

CO₂-assisted perfluorodecalin impregnation into silica aerogels

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ABSTRACT

Subcritical CO₂ is used to impregnate perfluorodecalin (PFD) into silica aerogels. Although as much as 45 wt% PFD can be impregnated at mild operating conditions of 25°C and 900 psia, thermogravimetric analysis (TGA) shows that PFD-loaded silica aerogels lose more than 80% of available PFD when maintained at 37°C for 60 minutes. Shelf-life studies also show that PFD-loaded silica aerogels lose ~10% and ~30% of available PFD in 30 days, when stored in closed bottles at 2-to-8°C and 20-to-23°C, respectively. To dramatically reduce the loss of PFD, the loaded aerogels are coated with PMMA using a solvent evaporation method. PMMA-coated, PFD-loaded silica aerogels retain 100% of the PFD for up to 30 days when stored at ambient conditions in a closed bottle. The coated aerogels lose less than 20% of the available PFD when maintained at 37°C for 60 minutes and an additional 10% when heated further to 100°C and held at this temperature for 30 minutes. The remaining 70% PFD is lost rapidly when the temperature is increased to 150°C, which is slightly above the boiling point of PFD and well above the glass transition temperature of PMMA. These materials offer a method for sustained topical oxygen delivery.

Key words: Supercritical CO₂, Impregnation, Silica Aerogel, Perfluorodecalin, and Oxygen delivery

INTRODUCTION

Perfluorocarbons (PFC) are chemically and biologically inert substances and able to dissolve significant amounts of gases especially O₂, which makes them attractive O₂ carrier materials. A considerable amount of research in the past three decades reports on the use of perfluorocarbon-based emulsions as artificial O₂ carriers. Several studies show the therapeutic benefits of oxygen for healing acute and chronic wounds [1, 2]. Although a common perception is that skin receives O₂ through internal blood circulation, a recent study shows that significant amounts of O₂ penetrate up to ~700 μm deep into human skin [3] from a topically applied source. Davis et al. show how the topical application of a perfluorocarbon emulsion, supersaturated with oxygen, significantly enhances the epithelialization of partial-thickness acute wounds and second-degree burns [4]. However, the application of perfluorocarbon emulsions is currently quite limited due to the difficulty in preparing the emulsion and maintaining its stability for extended periods of time. In addition, perfluorocarbons typically exhibit a very short *in vivo* half-life [5, 6]. Several

research groups addressed these deficiencies by synthesizing PFC-filled, core-shell micro- or nano-capsules with a silica or a polymeric shell [5, 7-9]. Although micro- or nano-encapsulation of PFCs is a promising technique, the capsules are susceptible to rupture and loss of PFC. In the present study, silica aerogels are impregnated with perfluorodecalin (PFD) using CO₂-assisted processing to create effective topical oxygen delivery devices. These studies demonstrate the effect of process parameters on the level of PFD impregnation and the minimization of evaporative losses of PFD. However, O₂ loading and *in vitro* O₂ release studies are currently in progress and are not presented at this time.

MATERIALS AND METHODS

Materials

Perfluorodecalin, is purchased from SynQuest labs, USA. Tetraethylorthosilicate (TEOS), Methanol, dichloromethane are purchased from Fischer Scientific, USA and used as received. Polyvinyl alcohol (PVA, ~86% hydrolyzed and M_w = 86,000 g/mol) and poly(methyl methacrylate) (PMMA, M_w = 15,000 g/mol) are purchased from Sigma Aldrich, USA.

Methods

CO₂-assisted impregnation of silica aerogel

Silica aerogels are prepared as described elsewhere using sol-gel and supercritical fluid processing [10]. A high-pressure apparatus (Parr instruments, model 5500 with magnetic stirrer drive) is used for CO₂-assisted impregnation. Silica aerogel, dried at 100°C for two hours prior to impregnation, is placed in a tea bag that is tied to the impeller shaft of the high-pressure apparatus. Enough PFD is placed at the bottom of the vessel so that CO₂ remains saturated at the operating temperature and pressure [11] of 25 ± 1°C and 900 ± 20 psia during the impregnation period. The PFD loading in the aerogels is determined gravimetrically.

Coating PFD-loaded silica aerogel particles

Figure 1 shows a schematic diagram of the oil-in-water (O/W) emulsification and solvent evaporation method used to coat the PFD-loaded aerogel particles with PMMA. The particles, created by crushing the PFD-loaded aerogels into fine powder, are suspended in dichloromethane containing PMMA (1:1 wt/wt ratio of PMMA/aerogel) and PFD. The dichloromethane-rich suspension is emulsified into an aqueous solution (1:3 wt ratio) containing PVA that acts as a stabilizer. Dichloromethane is then evaporated from solution by continuously stirring at ambient conditions for four hours. The resultant microparticles are recovered from solution by first centrifuging the solution followed by rinsing the recovered particles twice with distilled water and then drying the particles under vacuum at 25°C for three hours. In the remainder of this paper the PFD-loaded silica aerogels are called uncoated aerogels and the PMMA-coated, PFD-loaded silica aerogels are called coated aerogels.

