

INFLUENCE OF DIETHYL (DITHIOL) ANTIDOTE UNITHIOL UPON SOME HAEMATOLOGICAL INDEXES OF SUBCHRONICAL MERCURY INTOXICATION

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Our previous investigations (Jeljazkov D. et al. — 1978) show that Unithiol applied to rats in a double molar ratio to the single lethal doses of mercury bichloride, prevents mortality and makes the determination of LD₅₀ of the mercury compound impossible.

The effectiveness of Unithiol, applied in a double molar ratio to the mercury ion, was studied in rats with subchronical mercury intoxication concerning a great number of biochemical and morphological indexes. The influence and effect of antidote upon some of the basic haematological indexes related to erythropoiesis and subjected to a continuous application of mercury and its compounds, is the object of the present study. The conditions for the experiment are a subchronical intoxication with mercury bichloride (Oronshnikova et al. — 1971; Laskavaya et al. — 1971).

Material and methods

The study covers 197 male white rats with average weight 150—200 gm divided into groups: Ist — control; IInd — regularly injected with 0.38 mg/kg Unithiol i. m. for a period of 45 days; IIIrd — 0.25 mg/kg mercury bichloride s. c. for 45 days — the dose is $1/30$ LD₅₀ of the same compound for the same animal and way of application (Department of Pharmacology, Jeljazkov D. et al. — 1978); IVth — treated in the same way and period with 1 mg/ml mercury bichloride ($1/7.5$ LD₅₀ of mercury bichloride); Vth — treated with mercury bichloride, in the way the animals of the IIIrd group are treated, combined with applying of Unithiol 0.38 mg/kg i. m. to supply a double molar ratio of Unithiol to the injected quantities of mercury bichloride; VIth — treated with 1 mg/kg mercury bichloride and 1.55 mg/kg Unithiol i. m. in the same ratio.

4—6 animals of each group were killed periodically (on the 7th, 15th, 30th and 45th day of the experimental beginning) and the following indexes were studied: Hb-quantity, Erythrocyte-number, Reticulocyte-number, Haematocrite. The same was done 30 days (animals treated with 0.25 mg/kg mercury bichloride) and 60 days (animals treated with 1 mg/kg mercury bichloride) after the treatment was over.

Results and discussion

The doses of 0.25 mg/kg and 1 mg/kg mercury bichloride do not induce any considerable changes of the Hb-quantity (fig. 1). 0.25 mg/kg causes statistically unreliable tendency of Hb-quantity decrease until the 5th day

of the treatment. 1 mg/kg causes changes similar to the control group. Unithiol itself induces moderate amplitudes of Hb-quantity about the control value (fig. 1). When applied in combination with mercury bichloride (0.25 mg/kg), the Unithiol compensates the comparative Hb-decrease, under the

