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HYDROLYSIS OF SILICA SOURCES: APS AND DTSACl IN MICROENCAPSULATION PROCESSES

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Abstract. The process of formation of silica shells around emulsion droplets was investigated. The ^{1}H-NMR spectroscopy was applied to follow the silica shell formation around emulsion droplets by hydrolysis and condensation of selected silanes in the emulsion system. (3- aminopropyl) triethoxysilane (APS) and dimethyloctadecyl [3-(trimethoxysilyl) propyl] ammonium chloride (DTSACl) were used as silica sources in microencapsulation process. The NMR analysis revealed strong dependence of the hydrolysis reaction rate on pH. Obtained information allowed selecting the optimal conditions for the formation of the capsules with silica shells. The obtained capsules' suspensions were stable for several weeks.

keywords: encapsulation, emulsions, silica shells, capsules, ^{1}H -NMR

1. Introduction

Microencapsulation can be defined as a process in which colloidal particles or droplets are being enclosed in inert shells of various materials to obtain capsules (Swapan, 2006). Encapsulation has a potential to improve the compatibility of lipophilic, poorly water-soluble or even water-insoluble compounds with aqueous media and it can protect active molecules from the negative effect of external environment. The development of the microencapsulation technology started with introduction of capsules containing dyes, which were incorporated into paper for copying purposes and replaced carbon paper (Schleicher and Green, 1956). Since then the number of processes used to produce microcapsules has continued to grow and the development of functional micro or nano-containers is currently one of the main topics in pharmaceutical research. In particular, nanocapsules can be used in specific drug delivery system as they can penetrate the cell membrane. Moreover they can be functionalized to achieve "intelligent targeting", i.e. delivery to the specific cells or organs (Donath and Moya, 2002; Radtchenko and Giersig, 2002; Shchukin and

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Radtchenko, 2003; Shchukin and Sukhorukov, 2004; Georgieva and Moya, 2004; Sukhorukov and Dahne, 2000; Caruso and Fiedler, 2000; Schüler and Caruso, 2001). Application of mini- or micro-emulsion with silica sources as cores opens the possibility of formation of novel, oil core microcapsules with hydrolyzed silica shells with good control of their size (Grigoriev and Bukreeva, 2008; Szczepanowicz and Hoel, 2010) and functionality due to easy modification of the shell.

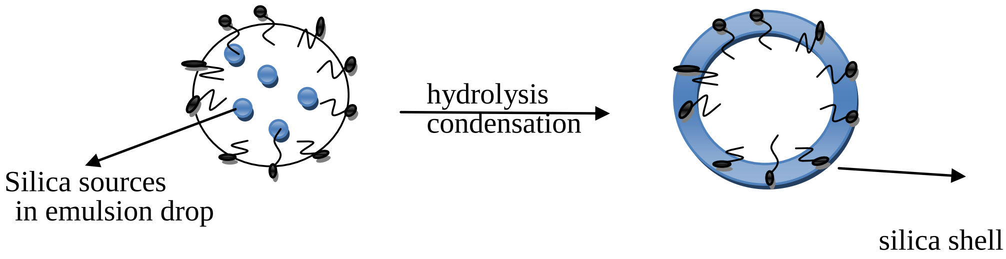


Fig. 1. Scheme of formation microcapsules with silica shells

In our previous work we have described the method of formation of emulsions containing silanes derivatives (Szczepanowicz and Dronka-Gora, 2009) for microencapsulation process, which is schematically presented in Fig. 1. The silanes undergo hydrolysis and condensation on the emulsion drop surface that leads to formation of a silica shell around liquid or semi-liquid core. We used APS and DTSACl as silica sources in emulsions of chloroform in water. The aim of our present work was to investigate the kinetics of the process of silica shell formation around emulsion droplets. We investigated the hydrolysis reaction of APS and DTSACl in chloroform emulsions systems in order to determine the conditions favorable for shell formation. The general scheme of polymerization reaction (hydrolysis and condensation) of silanes derivatives (alkoxysilanes) occurring at the interface and leading to silica shell formation is presented in Fig. 2 (Artaki and Bradley, 1985; Brinker and Scherer, 1990).

