Efficiency of Low-Esterified Pectin in Toxic Damage to the Liver Inflicted by Lead Treatment

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Study of the effects of low-esterified pectin in toxic damage to the liver caused by enteral treatment with lead acetate showed that pectin treatment promoted the decrease in lead content in the liver, reduction of LPO activity, and recovery of parameters of lipid metabolism.

Key Words: *liver; lead; pectin*

Lead has a negative impact on the majority of organs and systems, particularly on the nervous, hemopoietic, and endocrine systems and on the kidneys. Accumulation of lead in bone tissue of children impairs the development of the skeleton [1,2,8].

The use of the majority of modern drugs intended for elimination of heavy metal excess from the body is fraught with the development of toxic effects because of low selective activity of these drugs and disorders of electrolyte balance, which can sometimes result in deterioration of patient's condition [10,11]. Alternative drugs with complex-forming activity can be used in practical toxicology. It is primarily the group of substances united by the term "non-starch polysaccharides". An important characteristic of these compounds is their capacity to bind heavy metals [12]. Comparative study of various adsorbents demonstrated that the adsorption capacity of pectin with low etherification degree for lead, copper, cadmium, and mercury is by one order of magnitude higher than that of activated charcoal, microcrystal cellulose, or lignin [6]. The use of this pectin in rats with thyroid gland pathology caused by lead injections promoted a significant improvement of thyroid function [9]. The use of apple pectin in children with excessive mercury content in the body increases hemoglobin and erythrocyte levels, improves differential blood count, and cellular and humoral immunity [5].

We evaluated the efficiency of low-esterified pectin under conditions of experimental lead intoxication in rats.

MATERIALS AND METHODS

The study was carried out on 30 adult outbred male albino rats (150-195 g). The animals were kept in vivarium of Vladivostok Medical University in a separate room at 20-25°C in special plastic cages, 5-6 per cage. All manipulations on animals were carried out in accordance with the recommendations of the Working Group of Federation of European Scientific Associations for Laboratory Animals [3].

Before the experiment the animals were divided into 3 groups. Group 1 animals (control; n=12) received standard diet throughout the experiment. Animals of groups 2 (n=12) and 3 (n=6) received intragastrically (through a tube) aqueous solution of lead acetate (100 mg/kg in conversion to lead) 2 h after feeding daily for 14 days. After 2 weeks, lead treatment was discontinued, arterial blood was collected under light ether narcosis in half of animals in groups 1 and 2, after which the rats were decapitated and the livers were removed. During the subsequent 4 days the remaining animals received only standard diet, after which animals of groups 1 and 2 received

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standard diet and group 3 animals received 1% aqueous solution of low-esterified pectin (50 mg/kg) intragastrically (through a tube) 60 min before feeding for 14 days. After the experiment, the blood was collected under light ether narcosis, the animals were decapitated, and the livers were removed.

Blood levels of total cholesterol and triglycerides were measured. One part of the liver was used for measurements of MDA, reduced glutathione, thiol groups, total cholesterol, and triglycerides, while the other part of the organ was used for measuring lead content. Liver dysfunction was evaluated by the status of the prooxidant and antioxidant systems and parameters of lipid metabolism. The relationships between changes in these parameters, the organ weight and lead content were evaluated.

In order to evaluate the antioxidant system of the liver, the organ was homogenized in 50 mM Tris-chloride buffer (pH 7.8) in a glass homogenizer at 0°C. LPO products were measured in the supernatant. Liver content of MDA was evaluated by a previously described method [14], reduced glutathione as described previously [7], total cholesterol and triglycerides by spectrophotometry [4].

The results were statistically processed by unifactorial analysis of dispersions (ANOVA) with post hoc Tukey's test. The differences were considered significant at $p<0.05$. The results were processed using SPSS 11.0 software.

RESULTS

The content of lead acetate in liver tissue after 2-week intoxication almost 4-fold surpassed that in controls. Liver weight virtually did not change. Accumulation of lead in the liver parenchyma was paralleled by accelerated formation of free radicals initiating LPO with subsequent development of hepatitis. This was confirmed by increased content of MDA and decreased levels of reduced glutathione and thiol groups, which indicated disorders in the antioxidant systems of the liver. Disorders in lipid metabolism manifested in increased levels of total cholesterol and triglycerides in the blood and liver tissue (Table 1).

No appreciable changes in lead content in the liver and in biochemical parameters were detected during the next 14 days (after lead acetate treatment was discontinued). Hence, lead ions were not spontaneously released from the liver and, consequently, toxic hepatitis progressed.

