liver tissue was increased on average by 32-37% ($P < 0.01$) compared with the control. Determination of RP showed the same pattern as determination of pO_2.

It can thus be concluded from these investigations that the biological activity of the lipid extract of silt mud is due to substances concentrated in the polar part. Despite the presence of carotene, the hexane-soluble compounds had no significant biological action and, from the practical point of view, they can be regarded as inert components.

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ROLE OF THE MAJOR (H-2) HISTOCOMPATIBILITY SYSTEM IN THE RESPONSE OF MICE TO ETHANOL

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KEY WORDS: congeneic resistant lines of mice; major histocompatibility system in mice; ethanol.

The search for genetic markers can be undertaken if lines of mice differing in localized regions of the genome are used as biological model [2]. These include congeneic resistant lines (CR lines) of mice, characterized by differences in the major (H-2) histocompatibility system. Convincing evidence of the role of this sytem in the regulation not only of immune, but also of neuromediator, endocrine, and metabolic processes, has been accumulated [7, 10]. Considering the importance of the latter in the pharmacodynamics of ethanol [4, 6], it was decided to study the response of CR lines of mice to a single dose and chronic administration of ethyl alcohol.

EXPERIMENTAL METHOD

Experiments were carried out on male mice weighing 20-35 g belonging to two pairs of CR lines, namely B10·R107, B10·RIII, and A/Sn, A·SW, differing in their H-2 locus, kept on a standard laboratory diet. The progenitors of the lines used in the experiments were obtained from the Research Laboratory of Experimental Biological Models, Academy of Medical Sciences of the USSR.

After a single intraperitoneal injection of ethyl alcohol in doses of 1.0 and 2.5 g/kg, changes in the locomotor activity of the animals were estimated 15, 30, and 60 min after injection in chambers with a photoelectric cell [9]. Parallel studies were made of the motor activity of control animals receiving isotonic NaCl solution. The experiments were carried out from 10 a.m. to 2 p.m., in a period characterized by its ability of the parameter chosen for recording for these particular rodents [3]. The response of mice of the CR lines to a narcotic dose of ethanol (4 g/kg body weight [11]) was determined in "dropping off time" tests, recorded as the time between administration of ethanol and loss of the correct body position reflex by the animals, and the "duration of alcohol sleep," i. e., the time after

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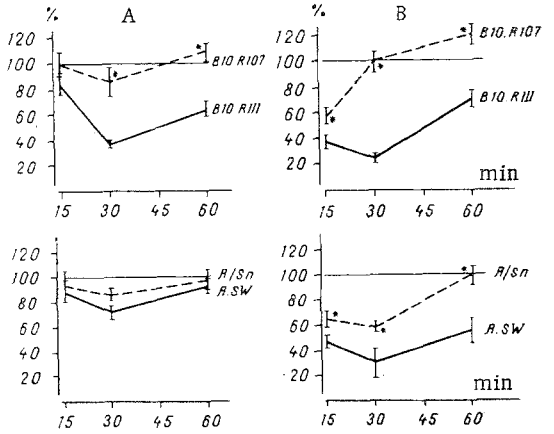

Fig. 1. Changes in locomotor activity of mice of congeneic resistant lines after a single does of ethanol. Dose: A) 1 g/kg, B) 2.5 g/kg body weight. *) Interlinear differences are statistically significant.

