

Research Article

Synthesis of Silicon-Containing Chitosan Hydrogels in a Glycolic Acid Medium

A. B. Shipovskaya,^{1,2} O. N. Malinkina,^{1,2} Yu. Yu. Zhuravleva,¹ and S. M. Rogacheva²

¹Chernyshevsky Saratov State University, 83 Astrakhanskaya St., Saratov 410012, Russia

²Yuri Gagarin State Technical University, 77 Politechnicheskaya St., Saratov 410054, Russia

Correspondence should be addressed to A. B. Shipovskaya; shipovskayaab@yandex.ru

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The present paper considers a “one-pot” green sol-gel synthesis of hybrid inorganic/organic hydrogels based on chitosan glycolate by using organically modified silica $\text{Si}(\text{OGly})_4 \cdot 2\text{GlyOH}$ as a precursor to form a network of $\equiv\text{Si}-\text{O}-\text{Si}\equiv$ bonds at 4, 20, and 37°C. The gelation time of the multicomponent chitosan-containing system was estimated as a function of the composition (the polymer template and precursor concentrations, introduction of a low-molecular-weight accelerator NaCl) and gelation conditions (the pH and temperature of the sol-gel process). It has been shown that an increased polymeric salt concentration, the introduction of an accelerator, and increased pH and temperature accelerate the gel-forming process.

1. Introduction

Inorganic/organic hybrid hydrogels, as well as aero-, cryo-, and xerogels obtained therefrom, are promising materials for practical applications in medicine (bioadhesive tissue-engineering constructions with anisotropic pore structures [1], wound dressings), pharmacology (soft dosage forms, controlled drug release systems [2]), and therapeutic cosmetology (transdermal compositions). Introducing an inorganic phase precursor (monomer) to an organic phase solution (e.g., a polymer solution) to form an inorganic network on the organic template matrix is one way to prepare hybrid hydrogels by sol-gel synthesis [3]. The possibility of “one-pot” quick obtaining homogeneous monolithic hydrogel systems is an important advantage of the sol-gel technology [4]. Nonaqueous solutions of alkoxy-silanes, such as tetraethoxy- or tetramethoxysilane (TEOS or TMOS), are most often used as the inorganic phase precursor [5], whose polycondensation, unfortunately, results in the formation of toxic products (ethanol and methanol, resp.), which limits their medical use. When such organic silicon derivatives as tetrahydroxyethyl- [6] and tetra- (dihydroxypropyl) silane are used [7], di- and trihydric alcohols, respectively, are formed, permitted for medical use. The nature of the organic template influences

the sol-gel synthesis kinetics and the stability of the systems produced. Shchipunov and Karpenko [8] used synthetic polymers (polyethylene oxide and polyvinyl alcohol PVA) and natural nonionic and ionic polysaccharides as the organic polymer matrix. It has been shown that the macromolecules with $-\text{OH}$ groups (PVA and polysaccharides) sharply accelerate the sol-gel kinetics and promote nucleation of silanol groups. Moreover, such charged polysaccharides as xanthan, carrageenan, and chitosan act as stabilizing agents to prevent syneresis.

The usage of a chitosan-containing matrix allows producing hydrogels and materials on their basis with rich morphology and high mucoadhesive and adjuvant properties [9]. For example, Larchenko et al. [10, 11] synthesized chitosan-containing glycerohydrogels with expressed hemostatic and transcutaneous activities. According to the modified classification of chitosan-containing hydrogels [12], chemical and physical hydrogels are distinguished, whose macrogel structure is fixed by covalent and ionic interactions, respectively. Covalent linking of chitosan macrochains with bifunctional agents, such as dialdehyde derivatives of nucleosides and nucleotides [13], genipin [14–16], diglycidyl esters [17], squaric acid esters [18], and enzyme aggregates [19], is accompanied by the formation of insoluble hydrogels with a

permanent 3D structure and good mechanical and absorptive properties. However, unwanted condensation products, the unreacted crosslinker, and a decreased number of free binding sites (the amino groups of chitosan) affect the gel's biological properties adversely. Physical hydrogels are free of these disadvantages of chemically linked ones, since they are formed via various reversible interactions, ionic ones, in ion-crosslinked hydrogels [20, 21], in polyelectrolyte complexes, or secondary interactions in grafted and interpenetrating hydrogels. For example, strong intermolecular hydrogen bonds are formed in the case of hybrid hydrogels of chitosan and gelatin [22], tripolyphosphate [23], glycerophosphate [24], agar [25, 26], sebacic acid [27], poly(lactic-co-glycolic acid) and polycaprolactone polyethers [28, 29], silk fibroin [30], and hyaluronan [31]. As the nonpermanent network of ion-crosslinked chitosan hydrogels is formed due to reversible bonds, such a structure is more sensitive to swelling at pH changes as compared with covalently crosslinked hydrogels and has the best biocompatibility, which enhances their potential medical usage.

