open pore structure, aerogels have been recognized as thermal insulators, effective adsorbents, energetic materials, sensors and many other fields. Versatile biofriendly materials can be turned into aerogels that opens up indeed boundless opportunities for conceivable application in life sciences. Since aerogels are originated from supercritical fluids, further processing in the supercritical media seems to be reasonable. When immersed in supercritical solution of a drug, aerogels adsorb it to some extend depending on the surface/solute chemistry. Drug loaded aerogels seem to be highly promising dosing vehicles for drug delivery. In this work adsorptive interactions between aerogels and model compounds are analyzed by supercritical fluid chromatography with regard to further prediction of adsorption on and crystallization in aerogels.

MATERIALS AND METHODS

Two types of aerogel particles were prepared to be used for the chromatographic experiments: silica aerogel and alginate aerogel particles. The particles were characterized by their shape, size and porosity. As a model system for separation a mixture of polycyclic aromatic hydrocarbons (benzene, naphthalene and anthracene) was chosen, since they can be easily separated with a silica-packed commercial column. In some tests methanol was added to mobile phase (CO_2) as a modifier.

Materials

Calcium carbonate used as a crosslinker was purchased from Magnesia GmbH, Germany. Span® 80 was purchased Merck (Germany) and paraffin oil from Carl Roth GmbH. Anhydrous ethanol (99.9%) that was used in the solvent exchange step was purchased from H. Möller GmbH & Co.KG. Carbon dioxide used for drying was from AGA Gas GmbH (Hamburg, Germany). Solutes (benzene, naphthalene and anthracene) were of HPLC grade (Merck). Other chemicals were obtained from Sigma Aldrich (Germany). All chemicals were used without further purification.

Aerogel preparation

Silica aerogel particles were prepared according the method reported elsewhere [1]. Briefly, a mixture of paraffin oil + Span® 80 was placed into a mixing vessel and homogenized with silica sol. Droplets of the dispersed phase were formed under continuous stirring. Oil-soluble amine was added to the emulsion. After 20–30 min of continuous stirring the emulsion converted into dispersion of spherical gel particles in the oil phase. The gel spheres were left for several hours for aging and harvested by washing consequently with hexane and ethanol.

Alginate aerogels microspheres were prepared according to previously described procedure [2]. In brief, 3 wt% alginate solution was vigorously mixed with $CaCO_3$ for 5 min. Continuous phase (Paraffin oil + Span® 80) was added to the mixture and homogenized. Upon formation of the stable emulsion, acetic acid was added into the emulsion while stirring by a marine propeller. After 10 min the propeller was stopped, suspension was aged for 1 night and filtered to obtain the gel particles. Finally, particles were washed with hexane and subjected to multistep solvent exchange in ethanol/water mixture.

To obtain aerogel, both silica nad alginate gels were placed into an autoclave and supercritical drying was performed with supercritical CO_2 at 100 bar and 40°C for several hours.

Characterization

The pore size distribution and surface area of the aerogels were determined via the nitrogen adsorption-desorption method, using a Nova 3000e surface area and pore analyzer (Quantachrome instruments). The particle size distribution was determined by a laser diffractometer model HELOS (Sympatec). The particle size and particle shape of aerogel particles were also investigated by means of a scanning electron microscope (SEM) model Leo 1530 (Gemini).

Column packing

As aerogels are extremely porous materials, with pore sizes in the order of few nanometers, the capillary forces generated by immersing them into a liquid would lead to the collapse of their structure. Thus, it was necessary to employ a dry method to pack the chromatographic columns. The method applied in this work consisted in successive filling of the column with the silica aerogel particles, followed by mechanical vibration and compression with supercritical CO_2. An empty HPLC column (4.6 mm inner diameter and 250 mm length) was left one head open and coupled to a sieve shaker. Subsequently aerogel particles were introduced into the vibrating column helped by a funnel. After the column was full, the second head of the column was screwed, and the column placed into an equipment for supercritical fluid extraction (Speed SFE, Applied Separations). At this point supercritical CO_2 was pumped at 300 bar and 40°C for several minutes. After fluid compression, one head was newly removed and the filling process was repeated until the column was filled completely.

