Synthesis of hydrogels based on silicon polyolates

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Biologically active hydrogels based on silicon polyolates, which are the products of reactions of tetraethoxy- and methyltriethoxysilanes with polyols (1,2-propanediol, glycerol, polyethylene glycol), were synthesized. The optimal conditions for hydrogel formation and hydrogel composition were determined. The acute toxicity and transcutaneous and wound-healing activities of the synthesized compounds were studied. The experimental results show that hydrogels based on silicon polyolates can be recommended for further preclinical and clinical tests with the purpose of their use in medical practice both as self-sufficient agents and ointment bases of pharmaceutical compositions with wound-healing, regenerative, and transcutaneous action.

Key words: organosilicon compounds, diols, glycerol, silicon polyolates, hydrogels, transcutaneous properties, wound-healing activity, ointment bases.

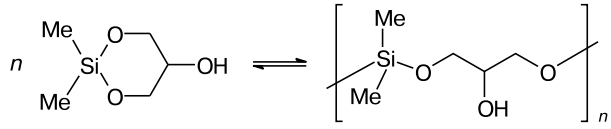
This communication describes the synthesis of new biologically active hydrogels obtained from silicon polyolates. These hydrogels are promising pharmaceutical agents with wound healing, regenerating, and transcutaneous action for as local and external application.

Silicon is a biogenic trace element needed for normal functioning of the human organism.[1,2] Extensive experimental material has now been accumulated on the search and development of various types of biologically active organosilicon compounds, potential pharmaceutical agents.[3]

Derivatives of polyols, silicon polyolates, form a promising class of organosilicon compounds. Some of them exhibit antiinflammatory, regenerating, and protector activities; they are able to penetrate through skin and promote the transcutaneous transfer of drugs.[4—6] They can be applied locally and orally both as such and in combination with active medical agents.

It is known that most often silicon polyolates cannot be isolated as monomers due to their propensity for polymerization or polycondensation transformations.[7] Indeed, the monomeric cyclic product formed in the reaction of dimethyldiethoxysilane with glycerol and isolated after vacuum distillation slowly polymerizes on storage and depolymerizes on heating[4] (Scheme 1).

Scheme 1



A similar polymeric product is formed as a result of polycondensation of the dimethyldiglyceroxysilane $Me_2Si[OCH_2CH(OH)CH_2OH]_2$; therefore, it cannot be isolated in a pure state. The polycondensation in this case is accompanied by glycerol liberation.

According to ^{29}Si and ^{13}C NMR data, the products of reactions of tetraethoxy- or tetramethoxysilane with glycerol in 1 : 2 and 1 : 4 molar ratio are not individual compounds either.[8] They are readily hydrolyzed and can be used for encapsulation or manufacture of membranes on the basis of enzymes, peptides, phospholipids, and other compounds.

In order to obtain stable silicon polyolates resistant against polymerization, polycondensation, and hydrolytic transformations, silicon glycerolates (glycerates) with excess glycerol described as $Si(C_3H_7O_3)_4 \cdot xC_3H_8O_3$ (where $3 \le x \le 10$) were prepared by glycerolysis of tetraethoxysilane, and hydrogels based on these compounds were obtained.[9] Glycerol contributes to stabilization of silicon glycerates through the formation of coordinatively saturated compounds;[10] this prevents the formation of cyclic

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and polymeric products. In the preparation of hydrogels, the excess of glycerol inhibits hydrolysis and subsequent condensation of the resulting silanols to biologically inert siloxane polymers. Silicon glycerates and hydrogels based on them are non-toxic and exhibit high transcutaneous activity. Using glycerohydrogel, a number of medications with antiinflammatory, wound-healing, regenerating, and transcutaneous action have been developed.[11–13]

In order to enhance the pharmacological activity of silicon glycerates and hydrogels based on them, it seemed expedient to replace the glyceroxy groups at the silicon atom in the molecular structure of silicon glycerates by methyl groups, which should increase the lipophilicity of the molecule and promote the transport of silicon through the lipid bilayer of cellular membranes. In addition, this will increase the quantitative content of biologically available silicon.

Along with glycerol, the use of other polyols allowed for medical use, for example, 1,2-propanediol and polyethylene glycol is of interest in this respect.

Thus, the purpose of this work is the synthesis of new biologically active hydrogels based on silicon polyolates of various functionality and study of their acute toxicity and wound-healing and transcutaneous properties.