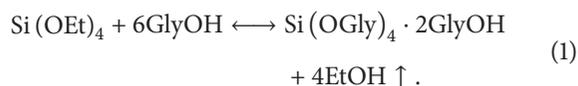
Hence, inorganic/organic Si glycerohydrogels based on an ion-crosslinked active chitosan matrix seem promising biocompatible systems not only with transport and transcutaneous activities (due to the precursor) but with mucoadhesive and bacteriostatic activities as well. The fact that the dissolution and, consequently, protonation of the amino groups of chitosan are performed in an acidic medium of nonpharmacopoeial grade, usually hydrochloric or acetic acid, substantially limits the use of such systems in pharmacology and medicine. Therefore, searching for biologically active solvents for chitosan is relevant and of great practical importance. For example, we have shown that the use of ascorbic acid as a chitosan solvent increases the biological activity of the corresponding gel composition [32], and glycerohydrogel based thereon is effective in the treatment of chronic generalized periodontitis and burn wounds [33, 34]. Here, the pharmacopoeial (0WT12SX38S UNII) glycolic acid (GA) was chosen to form chitosan polycations, which promoted cell regeneration and moisture retention in tissues [35, 36]. Due to its biologically useful properties, it is used for the production of dermatological and cosmetic products (scrubs and peels) with keratolytic and antiaging properties for the treatment of acne, scarring, and depigmentation [37]. Thus, research and development of inorganic/organic hybrid hydrogels and materials on their basis with preset parameters are relevant. In this connection, the aim of this work was the preparation of hybrid inorganic/organic hydrogels based on chitosan glycolate and silicon tetraglycerolate by using a "one-pot" sol-gel technology in situ under mild conditions, a study of the influence of the polymeric template and precursor concentrations and conditions (pH and temperature) on hybrid hydrogel formation.

2. Experimental

2.1. Materials. The following reagents were used: powder of chitosan with a viscosity-averaged molecular weight 38 kDa (CS), a degree of deacetylation 70 mol.% (Bioprogress Ltd., RF); tetraethoxysilane $\text{Si}(\text{OEt})_4$ ("Ekos-1" Ltd., RF); glycerol

(GlyOH) (Vekton Ltd., RF); glycolic acid 70% $\text{C}_2\text{H}_4\text{O}_3$ (GA) (Sigma-Aldrich, USA); NaCl and NaOH (NPO EKROS Ltd., RF); distilled water. All chemicals were of analytical grade or higher and used without further purification; freshly prepared solutions were always used in all experiments.

2.2. Synthesis of Organically Modified Silicon. The synthesis of silicon tetraglycerolates was performed by transesterification of tetraethoxysilane in a polyol excess without a catalyst according to Larchenko et al. [10]:



The first step was the esterification between tetraethoxysilane and glycerol within 70–80°C and under constant stirring until the disappearance of the phase interface. At the second step, the formed free EtOH was distilled off from the reaction mixture at 80°C and under atmospheric pressure. The completion of this stage was controlled by the temperature falling down to 73°C and by the volume of the EtOH distilled off as an azeotrope (~75% of the theoretical value). At the third step, EtOH was removed from the system at 140°C and under 15 mm Hg for 3 h. The reaction's completeness and the purity of the inorganic phase precursor were monitored using IR spectroscopy by no signals of $>\text{C}=\text{O}$ and $>\text{C}=\text{C}<$ at 1705–1685 cm^{-1} , which are specific to the product of the thermal oxidation of glycerol (acrolein). IR spectra were recorded on a Nicolet IR-6700 spectrometer, FT-IR (US) with a resolution of 4 cm^{-1} in the range of 4000 ÷ 5000 cm^{-1} .

2.3. Chitosan Solution Preparation. Solutions of CS with polymer concentrations $C_{\text{CS}} = 2$ and 4% (w/v) in aqueous glycolic acid with acid concentrations $C_{\text{GA}} = 1.5\%$ (v/v) were used. The choice of such polymer concentrations was due to the fact that when $C_{\text{CS}} > 1\%$ (w/v) chitosan accelerates gelation in weakly acidic media [34]. The solutions were prepared by dissolving polymer powder in an aqueous solution of GA at the ambient temperature without light for 24 h. The salt of chitosan glycolate was formed (CS-GA). The pH of the system was adjusted by adding 0.4 M aqueous NaOH solution.