Chromatographic tests

Model compounds (benzene, naphthalene, and anthracene) were dissolved in n-hexane in concentrations of 128.4, 17.3 and 1.1 mM respectively. The columns were installed into SFC equipment Model HP-G1205A (Hewlett-Packard). Carbon dioxide flow rate was kept constant at 2.5 cm^3/min. The hydrocarbons were detected at 254 nm by a UV-Detector (HP Series 1050). Different operating conditions of pressure, temperature were applied to obtain thermodynamic quantities (see below). The influence of the modifier on the elution of aromatic hydrocarbons was investigated by adding methanol to the mobile phase in concentrations of 0.05, 1.00, 2.00 and 5.00%.

Determination of interactions between active compounds and silica aerogels

For quantitative determination of the interactions between the aerogels and the solutes naphthalene was used as the model compound since its crystallinity in the aerogel pores was studied in our previous work [3, 4]. Instead of the mixture of aromatic hydrocarbons the solution of naphthalene in n-hexane was injected into the column accordingly. The retention times of the compound were determined for temperatures and pressures. Each set of the experiments was performed at constant CO_2 density. To calculate the thermodynamic parameters the retention factor k' was determined from the retention times (t_R) and the hold-up time (t_0) and the plot of $\mathbf{ln}\, k'$ *vs.* $1/T$ was constructed [5]. The enthalpy and entropy of adsorption were determined respectively from the slope and intersection of the straight line according to

$$\ln k' = -\frac{\Delta H}{RT} + \frac{\Delta S}{R} - \ln \beta$$

The phase ratio β is defined as the ration between volume of the stationary and mobile phase respectively. The operating conditions were selected in order to obtain average densities of CO_2 inside the column in the range of 0.22 and 0.86 g/cm^3. The influence of the CO_2 density on the thermodynamics of adsorption was then investigated.

RESULTS AND DISCUSSION

Particle morphology

Both silica and alginate aerogel microparticels are almost spherical. Agglomeration is more pronounced for silica particles, whereas alginate microspheres are well separated from each other (Fig. 1). SEM analysis does not indicate macroporosity what is typical for aerogels produced by sol-gel method. Average particle size measured by laser diffractometry is ca. 23 µm for silica, whereas ca. 8 µm for alginate aerogel. Particle size highly depends on processing parameters such as stirring rate and amount of surfactant. Too small particles

(<3 µm) create high pressure drop along the column, which is in turn affect retention since CO_2 solvation power depends on pressure. Too big particles (>30 µm) lead to poor separation performance, however can still be used to measure thermodynamic quantities.

