SYNTHESIS AND BIOLOGICAL ACTIVITY OF ORGANOSILICONTITANIUM GLYCEROHYDROGELS

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Translated from Khimiko-Farmatsevticheskii Zhurnal, Vol. 43, No. 2, pp. 26 – 32, February, 2009.

Original article submitted August 25, 2008.

A series of organosilicontitanium (OST) glycerohydrogels with the general formula $2Si(C_3H_7O_3)_4 \cdot Ti(C_3H_7O_3)_4 \cdot xC_3H_8O_3 \cdot yH_2O$ (where $9 \le x \le 30$ and $60 \le y \le 120$) were synthesized and some of their pharmacological properties were studied. High percutaneous activity of the compounds was revealed by measuring the diffusion of sodium diclofenac through intact skin membranes *in vitro*. It was established that all of the synthesized substances are nontoxic. The wound-healing and antioxidant properties of the glycerohydrogels were studied. The experimental results show that OST glycerohydrogels can be recommended for further testing as effective percutaneous vehicles of medicines with wound-healing, burn-healing, and antioxidant action.

Key words: synthesis, organosilicontitanium glycerohydrogels, wound-healing activity, antioxidant activity.

Oil bases of various nature such as lipophilic, hydrophilic, and lipohydrophilic are currently used to prepare soft drug forms. Each of these has its advantages and disadvantages. The ideal base does not exist. However, hydrophilic gels have recently been used more and more [1]. Bases of this type do not contain lipophilic compounds, are easily dissolved in water or mixed with it, have good consistency, are evenly distributed in the mucous, and readily release drugs. They have a cooling action when placed on skin due to evaporation of water. Hydrophilic gels are capable of absorbing significant volumes of intercellular exudate of inflammatory or other origin owing to their high osmotic activity and are often used in ointments for treating purulent wounds. They can dehydrate cells after prolonged contact with skin or mucous.

Transcutaneous (transdermal) vehicles are used in order to enhance the pharmacological activity and, as a result, the therapeutic efficiency of drugs and to reduce their concentration in pharmaceutical compositions for local and topical application. The most well-known of these is dimethylsulfoxide (DMSO) [2]. DMSO produces good transdermal penetration of drugs and has anti-inflammatory, antimicrobial, and fibrinolytic activity. However, its use is limited because of its unpleasant odor, the possibility of allergic reactions, reduced tissue oxygenation, and inhibition of endogenous cell respiration.

Titanium-containing glycerohydrogels such as tisol of composition $Ti\text{-}[O\text{-}CH_2\text{-}CH(OH)\text{-}CH_2\text{-}OH]_4 \cdot 10C_3H_8O_3 \cdot 40H_2O$ [3] and eftiderm of composition $20Ti\text{-}[O\text{-}CH_2\text{-}CH(OH)\text{-}CH_2\text{-}OH]_4 \cdot 160C_3H_8O_3 \cdot 940H_2O \cdot 9HCl$ [4] are also known. These compounds are transcutaneous vehicles of drugs; intensify and prolong their therapeutic effect; possess anti-inflammatory, anti-edema, and antipruritic activity; are nontoxic; do not have cancerogenic, mutagenic, or allergenic activity; and are not capable of accumulating in organs and tissues. Various pharmaceutical compositions for local and topical application in medical practice are based on them. However, the rather high concentration of HCl in the gel can irritate skin and lead to various types of dermatitis with prolonged use. Furthermore, these bases cannot be used with certain drugs that are decomposed by acid.

Silicon glycerates with transdermal penetration and hydrogels based on them of composition $Si(C_3H_7O_3)_4 \cdot xC_3H_8O_3 \cdot yH_2O$, where $3 \le x \le 10$ and $20 \le y \le 40$ were synthesized and patented at the Institute of Organic Synthesis of the Ural Branch of the Russian Academy of Sciences [5]. The main features of the gelation process have been investigated [6]. The optimum conditions for preparing hydrogels

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were determined. A polycondensation mechanism of formation of the dispersed phase was postulated. The synthesized compounds were nontoxic and contained Si, which had an active stimulating effect on all types of tissues [7, 8]. The transdermal penetration of Si in glycerates was 10 times greater than that of Ti according to atomic-emission spectrophotometry [5].