2.4. Sol-Gel Synthesis of Hydrogels. To synthesize hydrogels, chitosan and $\text{Si}(\text{OGly})_4 \cdot 2\text{GlyOH}$ solutions were used in weight ratios from 1 : 1 to 13 : 1 with/without a low-molecular-weight accelerator (NaCl powder, 1 wt.%). The component concentrations were controlled gravimetrically on Ohaus Adventurer AR 1530 scales (the accuracy of weighing ± 0.002 g) and were expressed in wt.%. The mixed solutions were stirred carefully until homogeneity (1–2 min) and kept at 4 ± 0.5 , 20 ± 2 , or $37 \pm 0.5^\circ\text{C}$ under atmospheric pressure for the sol-gel synthesis. The gel point was fixed by the loss-flow time of the system, using "the test tube inverting method." The gel point corresponded to the instant of time after which the system "did not flow" within 40 seconds after the tube had been turned over at a given temperature. The physicochemical parameters (pH and the refractive index n_D^{25}) of the mixed solutions were measured on a Mettler

TABLE 1: Characterization of the hybrid silicon-chitosan-containing hydrogels.

Number	Component of the hydrogel, wt. %			CS/Si ratio	Physicochemical parameter		Gelation time, days		
	CS	Si	NaCl		n_D^{25}	pH	4 °C	20 °C	37 °C
1	2.0		—		1.4051	2.15	5.15	4.12	2.08
2	2.0*	2.43	—	0.82	1.3996	3.85	4.10	0.22	0.09
3	2.0*		1.0		1.4040	4.31	1.22	0.13	0.03
4	1.0*		—	0.41	1.3924	5.39	0.68	0.03	0.01
5	2.67		—		1.3854	2.13	6.88	5.95	2.13
6	2.67*	1.62	—	1.65	1.3821	3.81	5.33	0.40	0.16
7	2.67*		1.0		1.3870	4.22	2.41	0.14	0.05
8	1.3*		—	0.82	1.3753	5.34	0.69	0.03	0.02
9	3.0		—		1.3725	2.09	14.0	10.7	3.31
10	3.0*	1.21	—	2.48	1.3699	3.79	9.45	0.75	0.28
11	3.0*		1.0		1.3655	4.25	2.98	0.32	0.15
12	1.5*		—	1.24	1.3733	5.33	0.71	0.04	0.02
13	3.2		—		1.3740	2.09	17.6	12.0	3.88
14	3.2*	0.97	—	3.29	1.3636	3.78	10.0	1.35	0.47
15	3.2*		1.0		1.3639	4.22	3.30	0.36	0.23
16	1.6*		—	1.65	1.3646	5.33	0.75	0.04	0.03
17	3.56		—		1.3568	2.04	31.6	18.8	11.1
18	3.56*	0.61	—	5.74	1.3540	3.78	17.3	3.52	1.02
19	3.56*		1.0		1.3576	4.21	6.63	0.76	0.62
20	1.75*		—	2.87	1.3544	5.31	0.81	0.10	0.04
21	3.64*		—		1.3509	3.77	21.9	5.03	2.52
22	3.64*	0.48	1.0	7.50	1.3533	4.21	9.02	1.00	0.92
23	1.82*		—	3.75	1.3502	5.28	0.88	0.22	0.12

*pH of the system was varied by adding NaOH.

Toledo Five Easy FE20 pH-meter (Germany) and a Mettler Toledo RM40 refractometer (Germany).

2.5. Solid Phase Preparation. The preparation of the solid phase (xerogel) was performed by exhaustive cold extraction combined with cryotreatment and reextraction. Samples were placed into EtOH (95.6%) for 30 days. The choice of ethanol was caused by its being a nonsolvent (precipitant) for chitosan and silicon glycerohydrogel but a solvent for water, glycolic acid, and glycerol. The precipitant was replaced every 10 days. Then, the samples were cryofrozen in a refrigerator (Sanyo [ultra-low temperature freezer] mdF-U3286S) at -85°C for 24 h and were rekept in the precipitant (alcohol/acetone) for 3 days followed by drying in a desiccator (CaCl_2) within 24 h.