There are many works concerning the kinetics of TEOS (tetraethylorthosilicate) hydrolysis during the formation of monosize silica particles in the literature, but there are no reports concerning APS and DTSACl enclosed in emulsion systems. The following methods were used to determine the concentration of TEOS: ^{29}Si NMR (Bogush and Zukoski, 1991; Bailey and Mecartney, 1992), ^{13}C NMR (van Blaaderen and Geest, 1992) and Raman spectroscopy (Harris and Brunson, 1990; Matsoukas and Gulair, 1988). In order to study the kinetics of TEOS hydrolysis, Byers and Harris (1987) used gas chromatography for determining the concentration of ethanol, which is co-product of the reaction. Kinetic studies of the hydrolysis and condensation of TEOS were performed also by Chen (1996). That author determined concentration of TEOS by means of gas chromatography and conductometry and showed that both hydrolysis of TEOS and condensation of $Si(OH)_4$ are the first order reactions.

Relationships of the hydrolysis and condensation rate constants with reaction condition variables, such as temperature and H_2O concentration were also determined. In our study the progress of the shell formation by hydrolysis of silica sources was observed using NMR spectroscopy. Since we had found ^{29}Si-NMR spectra ambiguous, we proposed an alternative way to characterize the hydrolysis of silica sources in emulsion system by monitoring its progress by analysis of the ^{1}H-NMR signals from un-hydrolyzed APS and DTSACl and of the NMR spectra of co-products of their hydrolysis. Ethanol is a co-product of the hydrolysis of APS, while methanol is co-product of the reaction of DTSACl.

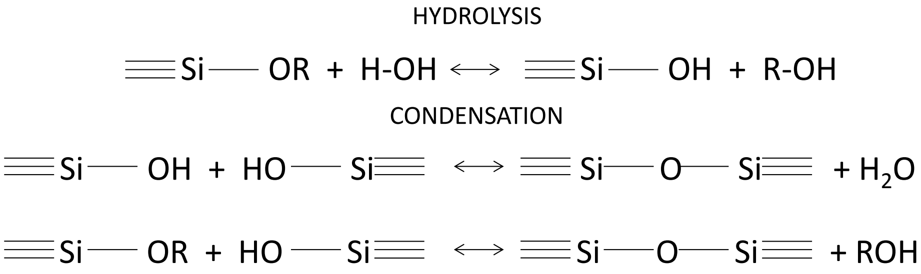
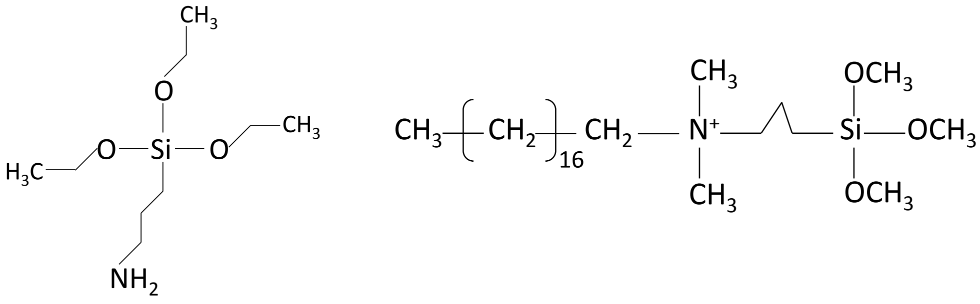


Fig. 2. The scheme of hydrolysis and condensation reactions of silanes (R is an alkyl group)

2. Materials and methods

APS ((3-aminopropyl)triethoxysilane), DTSACl (dimethyloctadecyl[3-(trimethoxysilyl)propyl]ammonium chloride), Tween 80 (polyoxyethylenesorbitan monooleate) were purchased from Sigma-Aldrich Co. Chloroform, HCl, NaOH were purchased from POCh SA. Water (Direct Q3 UV system, Millipore SA) was used for the preparation of solutions. All materials were used without further purification. Structural formulas of silica sources are shown in Fig. 3.