In contrast with Ti, Si is an essential element for the normal functioning of the human organism. It is present in practically all organs and tissues. Connective tissue is especially rich in Si. Silicon is a structural component in mucopolysaccharides and their protein complexes, which form the framework of connective tissue and determine their mechanical strength, elasticity, and resilience. Silicon contributes to the growth and hardening of connective tissue during both embryonic development and wound healing. It assists the biosynthesis of collagen and the formation of bone tissue, plays a significant role in metabolic processes, and prevents deposition of cholesterol on the walls of blood vessels [7].

Thus, the fabrication of drugs based on Si compounds is definitely justified on both biochemical and pharmacological bases. On the other hand, it is expected that introducing a Ti atom into the molecular structure of Si glycerates (or hydrogels based on them) will allow the improvement of several pharmacological properties, for example, increased transcutaneous and antioxidant activity, because Ti is more capable than Si of forming complexes due to its variable valence [9 – 12].

The goal of our work was to prepare new biologically active organosilicontitanium (OST) glycerohydrogels as bases for creating soft drug forms that can exert an additional positive action on the organism due to the presence of Si and Ti atoms simultaneously in its structure.

In the first step, we synthesized mixed Si and Ti glycerates (**I**) from $Si(OC_2H_5)_4$ and $Ti(OC_4H_9)_4$ in mole ratio 2:1 through an alcoholysis reaction in an excess of glycerine (Scheme 1) [13].

The prepared compounds **I** resulted from the formation of a complex of tetraethoxysilane with tetrabutoxytitanium of composition $2Si(OC_2H_5)_4 \cdot Ti(OC_4H_9)_4$ [12]. This complex formed readily upon mixing the starting materials at room temperature and was a transparent yellow liquid. The complex between these reagents was most probably formed by donor-acceptor interaction between the Ti atom(s) and an O atom of a siloxane bond: $(RO)_4Ti \leftarrow O(R')\text{-}Si(OR')_3$. This interaction was due to the high electron-accepting capability of the Ti atom and the significant nucleophilicity of the O atom in the siloxane bond. Furthermore, donor-acceptor interaction involving the Si atom and an O atom of the titanoxane bond is also possible: $(RO)_3Ti\text{-}(R)O \rightarrow Si(OR')_4$ [12]. Apparently the latter type of interaction dominates in Si and Ti glycerates because complexes of titanates with alcohols of the type $(RO)_4Ti \leftarrow O(H)\text{-}R''$ [11] are known to form. This prevents coordination of the siloxane O atom to the Ti atom. Formation of complexes with glycerine molecules through Si-O-C, Ti-O-C, and C-O-H bonds in solvated complexes **I** also stabilizes the resulting mixed Si and Ti glycerates [13]. These compounds are thick white liquids that are characterized by elemental analyses, refractometry, IR spectroscopy, differential thermal analysis (DTA), and dynamic viscosity.

Scheme 1

$$2Si(OC_2H_5)_4 + Ti(OC_4H_9)_4 + (x + 12)C_3H_8O_3 \rightarrow$$
$$\rightarrow \underset{\mathbf{I}}{2Si(C_3H_7O_3)_4 \cdot Ti(C_3H_7O_3)_4 \cdot xC_3H_8O_3} +$$
$$+ 8C_2H_5OH + 4C_4H_9OH,$$

where $9 \le x \le 30$

In the second step, hydrogels **II** with the following component ratios (mass%) were prepared according to Scheme 2 through reaction of solvated complexes **I** with aqueous solutions of a gel-forming additive:

solvated complexes of Si and Ti glycerates **I**	48,4 – 65,2
gel-forming additive	0,1 – 0,6
water	remainder

Various electrolytes such as NaCl, $CaCl_2$, NaF, and others can be used as the gel-forming additive. Hydrogels based on solvated complexes of Si and Ti glycerates **II** are white odorless compounds that are stable upon storage. Hydrogels were characterized by elemental analyses, refractometry, IR spectroscopy, and DTA.