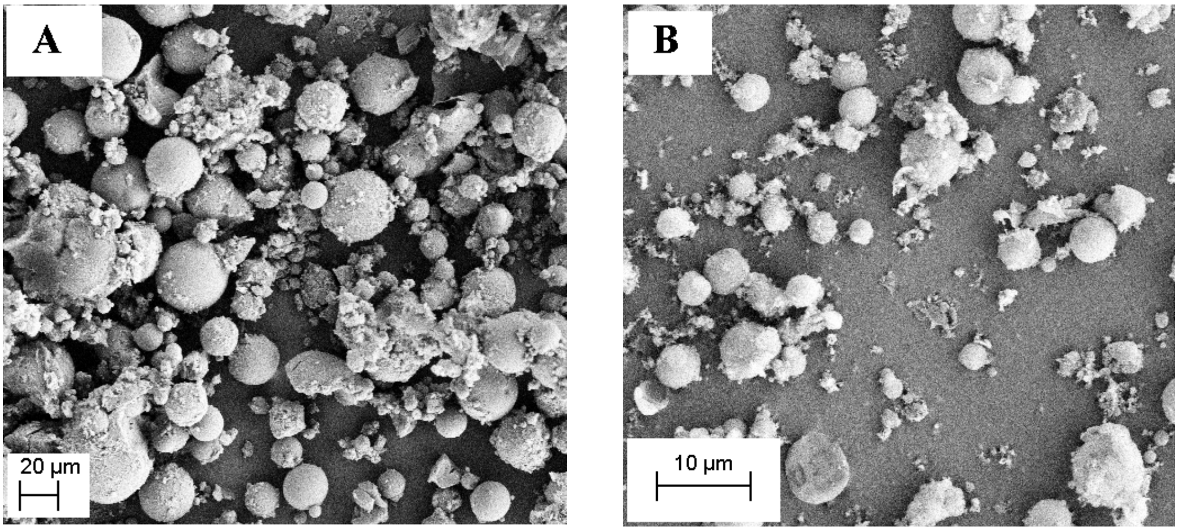

Fig. 1 SEM images of (a) silica and (b) alginate aerogel microparticles

Nitrogen adsorption indicates that silica microspheres have specific surface area of ca. 1000 m^2/g, while alginate shows somewhat lower specific surface of ca. 500 m^2/g. Specific pore volume is similar for both aerogels (ca. 3 – 4 cm^3/g).

Separation feasibility

The chromatographic experiments were then performed with the columns packed with both silica and alginate aerogel particles. According to the resulting chromatogram (Fig. 2) it is demonstrated that silica aerogels have potential to be used in SFC, as they proved to separate polycyclic aromatic hydrocarbons with adequate resolution. Since no appreciable tailing is observed, Gaussian peaks were assumed to perform the plate number calculations. The plate number calculated for this column was approximately 270 (silica aerogel). This value is rather low in comparison with typical values in HPLC. The reason for this may be due to agglomeration and bigger size compare to commercial stationary phases. Nevertheless a satisfactory and complete separation of the hydrocarbons was reached.

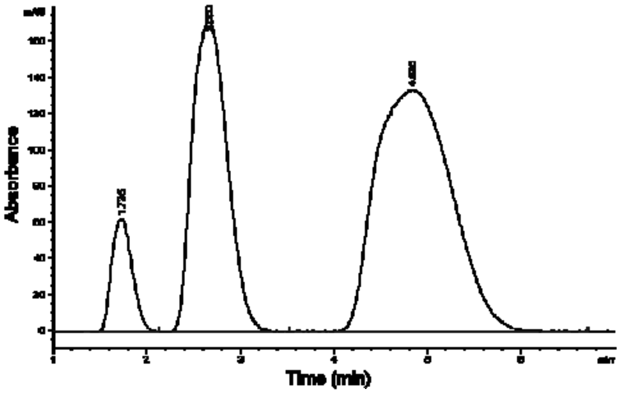

Fig. 2 Chromatogram of benzene, naphtalene and anthracene. Stationary phase: silica aerogels; mobile phase: supercritical CO_2 at100 bar, 40° C

Effect of a modifier

Since the polarity of carbon dioxide is similar to hexane, organic modifiers, such as methanol or acetonitrile, are frequently added to the eluent, since otherwise SFC would be limited to compounds of low polarity. It means that if aerogel columns are to be applied in SFC separations it should be possible to use modifiers.

To determine the influence of modifiers methanol was used to modify the polarity of the mobile phase at concentrations of 0.05, 1, 2 and 5 vol%. Tests with CO_2 free of methanol were performed before and after the tests with modifier to determine firstly how it influences retention times and secondly to determine if the modifier damaged the aerogel skeleton.
In Fig. 3A some peaks of the aromatic hydrocarbons for different modifier concentrations are shown. The addition of small amounts of methanol has a positive effect in our system as the analysis time becomes shorter and the peak width tends to decrease. However for too large amounts of modifier, larger than 1%, the resolution is not enough to elute benzene and naphthalene separately. Anthracene eluted normally at last as a single peak for concentrations as high as 2%. This behavior comes into agreement with the literature which states that to avoid excessive retention on packed columns, the mobile and the stationary phases should be relatively similar.