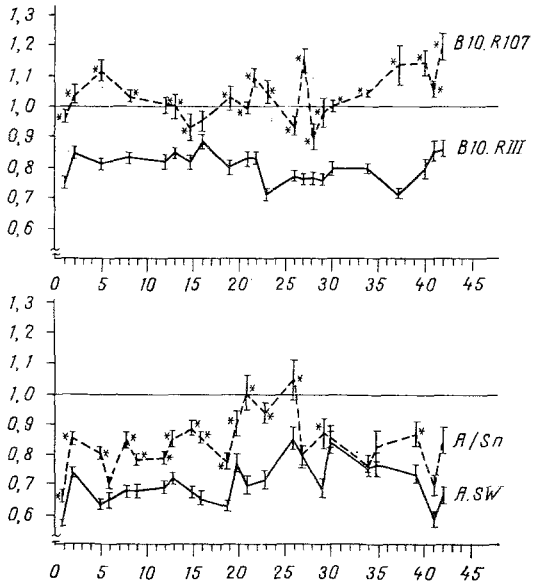

Fig. 2. Ethanol consumption by mice of congeneic resistant lines. Abcissa, duration of alcoholization (in days); ordinate, ethanol consumption (experiment/control). *) Interlinear differences statistically significant.

disappearance of the reflex to its recovery. The level of consumption of 10% ethanol solution by the experimental mice (in the course of 6 weeks) was assessed by comparison with control animals, which were given water.

The experimental results were analyzed by computer in the Medico-Biological Experimental Automatic Control Unit, Central Research Laboratory, N. I. Pirogov Second Moscow Medical Institute.

EXPERIMENTAL RESULTS

Statistically significant differences in locomotor activity of the animals were found after administration of a single dose of 1.0 and 2.5 g/kg of ethanol (Fig. 1). The B10·R107 line proved to be most resistant to the action of alcohol in respect of this parameter. In a dose of 1.0 g/kg alcohol did not change the motor activity of the mice, but in a dose of 2.5

TABLE 1. Ethanol Consumption and Duration of Alcohol Sleep in Mice of Congeneic Resistant Lines

Parameter studied	Line			
	B10.R107 (1)	B10.RIII (2)	A/Sn (3)	A.SW (4)
10% Ethanol (in ml)	1,059±0,015	0,814±0,012	0,830±0,017	0,706±0,014
	$P_{1-2}<0,001$		$P_{2-3}>0,05$	$P_{3-4}<0,001$
Duration of sleep, min	81±5,4	119±5,9	100±10,5	130±9,0
	$P_{1-2}<0,001$		$P_{2-3}>0,05$	$P_{3-4}<0,05$

g/kg it inhibited locomotion after 15 min but the effect disappeared after 30 min. For the B10·RIII line, congeneic (for the H-2 locus) with the B10·R107 line, a considerable decrease in locomotor activity with maximal effect after 30 min was observed in response to both doses. In the case of the second pair of CR lines compared (A/Sn and A·SW) no significant deviation of this parameter from the control level was observed in response to a dose of 1.0 g/kg (Fig. 1). However, with an increase in dose to 2.5 g/kg, an inhibitory action of alcohol was manifested within these lines with a maximal effect after 30 min. In this case statistically significant interlinear differences in changes in locomotion at all points of the experiment indicate that the A/Sn line was the most resistant to the depressive action of ethanol. Differences in the intensity of locomotor activity in animals with an increased intake of ethanol indicate that this effect is dose-dependent.

The "dropping off time" during administration of ethyl alcohol in a dose of 4.0 g/kg did not differ significantly in mice of lines A·SW and A/Sn (86 ± 5.4 and 83 ± 6.6 sec, respectively; $P > 0.05$). This parameter was higher for B10·R107 mice than for B10·RIII mice (81 ± 2.8 and 71 ± 3.4 sec, respectively; $P > 0.05$). Just as during analysis of changes in locomotor activity, these results point to greater resistance of B10·R107 mice to the depressive action of alcohol than of B10·RIII mice.

Lines B10·R107 and A/Sn had the shortest duration of sleep compared with their congeneic resistant B10·RIII and A·SW partners (Table 1). They could accordingly be characterized as most resistant to the narcotic effect of ethanol.

After only a single dose of ethyl alcohol, lines B10·RIII and A·SW thus showed themselves to be alcohol-sensitive compared with their congeneic B10·R107 and A/Sn partners, which were more resistant.