The contents of Si and Ti glycerates, glycerine, and water in gels **II** were determined by the optimum ratio of Si and Ti atoms from the viewpoint of complex formation, the synergetic effect with respect to transcutaneous activity, the resistance to syneresis, and the more acceptable consistency of the gel for practical use.

TABLE 1 lists results from thermogravimetric analysis of Si and Ti glycerate solvated complexes **I**: $2Si(C_3H_7O_3)_4 \cdot Ti(C_3H_7O_3)_4 \cdot 30C_3H_8O_3$ and the hydrogel based on them **II**: $2Si(C_3H_7O_3)_4 \cdot Ti(C_3H_7O_3)_4 \cdot 30C_3H_8O_3 \cdot 120H_2O$ in addition to the mechanical mixture consisting of solvated complexes **I** and an aqueous solution corresponding to the composition of hydrogel **II**. The results indicated that the hydrogel was thermally more stable than the mechanical mixture, which confirmed that it was formed.

Any solvated complexes **I** of composition $2Si(C_3H_7O_3)_4 \cdot Ti(C_3H_7O_3)_4 \cdot xC_3H_8O_3$, where $9 \le x \le 30$, and any hydrogels **II** based on them of composition $2Si(C_3H_7O_3)_4 \cdot Ti(C_3H_7O_3)_4 \cdot xC_3H_8O_3 \cdot yH_2O$, where $9 \le x \le 30$ and $60 \le y \le 120$ can be prepared by analogous methods [13].

Scheme 2

$$2Si(C_3H_7O_3)_4 \cdot Ti(C_3H_7O_3)_4 \cdot xC_3H_8O_3 + yH_2O \rightarrow$$

I

$$\rightarrow 2Si(C_3H_7O_3)_4 \cdot Ti(C_3H_7O_3)_4 \cdot xC_3H_8O_3 \cdot yH_2O,$$

II

where $9 \le x \le 30$, $60 \le y \le 120$

EXPERIMENTAL CHEMICAL PART

IR spectra in a thin layer of pure compound were recorded on a Spectrum One IR-Fourier spectrometer (Perkin-Elmer) in the range 400 – 4000 cm^{-1}. Indices of refraction were determined on an IRF-456 refractometer (Russia). Thermogravimetric studies (DTA) were performed on a type OD-102 MOM derivatograph (Hungary) at heating rate 5°C/min. Dynamic viscosity was determined in a Viscotester 6® rotational viscometer (Germany) with relative uncertainty ±6%. Elemental analyses agreed with those calculated.

Starting materials, $Si(OEt)_4$ (high purity), and glycerine (analytically pure) were used without further purification. $Ti(OBu)_4$ was purified by double vacuum distillation before use.

Solvated complexes of Si and Ti glycerates (I). Glycerine (63.82 g, 693.0 mmol) was placed into a one-necked round-bottomed flask equipped with a three-hole adapter, mechanical stirrer, dropping funnel, and reflux condenser; heated to 60°C; treated dropwise with stirring with a thoroughly mixed mixture of $Si(OEt)_4$ (6.88 g, 33.0 mmol) and $Ti(OBu)_4$ (5.62 g, 16.5 mmol), and held for 3 h at 130°C with vigorous stirring. The produced alcohols were removed in vacuo in a rotary evaporator at 2 – 5 mm Hg and 120 – 130°C to constant mass (which corresponded to loss of the theoretical amount of ethyl and butyl alcohols). Yield, 64.71 g (99%). **I** was a white liquid with dynamic viscosity 6.5 Pa · s (20 ± 0.5°C) and n_D^{20} 1.4760 and was infinitely miscible with water. The composition of the product agreed with the formula $2Si(C_3H_7O_3)_4 \cdot Ti(C_3H_7O_3)_4 \cdot 30C_3H_8O_3 \cdot C_{126}H_{324}O_{126}Si_2Ti$.

IR spectrum (ν, cm^{-1}): 995, 1050, 1115 (Ti-O-C, Si-O-C), 1050 (C-O in primary C-O-H), 1110 (C-O in secondary C-O-H), 1220 (CH_2), 2935, 2880 (C-H), 3400 (OH).

