A study of the effects of the polypropylene glycols on intermediary carbohydrate metabolism showed that these compounds have no direct inhibitory action on anaerobic glycolysis, but all three exerted an inhibitory effect on the oxidative phase of the process. At the 5×10^{-3}M concentration polypropylene glycol 425 produced approximately 44 per cent inhibition; polypropylene glycol 1025, 64 per cent; polypropylene glycol 2025, 75 per cent. No attempt was made to localize further the exact site of this action, other than the work with succinic dehydrogenase noted above. The involvement of this enzyme does not fully explain the results obtained on aerobic glycolysis since the dehydrogenase was unaffected by polypropylene glycol 425 in the concentration used, whereas the oxidative process was inhibited to the extent of about 44 per cent.

In testing the influence of these compounds on aerobic glycolysis, all the components of the reaction mixture except the tissue were added to the main compartment of the Warburg vessel and equilibrated for 10 to 20 minutes in the water bath before the homogenate was added from the side arm. Manometer readings were taken approximately two minutes after tipping in the homogenate, and again at 10 minute intervals thereafter for a total of 40 minutes. Under these conditions, there was a progressive increase in the amount of inhibition exerted by each of the polypropylene glycols. The figures given above represent maximal inhibition, based on the last observation period. In a separate set of experiments, the inhibitor (polypropylene glycol 425) was incubated with the homogenate in the side arm for a period of 20 minutes before mixing with the contents of the main compartment; however, this preliminary incubation did not appreciably increase the degree of inhibition in the initial periods of measurement.

This progressive increase in inhibitory activity was observed with polypropylene glycol 1025 acting on the succinoxidase system. The situation is comparable to that of a compound studied by Herrmann and DuBois.[15] The explanation advanced by these authors, namely, that the tissue is capable of effecting a change in the test material resulting in the production of an inhibitory substance, would seem to be applicable in the present case.

SUMMARY

Three polypropylene glycols of mean molecular weights of 425, 1025, and 2025, respectively, have been studied. These exhibited considerable acute toxicity by the oral, intravenous, and intraperitoneal routes, as compared with propylene glycol and the polyethylene glycols. Toxicity was greatest in the case of the compound of intermediate molecular weight (1025). Lethal single doses administered to rats produced hyperexcitability of the central nervous system, as evidenced by tremors or convulsions, with death occurring from respiratory arrest during convulsive seizures.

The toxicity of these compounds by the cutaneous and respiratory routes was low. Skin irritation was minimal, and eyes were not injured by the undiluted materials.

The ability of certain members of this series to produce ventricular extrasystoles in the anesthetized dog has been confirmed. Data are presented on the extent to which these compounds are absorbed from the gastrointestinal tract of the rabbit, together with some information on the nature of the urinary excretory product. Their behavior toward certain isolated enzyme systems is reported.

15. Herrmann, R. G., and DuBois, K. P.: The Effect of p-Dimethylaminobenzenediazo Sodium Sulfonate (DAS) on the Enzymatic Reactions of Intermediary Carbohydrate Metabolism, J. Pharmacol. & Exper. Therap. **95**:272-284, 1949.