# Cellulose Aerogel Microparticles via Emulsion-Coagulation Technique

Lucile Druel, Amelie Kenkel, Victor Baudron, Sytze Buwalda, Tatiana Budtova

*Submitted to Biomacromolecules 14 December 2019*
*Revised 30 January 2020.*

# Cellulose aerogel microparticles via emulsion-coagulation technique

*Lucile Druel[1], Amelie Kenke1[1, 2], Victor Baudron[2], Sytze Buwalda[1], Tatiana Budtova[1]**

1 - MINES ParisTech, PSL Research University, Center for Materials Forming (CEMEF), UMR CNRS 7635, CS 10207, 06904 Sophia Antipolis, France

2 - Institute of Thermal Separation Processes, Hamburg University of Technology, Eißendorfer Straße 38, 21073 Hamburg, Germany

*Corresponding author: Tatiana Budtova, Tatiana.budtova@mines-paristech.fr

**Abstract**

Cellulose aerogel microparticles were made via emulsification/non-solvent induced phase separation/drying with supercritical $CO_2$. Cellulose was dissolved in NaOH-based solvent with and without additives in order to control solution gelation. Two emulsions, cellulose solution/oil and cellulose non-solvent/oil, were mixed to start non-solvent induced phase separation (or coagulation) of cellulose inside each cellulose droplet leading to the formation of so-called microgels. Different options of triggering coagulation were tested, by coalescence of droplets of cellulose solution and cellulose non-solvent, and by diffusion of non-solvent partly soluble in the oil, accompanied by coalescence. The second option was found to be the most efficient for stabilization of the shape of coagulated cellulose microgels. The influence of gelation on particle formation and aerogel properties was investigated. The aerogel particles' diameter was around few tens of microns and the specific surface area was 250 - 350 $m^2/g$.

**Keywords**

Cellulose; microgel ; microparticle; aerogel; emulsification.

## Introduction

Bio-aerogels are a special class of dry, highly porous, nanostructured polysaccharide materials with growing interest for biomedical and pharmaceutical applications due to their low density (below 0.2 g/cm$^3$), open pore structure and high specific surface area (above 100 m$^2$/g).[1-3] Bio-aerogels are recent materials which are prepared via polymer dissolution, gelation or direct non-solvent phase separation and drying with supercritical $CO_2$.

Bio-aerogels have the same advantages as conventional hydrogels. In addition, the specificities of shaping bio-aerogels allow their structure and properties to be varied more widely making, for example, organic-organic or organic-inorganic composites or hybrids.[4, 5] Another advantage is that being dry, aerogels are much more stable with respect to hydrogels, contamination during storage is avoided and their transport is facilitated thanks to their low density.

Most bio-aerogels reported in literature are in the form of monoliths of several cm$^3$; only a limited number of publications deal with bio-aerogels in the form of microparticles, as reviewed recently by Ganesan et al.[6] By "microparticle" we assume a particle "of any shape with an equivalent diameter of approximately 0.1 to 100 μm".[7] The production of bio-aerogels in the form of microparticles significantly reduces the process costs and duration, especially with regard to the time needed for solvent exchange and supercritical drying.[8] In addition, bio-aerogel microparticles are preferred over other aerogel forms when it comes to drug delivery, thanks to their high flowability, facile handling, improved processing reproducibility as well as a reduced inflammatory response due to the absence of sharp edges.[9] A number of polysaccharides have been employed for the preparation of bio-aerogel microparticles, including alginate,[10, 11] carrageenan[12] and pectin.[13]

Cellulose, the most abundant renewable resource on earth, has not yet been explored for bio-aerogel microparticles. Thanks to its excellent availability, environmental friendliness, biodegradability

and biocompatibility, cellulose has been widely used for biomedical and pharma applications.[14, 15] In this sense cellulose aerogels have a huge potential, in particular, when made using a non-toxic and easily recyclable solvent such as aqueous NaOH. Most cellulose aerogels are produced from solutions followed by non-solvent induced phase separation (or coagulation), solvent exchange to a fluid miscible with $CO_2$ (usually ethanol or acetone) and drying in supercritical conditions.[16] One exception is cellulose dissolved in NaOH-water based solvent: these solutions are gelling with time and temperature increase.[17]

It is important to define the terminology that will be used in the following: we will distinguish two cases, particles before drying ("wet" particles or "microgels") and dry ones. For the majority of polysaccharides, their aqueous solutions are gelling triggered by pH, or ionic strength, or temperature. A well-known way to prepare polysaccharide microgels is to use microfluidics or to emulsify a solution in a non-miscible liquid phase, both approaches followed by triggering gelation to stabilize the droplet shape and then separating the microgels from the oil. They can then be dried in different ways, either by lyophilization, or vacuum, or ambient pressure drying, or with supercritical $CO_2$. However, cellulose is not an "easy-gelling" polysaccharide as alginate, pectin or starch. For simplicity, we will use the term "microgel" for cellulose when a "wet" microparticle is obtained. It should be noted that most cellulose "wet" particles are obtained not via gelation of a droplet of cellulose solution, but via non-solvent induced phase separation (coagulation), for example, by dropping cellulose solution in a bath of non-solvent.

As far as cellulose dry particles are concerned, most are known to be of the size of few millimeters down to several hundreds of microns,[18] and in most cases they are not porous as drying is performed in ambient conditions which leads to pores' collapse due to the capillary pressure. Cellulose aerogel beads of millimeter size were made via dropping cellulose-NaOH-water solution in water[19] and of sub-millimeter size by using Jet-Cutting technique applied to cellulose-ionic liquid solution[20] and

to cellulose-N-methyl-morpholine-N-oxide monohydrate hot solution[21] falling in various coagulation baths. Dropping usually does not result in particles with diameter below 100 μm. High-pressure atomization allowed production of cellulose microparticles of 1 to 3 μm in diameter, however, their porosity was not reported.[22] To the best of our knowledge, just few publications report on cellulose microparticles through emulsification technique. For example, droplets were made using cellulose-NaOH-urea-water solution dispersed in paraffin oil/Span 80, followed by coagulation in hydrochloric acid; the diameter of microgels varied from 5 μm to 1 mm.[23] Since drying was performed via lyophilization, the specific surface area of microparticles was low. In another case, cellulose-ionic liquid-N,N-dimethylformamide solution was dispersed in hexadecane containing either Span 80 or Silaplane FM-3321 and then cellulose was coagulated in butanol; microgels of few tens of microns were obtained.[24] As in the previous case, freeze-drying resulted in a low specific surface area. Non-porous crosslinked cellulose microparticles were produced from cellulose-ionic liquid solutions using cross-flow membrane emulsification followed by coagulation in ethanol.[25] Cellulose microgels were obtained via emulsification of cellulose-ionic liquid solution/cyclohexane/Tween 60/oil/Span 85 and Span 85/oil/aqueous sodium sulfate; microgels were double cross-linked with epichlorohydrin and glycol diglycidyl ether[26] Despite drying with supercritical $CO_2$, the specific surface area was low, around 30-50 $m^2/g$.

The goal of this work is to combine the approach and advantageous properties of bio-aerogel microparticles and cellulose. We present an original, simple and reproducible emulsification method for the preparation of cellulose microgels from droplets of cellulose using only non-harmful compounds, and we describe the properties of the aerogel microparticles that are obtained following supercritical $CO_2$ drying. We control cellulose solution gelation via the presence or

absence of additives (urea or ZnO), and we demonstrate that gelation is detrimental for particles' shaping.