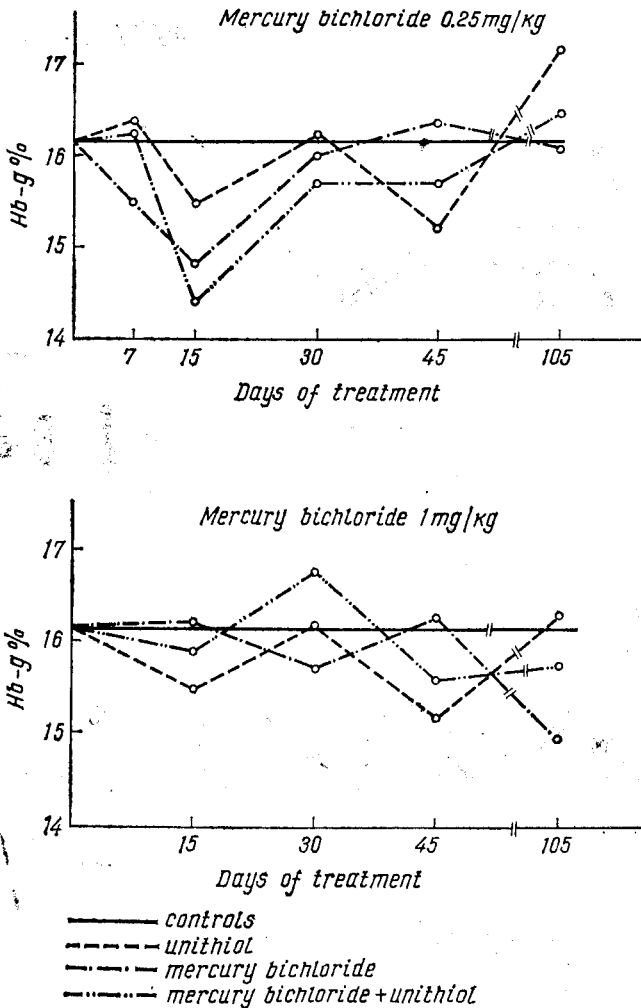


Fig. 1: Haemoglobin in mg%

influence of mercury bichloride, on the 7th day. If the dose of mercury bichlorides is 1 mg/kg, the Unithiol (similar to the single application of mercury bichloride) does not cause considerable changes of Hb-values in all investigated intervals.

0.25 mg/kg mercury bichloride induces a statistically reliable decrease of the erythrocyte-number on the 7th and and 30th day of the treatment, while on the 45th day a statistically reliable increase is registered (fig. 2).

The bigger dose of mercury bichloride causes greater number of erythrocytes (above the control) on the 30th and 45th day. Single application of Unithiol causes amplitudes very near to or above the control values. The combined application of Unithiol and mercury bichloride (0.25 mg/kg) induces stati-

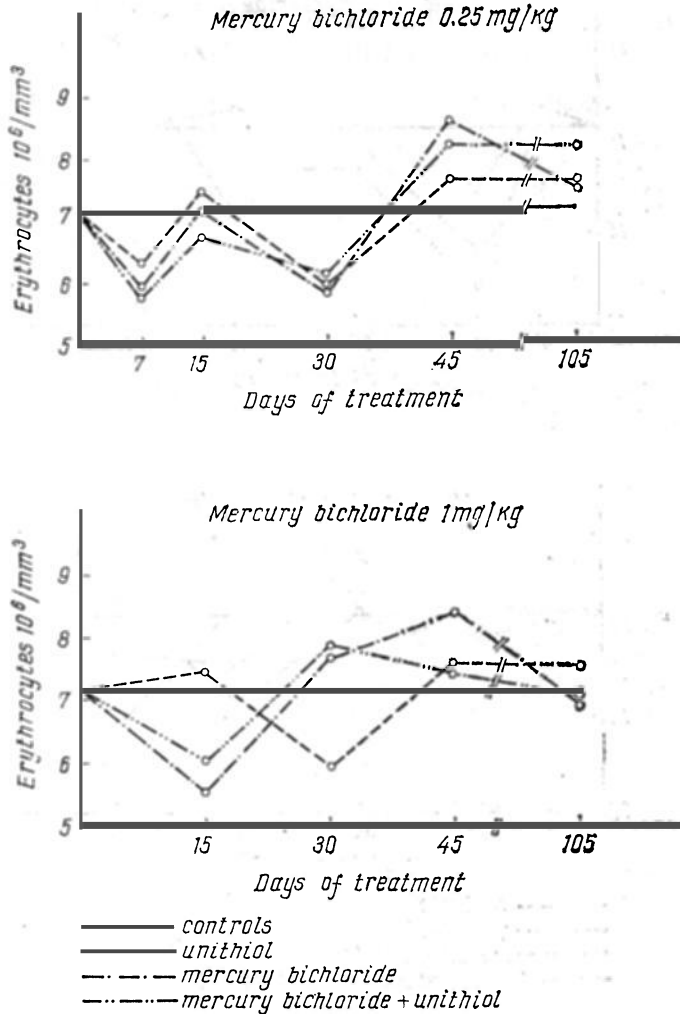


Fig. 2: Erythrocytes in mln/mm³

stically unreliable changes of the erythrocyte-number on the 30th and 45th day (fig. 2). The bigger dose of mercury bichloride and Unithiol in combination causes changes of the erythrocyte-number, similar to those under the influence of mercury bichloride only (until the 30th day), but after that (until the 45th day) the increase is statistically unreliable.