Results and Discussion

Synthesis of hydrogels based on silicon polyolates

Hydrogels based on silicon polyolates were prepared in two steps. In the first step, tetraethoxy- and methyltriethoxysilane were converted into silicon polyolates **1a**–**f** of different functionality in an excess of polyol such as 1,2-propanediol, glycerol, and polyethylene glycol (Scheme 2). In the second step, silicon polyolates **1a**–**f** were made to react with water or aqueous solutions of electrolytes to give hydrogels **2a**–**f** (Scheme 3).

Scheme 2

$$Me_{4-n}Si(OEt)_n + (x+n)\ HOROH \rightleftharpoons$$

$$\rightleftharpoons Me_{4-n}Si(OROH)_n \cdot x\ HOROH + n\ EtOH$$

1a—f

Compound	R	n	x
1a	$-CH_2CH(Me)-$	4	2.9
1b	$-CH_2CH(OH)CH_2-$	4	2.9
1c	$-(CH_2CH_2O-)_{12}CH_2CH_2-$	4	0.5
1d	$-CH_2CH(Me)-$	3	0.5
1e	$-CH_2CH(OH)CH_2-$	4	0.5
1f	$-(CH_2CH_2O-)_{7.7}CH_2CH_2-$	4	0.5

The composition of silicon polyolates and hydrogels based on them is summarized in Table 1.

Scheme 3

$$Me_{4-n}Si(OROH)_n \cdot x\ HOROH + y\ H_2O \longrightarrow$$

1a—f

$$\longrightarrow Me_{4-n}Si(OROH)_n \cdot x\ HOROH \cdot y\ H_2O$$

2a—f (gel)

n = 4 (**a—c, e, f**); 3 (**d**)
x = 2.9 (**a, b**), 0.5 (**c—f**)
y = 37 (**2a,b**), 3 (**2c—f**)

Ethanol liberated in the first step was removed until the loss was equal to its theoretical amount. The course of the reaction was also monitored by ^{1}H NMR, its completion being stated by the absence of the signals of residual ethoxy groups at silicon at δ_H 1.08—1.18 (t, 3 H, Me) and 3.69–3.79 (q, 2 H, CH_2).

Silicon polyolates in excess polyol **1a**—**f** are transparent colorless liquids with different viscosity, readily soluble in water; on attempted vacuum distillation, they decompose. They were characterized by elemental analysis, refractometry, and IR spectroscopy data. Due to the excess of polyol, the ^{1}H NMR spectra provide little information as regards the composition and structure of silicon polyolates.

Hydrogels **2a**—**f** were obtained at 85—90 °C; to accelerate gelation, aqueous solutions of electrolyte salts (NaCl, NaF) were used. The gelation rate was estimated from the time of fluidity loss in the system. The hydrogels thus formed do not melt up to decomposition temperature and are incompletely water-soluble; they were characterized by elemental analysis, refractometry, and IR spectroscopy data.

A study of the formation process of hydrogels based on silicon polyolates confirmed the key regularities found previously for gels based on silicon glycerates:[10] accelerating effect of temperature or a gel-forming additive, polycondensation mechanism of formation of the disperse phase involving partial hydrolysis of Si—O—C bonds to give silanol groups Si—OH followed by their condensation to disiloxane groups Si—O—Si functioning as cross-links in the disperse phase.

The polycondensation mechanism of formation of hydrogels is additionally supported by the fact that in the case of difunctional dimethylbis(2,3-dihydroxypropoxy)-silane in excess glycerol $Me_2Si(C_3H_7O_3)_2 \cdot C_3H_8O_3$ (**1g**), the hydrogel is not formed.

It should be noted that the introduction of methyl groups into the silicon polyolate structure affects considerably their gelation behavior (see Table 1). In the case of tetrafunctional silicon polyolates, the time of formation of hydrogels **2a**—**c** did not exceed 1 h, while for trifunctional derivatives it increases to 12 h (**2d**,**f**).