## Experimental section

### Materials

Microcrystalline cellulose (MCC, Avicel PH-101, degree of polymerization ≈ 350 as determined via viscometric method,[27] see Methods section) was from Sigma-Aldrich (St-Quentin Fallavier, France). Urea (purity > 99.5%), sodium hydroxide in pellets (purity > 98%), absolute ethanol (purity > 99%), glacial acetic acid (purity > 99%), 32% aqueous hydrochloric acid (HCl, analytical grade) and paraffin oil were from Fisher Scientific (Illkirch, France). ZnO (ReagentPlus, purity > 99.9 %) was from Sigma Alrdrich and the non-ionic surfactant polysorbate 80 (polyoxyethylene 20 sorbitan monooleate) was purchased from Alfa Aesar (Haysham, United Kingdom). Water was distilled.

### Methods

#### Preparation of cellulose aerogel microparticles

*Cellulose dissolution.* MCC was dried under vacuum at 50 °C for at least 3 h and then swollen in distilled water at 5 °C for 3 h. Cellulose was dissolved either in 8% NaOH-water or in the same solvent but in the presence of additives, either ZnO or urea. If the additive was used, it was first dissolved in NaOH-water. The solvent was cooled to –12 °C. Swollen cellulose and NaOH-based solvent were mixed at 1000 rpm and -3 °C for 3 min. The final concentration of cellulose was always 5 wt% and of NaOH in water 8%. The concentration of urea was 11.5 wt% and of ZnO 0.5 wt%.

*Emulsification method.* Cellulose solution was added dropwise to paraffin oil and emulsified with a marine-style impeller for 30 min at 700 rpm.[27] Acetic acid (8.6 M) or HCl (0.5 M), which are non-solvents for cellulose, were emulsified separately in paraffin oil with 1 v/v % of polysorbate 80 using a flat impeller for 30-45 min at 700 rpm.[27] The ratio cellulose solution/paraffin oil in the first emulsion was 1:10 and the ratio non-solvent/paraffin oil in the second emulsion was 1:2. The cellulose emulsion and non-solvent emulsion were then mixed at 1000 rpm for 2 h in order to trigger cellulose coagulation, after which the resulting suspension was left to stand for the cellulose microgels to settle. The ratio cellulose solution/non-solvent in the final emulsion was 4:1. All manipulations concerning the emulsification were carried out at room temperature.

*Cellulose microgels collection.* After the cellulose microgels had settled, the suspension was mixed with twice its volume of ethanol/water (1/1 v/v) and centrifuged at 9000 rpm for 5-10 min.[27] The reason for using an ethanol/water mixture was to avoid interfacial jamming if only water is used and to avoid ethanol floating on the top of the oil because of the density difference if only ethanol is used. After each centrifugation, the paraffin oil was progressively removed and replaced by the ethanol/water mixture. Once the majority of the oil was removed, the cellulose microgels were washed at least 6 times in pure ethanol prior to supercritical drying with $CO_2$.

*Supercritical drying.* The cellulose microgels were dried using a home-made supercritical $CO_2$ installation. After placing cellulose/ethanol microgels in an autoclave, the system was pressurized at 50 bar and 37 °C with gaseous $CO_2$ while the ethanol was slowly drained. The pressure in the autoclave was subsequently increased to 80 bar, which is above the critical point of $CO_2$, in order to let the supercritical $CO_2$ solubilize the residual ethanol inside the pores of the cellulose particles. A dynamic washing step was performed at 80 bar and 37 °C at an output of 5 kg $CO_2$/h for 1 h. This was followed by a static step for 1-2 h, without $CO_2$ flow, and another dynamic washing step

for 2 h at the same pressure and temperature. Lastly, the system was depressurized at 4 bar/h and cooled to room temperature before being opened to collect the cellulose aerogel microparticles.

Characterization

*Determination of cellulose degree of polymerization (DP)*. The intrinsic viscosity [η] of MCC was measured by dissolution in cupriethylenediamine (CED) following the SCAN-CM standard 15:88 according to the requirements of the ISO 5351. Viscosity of solvent and cellulose solutions was measured with a LAUDA iVisc equipped with an Ubbelohde-type viscometer. Cellulose DP was calculated according to the Mark-Houwink equation: $(DP)^{0.90} = 1.65 \times [\eta]$.[28]

*Rheological properties of solutions*. Gelation of cellulose solutions was traced using a Bohlin Gemini rheometer equipped with cone-plate geometry (2°, 60 mm) and a Peltier temperature control system. Oscillation rheology was performed in the linear region (frequency of 1 Hz and a stress of 0.01 Pa) in the temperature interval from 10 to 40 °C. The evolution of elastic (G') and viscous (G") moduli and dynamic viscosity was followed as a function of time at a fixed temperature (see examples in Figure S1). Gelation time was taken from gel point which is, in the first approximation, when G' = G".[29]

The viscosity of paraffin oil was measured in the steady state regime as a function of shear rate (interval from 0.05 to 200 $s^{-1}$) at fixed temperatures.

*Optical microscope.* A Leica DP 4500 optical microscope in transmission mode was used to observe droplets in emulsion.

*Scanning electron microscopy (SEM)*

The morphology of the cellulose aerogel microparticles was examined using a Zeiss Supra 40 microscope equipped with a field emission gun. The observations were performed with diaphragms

from 7.5 to 20 μm in diameter and the acceleration voltage was set between 1 and 3 kV. Prior to the observations, a thin layer of platinum was applied on the surface of the particles with a Quorum Q150T metallizer to prevent the accumulation of electrostatic charges. SEM images were also used to estimate the size distribution of the cellulose aerogel microparticles, mean diameter was calculated as arithmetic average. At least 100 particles were measured.

*Specific surface area.* The specific surface area was measured with a Micromeritics ASAP 2020 instrument using nitrogen adsorption and the Brunauer–Emmett–Teller (BET) method. The samples were degassed under high vacuum at 70 °C for 10 h prior to the measurements.

## Results and Discussion

Before presenting the results, we first explain the logics behind our approach. As mentioned in the Introduction, the majority of polysaccharide gel particles are made via gelation of droplets of solutions triggered by various external inputs. However, when cellulose "wet" or dry particles are concerned, droplets' shape is always stabilized by non-solvent induced phase separation caused by the contact with non-solvent. Probably, the reason is "historical": spinning fibers and making films is performed by placing cellulose solution in a non-solvent. 7-9% NaOH-water is cellulose solvent in which solutions are gelling. Can the approach used for "easy-gelling" polysaccharides be applied to cellulose-NaOH-water solutions, when making microgels via emulsification? It would be logical to assume that gelation of cellulose-NaOH-water solutions' droplets is beneficial for stabilization of microgel shape and facilitation of further processing steps to obtain spherical cellulose aerogel microparticles. To answer this question, we used the unique property of 7-9%NaOH-water as cellulose solvent: it allows varying gelation time by using or not specific additives. By controlling gelation kinetics, cellulose aerogel microparticles can thus be made either via droplet gelation

(quick gelation) or via non-solvent induced phase separation (avoiding gelation due to slow kinetics). First, we briefly present rheological results showing the influence of additives on gelation kinetics. Then we describe the preparation and properties of cellulose aerogel microparticles using emulsion approach and non-solvent induced phase separation. A special attention is paid on the influence of non-solvent's type that turned out to be crucial for fixing microgel shape. Finally, we demonstrate the influence of gelation on the shape and size of aerogel microparticles.