The surface morphology of the xerogel samples was evaluated by SEM on a MIRA/LMU scanning microscope (Tescan, Czech Republic) at a voltage of 8 kV and a conductive current of 60 pA. A 5 nm thick golden layer was sprayed onto each sample with a magnetron sputtering installation K450X carbon coater (Germany) at a spraying current of 20 mA and a spraying duration of 1 min.

3. Results

3.1. Effect of the Weight Ratio Template/Precursor, pH, Temperature, and Additives of a Salt-Electrolyte on the Gelation Time. The gelation time of several inorganic/organic systems

obtained by mixing the stock solutions of an organic template (an aqueous solution of CS-GA) and an inorganic phase precursor (glycerol $\text{Si}(\text{OGly})_4$) in a weight ratios range from 1 : 1 to 13 : 1 was measured. The effects of the CS and $\text{Si}(\text{OGly})_4$ concentrations, the accelerating NaCl addition, and the pH and temperature of the sol-gel process on the gelation time were examined. We selected three incubation temperatures for the sol-gel synthesis, namely, standard medical storage temperatures (4 ± 0.5 , $20 \pm 2^{\circ}\text{C}$) and the physiological one ($37 \pm 0.5^{\circ}\text{C}$). pH was varied by addition of small amounts of NaOH into the initial solution of CS-GA. At the same time, increasing of the medium pH increased the amount of the deprotonated amino groups of CS without polymer precipitation. To reduce the gelation time, a low-molecular-weight accelerator NaCl was selected, with the least toxic effect from the lyotropic anion series [10].

In all cases, the formation of monolithic shape-stable transparent light-beige systems was completed within each sol-gel reaction. Table 1 shows the physicochemical characterization (n_D^{25} , pH) of some initial mixed solution template/precursor and the value of the gelation time of these synthesized samples. The component composition of our mixed systems was expressed by the concentrations of CS and Si (wt.%) and their CS/Si ratios for convenience.

The data in Table 1 show that the gelation time of these systems is strongly influenced by both the conditions of the sol-gel process (pH, temperature) and the initial component

concentrations of the gel-forming system. The gelation time may change over a wide range (from 10 min till 32 days). For example, even a slight increase in the pH (*ceteris paribus*) reduces the gelation time (see, e.g., systems 1 and 2, 5 and 6, 9 and 10, 13 and 14, and 17 and 18 in Table 1). The accelerated gelation effect depends on temperature and the concentration ratio of the components. For example, the greatest effect of gelation time reduction at an increased pH is observed at 20 and 37°C and at a small CS/Si ratio. With increased CS/Si ratios, the accelerated gelation effect reduces. This effect is substantially lower at 4°C than within 20–37°C and is most pronounced at relatively high CS/Si ratios. Introduction of an electrolyte salt (NaCl) into the source mixed solution increases the pH and accelerates gelation (see, e.g., systems 2 and 3, 6 and 7, 10 and 11, 14 and 15, 18 and 19, and 21 and 22 in Table 1).

Let us consider individually the impact of each tested parameter on the gelation time of our inorganic/organic silicon-containing chitosan hydrogel. Note that the selected method of varying the CS/Si ratio in the hydrogel composition was implemented by mixing different volumes of the precursor and template solutions. Since fixed-concentration CS and Si(OGly)₄·2GlyOH solutions were used (see Experimental, Sections 2.2 and 2.3), their mixing was accompanied by an increase in the chitosan concentration by reducing the silicon tetraglycerolate concentration. In this regard, the template/precursor mass ratio (C_{CS}/C_{Si}) was used to express the component composition of the final hydrogel system.

Figure 1 shows the gelation time of our mixed compositions based on Si(OGly)₄·2GlyOH and 2.0 (4.0) wt.% CS-GA as a function of the template/precursor weight ratio at several pH values and temperatures. It can be seen that the gelation time regularly increases with the C_{CS}/C_{Si} ratio. The gelation time dependence on C_{CS}/C_{Si} is described by monotonic curves in almost all cases. The only exceptions were the systems within the 4.2–5.3 pH range, whose gelation was implemented at 4°C (curves 1 c-d). For these systems, the gelation process was much more decelerated when $C_{CS}/C_{Si} > 4-5$ as compared to $C_{CS}/C_{Si} < 4-5$.

In a low-pH medium (2.2–3.8) the gelation time in the studied systems was substantially longer (Figures 1(a), 1(c), and 1(d)) than in media with pH = 4.2–5.3 (Figures 1(c) and 1(d)). Furthermore, an increased pH, as well as a lowered template/precursor weight ratio, led not only to accelerating the sol-gel process but also to leveling the difference in the gelation times at 20 and 37°C (Figures 1(b), 1(c), and 1(d), curves 2 and 3). The pH effect on the gelation time is most clearly observed in Figure 2(a).

