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NATURAL OCCURING ORAL CHELATORS AGAINST LEAD AND COBALT TOXICITY

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It is known that exposure to cobalt-contaning dust is associated with the development of lung disease characterized in its extreme by a potential fatal interstitial fibrosis. At the same time, exposure to lead causes hematological, gastrointestinal, and neurological dysfunctions. However, despite the difference in their toxic manifestations, both metals seem to be able to stimulate the overproduction of free radicals and destroy endogenous antioxidants. Therefore, it may be suggested that damaging free radical-mediated processes can mainly or partly be responsible for the toxic effects of both cobalt and lead. Early, we have shown [1,2] that Japanese health food supplementation Bio-normalizer (a natural nontoxic substance possessing antioxidant and chelatory properties) can control free radical-mediated processes in the *in vitro* and *in vivo* systems. Because of that, we have studied the possibility of application of Bio-normalizer for suppressing the toxic activities of cobalt and lead in humans and animals.

The toxic effects of cobalt were studied in animal model of lung injury. Cobalt sulfate was injected intratracheally to male Wistar rats, which then were sacrificed on 1st, 3d, 7th days. Simultaneously, cobalt injections were given to rats, which were fed with Bio-normalizer (BN). In all cases animal survival, cobalt-induced lung edema, and the

parameters of rats free radical status (GSH content, erythrocyte and leukocyte SOD activities, and oxygen radical release by leukocytes and alveolar macrophages) were determined.

As it should be expected, in all cases the administration of cobalt sulfate to rats resulted in acute toxic effects. Intracheal instillation of cobalt sulfate decreased the survival of rats by more than 50%. Feeding rats with BN after cobalt administration sharply increased the survival rate in the last 3 days. In contrast, BN administration before Co instillation suppressed its toxic effect in the first 3 days. Cobalt administration to rats induced lung edema that achieved a maximum already on 3th day; BN administration diminished it by 15-20% to the end of the experiment.

In contrast to previous findings obtained with cobalt instillation to hamsters [3], we found that cobalt sharply increased GSH level in the rat lung. BN administration enhanced sinergistically GSH level in the cobalt-treated animals. SOD activity in erythrocytes of cobalt-treated rats decreased by 1.5-2 times in comparison with control animals, but BN admistration temporary restored SOD activity on the 3d day. SOD activity in leukocytes practically was not affected by Co instillation. Cobalt administration significantly enhanced oxygen radical release by leukocytes (measured by lucigenin-amplified chemiluminescence, CL) and decreased CL produced by alveolar macrophages. BN suppressed both inhibitory and stimulatory effects of cobalt (Table 1). This finding possibly shows the most important beneficial effect of this nontoxic natural substance because BN turns out to be able to suppress the inflammation stimulated by leukocytes and increase the phagocytic activity of macrophages.

Table 1

Lucigenin-amplified CL by leukocytes and alveolar macrophages from Co-treated rats

	CL intensity in leukocytes (mV)	CL intensity in alveolar macrophages (mV)
Control rats	44±15	146±35
Co-treated rats	75±20	82±16
Co-treated rats + BN	56±10	134±25

In the second part of this work we investigated the effects of BN administration to patients with chronic lead intoxication. For this purpose, a phase II double-blind case-controlled randomized clinical trial has been performed with 40 patients (manual workers in radio industry, printing, glass and electric charge battery manufacturing and liquidators from Chernobyl atomic power station), having lead blood content about 0.4-0.6 mg/L. Experimental group was divided into 3 subgroups: the patients of Group A were given 3 g BN a day, the patients of Group B were given 6 g BN a day, and the patients of Group C were given 9 g BN a day. The control group patients were given 3 g sugar powder a day as a placebo.

It was found that the consumption of BN was not associated with any adverse effects in patients; on the contrary, the clinical conditions of most patients were improved. Chelatory effect of BN was dose-dependent: the administration of 6 g BN a day to patients of Group B significantly enhanced lead level in the blood (Table 2), while there was no change in the lead level of the patients of Groups A and C. Interestingly, that the patients of Group B are also characterized by the diminished ALA and coproporphyrin contents, the parameters of lead-induced damage. Therefore, this dosage seems to be optimal in combating the consequences of lead intoxication.

Table 2

The effect of BN administration (6 g a day) on the lead blood level and the parameters of lead-induced damage

	Pb content in the blood (μM/L)	ALA (μM/g creatinin)	Coproporphyrin (mM/g creatinin)
Before BN treatment	2.04±0.95	12.1±2.8	107±20
After BN treatment	3.56±0.95	9.7±2.5	80±15

Thus, we concluded that due to its chelatory and antioxidant activity, BN is capable of mobilizing lead from the organism's storage, removing it from the organism, and improving impaired porphyrin metabolism of patients with lead intoxication.

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