Aerogel Characterization

Nitrogen adsorption/desorption measurements are used to determine the aerogel surface area and pore size distribution. The pre-weighed aerogel sample is degassed in vacuum at 120°C for four hours prior to performing the nitrogen adsorption/desorption measurements at 77 K (Quantachrome Instruments, Nova 2200e). The specific surface area of the aerogel is calculated with the multipoint BET model in the relative pressure range of 0.05 to 0.30. The pore size

distribution is calculated with the BJH model using a desorption isotherm for a relative pressure of less than 0.35.

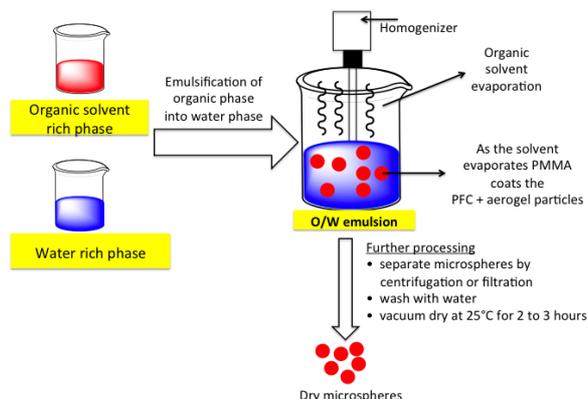


Figure 1. Schematic diagram of the oil-in-water (O/W) emulsification and solvent evaporation method used to coat aerogel particles with PMMA.

Thermal gravimetric analysis (TGA) (Perkin–Elmer USA, Model Pyris 1) is used to determine the PFD loading in the uncoated aerogels, where the sample is heated to 150°C at a rate of 10°C/minute and held at this temperature for 60 minutes. TGA is also used to determine the PFD loading and the weight of PMMA for the coated aerogels by step-wise heating from 20 to 700°C. Inverted light microscopy and scanning electron microscopy (SEM) are used to determine the morphology of coated aerogels.

RESULTS AND DISCUSSION

PFD is a hydrophobic and lipophobic compound, hence it is expected to be highly soluble in CO₂. Figure 1 shows vapor-liquid equilibrium literature data for the PFD–CO₂ system [11] 20°C, which suggests that operating the CO₂-assisted processing at 25°C and 900 ± 20 psia will be sufficient for an effective PFD impregnation process. Figure 2 shows the effect of contact time on the amount of PFD loaded in the aerogels. As the contact time increases from 15 to 80 minutes the PFD loading in the silica aerogels initially increases and ultimately reaches a plateau. Approximately 40-to-50 wt% of PFD is loaded into the aerogels at 25°C and 900 psia.

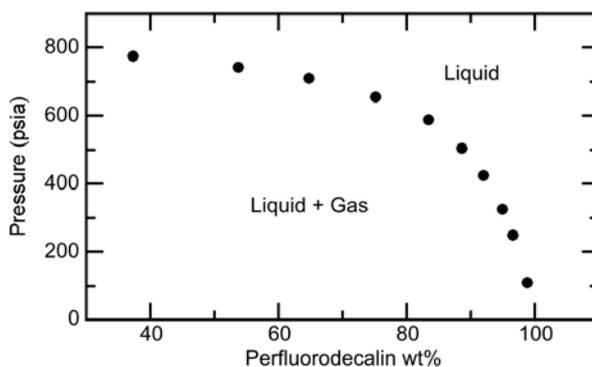


Figure 1. Vapor–liquid equilibrium of the PFD–CO₂ system at 20°C [11].

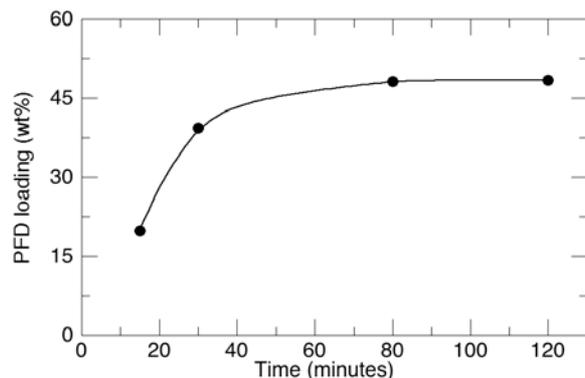


Figure 2. Effect of contact time on the PFD loading of silica aerogels at 25°C and 900 psia obtained in this study.