For example, the gelation time decreased monotonically with increasing pH for the system with $C_{SC} = 2.67$ wt.% and $C_{Si} = 1.62$ wt.% (37°C), so the sol-gel process lasted substantially slower in an acidic medium than in a neutral one (pH > 5.5). The shortest gelation time (shorter than 1 h) was achieved even at pH ~ 4.5.

Addition of the electrolyte salt (NaCl) in an amount of 1 wt.% reduces the gelation time of the system (Figure 1(c)) in comparison with the original system without any accelerator (Figure 1(b)). For example, even at 4°C the gelation time may increase ~1.5–3.0 times. As noted above, the gelation time in

the CS-GA + Si(OGly)₄·2GlyOH system is determined by the pH at which the process proceeds. According to Figures 1(b) and 1(c) and Table 1, introduction of NaCl into the source mixed solution reduces the acidity of the medium, which leads to a pronounced catalytic effect on the gelation process.

Raised temperatures also significantly accelerate the formation of silicon-chitosan-containing hydrogels (Figure 1). Figure 2(b) exemplifies the temperature dependence of the gelation time for the systems with $C_{SC} = 3.43$ wt.% and $C_{Si} = 0.69$ wt.% with/without addition of NaCl (pH = 3.8–4.3). It can be seen that the temperature increase in the range 4–37°C accelerates the gelation process ~7 and ~2 times for the chitosan-containing systems with and without the accelerator, respectively.

It seemed interesting to examine the effect of the organic template concentration at a constant precursor amount on gelation time. For this, few systems were selected with a constant concentration of silicon $C_{Si} = 1.21$ or 1.62 wt.%, where gelation proceeds 3 hours or shorter (to fix the gel point with a lesser measurement error). Gelation was carried out at 20 and 37°C. Higher template contents in the system promote the sol-gel process, and this effect is more expressed at lower Si contents (Figure 3). For example, an increase of the CS content from 1.6 to 3.2 wt% reduces the gelation time at 37°C almost twice (curve 1) at $C_{Si} = 1.21$ wt.% and almost ~1.2 times when $C_{Si} = 1.62$ wt.% (curve 2). The same pattern of the CS concentration influence (if $C_{Si} = \text{const}$) on the gelation kinetics is observed if the reaction proceeds at 20°C.

Similar acceleration of the gelation process (at the formation of silicon-chitosan-containing hydrogels) with increasing concentration of the organic template was noted when using hydrochloric (pH ~ 3.6–4.2) and acetic acid solutions of CS [34]. It is believed that this acceleration may be due to the formation of multiple hydrogen bonds between the hydroxyl groups of chitosan macromolecules and the precursor [6, 8]. Moreover, the resulting gelation time dependence on the chitosan concentration (Figure 3) correlates with the pH dependence of the gelation time (Figure 2(a)). The free –NH₂ groups of chitosan macromolecules may therefore participate in the formation of intermolecular hydrogen bonds with the ≡Si–OH groups formed by hydrolysis of the precursor. All this should determine the morphostructure of the resulting hybrid inorganic/organic hydrogel.

3.2. SEM of the Xerogel Solid Phase Prepared from Silicon-Chitosan-Containing Hydrogel. In order to study structural features of the hydrogel solid phase, several samples were treated by exhaustive cold extraction combined with cryotreatment. SEM images show that the morphology of the isolated solid phase of our inorganic/organic hybrid xerogel is represented by a matrix of evenly distributed agglomerated particles (Figure 4). The globular structures on the sample surface exhibit the formation of a 3D network of ≡Si–O–Si≡ bonds.

4. Discussion

Our experiments show that raising the pH and incubation temperature and addition of an electrolyte salt accelerate the

