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(Translated by Ostertag)

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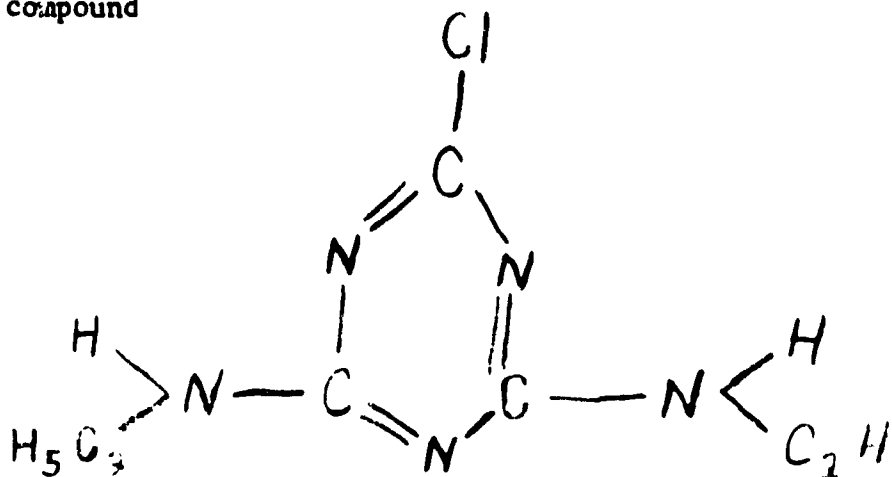
ON THE TOXICITY OF "SIMAZIN", A HERBICIDE PREPARATION

[Following is a translation of an article by A. V. Kovalenko and V. V. Svyatoslavova (Saratov), Institute of Rural Hygiene, published in the Russian-language periodical Gigiyena Truda i Professional'nyye Zabolevaniya (Industrial Hygiene and Occupational Illnesses), 7(5), 1963, pages 54-56. Translation performed by Sp/6 C. T. Ostertag Jr.]

Recently, works on the study of the herbicidal activity of heterocyclic amines (derived triazines) have acquired particular importance. According to facts from native and foreign investigators these preparations are extremely effective against annual and some perennial weeds. One of the main representatives of this group, simazin (systemic herbicide), destroys the majority of monocotyledonous and dicotyledonous weeds. According to the evidence of Yu. I. Shillinger, Bartley, and Domenjoz, simazin is mildly toxic for mice, rats, chickens, and pigeons; upon the introduction into the stomachs of a dose of 5g to 1 kg of body weight, half of the experimental animals and birds perish. Information concerning the toxicity of the preparation under the conditions of an inhalation experiment we haven't encountered. We studied the toxicity for laboratory animals (mice, rats, rabbits) of native simazin and the Swiss preparation of the firm Geiga during its action through the digestive and respiratory tracts and through the skin.

Simazin-2-chloro-4,6-bis(ethylamino)-s-triazine ($C_7H_{12}N_5Cl$) is a white crystalline powder, melting point 207° , $d_{20} = 1.0956$, poorly soluble in water and organic solvents, and almost odorless.

This compound



is very stable, the chlorine atom converts into a hydroxyl under the action of strong bases or acids at a high temperature. The preparation is issued mainly in the form of a wetting powder of a 50% concentration which includes a 2% OP-10 emulsifier, 3% sulfite lye, and 45% kaolin (nameplate data from the NIUIF laboratory, S. S. Kukalenko). [NIUIF -- Nauchnyy Institut po Udobreniyam i Insektofungisidam (im. Ya. V. Samoylova), Scientific Research Institute of Fertilizers and Insectifuges.] In the field simazin is used in the form of an 0.5 - 3% aqueous suspension.

The toxicity of the native and foreign preparation for rats is almost the same. The LD_{50} , obtained by the probit-method*, is correspondingly 1390 ± 218 and 1900 ± 260 mg/kg. From the results of computing the reliable limits it follows that the difference of the toxic effect on rats of the native and foreign preparation is insignificant. [*Probit is a literal transliteration from the Cyrillic. It evidently comes from the verb probivat' (to puncture or perforate) or probovat' (to test or sample).]