## Influence of additives and temperature on gelation of cellulose solutions

It is known that cellulose-NaOH-water solutions are gelling with time and temperature increase.[29] The mechanism of gelation is still under discussion. Traditionally, it is supposed to be due to the decrease of solvent quality with temperature increase leading to the preferential interactions between cellulose chains via hydrogen bonding and formation of polymer-rich and polymer-poor domains.[17, 30] Another option was suggested recently: gelation is due to the formation of carbonate bridges between deprotonated cellulose and $CO_2$, the latter always present in air.[31] Additives as urea and ZnO are known to delay gelation[32-34] most probably by preventing cellulose chains to interact with each other. As the preparation of emulsions takes a certain time, the evolution of cellulose solutions' viscoelastic properties in time needs to be evaluated to be further used in the understanding and control of shaping of cellulose microparticles.

The influence of temperature on gelation time $T_{gel}$ of cellulose-NaOH-water solution without additives and in the presence of either 11.5 wt% urea or 0.5 wt% ZnO is shown in Figure 1. Higher solution temperature results in a faster gelation, and the presence of urea or ZnO delays gelation. For example, at 20 °C a solution without additives is gelling within 40 min and in the presence of ZnO or urea in about 8 h (Figure 1). As suggested in ref. 29, gelation time was approximated by

$T_{gel} \sim exp(-aT)$ where $a$ is a constant and $T$ is temperature. Most of the work on making cellulose aerogels microparticles was performed using NaOH-urea-water solvent which allows keeping stable viscoelastic properties within the first hour of mixing (Figures S1 and S2 in the Supporting Information). The option of NaOH-water solvent without additives was used for the case of testing the influence of gelation on particles' shaping. NaOH-ZnO-water solvent was used as a proof of concept, i.e. to demonstrate that non-gelling cellulose solutions are favorable for making cellulose aerogel spherical microparticles.

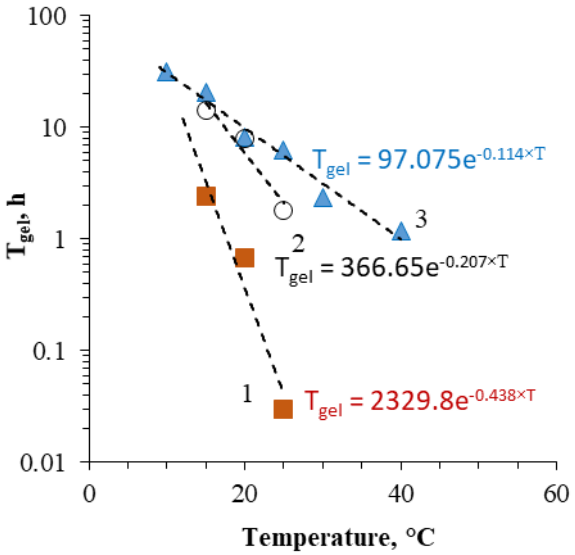



**Figure 1.** Gelation time as a function of temperature for 5wt% cellulose-8wt% NaOH-water (1), 5wt% cellulose-8wt% NaOH-0.5 wt%ZnO-water (2) and 5wt% cellulose-8wt% NaOH-11.5wt% urea-water (3). Dashed lines are $T_{gel} \sim exp(-aT)$ approximations shown with the corresponding fitting parameters.

When mixing immiscible fluids with the goal of making droplets of one phase in another, one of the important parameters controlling the breakage of the dispersing phase is the viscosity ratio

between the two fluids. It is known that in the simplest case of shear flow and Newtonian fluids, droplet breakage occurs when the ratio of droplet viscosity $\eta_d$ to continuous matrix viscosity $\eta_m$ is below 4 with the most efficient breakage at $\eta_d/\eta_m = 1$.[35] We made a rough estimation of the viscosity ratio not considering the elongation stresses. $\eta_d$ was taken as the dynamic viscosity of the cellulose solution at the beginning of oscillation measurements (Figure S2) as fresh cellulose solutions were always used for emulsion preparation. $\eta_m$, the viscosity of paraffin oil, is Newtonian (Figure S3) with no special temperature induced behavior as it obeys Arrhenius' law (Figure S4). The viscosity ratio was around 0.4 and 1.2 at 20 °C in cases when urea and ZnO were used, respectively. When no additives were used, $\eta_d/\eta_m$ was just below 4 within the first 30 minutes. It can thus be concluded that the viscosity ratio is favorable for the breakage of cellulose solution droplets in paraffin oil.

## Development of emulsification process

Luo et al. reported on a method for the preparation of cellulose microgels via emulsification of cellulose-NaOH-urea solution in paraffin oil in the presence of 1 vol% polysorbate 80 and subsequent coagulation in HCl.[23] Using these conditions, we observed that the cellulose droplets became irregular in shape over time with the formation of a roughly textured "skin" on their surface (Figure S5). We hypothesize that this is due to hydrolysis of polysorbate 80 in the highly alkaline solution, resulting in a loss of its amphiphilicity and emulsifying power. Emulsification of NaOH-water solution with 1 v/v % polysorbate 80, without cellulose, corroborated this hypothesis as a similar "skin" appeared on the surface of the aqueous droplets (Figure S6). For this reason, we emulsified cellulose-NaOH solution in paraffin oil without surfactant, which resulted in round, non-aggregated droplets, albeit with a bimodal size distribution (Figure S7). Following the protocol

proposed by Luo et al.,[23] we then attempted to coagulate the cellulose via the drop-wise addition of 0.5 M HCl in the cellulose-NaOH/oil emulsion. However, this procedure resulted in the formation of deformed and broken cellulose microgels. Possibly, the direct addition of the relatively large HCl droplets disturbed the stability of the emulsion, leading to fragmented, coagulated cellulose microgels.

In view of the above, we decided to develop an adapted, original emulsion technique. First, two separate emulsions were prepared: cellulose-NaOH-urea-water dispersed in paraffin oil and coagulant (either 0.5 M HCl or 8.6 M acetic acid) dispersed in paraffin oil in the presence of 1 v/v % polysorbate 80. The reason for using different coagulants will be explained later. The two emulsions were then mixed leading to cellulose coagulation and formation of microgels, and subsequently centrifuged with addition of 50% ethanol-water for the separation of phases (Figure S8). Lastly, the microgels were washed in ethanol to remove water and dried with supercritical $CO_2$. Figure 2 presents a schematic overview of the preparation of cellulose aerogel microparticles.