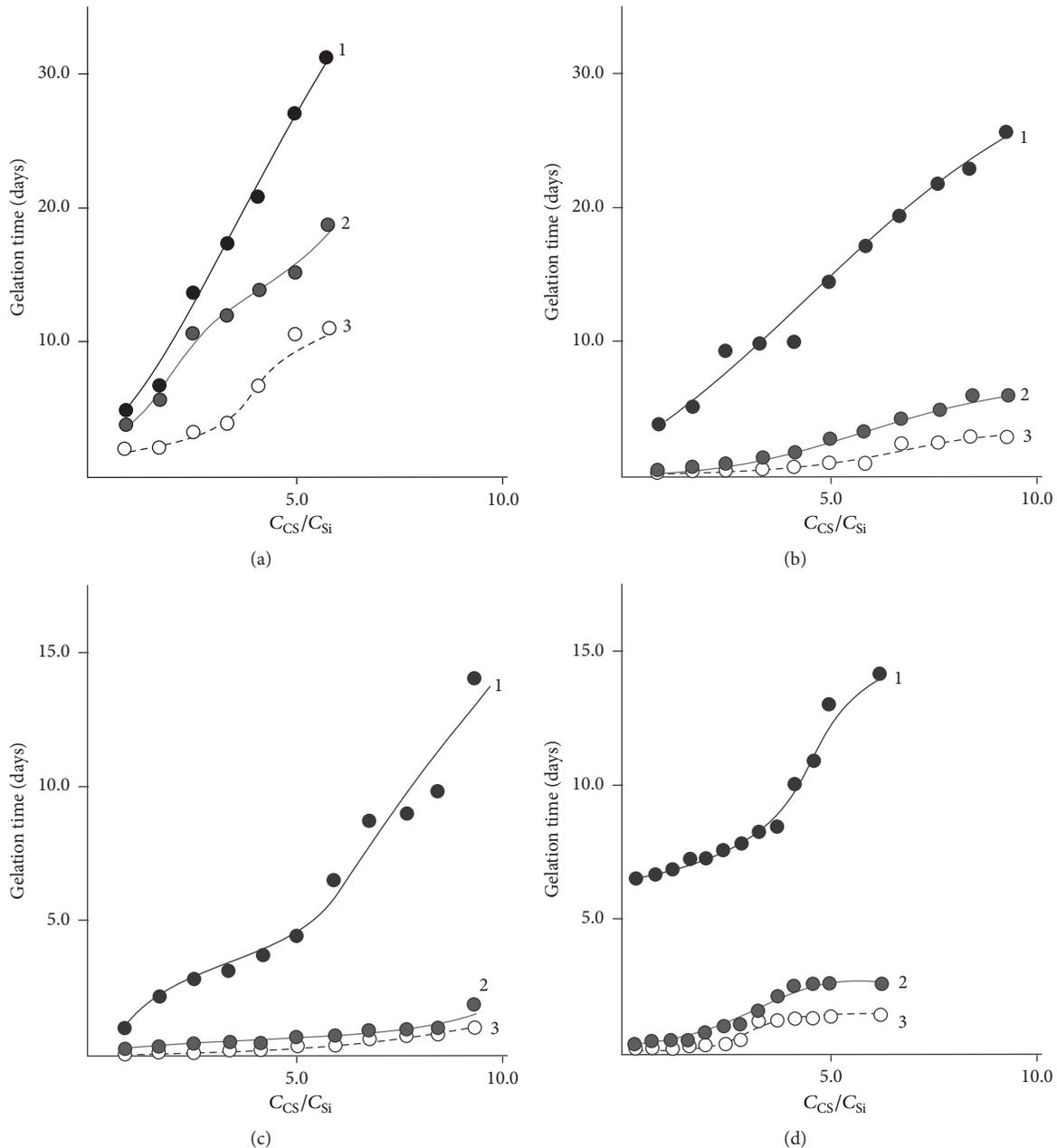


FIGURE 1: Dependence of the gelation time for systems CS-GA + Si(OGly)₄·2GlyOH on C_{CS}/C_{Si} at pH = 2.27 ± 0.13 (a), 3.81 ± 0.04 (b), 4.26 ± 0.05 (c), and 5.33 ± 0.08 (d), on the incubation temperatures 4 (1), 20 (2), and 37°C (3) without (a, b, and d) and with addition of 1 wt.% NaCl (c).

sol-gel process and, consequently, promote the faster loss of fluidity of the multicomponent silicon-chitosan-containing system. In addition, increased concentrations of the inorganic phase precursor (reduced C_{CS}/C_{Si} ratios) and increased concentrations of the organic template (for the systems with a constant C_{Si}) have the accelerating effect upon the course of the sol-gel synthesis. Therefore, the initial component composition of the gelling system and the reaction conditions (temperature and pH) are crucial sol-gel process parameters. The mechanism of interaction between the components is as follows.