Hydrogels based on solvated complexes of Si and Ti glycerates (II). Product **I** (64.67 g, 16.3 mmol) at 80°C was stirred and treated proportionally with an aqueous solution (35.33 g, 1960.0 mmol) of NaCl (0.6 g, 10.3 mmol, 0.6 mass% of the total weight). Gel formed upon heating (80°C) and stirring. Yield, 100.00 g (100%). **II** was a white gel with n_D^{20} 1.4385 that was soluble in ordinary organic solvents and completely soluble in water. The composition of the product agreed with the formula $2Si(C_3H_7O_3)_4 \cdot Ti(C_3H_7O_3)_4 \cdot 30C_3H_8O_3 \cdot 120H_2O$. $C_{126}H_{524}O_{246}Si_2Ti$.

IR spectrum (v, cm^{-1}): 995, 1050, 1115 (Ti-O-C, Si-O-C), 1050 (C-O in primary C-O-H), 1110 (C-O in secondary C-O-H), 1220 (CH_2), 1640 (H-O-H), 2935, 2880 (C-H), 3400 (OH).

EXPERIMENTAL PHARMACEUTICAL PART

The acute toxicity of OST glycerohydrogel **II** of composition $2Si(C_3H_7O_3)_4 \cdot Ti(C_3H_7O_3)_4 \cdot 30C_3H_8O_3 \cdot 120H_2O$ was studied as before [14] on white mice of both sexes (18 – 23 g) and Wistar white rats of both sexes (180 – 230 g). Experimental animals were kept in a vivarium at 18 – 20°C under a natural light cycle with a standard diet with free access to food and water. The studied compounds were injected into the stomach through a catheter and i.p. once as 50% and 10% aqueous gels. A total of 6 doses in 12 groups of mice (6 males and 6 females) and 12 groups of rats (also 6 males and 6 females) was tested. The behavior of the animals was observed every hour after injection of the glycerohydrogel for 1 d and daily for the next 13 d. The general motor activity of the animals, neuromuscular excitation, reflexes (pain, corneal), and vegetative reactions (salivation, diuresis, defecation) were recorded during the experiment.

Transcutaneous penetration was studied by measuring the degree of transdermal permeation of drug in the presence

TABLE 1. Thermogravimetric Analyses

Sample No.	Solvated complexes	Weight loss, %						Temperature of weight losses, °C			
		50°C	100°C	125°C	150°C	200°C	250°C	1 %	5 %	10 %	50 %
1	Solvated complexes of Si and Ti glycerates I	0.1	0.3	0.4	0.6	4.1	20.5	160	210	228	285
2	Hydrogel based on solvated complexes II	0.5	4.5	14.5	25	34.8	57.5	63	107	120	243
3	Mechanical mixture consisting of solvated complexes I and aqueous solution	0.2	4.8	19	27	35.5	57.2	65	102	108	240

of transcutaneous vehicles through natural biological membranes from intact skin (*in vitro*). Sodium diclofenac was used as the drug diffusing through the skin. Its initial concentration in isotonic saline was 2%. The studied transcutaneous vehicles were solvated complexes of Si and Ti glycerates **I** of composition

$2Si(C_3H_7O_3)_4 \cdot Ti(C_3H_7O_3)_4 \cdot 30C_3H_8O_3$ and hydrogel **II** based on them of composition $2Si(C_3H_7O_3)_4 \cdot Ti(C_3H_7O_3)_4 \cdot 30C_3H_8O_3 \cdot 120H_2O$. The references were known transcutaneous vehicles tisol $Ti(C_3H_7O_3)_4 \cdot 10C_3H_8O_3 \cdot 40H_2O$ [3], Si glycerates $Si(C_3H_7O_3)_4 \cdot 10C_3H_8O_3$, and organosilicon glycerohydrogel $Si(C_3H_7O_3)_4 \cdot 10C_3H_8O_3 \cdot 40H_2O$ [5]. Experiments were conducted using skin sacks of prepared frog legs with bone and muscle removed from them as the biological membranes. All frog legs were selected so that differences in their sizes and masses were less than ± 5%. Legs prepared in this way were firmly fixed to the bases of hollow glass tubes (1-cm diameter) with a groove for tying.