0.25 mg/kg mercury bichloride induces considerable (but statistically unreliable) changes of the haematocrite-values (fig. 3). Unithiol alone causes

slight amplitudes. The combination Unithiol and mercury bichloride (0.25 mg/kg) does not influence the changes caused by mercury bichloride only (until the 30th day). The haematocrite-value is the same with that of the control (45th day). 1 mg/kg mercury bichloride induces statistically reliable

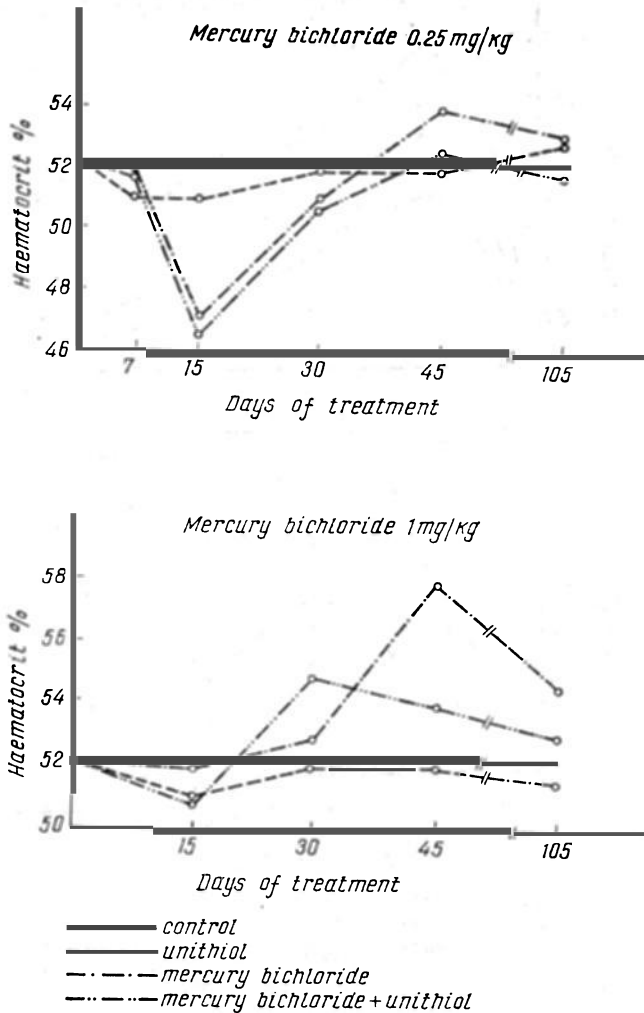


Fig. 3: Haematocrite in %

increase of haematocrite on the 45th day. The influence of Unithiol reduces the increase considerably (fig. 3).

Concerning the reticulocyte-number, a dose of 0.25 mg/kg mercury bichloride causes a considerable (statistically reliable) increase in all investigated intervals, including 30 days after the treatment itself is over (fig. 4). The combination of Unithiol and mercury bichloride makes the reticulocyte-number lower (nearly twice) in all intervals, which is very similar to the influence of the Unithiol alone.

1 mg/kg mercury bichloride increases the reticulocyte number but not so expressed as the dose of 0.25 mg/kg does. The combination with Unithiol in this case also induces an expressed reduction of the studied effect (fig. 4).