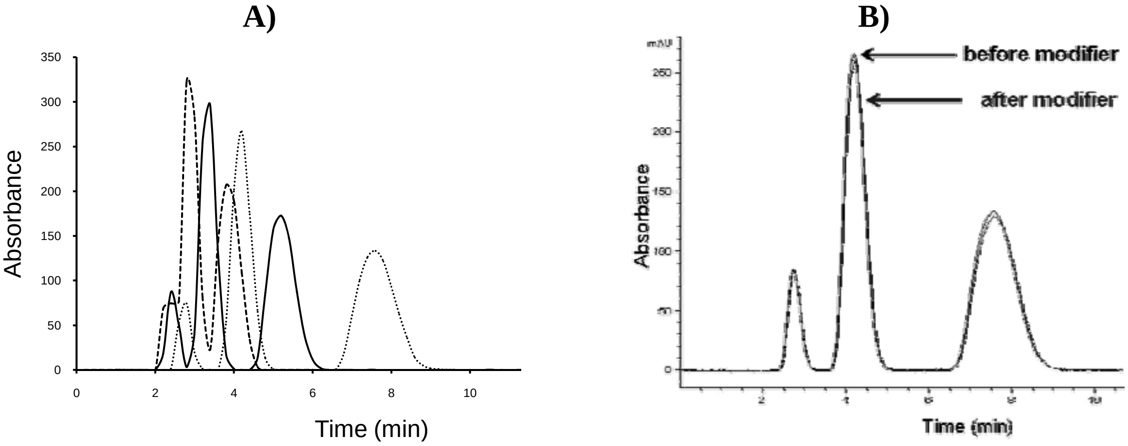

Fig. 3. A) chromatograms of the aromatic hydrocarbons for different methanol concentrations: 5% (striped line), 1% (solid line) and no modifier (pointed line);
B) chromatograms of the aromatic hydrocarbons before and after experiments with methanol

In Fig. 3B the chromatograms of the aromatic hydrocarbons before and after approximately 12 h of experiments with modifier are compared. Both chromatograms overlap very well to each other and only negligible differences are present. If the aerogel structure were damage by capillary forces originated by the modifier voids should appear in the packing material and peak broadening could be expected. As the peaks do not seem to be distorted after treatment with modifier it can be assumed that this additional solvent does not represent any risk for the aerogel packing and therefore can be used without drawbacks. The majority of the SFC separations involve the use of a solvent modifier, therefore the possibility of using modifiers with aerogel as stationary phase extends their spectrum of application.

Determination of interactions between solute and aerogel

The retention times of naphthalene at different temperatures for constant density were used to calculate the retention factors on silica and alginate aerogels. In accordance to the literature the plot $\ln k'$ vs. T^{-1} yielded straight lines at every constant density used (Fig. 4) for both columns. In the plots the slope represents the enthalpy of adsorption ΔH and the intersection with ordinate axis gives the entropy of adsorption ΔS.

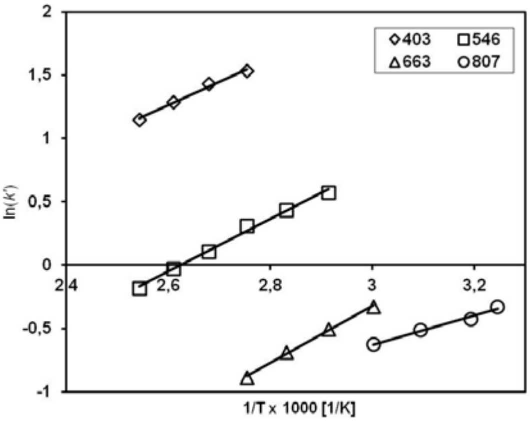

Fig. 4. Retention factor of naphthalene on silica aerogel column versus reciprocal temperature at different densities of the mobile phase (in kg/m^3)