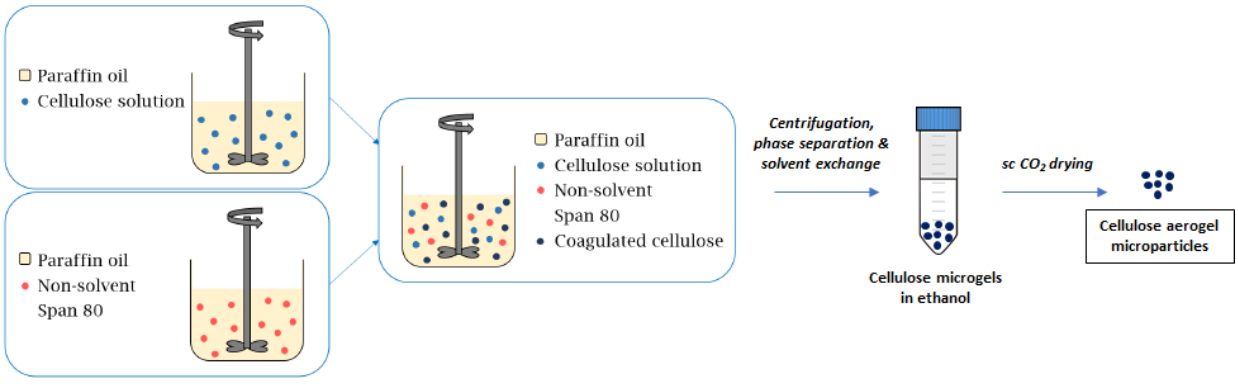



**Figure 2.** Workflow for the preparation of cellulose aerogel microparticles via emulsion technique.

## Characterization of cellulose aerogel microparticles

The choice of coagulant turned out to be very important in terms of "fixing" the macroscopic shape of the cellulose microgel, and as a consequence, of the cellulose aerogel microparticle.[27] Figure 3a shows that the acetic acid-coagulated cellulose microgels in ethanol are regular in shape and size with a mean diameter of approximately 35 µm. In contrast, HCl-coagulated microgels (Figure 3c) look agglomerated and have a smaller diameter of about 20 µm.

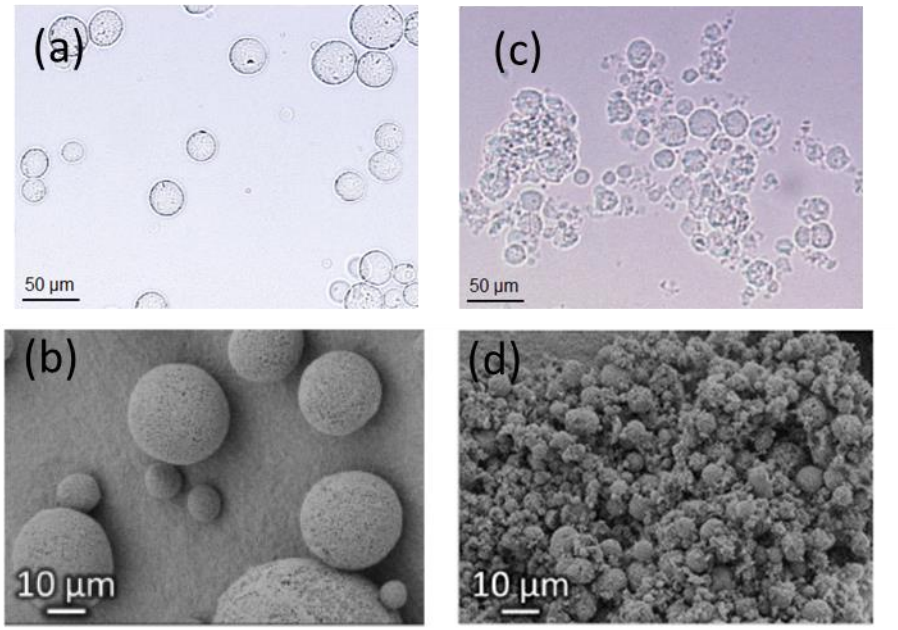



**Figure 3.** Cellulose microgels and aerogel microparticles after coagulation in acetic acid (a, b) or in HCl (c, d): optical microscopy images of microgels dispersed in ethanol (a, c) and SEM images of microparticles after drying with supercritical $CO_2$ (b, d)

Following supercritical drying, the differences in appearance persisted, as the acetic acid-coagulated cellulose aerogel microparticles were slightly larger, with well-defined spherical shape and without visible debris (Figure 3b) contrary to HCl-coagulated cellulose (Figure 3d). These

differences are resulting from different actions triggering cellulose coagulation and thus fixing the droplet and microgel shape. Since acetic acid is partly soluble in paraffin oil, it diffuses into the cellulose droplet as soon as the non-solvent emulsion is mixed with the cellulose solution emulsion (Figure 4, top). Non-solvent induced phase separation starts immediately and a skin of coagulated cellulose is formed on the surface of the cellulose solution droplet, helping to fix the droplet's shape. Then, upon continuation of the acetic acid diffusion and also because of coalescence with an acetic acid droplet, coagulation of the cellulose droplet is completed. In contrast, the insolubility of HCl in paraffin oil allows cellulose coagulation only upon coalescence with HCl droplet (Figure 4, bottom). Since in this case the coagulation is not starting immediately upon mixing of the two emulsions, the cellulose droplets may continue breaking-up and/or coalescing with each other during mixing. The impact produced during coalescence of cellulose solution and non-solvent droplets may induce cellulose solution droplet deformation and further breakage, leading to the formation of debris.

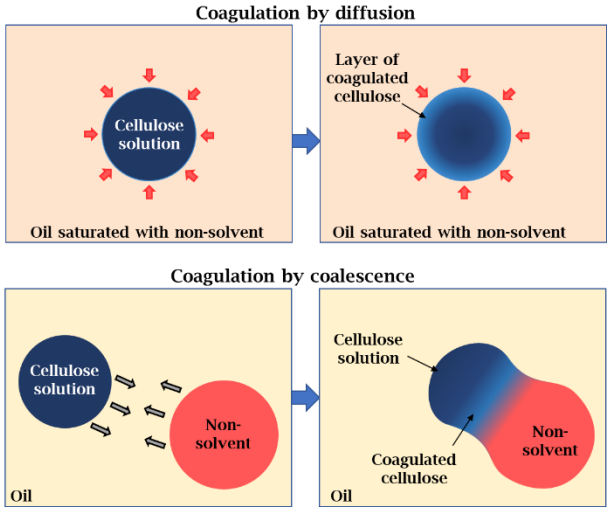



**Figure 4.** Proposed mechanism for the coagulation of cellulose via diffusion (top) or coalescence (bottom) after mixing cellulose/oil and non-solvent/oil emulsions.

The size distribution and mean diameter of the cellulose aerogel microparticles were obtained from the SEM pictures and are presented in Figure 5. Compared to their size in ethanol (Figure 3), the aerogel microparticles have a smaller size (mean diameter of around 21 and 5 µm for cellulose coagulated with acetic acid and HCl, respectively), which can be attributed to shrinkage during supercritical drying.[36] The size decrease is higher for HCl-coagulated particles compared to acetic acid-coagulated particles (volume shrinkage of 97 and 79 %, respectively), indicating that coagulating cellulose with acetic acid results in a network that is more resistant to shrinking, most probably due to the formation of a skin of coagulated cellulose as mentioned above.

