The effect of phosphatidic acid in a concentration of 15 moles % in the composition of DPPC liposomes on prolongation of the action of HC was demonstrated in [8]. This prolongation lasted 3-4 days. The authors cited interpret this phenomenon as the effect of coincidence between the melting point of this mixture of lipids and the temperature of inflammation, namely 36°C. Such an interpretation of the results is evidently incorrect because incorporation of phosphatidic acid in the lipid phase of LPPC liposomes leads not to a decrease in phase transition temperature, but to an increase in it to 58-67°C depending on pH of the microemulsion [1, 5]. Incorporation of 20 moles % cholesterol, which was done to increase the stability of the vesicles, is reflected also in the melting point of DPPC and shifts the beginning of phase transition from 41.5 to 37°C [1, 7], i.e., to a temperature that is close to the temperature of inflammation.

It can thus be postulated that the effect of prolongation of the anti-inflammatory action of HC incorporated into DPPC liposomes is due to two circumstances. In the first stage, because of closeness of the phase state of the liposomal lipids and cells at the temperature of inflammation, effective uptake of vesicles by the cells takes place. Later, because of the appearing hypothermic action of HC and the fall of temperature to 32°C, the vesicles taken up are converted into a solid-crystal state, in which their utilization time is considerably lengthened.

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EFFECT OF 1-(CHLOROMETHYL)SILATRANE ON TISSUE BIOCHEMICAL PARAMETERS IN EXPERIMENTAL GASTRIC ULCER

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KEY WORDS: experimental gastric ulcer; granulation and fibrous tissue; silatranes; oxyferriscorbone; methyluracil.

Silicon has been shown to be an essential trace element for higher animals and man [2]. Among compounds of this element many substances with high biological activity have been found. The silatranes, which stimulate protein and nucleic acid synthesis in cells [1, 12, 14] and also the proliferative-reparative function of connective tissue [1, 8, 12, 14], are particularly important in this respect. It was shown as long ago as in 1975 that certain

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TABLE 1. Hydroxyproline and Tyrosine Concentrations in Gastric Ulcer Tissue of Rats Treated with MU, OFS, and CMS (in g/100 g dried, defatted tissue)

Time, days	Hydroxyproline (1,44±0,13)				Tyrosine (2,75±0,50)			
	control	MU	OFS	CMS	control	MU	OFS	CMS
3	1,39±0,22	1,21±0,10	1,44±0,17	1,36±0,16	2,12±0,26	1,86±0,3	2,39±0,3	2,38±0,28
7	1,31±0,29	0,70±0,09	1,60±0,12	1,73±0,33	2,06±0,3	1,63±0,17	2,06±0,14	1,76±0,23
10	1,37±0,26	1,37±0,24	1,91±0,26	1,97±0,16	1,92±0,16	1,88±0,17	2,0±0,2	2,03±0,3
20	2,29±0,12	1,50±0,15	2,14±0,15	2,08±0,2	1,79±0,16	1,67±0,22	2,11±0,12	1,66±0,11
30	2,03±0,3	1,66±0,14	2,10±0,37	1,77±0,28	1,87±0,41	1,66±0,26	2,3±0,4	1,78±0,26

Legend. Content of hydroxyproline and tyrosine in intact rat stomach wall shown in parentheses.

TABLE 2. Effect of MU, OFS, and CMS on Total Content of Hexuronic Acids (in g/100 g dried, defatted tissue) and Determination of Their Fractions in Gastric Ulcer Tissue of Rats (in % of total hexuronic acid content) on 30th Day After Treatment

Experimental conditions	Total content of hexuronic acids	Fractions soluble in NaCl solution		
		0,4 M	1,2 M	2,1 M
Intact animals	0,66±0,12	35	27	37
Control	0,85±0,15	45	27	28
MU	0,51±0,2	31	45	24
OFS	0,54±0,2	45	35	20
CMS	0,49±0,11	38	24	38

TABLE 3. Effect of MU, OFS, and CMS on Content of Hexosamines, Hexoses, and Sialic Acid in Gastric Ulcer Tissue of Rats (in g/100 g dried, defatted tissue)