(a) (b)

Fig.3. Structural formulas of silica sources applied in our studies a) APS b) DTSACl

2.1. Emulsion preparation

The emulsions containing silanes (APS and DTSACl), and when it was necessary stabilized by addition of Tween 80, were prepared according to procedure described before (Szczepanowicz and Dronka-Gora, 2009) by continuous mixing of all components using magnetic stirrer.

2.2. Droplets size analysis

Size (hydrodynamic diameter) of emulsion droplets were determined by DLS (Dynamic Light Scattering) using Zetasizer Nano ZS from Malvern Instruments Ltd. with the detection angle of 173° in optically homogeneous square polystyrene cells. Measurements of the average size of emulsion droplets were performed at 298 K. Each value was obtained as average from three runs with at least 10 measurements.

2.3. Zeta potential measurements

The zeta potential of emulsion droplets was measured by the microelectrophoretic method using Malvern Zetasizer Nano ZS apparatus. Each value was obtained as an average from three subsequent runs of the instrument with at least 20 measurements. The zeta potential of capsules was measured in 0.015M NaCl.

2.4. ^{1}H-NMR spectroscopy

NMR-spectroscopy was applied to characterise the hydrolysis of the silica sources in emulsion systems. Spectra were obtained using a Varian VXR S 300 MHz and Varian GEMINI 300 MHz instruments. The volume of 0.7 ml of the solution was used in the NMR-tube. C_6D_6 in a capillary was used to lock the instrument. First spectre were taken 15 minutes after preparing of the sample.

3. Results and discussion

The emulsions were prepared by mixing all components (water with surfactant and chloroform with silica sources) using magnetic stirrer. Figure 4 shows size distributions of emulsions drops containing 20% of APS in chloroform stabilized by Tween 80 with various oil to surfactant ratios. As it can be seen, quite monodisperse microemulsions with the average drop size of 20, 50 and 100 nm and zeta potential of +15 mV were obtained. Therefore, by changing the proportion between oil phase (chloroform) and surfactant it was possible to vary the average size of emulsion drops.

Because DTSACl exhibits strong surface activity as it was demonstrated before (Szczepanowicz and Dronk-Gora, 2009), lowering the interfacial tension between chloroform and water below 5 mN/m at the concentration 10^{-4} mol dm^{-3}, emulsions containing various amounts of DTSACl in chloroform were prepared without any additional surfactant. It is advantageous for biomedical application as in that way the amount of free surfactant, which can be toxic to cells, should be minimized. Figure 5 presents the example of the size distribution of emulsion drops obtained using the ratio between chloroform and DTSACl equal to1:1. The average size of emulsion droplets was 10 nm and their zeta potential was +22 mV. It can be seen that quite monodisperse emulsions can be obtained with this surface active silica source contained in the non-aqueous phase.

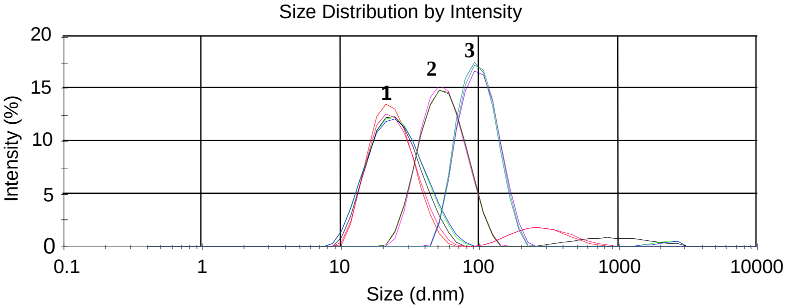


Fig. 4. Size distributions of emulsions - 20% APS in chloroform/Tween 80/water with various ratios between oil and surfactant: for 20 nm - 1:1, 50 nm – 3:1, 100 nm – 5:1.