In this study, we identified the optimal conditions for the preparation of hydrogels (see Table 1) and their composition as regards the polyol and water contents,

Table 1. Formation of the hydrogels $Me_{4-n}Si(OROH)_n \cdot xHOROH \cdot yH_2O$ (n = 3, 4) at 85—90 °C

Silicon polyolate	**1** : H_2O, mol/mol	Gelating additive[a]	t/h[b]	Hydrogel
$Si(OCH_2CH(Me)OH)_4 \cdot 2.9\ HOCH_2CH(Me)OH$ **(1a)**	1 : 37	—	1	**2a**
$Si(OCH_2CH(OH)CH_2OH)_4 \cdot 2.9\ HOCH_2CH(OH)CH_2OH$ **(1b)**	1 : 37	—	1	**2b**
$Si(O(CH_2CH_2O)_{12}CH_2CH_2OH)_4 \cdot 0.5\ HO(CH_2CH_2O)_{12}CH_2CH_2OH$ **(1c)**	1 : 3	NaF	0.5	**2c**
$MeSi(OCH_2CH(Me)OH)_3 \cdot 0.5\ HOCH_2CH(Me)OH$ **(1d)**	1 : 3	—	12	**2d**
$MeSi(OCH_2CH(OH)CH_2OH)_4 \cdot 0.5\ HOCH_2CH(OH)CH_2OH$ **(1e)**	1 : 3	NaCl	1	**2e**
$MeSi(O(CH_2CH_2O)_{7.7}CH_2CH_2OH)_4 \cdot 0.5\ HO(CH_2CH_2O)_{7.7}CH_2CH_2OH$ **(1f)**	1 : 3	NaF	12	**2f**

[a] A 1% solution of the electrolyte salt was used.
[b] Gelation time.

which is determined by the syneresis stability of hydrogels and the most suitable consistency for practical use both as self-contained pharmaceutical agents and as bases for pharmaceutical compositions. The hydrogels $Me_{4-n}Si(OROH)_n \cdot xHOROH \cdot yH_2O$ can also be obtained with other x and y in the ranges of $0.5 \le x \le 2.9$ and $3 \le y \le 37$ but these would not be the optimized compositions.

Pharmacological studies

Pharmacological studies of the hydrogels were carried out in comparison with silicon polyolates from which they were prepared.

A study of acute toxicity demonstrated that the compounds are non-toxic. It was impossible to determine LD_{50} for hydrogels **2a**—**f** as all of the test animals stayed alive; no reliable behavior deviations were found for them. For silicon polyolates in excess polyol **1a**—**g**, the LD_{50} values (for intragastric administration) are more than 6000 mg kg^{-1}. Thus, according to GOST 12.1.007-76, the test compounds are low-toxic (hazard class IV).

Table 2 summarizes the results of studies of the transcutaneous behavior of a number of synthesized compounds relative to penetration of diclofenac sodium through the rat skin (*in vitro*) in relation to the known transcutaneous agent (DMSO). It follows from Table 2 that all of the compounds under study promote the transcutaneous penetration of diclofenac sodium, being more active than DMSO. The difunctional silicon glycerate in excess glycerol **1g**, which does not form a hydrogel, was the most active transcutaneous conductor.

Table 3 presents the wound-healing times for second- and third-degree thermal burns of rat skin according to the stages: (1) formation of a granulation tissue, (2) granulation rejection, (3) active epithelization to form a scar. As can be seen from the Table, complete wound-healing in the control group (without treatment) was observed by about the 21st day. The most pronounced shortening of the healing period took place with silicon polyolates **1a** and **1g**. Generally, all the agents used exhibited pronounced wound-healing activity with respect to the control as regards the healing period: the treatment efficiency was 23.8—33.3%.

No reliable changes were detected in the common and biochemical blood tests after the treatment; the characteristics of the test animals did not differ from characteristics of the intact animals. The histological examination of the internals of the test rats showed no structural changes either.

It should be specially noted that in all cases, no inflammation or purulent exudate were observed as a result of treatment, and a much more elastic after-burn scar and a noticeably thicker hair coat formed.

Thus, biologically active hydrogels based on silicon polyolates in excess polyol were synthesized. The optimal conditions for hydrogel preparation and their composition were determined. It was shown that introduction of the methyl groups into the silicon polyolates structure inhibits the gelation process.

A set of primary pharmacological investigations of the obtained hydrogels was carried out; for comparison, silicon polyolates were studied. The synthesized compounds proved to be non-toxic and to exhibit clear-cut transcutaneous and wound-healing activities; they are also beneficial for the morphofunctional state of skin.

