Review József Kalmár

József Kalmár possesses 56 publication, from that 47 in referred journals with 1440 sovereign citation. The dissertation is 150 pages, its main part (70 %) is Results and Discussion. The dissertation is dealing with the structures and applications of various silica-based aerogels. The studies summarised in dissertation concentrate on the clarification of the relationships between the chemical structures, nanoscale architectures and physical chemical properties of the aerogels. The dissertation clears the mechanism of the hydration and the consequent structural changes in silica-gelatin, silica-casein, borosilicate-PVA, Ca- and Fe(III)-alginate, as well as polyamide hybrid aerogels. The clearing of the hydration mechanism and the structural changes in aqueous medium possesses serious importance in the biomedical application of aerogels as drug carriers.

Novel drug delivery systems were also developed by József Kalmár and coworkers. Best, real novelties offering parts of dissertation belong to the release of adsorbed drugs and to the determination of biocompatibility in vitro experiments. Micronized silica-gelatine hybrid aerogel particles suspended in physiological saline were tested in living organism.

József Kalmár and coworkers have constructed mechanistic models for the adsorption of a model dye and a model protein on suspended silica aerogel microparticles.

Thesis

Thesis is based on 17 publications from 2015 to 2024. Main part of the publications is represented by Q1 journals with excellent average 6-7 impact factor. József Kalmár is 2x first author and 14x correspondent author. Many thesis points can be admitted as separate scientific achievements.

I. Thesis points are accepted.
1/2: This Thesis point is also accepted, however, the reason of different hydration behaviours of hybrid aerogels is missing. The next expression in 1/4. point “kalciumionokkal teljesen mértékben térhálósított” is not typical for Ca ions.
II. Theses, which are dealing with the aerogels as drug delivery systems, are the most innovative thesis points. Every point provides new research achievements.
III. From these points 3/1 and 3/2 points are not acceptable. 3/1: The adsorption of methylene blue on silicate aerogels is frequently investigated. More than 50 000 hits are on the internet for search of “adsorption of methylene blue on silicate aerogels”. The description of the mathematic model application for adsorption does not give a right novelty. Thus, this point cannot be received as a real novelty.
3/2: The adsorption of methylene blue on quartz glass is completely not understandable to give a new thesis point.
3/3 Perhaps only one thesis point may be instead of 3 points containing some test measurements for adsorption of important serums.
3/4 can be accepted as new research achievement.

Introduction - Literature

Introduction and Literature are generally correct, well corresponding to the requirements of scientific dissertation.
The used structural characterisation techniques are adequate and suitable measuring techniques. The adaptation and application of various NMR techniques (e.g. MAS NMR, cryo-porosimetry, relaxometry) for characterisation of aerogels are prominently good. Application of SANS also provides very useful information for the hydration mechanism of aerogels.

Some remarks for Introduction:

- Some misprints there are in the Theses and Dissertation: e.g. EDS instead of XRF.
- It is not correctly written: "highly porous solids such as xerogel and aerogels" "nanostructured solids" The xerogels are not highly porous materials, the typical porosity is 10-40% in xerogels dried at ambient pressure and without any additional materials. The xerogels cannot be generally characterised by nanostructure. The preparation of xerogel does not require a solvent exchange (2 Scheme), according to the typical process the gel is directly dried at atmospheric pressure. The aerogels possess 70-90% porosity and real nanostructure.
  References: A.K. Nayak "Polymeric Gels" 1/10 Xerogel (2018)
  C.J. Brinker, G.W. Scherrer "Sol-Gel Science" Academic Press, (1990).
- "gels can be made of inorganic oxides, metals, carbon" etc. "Metals" expression is not correct, instead of metals - metal-organic/ metallogel (metal-ion containing) gels should be used.

Some remarks in the Literature:

- General problem is application of "solvated gel", it is not a really correct term:. The gel means: "Gels are consisting of a liquid and particles. The particles are either dispersed or arranged in a fine network in a liquid phase" Encyclopaedia Britannica. Thus, it would be enough to use only "gel" term instead of solvated gel.

Experiments

Some remarks in the Experiments

- From gelation processes only the hydrolysis has been mentioned, the condensation reaction not at al. However, continuous 3D network of gel can be obtained only by condensation.
- Various and contradictory pressure values are written in the part for supercritical drying: 140 bar, 140 kPa, 120 kPa, 5,4MPa. kPa seems to be not correct measurement unit.

Questions:

- *IV/1* What was the temperature in the silica gel preparation? 24 h seems to be too long for formation of alcogel in a basic conditions.
- What was the reason of the soak of methanol-containing gel in methanol?
- What kind of condition was used for solvent change before supercritical drying? Simple soak is not enough for the solvent change.
- IV/3 Hydration and wetting of aerogels*:* "a 24‑48 h equilibration period before the measurements" What kind of measurement? The measurement is mentioned only as characterization measurement. Perhaps, swelling or NMR cryoporometry?
- IV/7 Why must be much higher pressure (200 bar) used during the impregnation of aerogels with drug than in supercritical drying of aerogels (120, 140 bar)?
- - IV/8 In this part "the released nicotine acid" is mentioned only here, but no before and no after anymore. What is the role of nicotine acid?