Two series of experiments were carried out. In the first series, tested mixture consisting of sodium diclofenac solution (4.5 mL, 2%) and tested transcutaneous vehicle (0.50 g) were placed into the cylinders formed by the attached legs. The final sodium diclofenac concentration was 1.8%; transcutaneous vehicle, 10%. The base of each cylinder with the legs was immersed into a separate tube (cylinder) of larger diameter with isotonic saline (50 mL). In this instance, the permeation of sodium diclofenac from the inner side of the skin to the dermis side was investigated. In the second series, isotonic saline (5 mL) was poured into the inner cylinders. The studied mixture consisting of sodium diclofenac solution (45 mL, 2%) and studied transcutaneous vehicle (5.00 g) were placed into the outer reservoir. In this instance, permeation of sodium diclofenac from the outer side of the skin to the epidermis side was investigated. All experiments in each series (10 – 12 each) were conducted in parallel at identical temperatures (20 ± 1°C) and storage times (16 h).

The concentration of sodium diclofenac passing through the skin was determined by UV spectroscopy on a UV-2401 PC spectrophotometer (Shimadzu) that was calibrated using the absorption band at 275 nm. The molar concentration of sodium diclofenac passing through the whole skin thickness was determined from a calibration curve. Then, its mass was calculated by knowing the volume of the solutions in the corresponding cylinders. The degree of permeability was estimated in percent of the initial mass of sodium diclofenac. The relative uncertainty of a determination was ±5%.

Wound-healing properties were studied using a thermal burn model on 40 Wistar white rats (180 – 230 g). Rats were divided into four groups of 10 animals each. All rats were burned on a side previously shaved of skin in an area 15 × 15 mm. The burn area for rats of the first group was treated with an aqueous suspension (40%) of OST glycerohydrogel **II** of composition $2Si(C_3H_7O_3)_4 \cdot Ti(C_3H_7O_3)_4 \cdot 26C_3H_8O_3 \cdot 104H_2O$; of the second group, an aqueous suspension of organosilicon glycerohydrogel of composition $Si(C_3H_7O_3)_4 \cdot 6C_3H_8O_3 \cdot 24H_2O$; of the third group, an aqueous solution (40%) of DMSO; of the fourth group (control), with no treatment. Wounds were smeared daily for 21 d (0.50 g each) until wounds of all groups were healed. The orientation and exploratory behavior of the animals was determined by the open-field method before inflicting the burns and on the 14th day of treatment. Their vertical and horizontal activity was assessed using the following criteria: time to exit a circle, number of squares visited, number of standings, groomings, and looks into a hole.

Blood was drawn from the animals for general and biochemical analyses after the course of treatment. Organs and skin structure were examined morphologically. Histological preparations were prepared after preserving tissues (heart, lung, liver, kidney, adrenal, spleen, skin) in formalin solution (10%) and sealing with paraffin. Histological media were colored with hematoxilin-eosin (Van-Gieson).

Antioxidant activity of glycerohydrogels was studied using adult Wistar rats of both sexes (5 – 7 months). Studied groups of animals (10 animals per group) were injected with organosilicon and OST glycerohydrogels of composition $Si(C_3H_7O_3)_4 \cdot 6C_3H_8O_3 \cdot 24H_2O$ and

TABLE 2. Permeability of Sodium Diclofenac Through Frog Skin in the Presence of Various Transdermal Vehicles

Sample No.	Studied transdermal vehicles		Degree of transdermal permeability after 16 h at 20 ± 1°C, %	
	Name	Composition	Series I (dermis side)	Series II (epidermis side)
1	Solvated complexes of Si and Ti glycerates I	$2Si(C_3H_7O_3)_4 \cdot Ti(C_3H_7O_3)_4 \cdot 30C_3H_8O_3$	62.1 ± 2.6*	3.3 ± 0.1
2	OST glycerohydrogel II	$2Si(C_3H_7O_3)_4 \cdot Ti(C_3H_7O_3)_4 \cdot 30C_3H_8O_3 \cdot 120H_2O$	55.0 ± 2.2*	2.8 ± 0.1*
3	Si glycerates	$Si(C_3H_7O_3)_4 \cdot 10C_3H_8O_3$	55.0 ± 2.2*	2.7 ± 0.1*
4	Organosilicon glycerohydrogel	$Si(C_3H_7O_3)_4 \cdot 10C_3H_8O_3 \cdot 40H_2O$	44.4 ± 1.6*	2.3 ± 0.1*
5	Tisol (reference preparation)	$Ti(C_3H_7O_3)_4 \cdot 10C_3H_8O_3 \cdot 40H_2O$	31.1 ± 1.1*	1.8 ± 0.1