Preparation	Time of observation, days				
	3	7	10	20	30
			Hexosamine (0,43±0,2)		
Control	1,15±0,09	0,80±0,3	0,82±0,3	0,85±0,15	0,85±0,3
MU	0,84±0,07	0,77±0,13	0,76±0,16	0,76±0,07	0,89±0,12
OFS	0,80±0,14	0,70±0,09	0,71±0,17	0,73±0,09	0,58±0,04
CMS	0,80±0,3	0,59±0,15	0,74±0,2	0,67±0,2	0,72±0,2
			Hexoses (1,78±0,4)		
Control	2,68±0,04	2,36±0,7	2,86±0,25	3,33±0,7	2,23±0,28
MU	1,75±0,28	1,78±0,45	1,88±0,03	2,0±0,19	2,10±0,26
OFS	2,03±0,3	2,13±0,29	2,11±0,42	2,19±0,53	2,40±0,36
CMS	2,72±0,55	2,18±0,5	2,17±0,4	2,13±0,49	2,20±0,46
			Stalic acid (0,37±0,14)		
Control	0,83±0,01	0,89±0,01	0,81±0,1	0,48±0,03	0,57±0,17
MU	0,56±0,07	0,68±0,08	0,59±0,09	0,62±0,06	0,47±0,05
OFS	0,63±0,14	0,63±0,16	0,78±0,08	0,57±0,04	0,48±0,04
CMS	0,76±0,01	0,64±0,09	0,66±0,07	0,74±0,19	0,67±0,11

Legend. Content of hexosamine, hexoses, and sialic acids in gastric ulcer tissue of rats shown in parentheses.

silatranes have a wound-healing action [5]. In particular, this effect has been found in the case of 1-(chloromethyl)silatrane (CMS) and 1-(ethoxy)silatrane, which substantially improve biochemical parameters of granulation and fibrous tissue developing in wound defects [5, 6, 12, 14]. In experiments on rabbits silatranes inhibited the development of gastric ulcers [3, 4, 13].

This paper gives the results of a quantitative biochemical study of the dynamics of connective-tissue components in tissues of the stomach as an objective parameter of the reparative reaction under the influence of CMS. The effect of this compound was compared with that of other antiulcer preparations used in clinical practice: methyluracil (MU) and oxyferriscorbone (OFS). The biochemical investigation was supplemented by a histological study.

EXPERIMENTAL METHOD

Experiments were carried out on 228 albino rats weighing 150-180 g. Experimental gastric ulcer was produced by a modified method [11]. After the operation the compounds for testing were administered for 10 days: CMS in a dose of 50 mg/kg (orally), MU in a dose of 500 mg/kg (orally), and OFS in a dose of 30 mg/kg (intraperitoneally). The animals were sacrificed on the 3rd, 7th, 10th, 20th, and 30th days after the operation. The stomach was opened along the lesser curvature and the area of the ulcer was measured. Some stomachs in each group were investigated histologically, the remainder were used for biochemical analysis [7].

EXPERIMENTAL RESULTS

The planimetric data show that all three compounds accelerated reduction in area of visible ulceration of the mucosa. A central place among the biochemical parameters of granulation and fibrous tissue is occupied by the collagen concentration (estimated as hydroxypyroline, a specific amino acid for this fibrillary protein). In the absence of treatment, in the stage of ulcer formation, some collagen destruction takes place, and after the 20th day this is replaced by intensive collagen accumulation – a sign of fibrosis of the tissue (Table 1). Destruction of noncollagen proteins was even more intensive and progressed until the end of the experiment, as a result of which the developing scar tissue was distinguished not only by excess of collagen, but also by deficiency of noncollagen proteins (with tyrosine as their indicator). During treatment with MU the initial fall in the hydroxypyroline concentration in the ulcer tissue was particularly rapid, but later, after the 10th day, the collagen concentration was restored to normal, and on the 30th day it was only a little higher than the concentration in intact stomach wall. In other words, MU significantly inhibits excessive accumulation of collagen although the deficiency of noncollagen proteins in this case was no less than in the untreated rats. Conversely, from the very beginning OFS prevents collagen destruction. Starting from the 7th day, destruction increased progressively, and the degree of fibrosis in this case was just as high as in the control group, the only difference being that the scar tissue which formed was closer to normal in its content of noncollagen proteins. On treatment with CMS the dynamics of the collagen concentration until the 20th day coincided with that during treatment with OFS, but later the collagen level fell appreciably, the process of scar formation was accelerated, and regression of the scar tissue began, features which distinguish the effect of CMS advantageously from the effect of OFS. CMS has a weaker effect on the dynamics of noncollagen proteins than OFS.

