meability of the GIT barrier for proteins, which preserve their biological specificity, during starvation, discovered in this investigation, must be borne in mind when recuperative diets are drawn up for patients after short courses of therapeutic food deprivation, and in cases when starvation is used for diagnostic purposes, or when patients requiring enforced starvation are subjected to combined dietetic and detoxication therapy.

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EFFECT OF IONOL ON GASTRIC LESIONS IN RATS WITH IMMOBILIZATION STRESS

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KEY WORDS: antioxidants; ionol; experimental gastric ulcer.

Gastric ulcers regularly arise in rats with immobilization stress [12]. It is very likely that the free-radical lipid oxidation (FRLO) system, which is activated in stress [9] participates in ulcer formation. In the presence of a critical concentration of FRLO products, injury to the membranes, irreversible inactivation of enzymes, etc., are observed [2]. Activation of FRLO can be prevented by administration of the bioantioxidant α-tocopherol, or its synergist, ascorbic acid [6], and also by administration of the synthetic antioxidant, ionol* [5].

The effect of ionol on some mechanisms of gastric ulcer formation, including changes in FRLO, was studied in the investigation described below.

*2,6-Di(tert-butyl-4-methylphenol).

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TABLE 1. Values of JpH in Different Parts of the Alimentary Tract of the Rats (M ± m)

Part of alimentary tract	Groups of animals			
	1 (15)	2 (8)	3 (9)	4 (10)
Stomach	4,12±0,07	3,45±0,05	4,7±0,19	5,34±0,18
P_1		<0,001	<0,01	<0,001
P_2				<0,001
P_3				<0,05
Duodenum	8,95±0,11	8,01±0,12	8,05±0,13	7,25±0,23
P_1		<0,001	<0,001	<0,001
P_2				<0,01
P_3				<0,01
Gastroduodenal gradient	0,46±0,02	0,43±0,01	0,58±0,02	0,71±0,04
P_1			<0,001	<0,001
P_2				<0,001
P_3				<0,01
Jejunum	8,60±0,10	7,91±0,06	7,92±0,15	7,26±0,33
P_1		<0,001	<0,002	<0,001
Ileum	9,10±0,09	8,65±0,15	8,47±0,19	7,72±0,26
P_1		<0,01	<0,01	<0,001
P_2				<0,01
P_3				<0,05
Cecum	10,55±0,12	9,36±0,34	9,54±0,14	8,53±0,32
P_1		<0,01	<0,001	<0,001
P_3				<0,01
Ileocecal gradient	0,85±0,01	0,92±0,02	0,89±0,01	0,91±0,02
P_1		<0,01	<0,02	<0,01
Rectum	8,60±0,12	9,02±0,17	8,25±0,10	7,76±0,30
P_1		<0,05	<0,05	<0,02
P_2				<0,002

EXPERIMENTAL METHOD

Noninbred male rats weighing 150-200 g, kept on a standard animal house diet, were divided into four groups: 1) intact animals; 2) rats receiving ionol (in its therapeutic form of dibunol) in a dose of 50 mg/kg once a day for 7 days by gastric tube; 3) rats immobilized by Brodie's method [14] for 24 h after deprivation of food for 24 h with access to water ad lib.; 4) rats receiving ionol for 7 days, like animals of group 2, then immobilized like the animals of group 3. In rats of group 1, 24 h after food deprivation, and in the remaining animals at the end of the experiment, the juxtamural pH (JpH) was determined under urethane anesthesia (150 mg/kg) in the body of the stomach, duodenum, jejunum, ileum, cecum, and rectum [7]. The animals were then decapitated. The following tests were carried out with the N 334 coagulograph: the beginning (T_1), end (T_2), and duration (T) of coagulation of whole blood, its rate in the first minute (V_1) and its maximal amplitude (MA). Gastric ulcer formation was evaluated in the rats of groups 3 and 4. The following parameters of FRLO were determined in the tissues of the mucosal portion of the stomach wall and liver: concentrations of diene conjugates (DC) [11] and malonic dialdehyde (MDA) [10], intensity of peroxide formation (PF) [15] and the concentrations of disulfide bonds and sulfhydryl groups [13].

EXPERIMENTAL RESULTS

No gastric ulcers were present in the rats of groups 1 and 2. In rats of group 3 the stomach lesions consisted of twisted ulcers with hemorrhagic borders (3.2 + 0.5)/100%, erosions (7.3 + 0.7)/(88.9 + 10.5%), and petechial (4.2 + 0.4)/(77.8 + 13.9%) and massive hemorrhages (0.6 + 0.3)/(33.4 + 15.7%). In the rats of group 4 the number of ulcers (4.0 ± 0.4)/100%, and massive hemorrhages (0.5 + 0.3)/(30.0 + 14.5%) was unchanged, the number of petechial hemorrhages was increased (7.6 + 1.0)/100% ($P < 0.01$), but the number of erosions, on the contrary, was reduced (3.5 + 0.6)/(80.0 + 12.6%) ($P < 0.001$).

In the animals of group 2 the value of JpH was reduced in all parts of the alimentary tract studied, and so also was the ileocecal gradient (Table 1). In the rats of group 3 the value of JpH increased in the stomach, but in all other parts it decreased, and the gastroduodenal and ileocecal gradients almost disappeared. Similar but more profound structural changes in the JpH profile were observed in the animals of group 4. Consequently, ionol reduced JpH along the whole of the alimentary tract, and immobilization stress had the same effect (except on JpH in the stomach); in response to the combined action of stress and ionol, the effect was potentiated. Assessment of the coagulogram revealed a significant lengthening of the phases of blood coagulation (T_1, T_2, T), with a decrease in V_1 and MA ($P < 0.05$-0.001) in the rats of group 2. Similar changes also were found in the animals of group 3, but they reached their culmination under the combined influence of stress and ionol; T_1 was increased more than tenfold, T_2 fivefold, T 2.6-fold, whereas the decrease in V_1 was threefold and in MA twofold.

