

Detailed Synthesis Procedure for the preparation of silica-alginate layered aerogels

Initially, an equal weight percent mixture of tetraethylorthosilicate (TEOS) (from Alfa Aesar 98% purity) and ethanol (from Merck) was prepared. Afterwards, a CaCl_2 (from Sigma Aldrich) solution and then HCl (from Riedel-de Haen with 37% purity) was added to adjust the pH to 2.0 where the rate of hydrolysis of the silica precursor is sufficiently high to complete hydrolysis within 45 minutes. After hydrolysis, NH_4OH (from Aldrich 2.0 M in ethanol) as the condensation catalyst was added to accelerate condensation reactions leading to gelation at neutral conditions. The mole ratio of TEOS to water was 1:4, TEOS to HCl was 500:1, TEOS to ethanol was 1:4.5 and NH_4OH to TEOS was 1:96. The typical CaCl_2 concentrations in the final solutions ranged from 0.02 to 0.2 M. Just before gelation, the solution was poured into cylindrical molds. Later, the wet gels were taken out from their molds and placed in Na-alginate solution. The concentration of the Na-alginate in distilled water was varied between 0.5 wt. % and 1.5 wt. %. The diffusion of Ca^{2+} ions from the porous silica alcogel structure through the alginate solution resulted in the formation of an alginate layer around the silica alcogel core as shown in Figure 1. The resulting layered aerogel structure was then subjected to successive aging steps prior to supercritical drying. The samples were then successively placed in a series of ethanol-water baths with increasing alcohol concentrations (10, 30, 50, 70, 90 and 100). The reason of using this kind of aging was to prevent the structural changes which could have occurred if 100% ethanol was immediately added. These solvent exchange steps aimed to remove all the impurities and replace water remaining in the pores. The last step was to dry layered alcogels at 90 bar and 313 K with supercritical carbon dioxide using an Applied Separations Spe-ed SFE system with a 26 ml extraction vessel. Primarily, the vessel was filled with pure ethanol to prevent the contact of the samples with air and the synthesized composite gels were placed inside. Initially, ethanol which was used to fill the vessel was extracted. This was followed by

extraction of ethanol from the pores of the samples to dry them completely, which took about 5 hours. Subsequently, the vessel was depressurized slowly (around 0.3 ml/min) to prevent formation of cracks.

Procedure for Paracetamol Loading

The silica alcogel cores which were obtained after the gelation were taken out from their molds and placed in an equivolume mixture of ethanol and water at 323 K for the aging step. The purpose of performing aging was to improve the mechanical strength of the wet gels by inducing hydrolysis and condensation reactions of unreacted TEOS remaining on the gels. After 24 hours, these gels were placed in pure ethanol for 3 days. Replacing water ethanol mixtures with ethanol, namely solvent exchange step, aimed to remove all the impurities and water remaining in the pores. Subsequently, the wet gels were contacted with an aging solution containing paracetamol which diffused into the pores of the alcogel from the aging solution. The loading depended on the diffusion rate of the paracetamol into the pores of the alcogel. Finally, the alcogel containing the drug was dried with supercritical carbon dioxide at 313K and 90 bars.

Modified Synthesis Procedure for the preparation of drug loaded layered structures

The silica alcogel core was primarily loaded with paracetamol as the model drug following the procedure above and then immersed in a 0.2 M CaCl_2 solution. Subsequently, the silica alcogel was placed in Na-alginate solution for the layer formation. Without any aging step, the drug loaded layered aerogel was dried using scCO_2 at 313K and 90 bar. The extraction vessel was filled with hexane in which paracetamol was not soluble and which was soluble in scCO_2 . The aim of omitting aging steps and using hexane instead of ethanol was to minimize the drug loss which could occur due to the diffusion of paracetamol (which has a high solubility in ethanol) to the ethanol during aging or at the beginning of the supercritical drying.

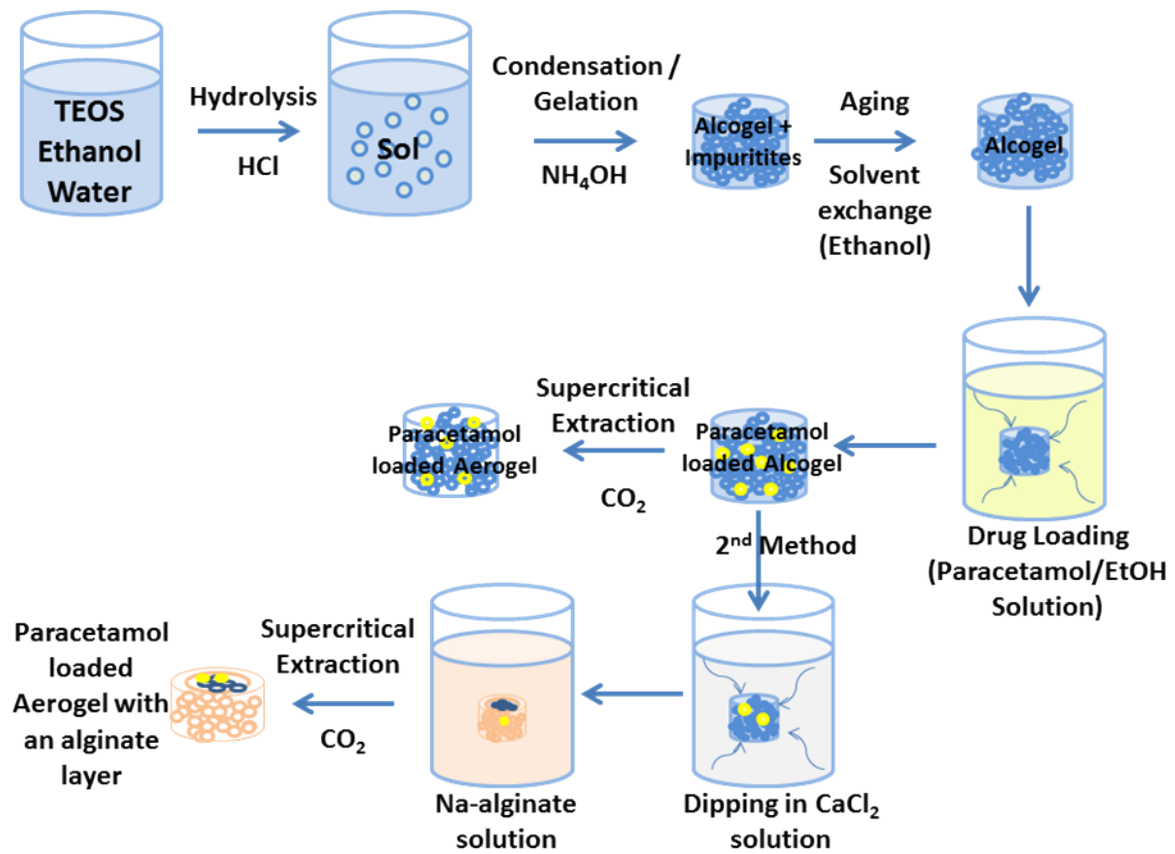


Figure 1: The procedure for the preparation of drug loaded silica aerogels