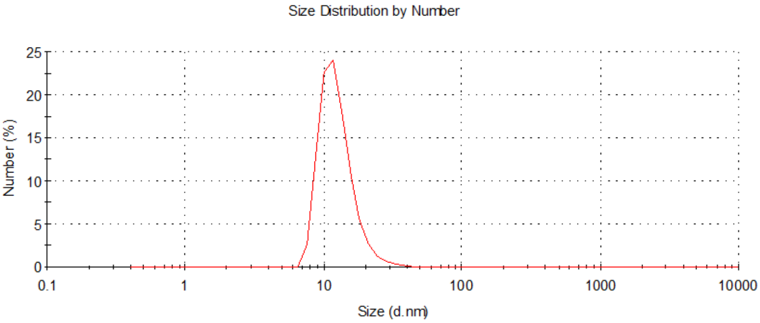


Fig. 5. Chloroform/DTSACl/water emulsions with the average drop size 10nm

NMR-spectroscopy was applied to characterise the hydrolysis of the silica sources in emulsion systems. However, since ^{29}Si-NMR spectra had been ambiguous, we proposed an alternative approach. The progress of the reaction was monitored by analysis of the ^{1}H-NMR signals from un-hydrolyzed APS/DTSACl and of ^{1}H-NMR spectra of co-products of their hydrolysis. Ethanol is a co-product of the hydrolysis of APS, while methanol is co-product of reaction of DTSACl. Progress of reaction was monitored at three conditions: basic (pH~10), acidic (pH~3) and natural (without any pH regulation). The spectra were taken immediately after the preparation of emulsion. In the ^{1}H-NMR spectra of the emulsion containing APS the quadruplet at 3.87 ppm was identified to belong to $–CH_3$ group from APS, the triplet at 1.26 ppm to $–CH_2$ group from APS and the triplet at 1.21 ppm to $–CH_2$ group from ethanol. Signals from unhydrolyzed APS were missing in spectra regardless of hydrolysis conditions, whereas ones corresponding to the ethanol were visible for all conditions studied, which means that hydrolysis of APS in the emulsion system was very fast (Fig. 6). The time needed to prepare emulsions was always longer than time of the hydrolysis reaction so APS was fully hydrolyzed.

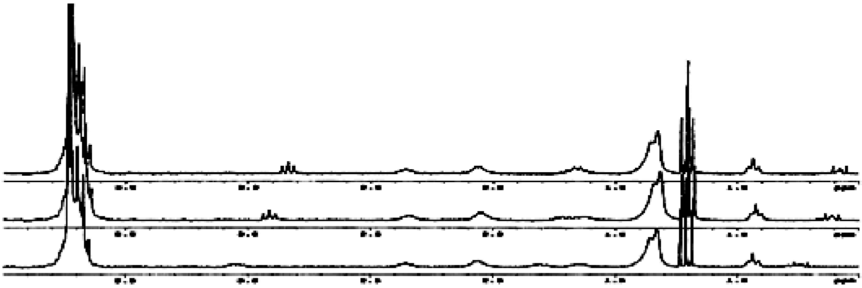


Fig. 6. The 1H-NMR spectra of emulsions containing APS. From the top: basic, natural, acidic

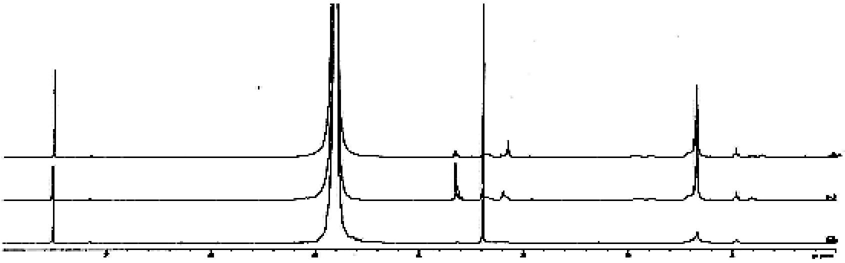


Fig. 7. The 1H -NMR spectra of emulsions containing DTSACl. From the top: acidic, natural, basic