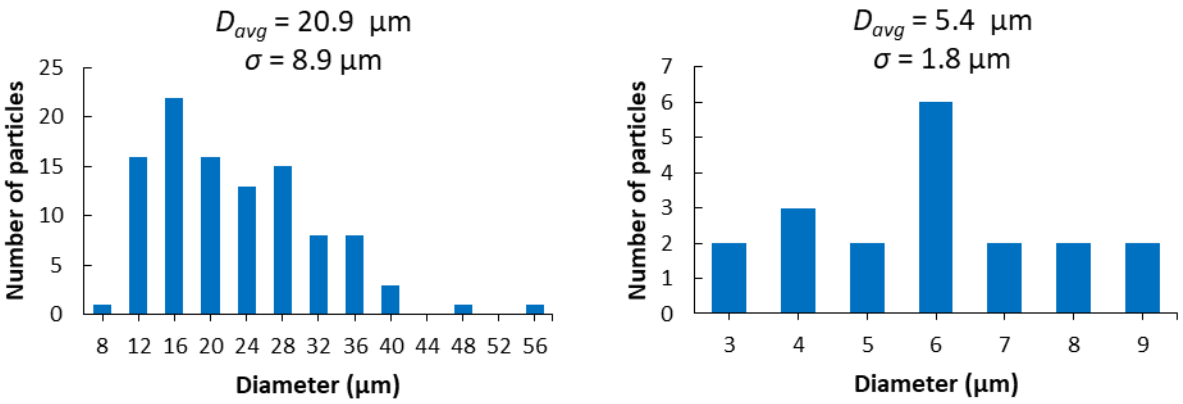



**Figure 5.** Size distribution of cellulose aerogel microparticles from cellulose-NaOH-urea-water solution coagulated by acetic acid (left) or HCl (right), debris were not taken into account.

The morphology of HCl-coagulated cellulose aerogel microparticles is slightly denser than that of acetic acid-coagulated cellulose (Figure 6), in accordance with the results regarding shrinkage upon supercritical drying. With HCl as the non-solvent, cellulose solution droplets are in direct contact with this strong acid upon coalescence. In contrast, the partial solubility of acetic acid in the oil

phase allows for gentle diffusion of this weak acid into the cellulose droplets leading to non-solvent induce phase separation, resulting in a more porous morphology.

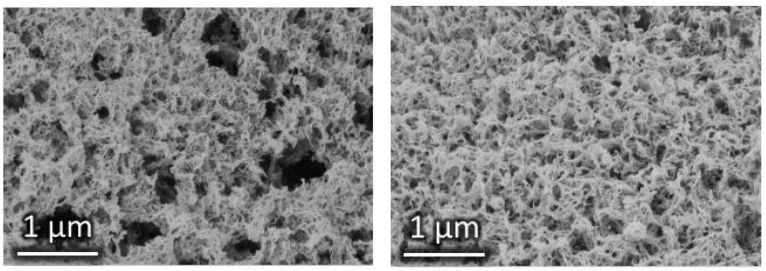
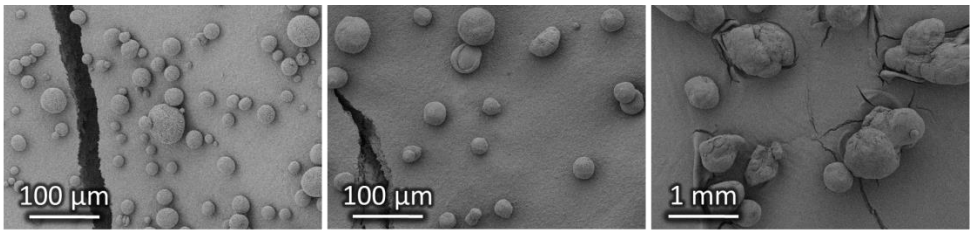



**Figure 6.** SEM images showing the porous structure of cellulose aerogel microparticles coagulated by acetic acid (left) or HCl (right).

The difference in morphology is also reflected in the specific surface area, which is higher for the acetic acid-coagulated cellulose aerogel microparticles (356 ± 50 $m^2/g$) in comparison with the HCl-coagulated ones (307 ± 34 $m^2/g$). Overall, the specific surface area of acetic acid-coagulated cellulose aerogel microparticles is within the highest values of surface area of micron-sized aerogel beads obtained from cellulose-ionic liquid solutions (240 - 340 $m^2/g$),[20] cellulose-N-methyl-morpholine-N-oxide monohydrate (300 – 350 $m^2/g$),[21] cellulose-NaOH-urea-ZnO-water (240 - 410 $m^2/g$)[37] and cellulose-NaOH-urea-water (340 - 470 $m^2/g$).[38]

Lastly, the influence of gelation on shaping of cellulose particles was investigated using acetic acid as coagulant as it was shown to give the best results in terms of shape and size homogeneity. Three cellulose solvents were compared: NaOH-urea-water, NaOH-ZnO-water and NaOH-water. In the latter case, the emulsion cellulose-NaOH-water/oil was kept for 3 h at 50 °C ensuring complete gelation of cellulose solution droplets. As mentioned at the beginning of the Results section, in order to stabilize the shape of a droplet of a polysaccharide solution, gelation is what is looked for

and is often used in case of "easy gelling" polymers such as alginate or carrageenan.[39] However, cellulose-NaOH-water solutions behave differently: the obtained aerogel particles from cellulose microgels are of large (several hundreds of microns) and irregular shape and with a lower specific surface area as compared to the cases when additives were used (Figure 7). The reason is that on one hand, cellulose-NaOH-water gels are weak and thus easily deformable and breakable, and on the other hand gelation is "pre-fixing" the droplet shape not allowing the interfacial tension to "correct" it.




| Cellulose solvent | NaOH-11.5 wt % urea-water | NaOH-0.5 wt % ZnO-water | NaOH-water |
|---|---|---|---|
| Specific surface area, $m^2/g$ | 356 ± 50 | 346 ± 35 | 279 ± 28 |

Figure 7

Influence of cellulose solvent and solution gelation on the shape of aerogel microparticles; coagulation was performed in 8.6 M acetic acid.

To demonstrate that cellulose solution gelation needs to be delayed to obtain spherical cellulose aerogel microparticles, ZnO was used, and cellulose aerogel microparticles were made from cellulose-NaOH-ZnO-water solutions in the same way as from cellulose-NaOH-urea-water solutions.[27] The result is shown in Figure 7: aerogel microparticles from cellulose-NaOH-ZnO-water are similar in shape and specific surface area to those made from cellulose-NaOH-urea-water; their mean diameter is around 33 µm (Figure S9).

## Conclusions

Cellulose aerogel microparticles were made by emulsion technique via cellulose dissolution in NaOH-based solvent, non-solvent induced phase separation and drying with supercritical $CO_2$. Emulsification was carried out by mixing two emulsions: cellulose solution/oil and cellulose non-solvent/oil. Gelation kinetics of cellulose solutions was varied by using or not additives such as urea or ZnO. The influence of non-solvent on droplet shape stabilization was also investigated. Spherical aerogel microparticles of few tens of microns in diameter and with a high specific surface of around 350 $m^2/g$ were obtained. This was possible when the following conditions were fulfilled:

- First, contrary to "easy-gelling" polysaccharides, gelation of the droplets of cellulose solution turned out to be detrimental for having well-defined particles with diameter below 100 μm. Thus additives (ZnO or urea) are needed to delay solution gelation.
- Second, quick cellulose coagulation is needed to stabilize the droplet shape. This can be achieved by using cellulose non-solvent (here, acetic acid) which is partly miscible with the dispersing medium (here, paraffin oil) providing cellulose coagulation via diffusion. A skin of coagulated cellulose is formed on the surface of the droplet helping to stabilize its shape. Coagulation is then continued due to coalescence of cellulose and non-solvent droplets.