TABLE 2. Parameters of FRLO in Tissues of Rats (M ± m)

Parameter	Groups of animals			
	I	II	III	IV
Stomach				
DC	0,32±0,03	0,25±0,01	0,40±0,02	0,34±0,02
P_1		<0,05	<0,05	
P_2				<0,01
P_3				<0,05
MDA	0,10±0,01	0,07±0,01	0,15±0,02	0,06±0,01
P_1		<0,05	<0,05	<0,05
P_3				<0,001
PF	0,19±0,01	0,12±0,02	0,16±0,01	0,11±0,01
P_1		<0,01	<0,05	<0,001
P_3				<0,001
SS-bonds	5,97±0,62	7,40±0,63	8,05±0,69	7,28±0,50
P_1			<0,05	
SH-groups	23,2±1,9	21,4±1,3	19,9±0,9	14,0±0,5
P_1				<0,001
P_2				<0,001
P_3				<0,001
Liver				
DC	0,35±0,03	0,30±0,02	0,54±0,03	0,51±0,06
P_1			<0,001	<0,02
P_2				<0,01
MDA	0,09±0,02	0,06±0,01	0,20±0,02	0,15±0,01
P_1			<0,002	<0,02
P_2				<0,001
PF	0,17±0,01	0,14±0,01	0,23±0,01	0,18±0,01
P_1			<0,001	
P_2				<0,05
P_3				<0,001
SS-bonds	5,69±0,39	8,79±0,75	6,16±0,63	8,19±0,89
P_1		<0,01		<0,02
SH-groups	17,5±1,5	21,2±0,7	26,5±1,2	14,8±1,2
P_1		<0,05	<0,001	
P_2				<0,001
P_3				<0,001

Legend. Parameters of FRLO for DC, MDA, and PF are given in millimoles/g tissue, and for SS-bonds and SH-groups in micromoles/g tissue.

In the animals of group 2 FRLO activity was reduced in the stomach tissues, and the concentrations of SS-bonds and SH-groups in the liver was increased (Table 2). Immobilization stress was accompanied by an increase in the concentration of both intermediate (DC) and end (MDA) products of FRLO in the stomach tissues, accompanied by reduced capacity for PF. In the liver the DC, MDA, and PF levels were raised, and the concentration of SS-bonds in the stomach and of SH-groups in the liver was increased. In the rats of group 4 the DC concentration in the gastric tissues was indistinguishable from normal, and the MDA and PF levels were depressed, whereas in the liver, the DC and MDA concentrations, on the contrary, were increased. The concentration of SH-groups in the stomach was reduced, but the concentration of SS-bonds in the liver was increased. Consequently, intragastric injection of ionol largely prevented stress-induced activation of FRLO in the stomach tissues but had no such effect on the liver.

The end products of FRLO are known to induce specific H^+/OH^- conduction through lipid biomembranes, which, it is suggested, may explain the reduction in the value of JpH in the intestine during stress [1]. The increase in the value of JpH in the stomach is probably connected with rediffusion of H^+ through the epithelial lining [8]. Injection of ionol caused JpH to fall along the whole of the alimentary tract. Similar results have been obtained by the use of α-tocopherol acetate [7], i.e., ability to lower the value of JpH is evidently a specific biological effect of antioxidants. The absence of a protective action of ionol on ulcer formation can be explained by the low value of its constant K_7, because of which ionol cannot compete with tissue antioxidants which, because of antagonism between antioxidants, are the first to be utilized [3]. Hence the decrease in resistance of the gastric mucosa. Inhibition of erosion formation is evidence in support of a different pathogenesis for different kinds of lesions of the gastric mucosa. Potentiation of the formation of petechial hemorrhages by ionol is explained by the hypocoagulation action of the compound.

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EFFECT OF LITHIUM NICOTINATE AND TETURAM ON THE COURSE OF SOME BIOCHEMICAL PROCESSES IN "ALCOHOLIC" RATS WITH INFECTIOUS-INFLAMMATORY LESIONS OF THE KIDNEYS

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KEY WORDS: lithium nitrate; teturam; experimental alcoholism; infectious-inflammatory lesions of the kidneys.

Infectious-inflammatory lesions of the kidneys are commonly associated with alcoholism [6, 9, 11]. There are twice as many urologic patients among alcoholics as among patients with any other disease [10]. An important problem which faces psychiatrists and nephrologists is therefore the search for and rational use of remedies which will not only have a marked depressant action, but will also benefit the course of infectious-inflammatory lesions of the kidneys in alcoholism. The writer showed previously that the new antialcoholic agent lithium nitrate (litonit), unlike teturam (disulfiram), increases the immunoglobulin and nonspecific antibody titers, stimulates release of cationic proteins from leukocytes of the blood and urine, and alleviates morphological disturbances in the kidneys.

The object of this investigation was to study the effect of lithium nitrate and teturam on the course of certain biochemical processes in the kidney tissues of infected "alcoholic" albino rats. Biochemical parameters which not only reflect the effectiveness of antialcoholic agents [5], but also characterize the development of inflammation, tissue damage, tissue function, and resistance to the introduced pathogenic microflora, were investigated, namely: activity of sorbitol dehydrogenase and catalase, intensity of lipid peroxidation (LPO) [3, 8, 14].

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