The total concentration of glycosaminoglycans (hexuronic acids, Table 2) in all series of experiments differed only a little from the control, but only when CMS was used was the ratio between glycosaminoglycan fractions characteristic of the intact wall restored in the ulcer tissue by the time of disappearance of visible ulceration of the mucosa; a characteristic feature of this ratio is a high content of the 3rd fraction (the fraction of heparin sulfate, heparin, and hypersulfated chondroitin sulfates) [9].

CMS has a more distinct effect than MU and OFS on hexosamine-containing glycoproteins in the ulcer tissue: Their concentration throughout the experiment was lower than in animals of the other series (Table 3).

All three preparations reduced the reactive hypersecretion characteristic of gastric ulcer, and for which the anthrone-positive hexoses (Table 3) can be taken as an indicator, for glycoproteins of the mucous secretion of the digestive tract are distinguished by a high content of hexoses [10]. At the same time, depending on the dynamics of sialoglycoproteins (sialic acids, Table 3), MU and OFS have a stronger antiexudative effect, especially in the early stage of ulcer development.

The favorable action of CMS on healing of experimental gastric ulcer was confirmed by the results of histological investigations. On the 3rd day after ulcer formation, necrosis of all layers of the stomach wall was observed. In untreated animals, young granulation tissue was formed after 7-10 days, and by 20-30 days scar tissue with hyalinosis appeared. Full recovery of the epithelium does not take place and a chronic ulcer is formed: Its base is covered with granulation tissue with a zone of necrosis and is saturated with fibrin, whereas along the edges repair of the mucosa continues. During treatment with MU and OFS synchronization of repair of the connective-tissue structures of the stomach wall is improved and, because of this, the healing process is accelerated. However, normal repair of the glandular structures of the mucosa does not take place. Under the influence of CMS, by the 3rd day fibroblasts and newly formed capillaries appear in the region of the ulcer. By the 7th-10th day granulation and fibrous tissue with a concentration of large fibroblasts develop. By the 20th-30th day well-formed connective tissue is observed and the ulcer defect is covered with epithelium, regeneration of which takes place with the formation of tubular and adenomatous structures, consisting of high prismatic cells.

CMS thus not only accelerates healing of the ulcer, but also optimizes restoration of the structure of the stomach wall.

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ADRENERGIC STRUCTURES AND MONOAMINE OXIDASE ACTIVITY IN DYSTROPHIC SKELETAL MUSCLES

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The study of hereditary neuromuscular diseases is becoming increasingly urgent in connection with the relative increase in the contribution of genetically determined diseases to the general structure of human pathology. Important advances in clinical neurogenetics have been achieved as a result of close collaboration with the basic natural sciences: molecular biology, biochemistry, etc. However, the absence of adequate animal models makes the study of such a large group of diseases as the progressive muscular dystrophies much more difficult.

In recent years, skeletal muscles from human patients taken at biopsy have been used on an increasing scale for study. Histochemical investigations [4] have revealed accumulation of catecholamines (CA) in the skeletal muscles of patients with Duchenne's progressive muscular dystrophy. More recent investigations [2, 6, 7] have demonstrated the important role of biogenic amines in the determination of the muscular dystrophic process. However, the causes of pathological accumulation of CA in the skeletal muscles of such patients have not yet been explained.

The aim of this investigation was to study the characteristics of adrenergic structures and monoamine oxidase (MAO) activity in skeletal muscles of patients with Duchenne's muscular dystrophy and with Charcot–

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