Chronic alcoholization of the animals also revealed differences in the consumption of 10% ethanol in the lines of mice compared. For B10·R107 and B10·RIII lines, for instances, interlinear differences for alcohol consumption were statistically significant throughout the 6 weeks of the experiment (Fig. 2). The higher level of alcohol consumption by B10·R107 mice than B10·RIII justified the description of "drinkers" for them. For the second pair of CR lines compared (A/Sn and A·SW) stable differences were observed during the first weeks of alcoholization, and these were subsequently maintained at individual points of the experiment (Fig. 2).

We were naturally concerned with the problem of the degree of correlation between the sensitivity of the animals to a single dose of ethanol and the consumption of 10% alcohol solution. The duration of alcohol sleep was found to correlate negatively with ethanol consumption of the mice. Further mathematical analysis, in which averaged values of consumption of 10% ethanol were compared with water consumption by mice of CR lines in the course of chronic alcoholization and comparison with durations of sleep revealed clear correlation, which could be expressed in the form of two inequalities B10·R107 > B10·RIII $\approx$ A/Sn > A·SW for the level of alcohol consumption, and B10·R107 < B10·RIII $\approx$ A/Sn < A·SW for the duration of alcohol sleep (Table 1). It must be emphasized that this negative correlation between these parameters was distinct and stable. A similar pattern was discovered previously both for noninbred rats [1] and for pure-line animals [5, 8]. Similar, i. e., negative correlation also was found between the degree of reduction of locomotion after administration of single increasing doses of ethyl alcohol and the quantity of alcohol consumed by mice of CR lines.

Pharmacological tests thus revealed clear differences in the response of CR lines of mice differing in their major histocompatibility system to ethyl alcohol.

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EXPERIMENTAL STUDY OF POLYVINYLPYRROLIDONE BINDING BY LYSOSOMES

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Lysosomotropic agents, which include chlorazine, streptomycin, iron compounds, etc., are a group of compounds which, when administered *in vivo*, are selectively accumulated in the subcellular particles known as lysosomes [4, 8]. Lysosomotropic properties of therapeutic compounds, both negative and positive, have been insufficiently studied; moreover, this effect has so far been virtually ignored both by clinicians and by pharmacologists [8].

Compounds of polyvinylpyrrolidone (PVP) are used in medicine [1, 2, 5, 6]. Low-molecular-weight PBP with mol. wt. 12,600 ± 2700, is a component of the Soviet product Gemodez, used for detoxication purposes [2, 6]. A PVP with average molecular weight (28,000-60,000) is a component of antishock fluids as a plasma expander [5, 6]. A characteristic property of PVP compounds is their marked ability to form complexes [6]; the preparations can bind toxins circulating in the blood stream and eliminate them by excretion through the kidneys [5, 6]. However, the mechanism of action of PVP has not been fully explained. It can be tentatively suggested that binding of PVP with the toxin also takes place in cells of the reticuloendothelial system, the intensive functioning of which leads to detoxication. It has been shown that repeated injections of low-molecular-weight PVP leads to an increase in specific activity of the lysosomal enzyme acid phosphatase [10]. However, binding of the compound with liver cells and changes in the physicochemical properties of lysosomes of the liver cells has not been studied. It can be postulated that the detoxication properties of PVP are largely associated with the affinity of preparations for lysosomes.

The aim of the present investigation was to study the structural and functional properties of lysosomes in rat liver cells after administration of PBP with mol. wt. of 24,000 and 30,000.

EXPERIMENTAL METHOD

Male Wistar rats weighing 180-200 g (15 control and 15 experimental animals) were used. PVP (mol. wt. 24,000, from Ferak, Berlin) was injected daily, intraperitoneally for 3 days at 25 h intervals, in the form of a 6% solution in 0.9% NaCl, in a dose of 3.3 ml/100 g body weight [10]. The animals were decapitated 48 h after the last injection. Intact rats served

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