Table 2. Study of the permeability of diclofenac sodium for Wistar rat skin in the presence of various transcutaneous conductors (*in vitro*)

Transcutaneous conductors[a]	Degree of transcutaneous permeability[b] after 20 h at 37 ± 2 °C	
	α (%)	α_{rel}
1a	1.20 ± 0.05	1.5
2b	0.99 ± 0.04	1.2
1e	1.62 ± 0.06	2.0
1d	1.04 ± 0.04	1.3
1g	1.71 ± 0.07	2.1
DMSO	0.82 ± 0.03	1.0

[a] 10% solutions were used.
[b] For comparison with DMSO, $p < 0.05$ in all cases.

Table 3. Healing times of thermal burns in test and control groups of Wistar rats

Test compounds	Healing times, stages[a]/days			Treatment efficiency[b] (%)
	1	*2*	*3*	
	Test groups			
1a	6.7±0.7	11.0±1.2	14.0±0.8	33.3
1g	6.7±0.9	13.0±1.8	15.2±0.8	27.6
2a	7.0±0.7	14.0±1.4	16.0±0.9	23.8
2f	7.0±0.8	14.0±1.4	16.0±0.9	23.8
	Control group			
—[c]	8.9±1.0	17.0±1.8	21.8±0.9	—

[a] Healing stages: (*1*) formation of a granulation tissue, (*2*) granulation rejection, (*3*) epithelization to form a scar.
[b] $p < 0.05$ in all cases, for comparison of experimental data with the control.
[c] No treatment.

It is also noteworthy that the gels represent a more convenient form for local and external application than liquid silicon polyolates, although they are somewhat less active.

In view of the results of investigations, hydrogels based on silicon polyolates can be recommended for further investigations both as self-contained agents and as ointment bases of various pharmaceutical compositions exhibiting wound-healing, antiinflammatory, regenerating, and transcutaneous action.

The physicochemical studies of the structure of hydrogels based on silicon polyolates and of the mechanisms of pharmacological action are in progress and will be the subject of subsequent communications.

Experimental

IR spectra were recorded on a Spectrum One Perkin Elmer FT-IR spectrometer at 400—4000 cm^{-1} for thin films of neat compounds. The refractive indices were determined on an IRF-456 refractometer. The ^1H NMR spectra were recorded on a Bruker AVANCE DRX-400 spectrometer operating at 400 MHz (DMSO-d_6 as the solvent and $SiMe_4$ as the standard).

All initial compounds except for polyethylene glycols PEG-400 and PEG-600, $HO(CH_2CH_2O)_mCH_2CH_2OH$ ($m = 7.7$ and 12.0, respectively) were distilled prior to use. Tetraethoxysilane $Si(OEt)_4$, 1,2-propanediol $HOCH_2CH(Me)OH$, and glycerol $HOCH_2CH(OH)CH_2OH$ were distilled *in vacuo* (glycerol was distilled from sodium metal), methyltriethoxysilane $MeSi(OEt)_3$, and dimethyldiethoxysilane $Me_2Si(OEt)_2$ were distilled under atmospheric pressure. Polyethylene glycol PEG-400 and PEG-600 were dried *in vacuo* at 100 °C.

Hydrogel based on tetrakis(2-hydroxypropoxy)silane (2a). 1,2-Propanediol (43.42 g, 0.573 mol) and tetraethoxysilane (17.23 g, 0.083 mol) were placed in a one-neck round-bottom flask equipped with a three-neck adapter connected to a mechanical stirrer, a reflux condenser, and a dropping funnel. The reaction mixture was stirred for 15 h at 120 °C, and the ethanol formed was removed first under atmospheric pressure and then on a rotary evaporator at 2—5 Torr and 130 °C to a constant weight of the reaction mixture (which corresponded to the removal of the theoretical amount of ethanol). The yield of tetrakis(2-hydroxypropoxy)silane in a 2.9-mole excess of 1,2-propanediol (**1a**) was 44.95 g (99%). The product was a transparent colorless liquid, n_D^{20} 1.4423, soluble in water, ethanol, and chloroform and insoluble in ether. The composition of the product corresponded to $Si(C_3H_7O_2)_4 \cdot 2.9C_3H_8O_2$. Found (%): C, 44.52; H, 9.70; Si, 5.08. $C_{20.7}H_{51.2}O_{13.8}Si$. Calculated (%): C, 45.28; H, 9.40; Si, 5.12. IR, ν/cm^{-1}: 3368 (OH); 2971, 2932, 2879 (C—H); 1139, 1083 (C—O in C—O—H sec.); 1046, 991 (C—O in C—O—H prim.); 1025 (Si—O—C).