The values for alginate column were between 5 and 12 kJ/mol. It has been observed that the values of the heat of adsorption on the alginate particles tended to decrease at higher $scCO_2$ densities in accordance to theoretical considerations [6]. In case of silica aerogel an opposite tendency observed: the heat of adsorption tends to increase with density; however a peak at densities between 550 and 650 kg/m^3 was observed. One probable explanation to this phenomenon lies in the competing character of the adsorption of $scCO_2$ and naphthalene from the supercritical solution. As reported by Strubinger et al. [7] the highest adsorption of CO_2 on silica takes place in the range of 300 to 600 kg/m^3 with coverage of more than 50% of the free surface. The results of Melnichenko et al. [8] indicate that adsorption of CO_2 is significantly stronger in aerogels than in xerogels due to the extremely high porosity and suitable pore sizes. It is possible that due to the extremely high specific surface area of the aerogel the naphthalene does not “feel” the presence of $scCO_2$ at low densities, thus the density of the CO_2 on the aerogel surface is low and there is abundance of adsorption sites. However, by increasing the density of the fluid the adsorption sites start not to be “enough” and the competition for these sites becomes more important. The adsorption of naphthalene may occur not directly over the aerogel surface because it is occupied by the $scCO_2$. The solvation layer can have a defined geometry or not depending on density as shown by Benmore et al. [9]. Another explanation may consist in high accessibility of OH-groups in $scCO_2$ [10].

The entropies of adsorption obtained from the experiments are negative what confirms that the adsorption of a solute, in this case naphthalene, involves entropy losses, reflecting the conversion of free translational and rotational degrees of freedom into bound motions.

Thermodynamic quantities, which can be obtained by SFC are a powerful tool to interpret adsorption on and crystallization in porous materials such as aerogels. To confirm this statement we have carried out crystallization experiments of naphthalene in silica aerogel at different densities, but constant temperature. Experimental procedure is described in detail elsewhere [3, 4]. Briefly, aerogel was exposed to naphthalene solution in $scCO_2$ to reach until adsorption equilibrium is reached. The system was depressurized fast to generate crystals of naphthalene in the aerogel. Degree of crystalllinity was measured using XRD. The results clearly indicate that there is correlation between heat of adsorption from SFC experiments and degree of crystallinity from XRD. More specifically, high adsorption enthalpy favors most amorphous sample and vice versa. Accordingly, lowest crystallinity was achieved at carbon dioxide density around 650 kg/m^3.

Although this effect is not fully understood, one should take into account the affinity of the solute to the matrix in order to control crystallinity of the end product. Since crystallization from supercritical solutions is widely adopted process, our findings give the problem a new dimension and force us to study phenomena behind in more detail. SFC seems in this context a efficient and reliable method to quantify interactions between a porous carrier and a solute.

CONCLUSIONS

The possibility to use silica and alginate aerogels as a stationary phase for supercritical fluid chromatography has been demonstrated. The separation of polycyclic aromatic hydrocarbons was achieved successfully in columns filled with aerogels. Performance of the aerogel packed columns in terms of the number of plates is not as good as that for a commercial columns but the separation is quite satisfactory. The use of methanol as a modifier can improve the peak shape and excessive retention of the aromatic hydrocarbons. Chromatograms obtained before and after modifier experiments suggest that aerogel structure is not damaged by the modifier.

An enthalpy and entropy of adsorption on the silica aerogel show extremum suggesting that the retention mechanism may differ from that on the alginate one. The test of active substances with different polarity as well as silica aerogel with different functional groups must still be performed in order to gain a better comprehension of the thermodynamics behind the adsorption on aerogels.

Thermodynamic analysis with help of SFC sheds light upon crystallization process in porous materials. Being a widely adopted process, crystallization process can also be optimized based on thermodynamic basis, which is easily obtainable through SFC measurements.

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