Here and in Table 3: * values are reliable for all compared groups at $p < 0.05$.

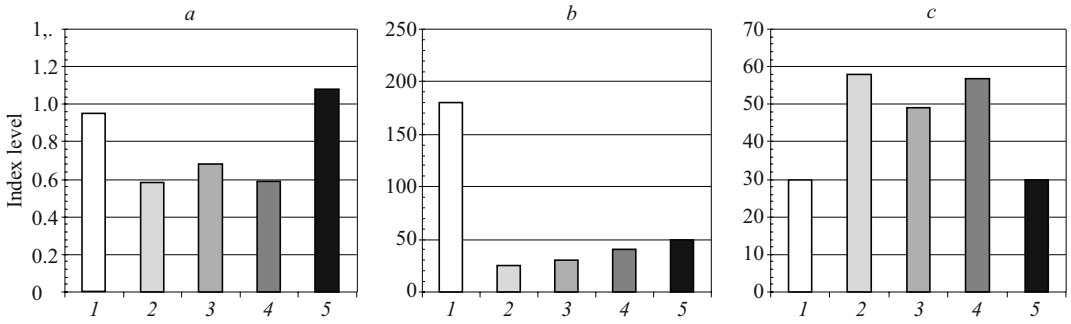

Fig. 1. Effect of studied preparations on level of enzyme-markers of the liver POL system in experimental animals: MDA (M) (*a*), SOD (arb. units/g Hb × min) (*b*), AOA (%) (*c*); control animal group (*1*), organosilicon gel i.p. (*2*), organosilicon gel into the stomach (*3*), OST gel i.p. (*4*), OST gel into the stomach (*5*).

$2Si(C_3H_7O_3)_4 \cdot Ti(C_3H_7O_3)_4 \cdot 26C_3H_8O_3 \cdot 104H_2O$, respectively, i.p. and into the stomach as 40% suspensions for 10 d. A section of the liver tissue was taken from anesthetized animals after 10 d of drug injection.

Changes in peroxide oxidation of lipid (POL) and antioxidant protection (AOP) systems of the liver were gauged from the quantitative content of peroxidation intermediates reacting with thiobarbituric acid (malonic dialdehyde, MDA), from the activity of superoxide dismutase (SOD), and from a determination of the total antioxidant activity (AOA) expressed as the ability of the endogenous system of antioxidants to regulate the POL level in the organism [15].

Results were treated statistically using Student t-criteria with calculated mean arithmetic values and average deviation from the mean arithmetic and mean-square deviations using Excel and Statistica programs for $p < 0.05$.

RESULTS AND DISCUSSION

Reliably significant deviations in the behavior of the animals were not observed during the study of the acute toxicity. The LD_{50} could not be determined. Thus, the tested OST glycerohydrogel **II** is nontoxic (class IV hazard) according to the literature [14].

TABLE 2 shows that solvated complexes of Si and Ti glycerates **I** and hydrogel **II** based on them are active transcutaneous vehicles and are more active than the corresponding Si-containing compounds and tisol. The increased transcutaneous activity of Si- and Ti-containing solvated complexes and hydrogels is probably explained by the fact that Si is less capable than Ti of forming complexes but has greater penetrating activity and increases the penetrating power of Ti by forming solvated complexes with it. This also increases the permeation of sodium diclofenac through the skin.

The open field test results from the wound-healing study showed that the control group had the greatest decrease of activity for all indicators. The horizontal activity of the rats did not practically change in the test groups. OST glycerohydrogel did somewhat reduce the activity in rats.