However, these PFD loadings are not yet optimized and further studies are in progress to elucidate the effect of other impregnation parameters including temperature and pressure.

Figure 3 shows the weight loss of unloaded aerogel and PFD-loaded, but uncoated aerogel determined by TGA. The unloaded aerogel loses ~8 wt% which is water that evaporates at 150°C. The ~40 wt% aerogel weight loss from the loaded, but uncoated aerogel exactly matches the amount of PFD in the aerogel as determined gravimetrically. The loaded PFD evaporates quickly from the aerogels when heated to 150°C. It should be noted that prior to loading with PFD, the aerogels are pre-heated at 100°C, so the weight loss obtained from the TGA is expected to be only from the PFD.

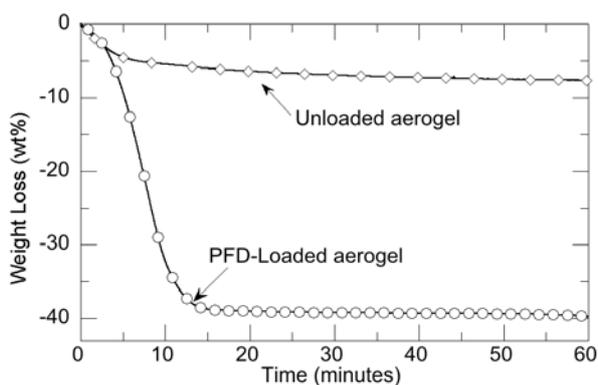


Figure 3. TGA curves for PFD-loaded, but uncoated aerogel (○) and unloaded aerogel (◇); in both the cases the aerogels are heated to 150°C and held at this temperature for 50 minutes.

Figure 4 shows the PFD shelf-life of the uncoated aerogels determined at 2-to-8°C and 20-to-23°C. The uncoated aerogels lose ~15% of the total loaded PFD (aerogel-free basis) when stored at 2-to-8°C for 30 days, whereas aerogels stored at 20-to-23°C lose twice as much total loaded PFD during the same time period. Given that the rate of PFD loss is fixed by the diffusion of

PFD through the pores of the aerogel, a thin polymer coating is expected to minimize the loss of PFD, and, hence, increases the shelf-life of the particles.

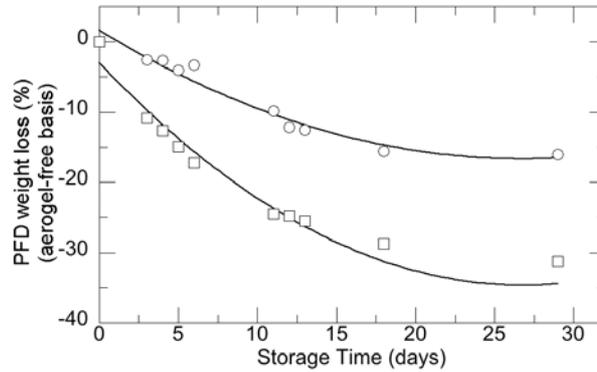


Figure 4. Storage stability of PFD from uncoated aerogels at 2-to-8°C (○) and at 20-to-23°C (□).

Figure 5 shows the weight loss of coated aerogel when heated from 20 to 700°C. The coated aerogel contains ~50 wt% PMMA, ~20 wt% PFD (40 wt% on a PMMA-free basis), and ~30 wt% silica aerogel based on the starting materials. The weight loss shown in Figure 5 exactly matches the theoretical weight composition of the coated aerogel. Note that the coating process is not yet optimized and related studies are in progress.

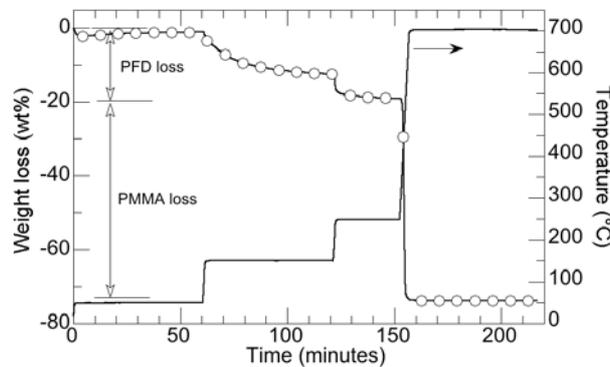


Figure 5. TGA curve for (○) coated aerogel and (—) sample temperature.