With mixing and thorough homogenization of the organic template (a chitosan solution in an aqueous solution of glycolic acid) and the inorganic phase precursor (a glycerol solution of tetraglycolate Si) there proceed fast reversible acid-catalyzed hydrolysis of Si(OGly)₄ to form silanol groups ≡Si-OH and their further slower condensation to form disiloxane groups ≡Si-O-Si≡, of the dispersed particles [10, 11]. The occurring polycondensation processes lead to the formation of a spatial network of the glycerohydrogel, and the dispersion medium is supplemented by the formed products of the reactions of hydrolysis and condensation, namely, the

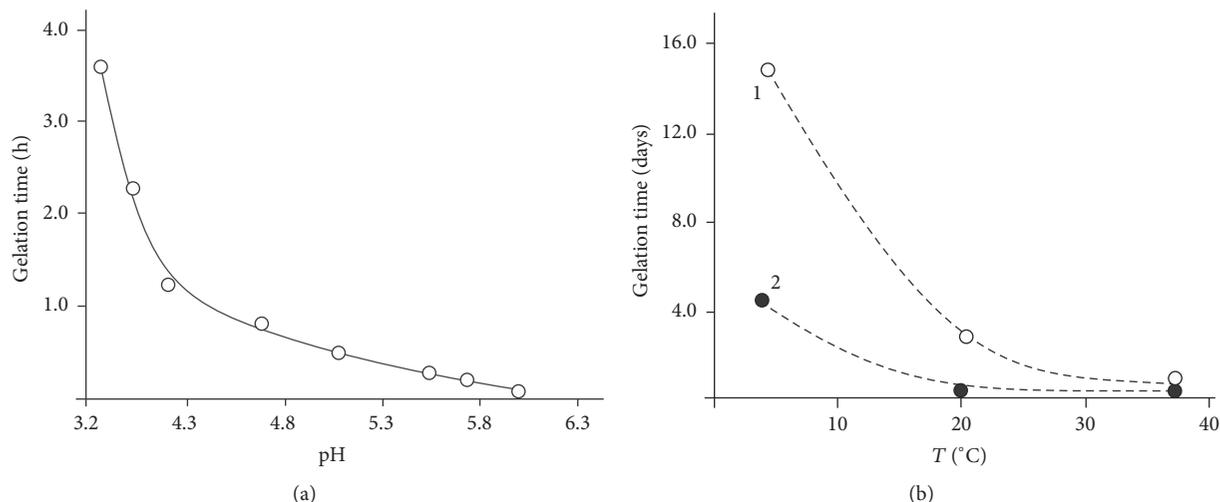


FIGURE 2: Dependence of the gelation time (a) on pH for the system with $C_{SC} = 2.67$ wt.% and $C_{Si} = 1.62$ wt.% at 37°C and (b) on the incubation temperature for the system with $C_{SC} = 3.43$ wt.% and $C_{Si} = 0.69$ wt.% without (1) and with 1 wt.% NaCl (2) at $\text{pH} = 3.81 \pm 0.04$ (1) and 4.26 ± 0.05 (2).

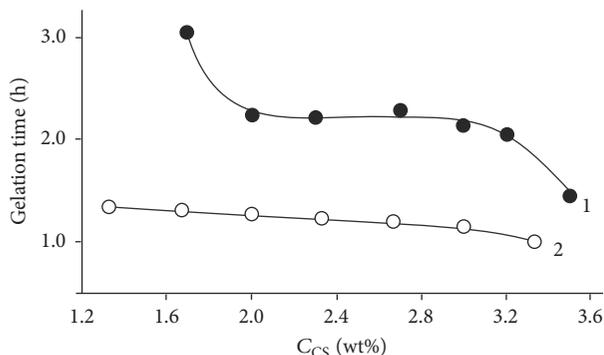


FIGURE 3: Dependence of the gelation time on C_{SC} for the system CS-GA + $\text{Si}(\text{OGly})_4 \cdot 2\text{GlyOH}$ at $C_{Si} = 1.21$ (1) and 1.62% (2), $\text{pH} \sim 4.47 \pm 0.03$, 37°C .

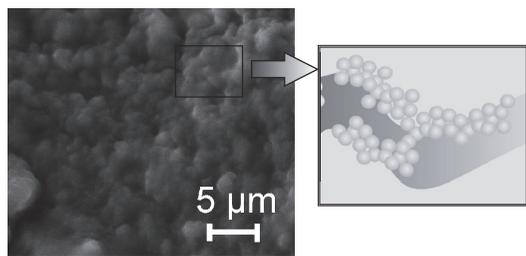


FIGURE 4: SEM image of the solid phase of the organic-inorganic xerogel prepared from the corresponding hydrogel based on CS-GA and $\text{Si}(\text{OGly})_4 \cdot 2\text{GlyOH}$. A schematic image of the distribution of globular particles of the branched 3D network of $\equiv\text{Si}-\text{O}-\text{Si}\equiv$ bonds on the CS matrix.

polyol and water, respectively. The free glycerol presented in the system prevents hydrolysis of the whole hydroxyl groups of $\text{Si}(\text{OGly})_4$. Depending on the pH, the condensation reaction proceeds involving the deprotonated or protonated silanol groups [11].