Results and Discussion

Many types of aerogels are studied in the Dissertation: silica, silica-gelatin, silica-casein, borosilicate-PVA, silica-PVA hybrid aerogels, Fe-alginate, Ca-alginate, polyurea cross-linked Ca-alginate, and polyamide aerogels. These aerogels have been investigated with various adequate, well-interpreted techniques, which are concentrated mainly on the atomic and

nanoscale structures. However, there is no aerogel sample, which has been studied in every aspect or with every technique. For example, the hydration mechanism is introduced in the silica-casein, borosilicate-PVA hybrid aerogels, and Ca-alginate aerogel; the drug delivery is described with metal alginates systems; the drug release kinetics with the silica-gelatin samples; the mechanical properties are reviewed only with polyamide aerogels. These diverse descriptions and a lot of technical details make "Results and Discussion" difficult to read and comprehend. Perhaps, it would be much easier for readers/reviewer to process the Results and Discussion parts of Dissertation, if it concentrates only on the detailed introduction of the most successful aerogel, the silica-gelation hybrid systems with a lot of results data of various measurements and tests; and in the case of other aerogels, only main characteristic features are to description.

The **Chapter V-1. "Hydration mechanisms of aerogels, structures of hydrated aerogels"** The main part of the studies represented in the Dissertation concentrates on the investigation of hydration mechanism of aerogels. This Chapter V-1. is dealing with very important aspect of biomedical utilisation of aerogels.

***Questions*:**

- A relevant results: "the carriers with low gelatin contents are rapid release systems, while the hybrid aerogels of high gelatin-content show sustained release properties." However, the specific surface area of aerogels is strongly reduced in the function of increasing gelatin content: 20% growth in gelatin yields about 65 % shrinkage in surface area. This reduction results in less adsorption/interaction possibility to drug. On the basic: What is the advantage of the using gelatin?

- What does regulate the hydration and wetting of silica and hybrid aerogels? Sometimes "the pores of a number of biopolymer-silica hybrids (e.g. silica-gelatin) close in water" in the other cases (e.g. borosilicate-PVA aerogels hybrid aerogel) does not close.

Chapters of "**Structural characteristics of silica and hybrid aerogels**" introduces versatile adequate structure investigation methods with correct evaluation. However, the application of every term is not really correct.

***Some remarks and questions*:**

- There are inconsistent sentences**,** which make difficult the text to understand.
  It is written: "The general conclusion is that during the hydration of silica aerogels, the monoliths disintegrate into microparticles, but the silica network and the pore structure of the microparticles remain intact." Disintegrate into micropart and the structure is remaining intact – simultaneously?? (Page 46)

- Many times, the application of aerogel' term is not adequate. The aerogel term is used in Dissertation even for solid foam or branched polymer structure.

"The results show that macropore contribution significantly increases with the increasing gelatin content of the hybrid aerogels." Increasing macropores in nanoporous aerogels? Already at 4wt% gelatin content the macropores is larger than 60%. That is rather a solid foam. In the case of silica-casein hybrid aerogel is written: "macropores is negligible" and mesopores are in the borosilicate-PVA hybrid aerogels, too. What is the explanation of this difference in hybrid aerogels?

- Why can the polyamide structure characterised as aerogels? It is written: "In this architecture "pores" are best defined as the void spaces among interweaved fibrils. Mesopores are evidently not visible in this magnification, but large macropores are." The specific surface area of polyamide system is only 251 m^2/g (95 Page). That is veery low for aerogels.

- What represents the SANS “p” values from Beaucage model in Table 2? The explanation of the p’ role is missing. That is the result of evaluation of Porod-region; represents the mass fractal dimension? If yes, those show more or less compact structure in silica-gelatin aerogels, the structure of silica-casein may be fractals. In V.1.4.2.Chapter is written about Ca alginate:” CaAG is a surface fractal (p = 3.5)”; on next page (on Scheme 6): “volume fractal (3 < p < 4)”. Volume or surface fractal? Generally at Porod evaluation: -μ = 3-4 means surface fractal dimension. What is the difference between ***p*** in Beaucage model and p derived from Power-law model (e.g. in Table 11, Page 91)?

Chapters of “Mechanism of drug release from aerogel carriers” V-1.1.2. and “Redox responsive drug release” V-2.1.2. are the most interesting parts of the dissertation, they represent many novelties compared with a typical paper on the aerogel fabrication. In these chapters, silica, silica-gelatin aerogels, and metal alginate aerogels were impregnated with ibuprofen and sometimes with ketoprofen. The mechanism of drug release is extensively studied and revealed in these 3 aerogel systems.

- The hydration mechanism of Fe(III)-alginate is strongly missing for its application as drug carriers. Thus, It is essential to understand the mechanism of the aerogels’ hydration the consequent changes in the aerogel structure in biomedical or environmental engineering application. The mechanical properties of Fe(III)-alginate and silica-gelatin aerogel are also missing.

First two parts of **V. 3, Chapter** should have skipped, because the research work was dealing with not pure silica aerogel and these part introduce the methylene blue adsorption on pure silica aerogel and - even more incomprehensible – on quartz glass. Many research data have already been published in this area. (As already mentioned: more than 50 000 hits are on the internet for search of “adsorption of methylene blue on silicate aerogels”. The description of the mathematic model application for adsorption does not give a right novelty.)

Final conclusion:
Apart from the difficult reading and comprehension of Dissertation and a not really focused description, the Dissertation represents many serious works with real novelties in a lot of cases. I would like to emphasize the adequate adaptation of various structure investigation methods (especially the excellent application of NMR techniques) and studies of using aerogels as drug deliverers (e.g. hydration behaviours, biocompatibilities, and sometimes in vitro investigation). I accept the results summarised in Thesis as novelties, exception of 3/1 and 3/2 points. Based on all this, I suggest the acceptation of József Kalmár’ submission for Doctor of the Hungarian Academy of Sciences and I propose the public defence of him dissertation.

Budapest, 2026. 21. 05.

Dr Sinkó Katalin, DSc
reviewer