Distilled water (55.05 g, 3.055 mol) was added in portions with stirring to obtained product **1a**. Gelation was carried out with heating (85—90 °C) and stirring. The yield of hydrogel **2a** was 100.00 g (100%). The product was a semi-transparent colorless gel, n_D^{20} 1.3917. The gel was insoluble in ordinary organic solvents and incompletely soluble in water. The hydrogel composition corresponded to $Si(C_3H_7O_2)_4 \cdot 2.9C_3H_8O_2 \cdot 37H_2O$. Found (%): C, 20.05; H,10.49; Si, 2.29. $C_{20.7}H_{125.2}O_{50.8}Si$. Calculated (%): C, 20.45; H, 10.38; Si, 2.31. IR, ν/cm^{-1}: 3340 (OH); 2976, 2936, 2884 (C—H); 1136, 1079 (C—O in C—O—H sec.); 1643 (H—O—H); 1044, 990 (C—O in C—O—H prim.); 1025 (Si—O—C).

Hydrogels **2b—f** based on silicon polyolates in excess polyol **1b—f** were prepared by a similar procedure (see Table 1).

Hydrogel based on tetrakis(2,3-dihydroxypropoxy)silane (2b). Tetrakis(2,3-dihydroxypropoxy)silane in a 2.9-mole excess of glycerol (**1b)** was synthesized in a 99% yield. The product was a transparent colorless thick liquid, n_D^{20} 1.4790, soluble in water and ethanol and insoluble in chloroform and ether. The product composition corresponded to $Si(C_3H_7O_3)_4 \cdot 2.9C_3H_8O_3$. Found (%): C, 37.28; H, 8.15; Si, 4.21. $C_{20.7}H_{51.2}O_{20.7}Si$. Calculated (%): C, 37.70; H, 7.83; Si, 4.26. IR, ν/cm^{-1}: 3358 (OH); 2937, 2884 (C—H); 1111 (C—O in C—O—H sec.); 1047 (C—O in C—O—H prim.); 1023 (Si—O—C).

Hydrogel **2b** was prepared in a 100% yield. The product was a semi-transparent colorless gel, n_D^{20} 1.4015. The gel was insoluble in ordinary organic solvents and incompletely soluble in water. The hydrogel composition corresponded to $Si(C_3H_7O_3)_4 \cdot 2.9C_3H_8O_3 \cdot 37H_2O$. Found (%): C, 18.71; H, 13.79; Si, 2.03. $C_{20.7}H_{125.2}O_{57.7}Si$. Calculated (%): C, 18.75; H, 13.41; Si, 2.11. IR, ν/cm^{-1}: 3390 (OH); 2944, 2888 (C—H); 1111 (C—O in C—O—H sec.); 1641 (H—O—H); 1046, 992 (C—O in C—O—H prim.); 1024 (Si—O—C).

Hydrogel based on tetrakis(ω-hydroxypolyethyleneoxy)-silane (2c). Tetrakis(ω-hydroxypolyethyleneoxy)silane in a 0.5-mole excess of PEG-600 (**1c**) was synthesized in a 99% yield. The product was a transparent colorless liquid, n_D^{20} 1.4688, soluble in water, ethanol, and chloroform and insoluble in ether. The product composition corresponded to $Si(O[CH_2CH_2O]_{13}H)_4 \cdot 0.5HO[CH_2CH_2O]_{13}H$. Found (%): C, 51.98; H, 9.12; Si, 0.97. $C_{117}H_{239}O_{63}Si$. Calculated (%): C, 52.39; H, 8.98; Si, 1.05. IR, ν/cm^{-1}: 3337 (OH); 2870 (C—H); 1107 (C—O—C); 1023 (Si—O—C).