As only non-toxic compounds were used, these new cellulose aerogel microparticles have a lot of potential to be used in life science applications as biodegradable and biocompatible carriers of active substances.

## Supporting Information

Supporting Information file contains figures concerning the rheological properties of cellulose-NaOH-water solutions and of paraffin oil, optical microscopy images of emulsified systems and size distribution of cellulose aerogel microparticles from cellulose-NaOH-ZnO-water solution.

## Acknowledgements

This project has received funding from the European Union's Horizon 2020 research and innovation program under grant agreement no. 685648. We thank Pierre Ilbizian (PERSEE, MINES ParisTech) for supercritical drying and Suzanne Jacomet (CEMEF, MINES ParisTech) for guidance in SEM.

## References


1. Soorbaghi, F. P.; Isanejad, M.; Salatin, S.; Ghorbani, M.; Jafari, S.; Derakhshankhah, H. Bioaerogels: Synthesis approaches, cellular uptake, and the biomedical applications. *Biomed. Pharmacother.* **2019***, 111*, 964-975.

2. Maleki, H.; Durães, L.; García-González, C. A.; del Gaudio, P.; Portugal, A.; Mahmoudi, M. Synthesis and biomedical applications of aerogels: Possibilities and challenges. *Adv. Colloid Interface Sci.* **2016***, 236*, 1-27.

3. Esquivel-Castro, T. A.; Ibarra-Alonso, M. C.; Oliva, J.; Martínez-Luévanos, A. Porous aerogel and core/shell nanoparticles for controlled drug delivery: A review. *Mater. Sci. Eng., C* **2019***, 96*, 915-940.

4. Demilecamps, A.; Beauger, C.; Hildenbrand, C.; Rigacci, A.; Budtova, T. Cellulose–silica aerogels. *Carbohydr. Polym.* **2015***, 122*, 293-300.

5. Lu, T.; Li, Q.; Chen, W.; Yu, H. Composite aerogels based on dialdehyde nanocellulose and collagen for potential applications as wound dressing and tissue engineering scaffold. *Compos Sci Technol* **2014***, 94*, 132-138.

6. Ganesan, K.; Budtova, T.; Ratke, L.; Gurikov, P.; Baudron, V.; Preibisch, I.; Niemeyer, P.; Smirnova, I.; Milow, B. Review on the production of polysaccharide aerogel particles. *Materials* **2018***, 11*, 2144.

7. Alemán, J.; Chadwick, A. V.; He, J.; Hess, M.; Horie, K.; Jones, R. G.; Kratochvíl, P.; Meisel, I.; Mita, I.; Moad, G. Definitions of terms relating to the structure and processing of sols, gels, networks, and inorganic-organic hybrid materials (IUPAC Recommendations 2007). *Pure Appl. Chem.* **2007***, 79*, 1801-1829.

8. Smirnova, I.; Gurikov, P. Aerogels in chemical engineering: Strategies toward tailor-made aerogels. *Annu. Rev. Chem. Biomol. Eng.* **2017***, 8*, 307-334.

9. García-González, C. A.; Jin, M.; Gerth, J.; Alvarez-Lorenzo, C.; Smirnova, I. Polysaccharide-based aerogel microspheres for oral drug delivery. *Carbohydr. Polym.* **2015***, 117*, 797-806.

10. Alnaief, M.; Alzaitoun, M.; García-González, C.; Smirnova, I. Preparation of biodegradable nanoporous microspherical aerogel based on alginate. *Carbohydr. Polym.* **2011***, 84*, 1011-1018.

11. Baudron, V.; Gurikov, P.; Smirnova, I. A continuous approach to the emulsion gelation method for the production of aerogel micro-particle. *Colloids Surf. A* **2019***, 566*, 58-69.

12. Alnaief, M.; Obaidat, R.; Mashaqbeh, H. Effect of processing parameters on preparation of carrageenan aerogel microparticles. *Carbohydr. Polym.* **2018***, 180*, 264-275.

13. García-González, C. A.; Carenza, E.; Zeng, M.; Smirnova, I.; Roig, A. Design of biocompatible magnetic pectin aerogel monoliths and microspheres. *RSC Adv.* **2012***, 2*, 9816-9823.

14. Kamel, S.; Ali, N.; Jahangir, K.; Shah, S.; El-Gendy, A. Pharmaceutical significance of cellulose: a review. *eXPRESS Polym. Lett.* **2008***, 2*, 758-778.

15. Gopi, S.; Balakrishnan, P.; Chandradhara, D.; Poovathankandy, D.; Thomas, S. General scenarios of cellulose and its use in the biomedical field. *Mater. Today Chem.* **2019***, 13*, 59-78.

16. Budtova, T. Cellulose II aerogels: A review. *Cellulose* **2019***, 26*, 81-121.

17. Budtova, T.; Navard, P. Cellulose in NaOH–water based solvents: a review. *Cellulose* **2016***, 23*, 5-55.

18. Gericke, M.; Trygg, J.; Fardim, P. Functional cellulose beads: preparation, characterization, and applications. *Chem. Rev.* **2013***, 113*, 4812-4836.

19. Sescousse, R.; Gavillon, R.; Budtova, T. Wet and dry highly porous cellulose beads from cellulose–NaOH–water solutions: influence of the preparation conditions on beads shape and encapsulation of inorganic particles. *J. Mater. Sci.* **2011***, 46*, 759-765.

20. Druel, L.; Niemeyer, P.; Milow, B.; Budtova, T. Rheology of cellulose-[DBNH][CO 2 Et] solutions and shaping into aerogel beads. *Green Chem.* **2018***, 20*, 3993-4002.

21. Innerlohinger, J.; Weber, H. K.; Kraft, G. Aerocellulose: aerogels and aerogel-like materials made from cellulose. *Macromol. Symp.* **2006**, *244*, 126-135.

22. Wang, Q.; Fu, A.; Li, H.; Liu, J.; Guo, P.; Zhao, X. S.; Xia, L. H. Preparation of cellulose based microspheres by combining spray coagulating with spray drying. *Carbohydr. Polym.* **2014***, 111*, 393-399.

23. Luo, X.; Zhang, L. Creation of regenerated cellulose microspheres with diameter ranging from micron to millimeter for chromatography applications. *J. Chromatogr. A* **2010***, 1217*, 5922-5929.

24. Suzuki, T.; Kono, K.; Shimomura, K.; Minami, H. Preparation of cellulose particles using an ionic liquid. *J. Colloid Interface Sci.* **2014***, 418*, 126-131.

25. Coombs OBrien, J.; Torrente-Murciano, L.; Mattia, D.; Scott, J. L. Continuous production of cellulose microbeads via membrane emulsification. *ACS Sustainable Chem. Eng.* **2017***, 5*, 5931-5939.

26. Du, K.; Yan, M.; Wang, Q.; Song, H. Preparation and characterization of novel macroporous cellulose beads regenerated from ionic liquid for fast chromatography. *J. Chromatogr. A* **2010***, 1217*, 1298-1304.