Possible interactions of the template are also determined by pH. In the source aqueous CS-GA solution, the polymer macromolecules are solvated due to the donor-acceptor interaction of chitosan's amino groups with glycolic acid molecules. The solvation degree of macrochains is determined by the protonation degree of $-\text{NH}_2$ groups and, therefore, by the pH of the aqueous acidic medium, which determines the gelation kinetics in general. Therefore, in an acidic medium ($\text{pH} < 3.5-4.0$), when the protonation degree of $-\text{NH}_2$ groups is maximum, the hydroxyl groups and the oxygen of the acetamide group of the glucopyranose ring of CS act as active sites for nucleation of the hydrolysis and condensation products of $\text{Si}(\text{OGly})_4$. In a slightly acidic or neutral medium ($\text{pH} \sim 5-6$) the formation of silicon-chitosan-containing hydrogels also involves the free amino groups of macrochains because lowering the medium acidity by NaOH introduction is accompanied by deprotonation of some amino groups involved in the donor-acceptor interaction with GA. This leads to additional nucleation sites and, accordingly, has an accelerating effect on the gelation process.

The results obtained in our work, as well as the available literature data on the sol-gel synthesis of silicon-containing and silicon-chitosan-containing glycerohydrogels [10, 11, 34], suggest a hypothetical scheme of the formation of hybrid chitosan-containing hydrogel systems. Stabilization of the hybrid hydrogel structure is due to the formation of a network of intermolecular hydrogen bonds among the functional groups ($-\text{OH}$, $-\text{NHCOCH}_3$, and $-\text{NH}_2$) of the chitosan macromolecules and the hydroxyl groups ($\equiv\text{Si}-\text{OH}$, $-\text{OH}$) of the products of the precursor's hydrolytic condensation, the inorganic network of $\equiv\text{Si}-\text{O}-\text{Si}\equiv$ bonds (Figure 5).

5. Conclusions

Inorganic/organic hydrogels based on CS-GA and $\text{Si}(\text{OGly})_4 \cdot 2\text{GlyOH}$ were obtained by the sol-gel technology. The effect of the component composition of the initial mixed

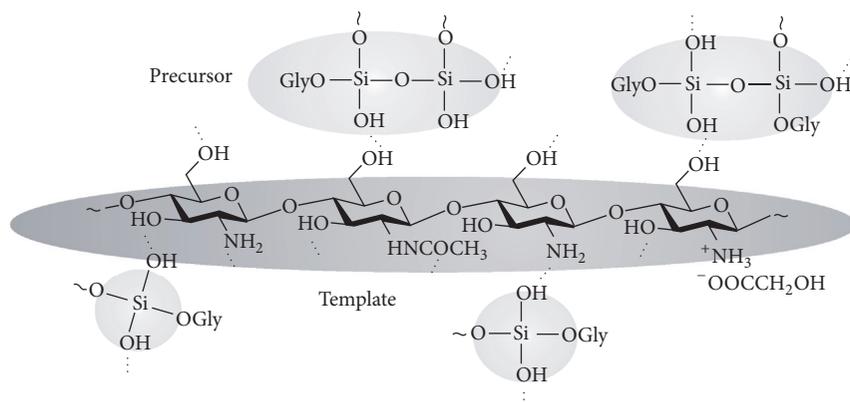


FIGURE 5: A hypothesized scheme of the intermolecular interactions in the chitosan-silicon-containing hydrogel based on CS-GA and $\text{Si}(\text{OGly})_4 \cdot 2\text{GlyOH}$.

solutions, temperature, and pH on the gelation time was estimated. Increased temperature and pH of the system and NaCl addition have been found to significantly accelerate the gelation process. Increasing the chitosan concentration in the gelation system (at both varying $C_{\text{CS}}/C_{\text{Si}}$ weight ratio and varying C_{CS} with $C_{\text{Si}} = \text{const}$) reduces the gelation time. A hypothetical scheme of intermolecular interactions in the silicon-chitosan-containing hydrogel is proposed.

Competing Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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