Subsequent 2-week treatment with low-esterified pectin led to an appreciable improvement of virtually all studied parameters. The content of lead in the livers of animals treated with pectin was significantly lower than in untreated animals. The decrease in lead concentration promoted normalization of the studied parameters of the prooxidant and antioxidant systems in comparison with untreated animals. Moreover, some parameters virtually did not differ from those in control animals. Significant signs of normalization of lipid metabolism were noted. Serum concentrations of total cholesterol and triglycerides virtually did not differ from those in control animals (Table 1).

These data indicate that low-esterified pectin effectively stimulates lead release from the viscera with good blood supply and promotes normalization of biochemical parameters of the liver, shifted as a result of toxic exposure to heavy metals. Presumably, low-esterified pectin treatment in exo-

TABLE 1. Effects of Low-Esterified Pectin on Liver Status in Rats with Experimental Lead Intoxication (*M±SEM*)

Parameter	Group, day of analysis				
	1 (14 days)	2 (14 days)	1 (28 days)	2 (28 days)	3 (28 days)
Liver weight, g/100 g body weight	3.520±0.204	3.615±0.152	3.670±0.232	3.682±0.201	3.551±0.189
Lead, μg/g dry tissue	3.6±0.7	12.4±1.8*	3.5±0.5	13.0±1.7*	7.3±1.1*ˣ
Liver MDA, nmol/mg protein	5.03±0.32	9.87±0.26*	3.85±0.34	8.85±0.16*	4.26±0.17ˣ
Glutathione, μg/mg protein	13.43±0.73	6.26±0.36*	12.45±0.45	4.95±0.17*	9.24±0.29*ˣ
Thiol groups, μg/mg protein	48.39±2.28	22.80±1.06*	41.38±1.85	19.34±0.68*	31.67±0.96*ˣ
Total cholesterol, mmol/liter					
serum	1.03±0.05	1.26±0.03*	1.00±0.06	1.32±0.05*	1.09±0.04ˣ
liver	10.35±0.72	14.20±0.34	9.87±0.46	14.80±0.46*	11.86±0.38*ˣ
Triglycerides, mmol/liter					
serum	0.98±0.07	1.11±0.04*	0.81±0.04	1.18±0.06*	1.04±0.03*ˣ
liver	15.73±0.54	19.09±0.40*	13.38±0.47	17.77±0.68*	14.37±0.53ˣ

Note. $p<0.05$ compared to: *group 1, ˣgroup 2.

genous lead intoxication will promote a reduction of lead concentrations in all viscera, including the brain and bone system. This hypothesis should be experimentally verified.

REFERENCES

1. Yu. E. Vel'tishchev, *Pediatriya*, No. 4, 26-33 (1995).
2. N. N. Klimkovich, T. I. Kozarezova, E. I. Slobozhanina, and L. I. Volkova, *Ibid.*, No. 2, 58-62 (1998).
3. R. E. Kopaladze, *Uspekhi Fiziol. Nauk*, No. 4, 74-92 (1998).
4. N. I. Portyanaya, B. G. Osipenko, P. A. Moskadynova, and N. K. Novokhatskaya, *Biochemical Studies in Toxicological Experiment* [in Russian], Irkutsk (1990).
5. M. B. Sobolev, S. B. Khatskel', and A. Yu. Muradov, *Vopr. Pitaniya*, No. 8, 28-30 (1999).
6. Yu. S. Khotimchenko, A. V. Kropotov, and M. Yu. Khotimchenko, *Efferent. Ter.*, No. 4, 22-36 (2001).
7. M. E. Anderson, *Methods Enzymol.*, **113**, 548-553 (1985).
8. I. A. El-Safty, A. M. Afifi, A. E. Shouman, and A. K. El-Sady, *Arch. Med. Res.*, **35**, No. 1, 59-65 (2004).
9. M. Khotimchenko, I. Sergushenko, and Y. Khotimchenko, *Environ. Toxicol. Pharmacol.*, **17**, 67-71 (2004).
10. C. D. Klaassen, *The Pharmacological Basis of Therapeutics*, McGraw-Hill, New York (1996).
11. W. J. Rogan, *Pediatr. Rev.*, **48**, 593-599 (2000).
12. H. E. Rose and J. Quarterman, *Environ. Res.*, **42**, 166-175 (1987).
13. K. Yagy, *Methods in Enzymology*, New York (1984).