Hydrogel **2c** was obtained in a 100% yield. The product was a transparent colorless gel, n_D^{20} 1.4673. The gel was insoluble in ordinary organic solvents and incompletely

soluble in water. The hydrogel composition corresponded to $Si(O[CH_2CH_2O]_{13}H)_4 \cdot 0.5HO[CH_2CH_2O]_{13}H \cdot 3H_2O$. Found (%): C, 51.04; H, 9.15; Si, 0.94. $C_{117}H_{245}O_{66}Si$. Calculated (%): C, 51.36; H, 9.03; Si, 1.03. IR, ν/cm^{-1}: 3340 (OH); 2871 (C—H); 1643 (H—O—H); 1111 (C—O—C); 1024 (Si—O—C).

Hydrogel based on methyltris(2-hydroxypropoxy)silane (2d). Methyltris(2-hydroxypropoxy)silane in a 0.5-mole excess of 1,2-propanediol (**1d**) was synthesized in a 99% yield. The product was a transparent colorless liquid, n_D^{20} 1.4500, soluble in water, ethanol, and chloroform and insoluble in ether. The product composition corresponded to $MeSi(C_3H_7O_2)_3 \cdot 0.5C_3H_8O_2$. Found (%): C, 45.13; H, 9.53; Si, 9.02. $C_{11.5}H_{28}O_7Si$. Calculated (%): C, 45.08; H, 9.21; Si, 9.17. IR, ν/cm^{-1}: 3370 (OH); 2972, 2932, 2877 (C—H); 1267 (Si—C); 1084 (C—O in C—O—H sec.); 1043, 990 (C—O in C—O—H prim.); 1023 (Si—O—C)); 842, 804 (Si—Me).

Hydrogel **2d** was obtained in a 100% yield. The product was a semi-transparent colorless gel, n_D^{20} 1.4287. The gel was insoluble in ordinary organic solvents and incompletely soluble in water. The hydrogel composition corresponded to $MeSi(C_3H_7O_2)_3 \cdot 0.5C_3H_8O_2 \cdot 3H_2O$. Found (%): C, 38.46; H, 9.67; Si, 7.56. $C_{11.5}H_{34}O_{10}Si$. Calculated (%): C, 38.32; H, 9.51; Si, 7.79. IR, ν/cm^{-1}: 3368 (OH); 2971, 2932, 2878 (C—H); 1643 (H—O—H); 1273 (Si—C); 1084 (C—O in C—O—H sec.); 1043, 991 (C—O in C—O—H prim.); 1023 (Si—O—C).

Hydrogel based on methyltris(2,3-dihydroxypropoxy)silane (2e). Methyltris(2,3-dihydroxypropoxy)silane **(1e)** in 0.5-mole excess of glycerol was synthesized in a 99% yield. The product was a transparent colorless thick liquid, n_D^{20} 1.4773, soluble in water and ethanol and insoluble in chloroform and ether. The product composition corresponded to $MeSi(C_3H_7O_3)_3 \cdot 0.5C_3H_8O_3$. Found (%): C, 37.90; H, 8.05; Si, 7.85. $C_{11.5}H_{28}O_{10.5}Si$. Calculated (%): C, 38.11; H, 7.79; Si, 8.11. IR, ν/cm^{-1}: 3368 (OH); 2937, 2884 (C—H); 1270 (Si—C); 1111 (C—O in C—O—H sec.); 1047 (C—O in C—O—H prim.); 1024 (Si—O—C); 868, 807 (Si—Me).

Hydrogel **2e** was obtained in a 100% yield. The product was a semi-transparent colorless gel, n_D^{20} 1.4554. The gel was insoluble in ordinary organic solvents and incompletely soluble in water. The hydrogel composition corresponded to $MeSi(C_3H_7O_3)_3 \cdot 0.5C_3H_8O_3 \cdot 3H_2O$. Found (%): C, 33.04; H, 8.55; Si, 6.42. $C_{11.5}H_{34}O_{13.5}Si$. Calculated (%): C, 33.17; H, 8.23; Si, 6.74. IR, ν/cm^{-1}: 3368 (OH); 2937, 2883 (C—H); 1273 (Si—C); 1643 (H—O—H); 1109 (C—O in C—O—H sec.); 1040, 994 (C—O in C—O—H prim.); 1024 (Si—O—C).