In the case of DTSACl a convenient way to characterize the progress of hydrolysis was the analysis of the ^{1}H-NMR peak at 3.6 ppm from –O-CH_3 groups in DTSACl and the peak at 3.4 ppm of –CH_3 group from methanol. During the course of hydrolysis reaction the integrals of peaks from –O-CH_3 group in DTSACl decreased and integrals of methanol peaks increased. The kinetics of the reaction revealed strong dependence of its rate on pH of the emulsion. In the basic conditions (pH 10) hydrolysis was very fast, since the signal from DTSACl was not visible in the first spectra taken just after the sample preparation. In the natural and acidic conditions hydrolysis reaction was much slower (Fig. 7). In the acidic conditions (pH 3) no changes in spectra were observed even after 18 hours after sample preparation (see Fig. 8). Results obtained from NMR measurements of hydrolysis rate are collected in Table 1. This information allows selecting the optimal conditions for the formation of capsules with silica shells, in which hydrolysis of selected organosilanes is favorable. On the other hand it was found that DTSACl under the natural conditions (pH 6) was almost fully hydrolyzed after 24 hours (Fig. 9). After two weeks, gradual growth of the emulsion containing APS in natural condition was observed due to continuing condensation of silica and thickening of the silica shell. The example of growth of the emulsion drops is illustrated in Fig. 10.

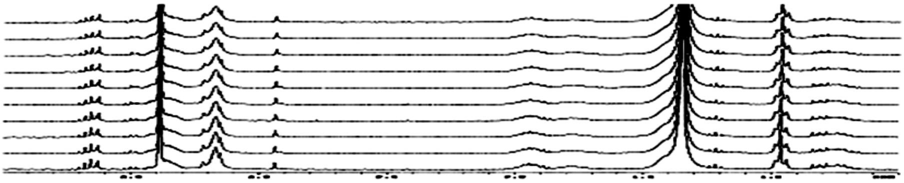


Fig. 8. The ^{1}H-NMR spectra of emulsions containing DTSACl in acidic conditions, sample has been tested over night with 1 hour period between spectra

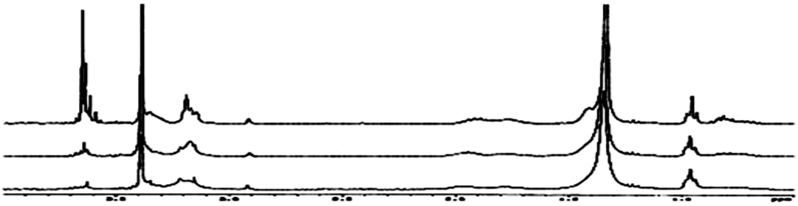
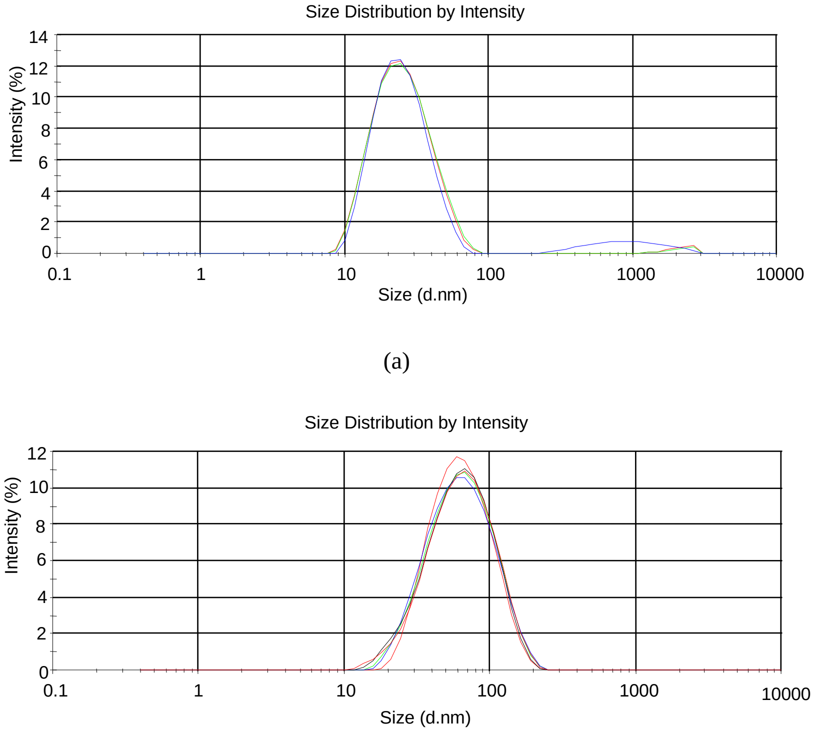