27. Druel, L., PhD thesis, MINES ParisTech, Sophia Antipolis, France, **2019**.

28. Evans, R.; Wallis, A. F. Cellulose molecular weights determined by viscometry. *J. Appl. Polym. Sci.* **1989***, 37*, 2331-2340.

29. Roy, C.; Budtova, T.; Navard, P. Rheological properties and gelation of aqueous cellulose− NaOH solutions. *Biomacromolecules* **2003***, 4*, 259-264.

30. Gavillon, R.; Budtova, T. Aerocellulose: new highly porous cellulose prepared from cellulose–NaOH aqueous solutions. *Biomacromolecules* **2008**, *9*, 269-277.

31. Gunnarsson, M.; Bernin, D.; Östlund, Å; Hasani, M. The CO2 capturing ability of cellulose dissolved in NaOH (aq) at low temperature. *Green Chem.* **2018**, *20*, 3279-3286.

32. Liu, W.; Budtova, T.; Navard, P. Influence of ZnO on the properties of dilute and semi-dilute cellulose-NaOH-water solutions. *Cellulose* **2011***, 18*, 911-920.

33. Cai, J.; Zhang, L. Unique gelation behavior of cellulose in NaOH/urea aqueous solution. *Biomacromolecules* **2006***, 7*, 183-189.

34. Egal, M., PhD thesis, MINES ParisTech, Sophia Antipolis, France, **2006**.

35. Grace, H. P. Dispersion phenomena in high viscosity immiscible fluid systems and application of static mixers as dispersion devices in such systems. *Chem. Eng. Commun.* **1982***, 14*, 225-277.

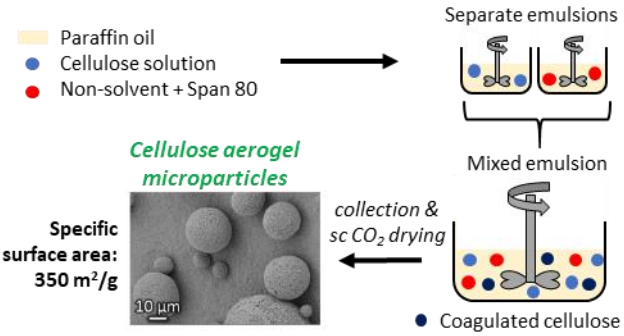
36. Buchtova, N.; Budtova, T. Cellulose aero-, cryo-and xerogels: towards understanding of morphology control. *Cellulose* **2016***, 23*, 2585-2595.

37. Mohamed, S. M. K.; Ganesan, K.; Milow, B.; Ratke, L. The effect of zinc oxide (ZnO) addition on the physical and morphological properties of cellulose aerogel beads. *RSC Adv.* **2015**, *5*, 90193-90201.

38. Trygg, J.; Fardim, P.; Gericke, M.; Mäkilä, E.; Salonen, J. Physicochemical design of the morphology and ultrastructure of cellulose beads. *Carbohydr. Polym.* **2013**, *93*, 291-299.

39. Quignard, F.; Valentin, R.; Di Renzo, F. Aerogel materials from marine polysaccharides. *New J. Chem.* **2008***, 32*, 1300-1310.

## Table of Contents



# Supporting Information

# Cellulose aerogel microparticles via emulsion-coagulation technique

*Lucile Druel[1], Amelie Kenkel[1, 2], Victor Baudron[2], Sytze Buwalda[1], Tatiana Budtova[1]**

1 - MINES ParisTech, PSL Research University, Center for Materials Forming (CEMEF), UMR CNRS 7635, CS 10207, 06904 Sophia Antipolis, France

2 - Institute of Thermal Separation Processes, Hamburg University of Technology, Eißendorfer Straße 38, 21073 Hamburg, Germany

**Figure S1**

Example of the evolution of elastic (G') and viscous (G") moduli of 5%cellulose-NaOH-urea-water solution in time at 20 and 25 °C.

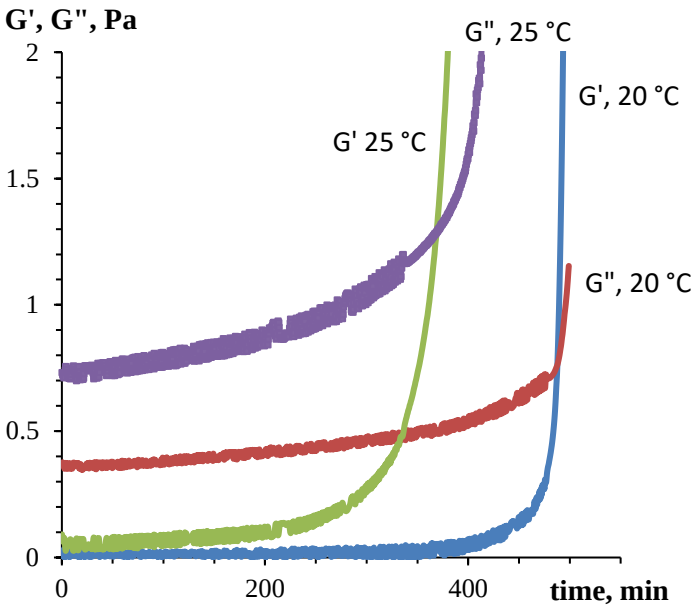



**Figure S2**

Example of the evolution of dynamic viscosity of 5%cellulose-NaOH-water (1), 5%cellulose-NaOH-ZnO-water (2) and 5%cellulose-NaOH-urea-water (3) solutions in time at 20 °C.

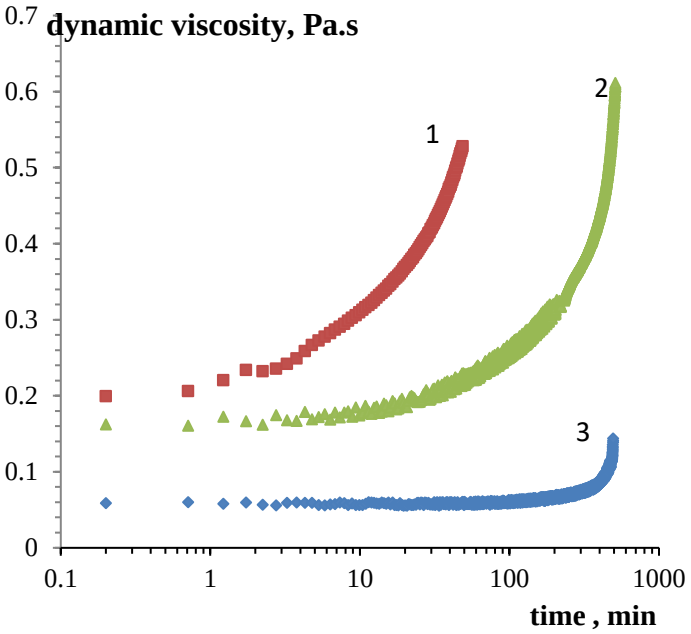

dynamic viscosity, Pa.s
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0.1
1
10
100
1000
time , min
1
2
3

**Figure S3.**

Examples of paraffin oil shear flow at 20 °C and 70 °C.