Hydrogel based on methyltris(ω-hydroxypolyethyleneoxy)-silane (2f). Methyltris(ω-hydroxypolyethyleneoxy)silane in an excess of PEG-400 **(1f)** was synthesized in a 99% yield. The product was a transparent colorless liquid, n_D^{20} 1.4643, soluble in water, ethanol, and chloroform and insoluble in ether. The product composition corresponded to $MeSi(O[CH_2CH_2O]_{8.7}H)_3 \cdot 0.5\,HO[CH_2CH_2O]_{8.7}H$. Found (%): C, 50.99; H, 9.25; Si, 2.14. $C_{61.9}H_{128.8}O_{34}Si$. Calculated (%): C, 51.47; H, 8.99; Si, 1.94. IR, ν/cm^{-1}: 3350 (OH); 2873 (C—H); 1272 (Si—C); 1111 (C—O—C); 1023 (Si—O—C).

Hydrogel **2f** was prepared in a 100% yield. The product was a semi-transparent colorless gel, n_D^{20} 1.4628. The gel was insoluble in ordinary organic solvents and incompletely soluble in water. The hydrogel composition corresponded to $MeSi(O[CH_2CH_2O]_{8.7}H)_3 \cdot 0.5HO[CH_2CH_2O]_{8.7}H \cdot 3H_2O$. Found (%): C, 49.49; H, 9.32; Si, 1.57. $C_{61.9}H_{134.8}O_{37}Si$. Calculated (%): C, 49.61; H, 9.07; Si, 1.87. IR, ν/cm^{-1}: 3350 (OH); 2872 (C—H); 1644 (H—O—H); 1273 (Si—C); 1111 (C—O—C); 1024 (Si—O—C).

Dimethylbis(2,3-dihydroxypropoxy)silane in 1-mole excess of glycerol (1g). Glycerol (83.16 g, 0.903 mol) and dimethyldiethoxysilane (50.56 g, 0.341 mol) were placed in a one-necked round-bottom flask equipped with a three-neck adapter connected to a mechanical stirrer, a reflux condenser, and a dropping funnel. The reaction mixture was stirred for 15 h at a temperature of 130 °C, and ethanol—dimethyldiethoxysilane azeotrope formed was then removed first under atmospheric pressure and then on a rotary evaporator at 2—5 Torr and 130 °C to a constant weight of the reaction mixture (which corresponded to the removal of the theoretical amount of ethanol). The product yield was 100.00 g (100%). The product was a transparent colorless thick liquid, n_D^{20} 1.4705, soluble in water and ethanol and insoluble in chloroform and ether. The product composition corresponded to $Me_2Si(C_3H_7O_3)_2 \cdot C_3H_8O_3$. Found (%): C, 39.33; H, 8.52; Si, 8.34. $C_{11}H_{28}O_9Si$. Calculated (%): C, 39.75; H, 8.49; Si, 8.45. IR, ν/cm^{-1}: 3368 (O—H); 2934, 2880, 1409 (C—H); 1260 (Si—C); 1111 (C—O in C—O—H sec.); 1047 (C—O in C—O—H prim.); 1025 (Si—O—C); 863, 802 (Si—Me).

Distilled water (16.27 g, 0.903 mol) was added in portions with stirring at 85—90 °C to product **1g**. No gelation took place.

Pharmacological studies were carried out according to the "Guidelines on experimental (preclinical) investigation of new pharmaceutical substances."[14] The acute toxicity of the compounds was studied on Wistar white rats by standard procedures.

The transcutaneous activity was estimated by measuring the degree of diffusion of the diclofenac sodium drug through natural biological membranes of the intact skin of Wistar white rats (*in vitro*) by a previously described procedure.[9] The compounds used as transcutaneous conductors were taken in concentration of 10% in isotonic solution and were compared with DMSO taken in the same concentration. The transcutaneous penetration of diclofenac sodium was estimated in percent of its initial weight.

The wound-healing action was studied in relation to healing of model burns of Wistar while rats by a reported procedure.[12] The rats were divided into six groups each group comprising 10 animals. All rats were thermally burnt to form 20×60 mm second- or third-degree burns of the skin at the side area. For test rats, the burn area was treated with test compounds, while the rats of the sixth (control) group received no treatment. Smearing with 0.5 g of the compound was performed daily for 18—22 days until the wounds were completely healed in all groups. The efficiency of treatment was calculated as the ratio of healing times in the test and control groups expressed in percent.

After the course of treatment, common and biochemical blood tests of the animals were taken and morphological studies of the internal organs and skin structure were performed.

The statistical processing of the experimental results was carried out using the Excel and Statistical programs at $p < 0.05$.

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