The clinical picture of acute poisoning by simazin testified to the affection of the central and vegetative nervous system and also the parenchymatous organs. Depending on the dose received, death began in 24 hours, 48 hours, and at the latest, on the fourth day. Histological changes in the organs of animals which perished in the first hours or day amounted to a sharply expressed plethora of the internal organs. In animals which died in later periods, in place of vascular disorders, deep dystrophic changes took place, plethora was noted in the lungs along with general hemorrhage and edema.

In a series of experiments, directed at clearing up the possibility of cumulative effects of simazin when introduced into the stomach, 30 mice and 26 rats were used. The animals were divided into three groups: One was a control group, the other two received daily for 30-50 days $1/10$ and $1/20$ of a LD_{100} preparation. The control group in this period received the corresponding volume of water.

The rats turned out to be the most sensitive to the repeated administration of simazin. The weight, especially of those to whom 1/10 of the LD₁₀₀ (200-250 mg) was administered daily, initially in the course of 2-3 weeks steadily decreased (an average of 15% of the original). In individual animals, it periodically increased due to developing edemas. Changes were also observed in the peripheral blood. By the end of the experiment, when the rats on the whole had received around 10g of substance, the average erythrocyte content in comparison with the original amount was reduced to 1.76 million ($m = \pm 0.54$, $P < 0.05$). In this same period a tendency to the lowering of hemoglobin was observed. In regard to the white blood the displacements led to statistically reliable accumulation of the amount of ion forms of neutrophils with an insignificant increase of the general number of leukocytes (the average difference in the content of ion forms in comparison with the initial amount was 31%; $m = \pm 5.09$, $P < 0.05$). The displacement of the leukocytic profile turned out to be more stable and was observed two months later after the cessation of the experiment.

Out of 26 rats in the specified series of experiments, 4 died which had received on the whole from 2.3 to 5.3 g of simazin (accumulation coefficient 1.2 - 2.8). In these animals they detected interstitial bronchopneumonia, hemorrhage and edema of the lungs, plethora of the organs of the abdominal cavity, and deep dystrophic changes in the liver, kidneys and cardiac muscle. Precisely the same changes were detected in the organs of animals which were slaughtered a week following the cessation of the oral administration of the herbicide. After two months the dystrophic changes in the organs of rats being investigated which were slaughtered by decapitation, were weakly expressed or lacking. Mice which were in an identical experiment didn't die and only somewhat of a lag in their gaining of weight was noted.

With the application of an aqueous suspension of simazin to the skin of rabbits (by the generally accepted method for 30 days), reactions indicating the resorptive effect of the preparation weren't noted. The applications were carried out on 8 rabbits of which 4 served as control. The dose of simazin was 500 mg/kg. The local reaction came to a light hyperemia which disappeared in 15-30 minutes after removing the application.

Several series of inhalation experiments were conducted with various concentrations of a native and Swiss preparations. Altogether, including the control, 8 rabbits and 100 rats were used. The disturbances originating in the organism of the rats by the repeated inhalatory influence of simazin in concentrations from 0.58 to 1.31 mg/l were so profound that they led to the death of some of the animals. In concentrations of 0.3 - 0.5 mg/l the toxic effects of simazin came to an irritation of the upper respiratory tracts, increased diuresis, and a slowing down of weight gaining and also to hematological displacements and pathohistological changes, detected in the organs of rats which

were slaughtered a month after the termination of the inhalations. In rabbits the specified concentrations didn't show a toxic effect. During the prolonged influence by simazin in concentrations of 0.05 - 0.1 mg/l, the variation of the indices of peripheral blood didn't go beyond the limits of the physiological norms and were observed only in the beginning of the experiment, and increases of weight in the experimental rats proceeded far more intensely than in the control.

Hygienic observations, conducted by T. K. Voskanova during the manual and tractor spraying methods in industrial testing of the herbicide, showed that in the zone of respiration of the workers, the concentration fluctuated in the limits of 0.35 - 0.53 mg/l. Upon examination of persons working with simazin, disruptions of physiological functions didn't develop, excluding the tendency toward the lowering of sensitivity of the olfactory analyzer.

Conclusions

1. Simazin is a mildly toxic substance, the danger of acute poisoning by it is not great.
2. Simazin is capable of exerting a toxic effect when taken through the organs of the respiratory and digestive tracts. Its effect on the skin doesn't present a serious hazard.
3. Simazin possesses a comparatively weak capability for accumulation.
4. From a hygienic point of view this herbicide may be used in agriculture.

Footnote¹. Pathohistological investigations performed by S. A. Stepanov.