5. J. R. Kaplan, Eur. Heart J., **8**, 928 (1987).
6. P. Leren, Am. J. Med., **82**, 31 (1987).
7. P. Lindqvist, C. Olsson, C. Nordborg, et al., Atherosclerosis, **72**, 163 (1988).
8. A. N. Orekhov, E. R. Andreeva, V. V. Tertov, et al., Acta Anat. (Basel), **119**, 99 (1984).
9. A. N. Orekhov, V. V. Tertov, and I. D. Vovikov, Exp. Molec. Path., **42**, 117 (1985).
10. A. N. Orekhov, E. R. Andreeva, A. V. Krushinsky, et al., Am. J. Path., **125**, 902 (1986).
11. A. N. Orekhov, V. V. Tertov, S. A. Kudryashov, et al., Atherosclerosis, **60**, 101 (1986).
12. A. N. Orekhov, M. Ya. Ruda, G. N. Baldenkov, et al., Am. J. Cardiol., **61**, 1116 (1988).
13. H. Stegemann and K. Stalder, Clin. Chim. Acta, **18**, 267 (1967).
14. P. J. Whittington-Coleman, O. Carrier, jr., and B. H. Douglas, Atherosclerosis, **18**, 337 (1973).

Laminaria saccharina EXTRACT LENGTHENS SURVIVAL OF MICE DURING ACUTE EXPOSURE TO COLD

Yu. V. Drozd, S. V. Bondarenko, V. V. Yasnetsov, S. G. Batrakov, O. G. Sakandelidze, and V. S. Shashkov

UDC 616-001.18-036.11-092.9-085.322:582 272.462-036.8

KEY WORDS: exposure to cold; survival rate.

Hypothermia in man is a widespread pathological process which in some occupations occurs on a massive scale [1-5]. Under the conditions of the Arctic, Antarctica, and the Far North, even the warmest clothing can maintain a positive heat balance in an ambient temperature of below −12°C only for a strictly limited time [1, 3, 9]. Attempts at pharmacologic correction of cooling have been limited in number, and have included administration of sodium bicarbonate in order to counter cold-induce acidosis [8], vitamin C and protein–vitamin concentrates [3], and sydnocarb with glutamic acid [2]. However, we know that animals living in the polar region, the tundra, and the Arctic Ocean have developed in the course of evolution a combination of protective reactions and adaptive substances, regulating resistance to exposure to cold [1, 5]. These substances include natural antifreezes, which are glycoproteins and glycolipids, that enable Arctic fishes to exist with a blood temperature of −2.2°C [9].

The aim of this investigation was to look for agents against hypothermia among preparations isolated from *Laminaria saccharina,* caught in the Barents Sea.

EXPERIMENTAL METHOD

Experiments were carried out on 100 (CBA × C57BL/6)F_1 mice, divided into five groups with 20 in each group. The pharmacologic agents were injected intraperitoneally 30 min before the experiment began, dissolved in 0.1 ml. The model of acute hypothermia consisted of placing the animals in plastic cages measuring 8 × 8 × 8 cm, which were placed in the Minsk-18 cold chamber at −18°C. Every 15 min the number of animals dying in each group was noted. The preparation isolated from *Laminaria saccharina* (LSP) was the batch end product obtained on crystallization of mannitol from the aqueous solution remaining after distillation of ethyl alcohol from an extract of *Laminaria saccharina.* The LSP was a brown opaque liquid with density 1.28-1.40, pH 3.5-5.0, and containing 40-60% of dry substance. Its composition was as follows: amino acids – asparagine

Institute for Medico-Biological Problems, Ministry of Health of the USSR. Research Laboratory of Biologically Active Substances from Hydrobionts, Moscow. Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 111, No. 4, pp. 383-384, April, 1991. Original article submitted May 7, 1990.

 0007-4888/91/0004-0488$12.50

TABLE 1. Effect of Therapeutic Preparations on Survival Time of Mice Exposed to Acute Cooling (M ± m)

Preparation	Number of animals	Dose	Survival time, min	Per cent of control
Control (physiological saline)	20	0,1 ml, i.p.	136,2±8,3	100
LSP	20	0,1 ml 10 % i.p.	219±21**	161
Ethyl alcohol	20	50 % 0,1 ml, i.p.	119,2±9,0	87
Sydnocarb + glutamic acid	20	30 μg + +400 μg 0,1 ml i.p.	159,6±7,9*	117
Pyrogenal	20	0,1 μg 0,1 ml i.p.	154,8±10,1	114

Legend. *p < 0.05, **p < 0.01 Compared with control (Student's test); i.p.) intraperitoneal injection.

0.24%, threonine 0.45%, serine 0.21%, glutamic acid 3.94%, proline 2.26%, glycine 0.86%, alanine 9.61%, valine 0.61%, isoleucine 0.21%, leucine 0.20%, lysine 0.12%, and arginine 0.23%; the mineral composition was: iodine up to 1 g/liter, Cu 0.1-0.4 · 10^{-3}, Pb 0.4 · 10^{-3}, Ni 0.261 · 10^{-3}, Ag 8-20 · 10^{-5}, Ti 3-4 · 10^{-3}, Zr 1-2 · 10^{-3} of the total weight of the sample.

EXPERIMENTAL RESULTS

It will be clear from Table 1 that LSP was the most effective agent as regards increasing the survival time of the animals, and superior to sydnocarb with glutamic acid, which in experiments on volunteers in an analogous dose per kilogram body weight, increased the length of stay in cold water from 6 to 20 h [2]. Preparations increasing basal metabolism, namely ethyl alcohol and pyrogenal, were either ineffective or had only a weak protective action respectively.

In view of these findings, the further search for new and even more effective preparations against freezing in the organs of Arctic animals and plants is interesting.

LITERATURE CITED

1. D. E. Al'pern, Pathological Physiology [in Russian], Moscow (1965).
2. A. S. Barer, N. G. Lakota, and V. S. Shashkov, Kosm. Biol., No. 6, 66 (1988).
3. V. G. Volovich, Man under Extremal Natural Environmental Conditions [in Russian], Moscow (1980).
4. D. T. Eastman and A. L. De Vries, V Mire Nauki, No. 1, 58 (1987).
5. E. V. Maistrakh, Pathological Physiology of Cooling in Man [in Russian], Leningrad (1975).
6. E. M. Khvatova, E. L. Davydova, and I. I. Mikhalev, Neirokhimiya, **6**, No. 2, 57 (1987).
7. É. Z. Émirbekov, Neirokhimiya, No. 7, 247 (1987).
8. R. H. Bader, J. Appl. Physiol., No. 4, 649 (1952).
9. S. Lutz, Military Med., No. 3, 210 (1957).