Figure 6 compares the PFD weight loss (aerogel-free basis) from uncoated aerogel, coated aerogel, and pure PFD. All three samples are held at 37°C for 60 minutes. During this period 20% of the available PFD is lost from the coated aerogel, more than 80% of the PFD is lost from the uncoated aerogel, and 100% of the pure PFD is lost. For the next 30 minutes the temperature is held at 100°C. During this next period another 10% PFD is lost from the coated aerogel and the remaining 20% PFD is lost from the uncoated aerogel. It is evident that the PMMA coating significantly reduces the evaporative loss of PFD.

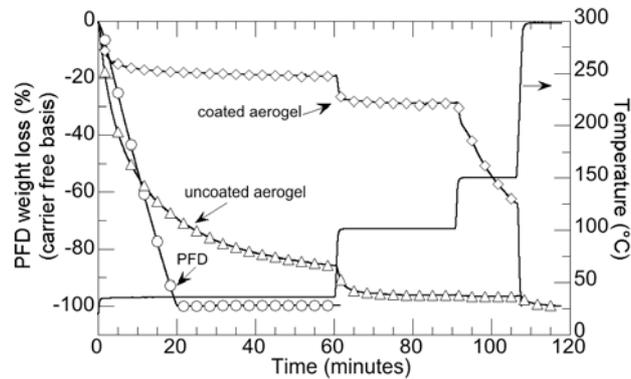


Figure 6. PFD weight loss comparison from (\diamond) coated aerogel, (Δ) uncoated aerogel, and (\circ) as received PFD.

Figure 7 shows the morphology of the coated aerogel. The inverted light microscopy image (Figure 7A) shows that the bright PFD-loaded aerogel particles are encapsulated within a dark PMMA shell. Figure 7B shows the SEM image that is used to further evaluate the morphology of the coated aerogels. These SEM results further confirm that PMMA coats the PFD-loaded aerogels and slows the evaporation of PFD from the coated aerogel as seen in Figure 6. The red circles in the Figure 7B highlight the broken PFD-filled PMMA microcapsules that are likely formed during the PMMA coating process. Further studies are in progress to load the PFD in these coated aerogels with oxygen and then to determine the in vitro oxygen release kinetics.

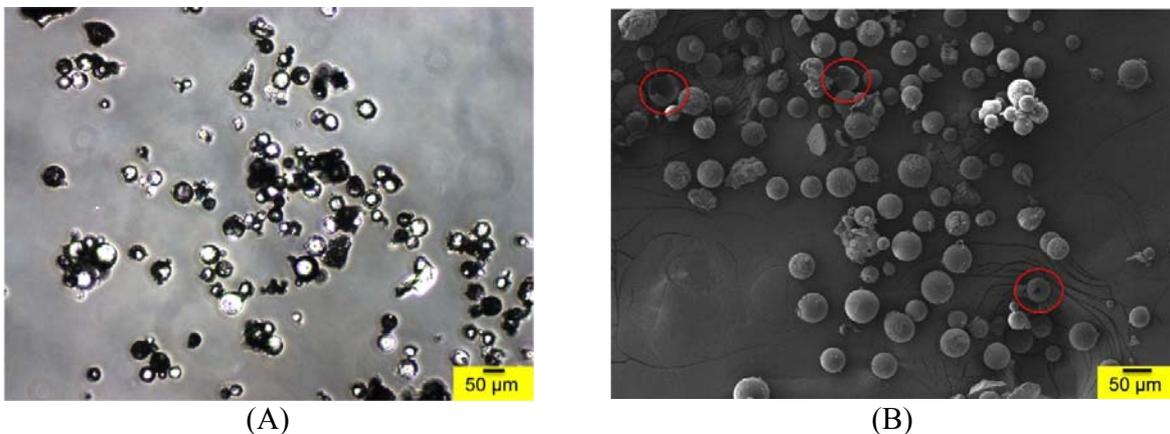


Figure 7. (A) Inverted light microscopy image where PMMA appears dark and PFD-loaded aerogel appears bright and (B) scanning electron microscopy image of coated aerogel.

CONCLUSIONS

In this study silica aerogels are successfully impregnated with PFD using subcritical CO_2 at mild operating temperatures and pressures. The PFD loading in the aerogels can be tailored between 18-to-50 wt% by manipulating the impregnation contact time. Maximum PFD loading in the aerogels is achieved at a contact time of 60-to-80 minutes. Shelf-life studies show that storing the PFD-loaded aerogels at 2-to-8°C retains more than 85 wt% of the loaded PFD and thus storing in the refrigerator is preferred over room temperature. PMMA coating significantly

improved the shelf-life of the PFD-loaded aerogels. We anticipate that the coated aerogels can find potential applications in advanced wound care for sustained oxygen delivery.

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