

## **EXAMINING ALKALI PHOSPHATASE ACTIVITY AFTER APPLYING THREE INCREASING DOSES OF SULFADIMIDINE IN RATS**

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### **Summary**

In this work we examined the toxicity of sulfadimidine sodium that was administered to Wistar strain through drinking water supplemented with three increasing doses (0.066%, 0.2% and 0.6%) during 8 weeks. We observed the influence of this treatment on creating alkali phosphatase in blood sera of the rats. The trial was carried out on 96 female rats Wistar strain, body weight ranging from 172.6 to 179.5 g. The rats were divided in 4 equal groups, out of which one was a control group. Weeks 2, 4, 6 and 8 of the experiment were used as time for observing alkaline phosphatase. Based on the experiment and the obtained results it can be concluded that sulfadimidine sodium administered in drinking water, as a therapeutic dose, but also in three time lower concentration, resulted in the changes of alkaline phosphatase activity in blood sera of the rats, but its intensity depended on the doses. However, alkaline phosphatase concentration in the control group, that received the highest tested concentration of the drugs, was significantly higher than the findings in the control group and other two experimental groups of the animals.

Sulfonamides have a wide spectrum in the treatment of intestinal infections, poultry coccidiosis, bacillary dysentery in humans, urinary and meningeal infections, primary and secondary pneumonia, actinobacillosis as well in treating of the infections caused by staphylococcus, streptococcus and pneumococcus that are resistant to the antibiotics (1, 2, 4). The wide application of sulfonamide in human and veterinary medicine resulted in undesired effect and toxicity of these chemotherapeutics. The unwanted acute effect of sulfonamide was registered in the application of recommended doses for cattle and dogs, as well as chronic toxic effect on the lungs, nervous system, elements of blood, skin and reproductive process in the treated animals (6,7).

Our goal was to examine the effect of sulfadimidine sodium on the organism of a mammal in therapeutic and higher doses, having in mind that this chemotherapeutic has not been sufficiently tested on the rats. Its unwanted effect and toxicity were examined on some animal species and, after shorter or longer period of administration, the changes were observed like, for example, suppression of saprophyte microflora, loss of appetite, reduced gain, diarrhoea, lethargy, uncoordination, leucopenia, renal damages and many others (10,11,12).

### Materials and methods

The trial was carried out on 96 male rats of Wistar strain (7 weeks old) in strictly controlled laboratory conditions. From littering until the time of the trial all the rats were kept under the same regime of nutrition and care. Also in the trial we used the preparation "Sulfadimidine sodium" ad us. vet, a dilution containing 16% of the active substance. The rats were divided in four equal groups, out of which one was a control, untreated group (K). The experimental groups were given sulfadimidine sodium in drinking water during 8 weeks, in concentrations of 0.066% (administered to the experimental group O-I), 0.2% (administered to the group O-II) and 0.6% (O-III). During the experiment the rats were fed with "Food for laboratory rats" and were given water *ad libitum*. In the intervals of 2 weeks (weeks 2, 4, 6, and 8) in the control and the experimental groups, six rats were sacrificed. The blood was punctuated from the heart and than centrifugated (15 min at rotation of 3000) with the aim to abstract sera. The obtained sera was used for determining alkali phosphatase on a SMAC (Segmental Multiple Analysis plus Computer).

### Results

In Table 1 are displayed the variation in the average concentration of alkali phosphatase in blood sera in rats, both in the control group and in the groups treated with 0.066% and 0.2% concentrations of sulfadimidine sodium in drinking water. No statistically important difference was observed.

In the rats that were administered 0.6% of sulfadimidine sodium in drinking water (O-III), concentration of the alkali phosphatase in blood sera developed to a statistically important level ( $p < 0.05$ ) up to the second week what is higher than the findings in K, O-I and O-II. High activity of this enzyme in the sera of rats belonging to O-III group remained, with certain variations, until the end of the trial, when it was significantly above the findings in K ( $p < 0.01$ ) and O-I ( $p < 0.05$ ). On the sixth week of the trial the concentration of alkali phosphatase in the rat sera from this experimental group was significantly above the results in the animals from the group K ( $p < 0.01$ ), O-I ( $p < 0.01$ ) and O-II group ( $p < 0.05$ ).

**Table 1.**  
**Influence of sulfadimidine sodium administered in drinking water (0.066%; 0.2%; 0.6%) on concentration of alkali phosphatase (U/l) in blood sera of the rats**

Weeks	Control group	0.066 % (O-I)	0.2 % (O-II)	0.6 % (O-III)
2	310.5± 67.4	293.3± 79.5	308± 67.4	462.5± 126.3 a,b,c
4	262.3±130.4	247.7±104.7	264.2± 56.1	207.4± 89.1
6	274.3± 33.2	247.2± 78.0	220.8± 53.4	437.3 ±100.0 aa,bb,c
8	191± 84.6	232.3±141.8	189.3± 280	409.8±114.0 aa,b

\*Values expressed as X ±SD;

- a – statistically important difference comparing to the control findings (a-p<0.05; aa-p<0.01);  
b – statistically important difference comparing to the findings in O-I (b-p<0.05; bb-p<0.01);  
c – statistically important difference comparing to the findings in O-II (c-p<0.05).

### Discussions

Alkali phosphatase can be found in all the tissues and organs, especially in mucous membrane of duodenum, bones, gristle, liver, kidneys, prostate and spleen. This enzyme catalase synthesis and the hydrolysis of ester phosphorous acid in alkali environment. Phosphorization and dephosphorization are the most important metabolic processes, therefore they have a key role in an organism. Namely, phosphatases are primarily intracellular enzymes and their concentration in plasma increases only when a larger number of the cells is damaged or enzyme synthesis shows abnormal increase. In our experiment there was a significant increase in concentration of this enzyme observed in the rats that were administered three time higher doses of sulfadimidine in weeks 2, 6 and 8. The similar results were obtained by Atef et al. (13,14) after repeated application of the sulfadiazine oral does in the rabbits. The highest activity of alkali phosphatase was observed in the experimental weeks 4 and 8. Also, in our experiment low activity of alkali phosphatase was recorded in all the experimental groups, but reached no statistically important difference. According to some authors (5,8) besides antimicrobial activity, sulfonamide can be a strong inhibitor for alkali phosphatase. The mechanism of inhibition is based on the binding with zinc that is a constituent part of the active form of enzyme for sulfonamide nitro group. The consequence is a transfer of the active enzyme into an inactive form. This pharmacology mechanism may probably explain the reduced enzyme activity in certain intervals in our experiments.

### Conclusions

Sulfadimidine sodium, continually administered in the drinking water, for therapeutic purpose but also in three times lower and higher concentration, caused changes in alkali phosphatase activity in the blood sera of the rats and the intensity of these changes was correlated to the doses. A significant increase of activity was observed in the groups that were given higher doses of sulfadimidine in the weeks 2, 6 and 8 of the experiment, both in the control group and in the remaining two experimental groups.

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