Fig. 9. The 1H -NMR spectra of emulsions containing DTSACl in natural condition, spectra taken just after preparing (top) after 3 hours (middle) and after 24 hours (bottom)

Table 1. Summary of results obtained from NMR measurements of hydrolysis of selected silanes

	APS	DTSACl
Acidic	fast	Slow (>12 days)
Neutral	fast	c.a. 24 h
Basic	fast	fast

One can see that the increase of the average size of the emulsion’s drops is not accompanied by significant broadening of the size distribution. Thus, one can assume that the increase of the size is caused by the silica condensation on emulsion’s drops instead of coalescence (or aggregation) of the emulsion. In the case of emulsion containing and stabilized by DTSACl, after half an hour in the alkaline conditions, growth of emulsion’s drops was observed as it is illustrated in Fig. 11. Since that growth was not observed in acidic condition, we assumed that it was the result of silica condensation and shell thickening following its formation due to hydrolysis.



(a)

(b)

Fig. 10. Size distributions of emulsions - 20% APS in chloroform/Tween 80/water: (a) before and (b) after hydrolysis and condensation

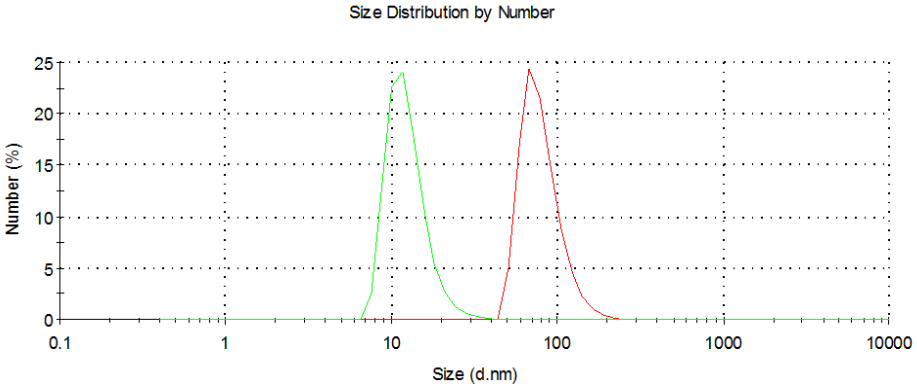


Fig. 11. Size distribution of emulsions - chloroform/DTSACl/water a) before (green line) and b) after hydrolysis and condensation (red line)

4. Conclusions

Chloroform solutions of silane derivatives APS or DTSACl were used as oil phase to prepare microemulsions, which play the role of cores for nanocapsules with silica shells. The size of obtained emulsion droplets ranged from 10 to 100 nm. The ^{1}H-NMR spectroscopy was applied to follow the silica shell formation around obtained emulsion droplets by the hydrolysis of silanes. The results revealed some dependence of the hydrolysis reaction rate on pH. In the case of the emulsion containing APS and stabilized by Tween 80, the rate was fast in all pH conditions studied, i.e., APS was fully hydrolyzed. On the other hand in the case of emulsion containing surface active DTSACl, the rate of its hydrolysis was strongly pH dependent - fast in the alkaline conditions, slow in acidic ones. The obtained information concerning the hydrolysis rate allows selecting the optimal conditions for the formation of capsules with silica shells. Gradual growth of the emulsion drop size observed under the conditions of fast hydrolysis, which was not accompanied by significant broadening of the size distribution by coalescence (or aggregation), was attributed to the silica condensation on emulsion's drops surface and shell thickening. Obtained nanocapsules with silica shells can be used for encapsulation and further surface modification (e.g. by layer-by-layer adsorption of polyelectrolytes).

Acknowledgements

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