Wounds healed completely in 14 d for about 60% of the test rats. Reliable differences in the healing times were not observed in the test groups. Complete epithelization and formation of a scar that was more elastic for Si- and OST glycerohydrogels were observed on the 21st day. Wounds in the control group healed on the 24 – 26 day.

Blood analysis in general did not show reliable changes (indicators of animals in test groups did not differ from those of intact animals).

Biochemical analysis of blood (Table 3) drew attention to the increased levels of aspartateaminotransferase (AST) in the second group of rats and alanineaminotransferase (ALT) in all experimental groups. The alkaline phosphatase indicator showed various changes depending on the preparation,

TABLE 3. Effect of Studied Preparations on Blood Biochemical Indices

Group No.	Studied preparation	AST, ME/L	ALT, ME/L	Alkaline phosphatase, mmol/L	Cholesterol, mmol/L
1	OST glycerohydrogel $2Si(C_3H_7O_3)_4 \cdot Ti(C_3H_7O_3)_4 \cdot 26C_3H_8O_3 \cdot 104H_2O$	116.21 ± 6.31	70.61 ± 3.57*	798.24 ± 38.75*	2.26 ± 0.09*
2	Organosilicon glycerohydrogel $Si(C_3H_7O_3)_4 \cdot 6C_3H_8O_3 \cdot 24H_2O$	157.24 ± 5.55*	113.62 ± 4.60*	1360.64 ± 50.84*	1.41 ± 0.07*
3	Dimethylsulfoxide (DMSO)	134.43 ± 11.62*	79.63 ± 4.71*	956.33 ± 52.17*	2.31 ± 0.10*
4	Without preparation (control)	121.42 ± 10.58	60.02 ± 3.66	1157.01 ± 58.60	1.83 ± 0.15

i.e., was reliably lower for OST glycerohydrogel in DMSO. Indicators for cholesterol were also inconsistent. They were higher than the control group in the first and third groups and lower in the second. The reduced activity indicators of enzymes for OST glycerohydrogel is evidence that this compound had a favorable influence on the functioning of the liver.

Structural changes were not observed in histological tests of internal organs of the rats.

Histological sections of burned skin areas in control rats showed that necrosis of the epidermis with perifocal granulocytic-leucocytic reaction did occur in the burn area. Capillaries and venules of papillary and subpapillary layers were expanded with appearances of adiemorrhysis. Proliferation of fibroblast cells was observed in the perifocal region in the papillary layer. Perivascular lymphoid infiltrations localized focally were seen in the dermal layer and hypodermis. Rats of the third group also had near the focus necrosis with peripheral granulocytic-leucocytic infiltrations. More favorable results were observed for rats in the first two groups. The perifocal lympho-leucocytic wall was better formed. Destruction and necrosis of the epidermis was decreased. In both instances treatment led to the formation of a more elastic post-burn scar. Thus, the morphological investigations indicated that organosilicon and OST glycerohydrogels had a substantial positive influence on the morphological and functional condition of the skin.

Levels of enzyme markers of POL in the liver of experimental animals (Fig. 1). showed that the MDA level decreased in all groups compared with the control group with the exception of OST glycerohydrogel injected into the stomach. The SOD activity decreased reliably in all instances. The total AOA increased reliably most noticeably after i.p. injection of the tested compounds.

These changes indicate clearly that the studied compounds influenced the POL system and the AOP of the liver of experimental animals already after 10 d of injection. It can be assumed that the corrective influence of the studied compounds on POL processes in the liver of animals was related to their distinct membrane-stabilizing properties and to the ability to modulate directly the activity of membrane-bound enzymes (SOD) in hepatocytes.

The results lead to the conclusion that OST glycerohydrogel is a physiologically active substance that enhances transcutaneous penetration of medicinal agents and possesses additional advantageous properties.

Thus, OST glycerohydrogel can be recommended for use as a new oil base of pharmaceutical compositions for local and topical application in various branches of medicine.

ACKNOWLEDGMENTS

The work was supported financially by the RFBR Project No. 07-03-97638 p ofi (Regional Competitions of Directed Basic Research).

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