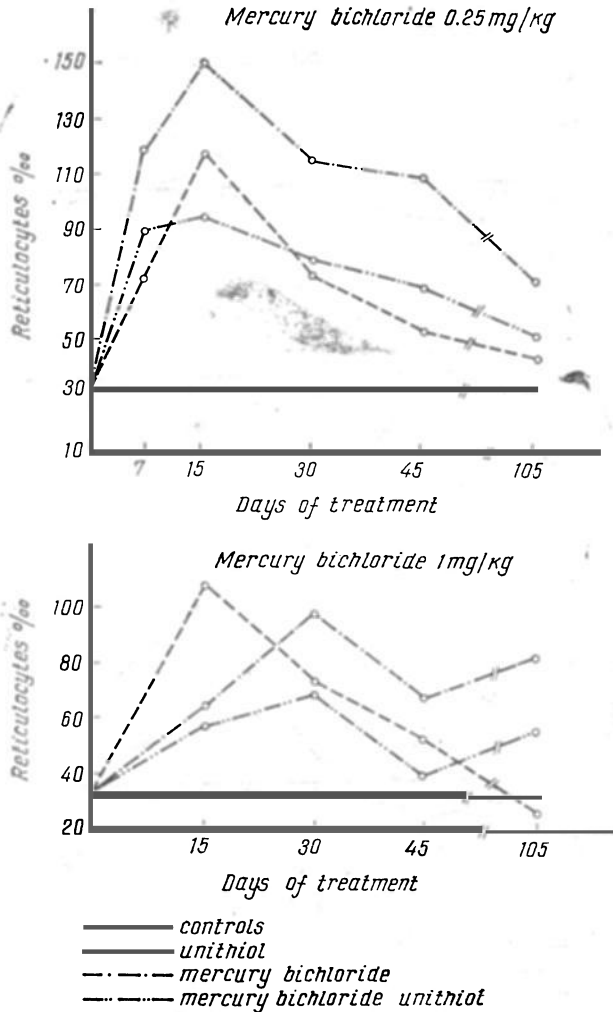


Fig. 4: Reticulocytes in %

The experimental data show the comparatively slight effect on the Hb-quantity, erythrocyte-number and haematocrite, concerning the treatment with both doses of mercury for a period of 45 days. The investigated amplitudes of the indexes under study, although statistically reliable at certain points, are about the physiological ones. The applying of Unithiol under these conditions is expected to be ineffective concerning considerable changes of the values. However, our results show a positive effect of the antidote upon Hb during the initial period of intoxication with 0.25 mg/kg mercury

bichloride. A positive effect of the antidote on the erythrocyte-number influenced by both doses mercury bichloride is also registered, because most of the cases have statistically unreliable changes after its application. The same is found for the haematocrite-values and their amplitudes at final stages of the treatment. Concerning the reticulocyte-number, however, which is most influenced by mercury bichloride, the effect of the antidote is considerably expressed.

The similar effect of Unithiol, applied in a same molar ratio to mercury ions, when there is an intoxication with both doses mercury bichloride, shows the necessity of a proper dose Unithiol itself, corresponding to the eventual quantities of mercury bichloride in the organism. Concerning the investigated indexes, our study establishes the effectiveness of a double molar ratio of antidote to mercury ion.

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ВЛИЯНИЕ ДИТИОЛОВОГО АНТИДОТА УНИТИОЛА НА НЕКОТОРЫЕ ГЕМАТОЛОГИЧЕСКИЕ ПОКАЗАТЕЛИ ПРИ СУБХРОНИЧЕСКОЙ РТУТНОЙ ИНТОКСИКАЦИИ

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РЕЗЮМЕ

В ходе исследования предохраняющего действия унитиола при субхроническом введении крысам двухлористой ртути было изучено влияние антидота на содержание гемоглобина, на число эритроцитов и ретикулоцитов и на количества гематокрита.

Двухлористая ртуть вводилась в дозах 0,25 мг/кг и 1 мг/кг в течение 45 дней. Унитиол вводился в количествах, обеспечивающих двойное молярное соотношение сульфидрильных групп по отношению к ртутному иону. Показатели прослеживались периодически во время затравки и восстановительного периода (один и два месяца).

Установлено подобие в изменениях, вызванных самостоятельным применением использованных доз двухлористой ртути и их комбинаций с унитиолом по отношению к содержанию гемоглобина, количеству эритроцитов и гематокрита. Установленные изменения находятся в интервалах физиологических норм для данного вида животных.