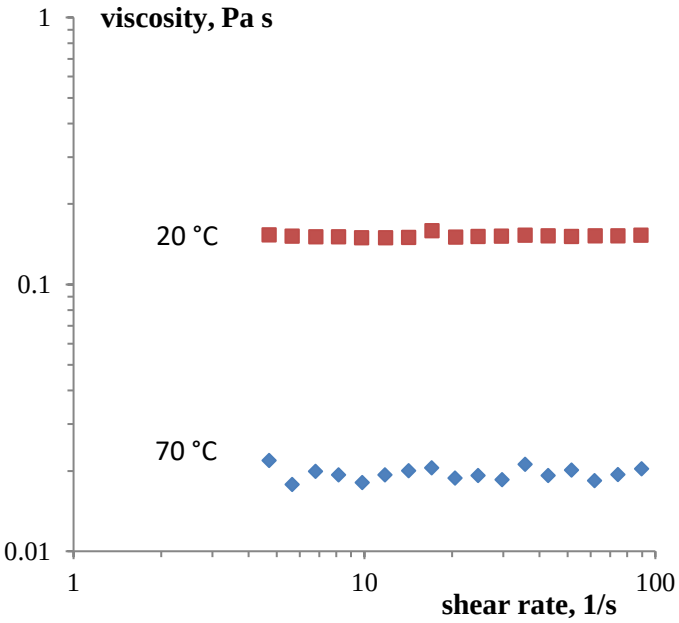



**Figure S4**

Arrhenius plot for paraffin oil viscosity

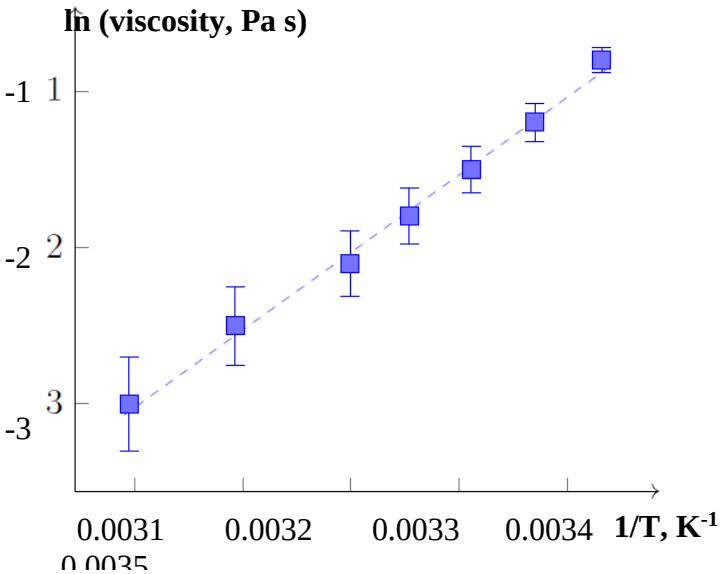

ln (viscosity, Pa s)
-1
1
-2
2
-3
3
0.0031
0.0032
0.0033
0.0034
1/T, K-1
0.0035

**Figure S5.**

Optical microscopy image of a cellulose-NaOH-urea solution emulsified in paraffin oil in the presence of 1 v/v % polysorbate 80 after 2 h of stirring.

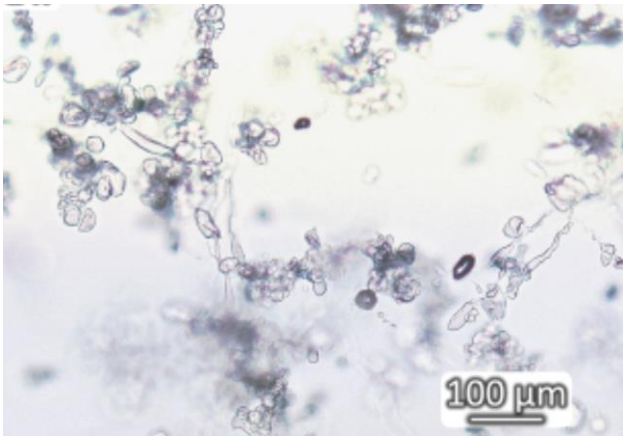



**Figure S6**

Optical microscopy image of NaOH/urea solution emulsified in paraffin oil in the presence of 1 v/v % polysorbate 80 after 2 h of stirring.

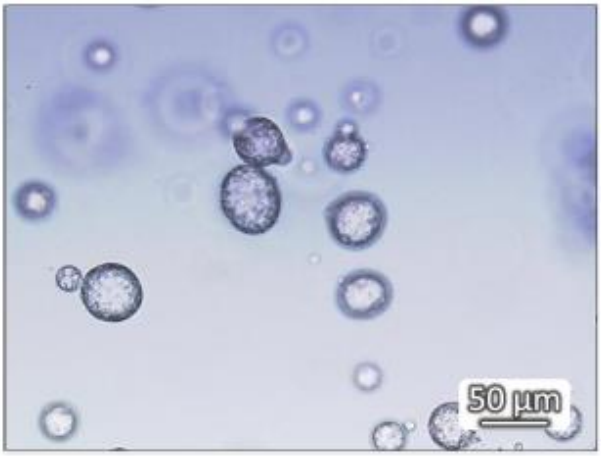


**Figure S7**

Microscopy image of a cellulose-NaOH-urea-water solution emulsified in paraffin oil without surfactant after 30 min of stirring.

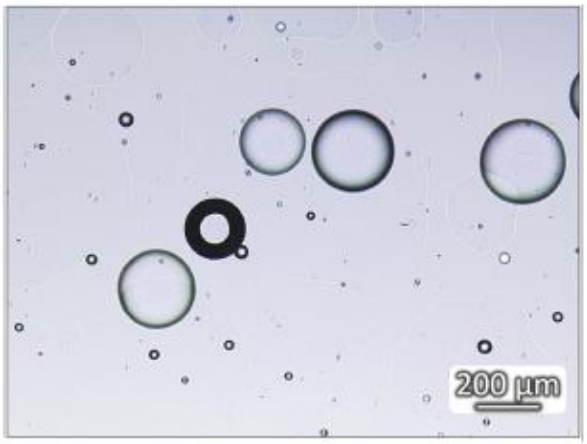



**Figure S8**

Test tube showing cellulose microparticles, the aqueous phase and the paraffin oil after centrifugation.

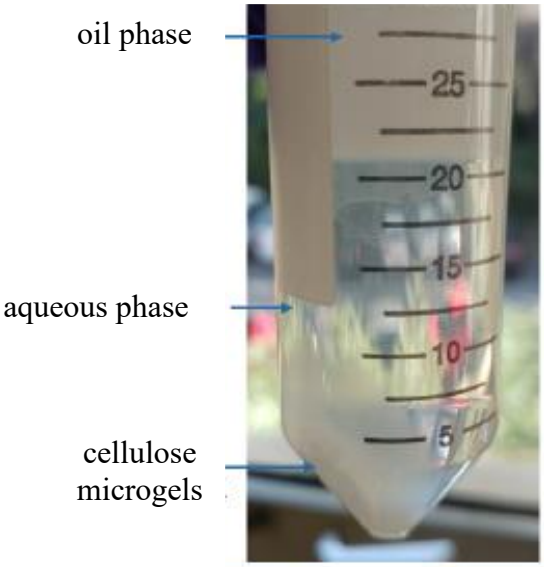


**Figure S9**

Size distribution of cellulose aerogel microparticles from cellulose-NaOH-ZnO-water solution coagulated in acetic acid.