

Shideman³ of the cardiac effects of a polypropylene glycol and dipropylene glycol methyl ether, respectively. The polypropylene glycol used had an average molecular weight of 750 and produced ventricular extrasystoles when administered intravenously to the anesthetized dog in total amounts ranging from 10 to 90 mg./Kg. Dipropylene glycol methyl ether was found to be a central nervous system depressant of relatively low toxicity. Injected intravenously in the anesthetized dog, with the animal under artificial respiration, it consistently produced auricular fibrillation at a dose level of 0.65 to 0.75 ml./Kg.

Mono-ethers and di-ethers of glycerol substituted in either or both the 1 and 3 positions may be regarded as derivatives of propylene glycol (1,2-propanediol). Certain compounds of this type cause flaccid paralysis, without loss of consciousness, and are capable of protecting animals from death of metrazol and strychnine convulsions. Mephenesin N.N.R. (3-*o*-toloxy-1,2-propanediol) has been extensively studied as an anticonvulsant. More recently, Berger⁴ has reported that 2-diethyl-1,3-propanediol possesses unusually effective action in this regard. Although these compounds are not directly concerned in the present discussion of propylene oxide polymers, they are nevertheless mentioned to indicate the pharmacological potentialities of the basic structure.

MATERIALS INVESTIGATED

The manufacture of the polypropylene glycols is customarily effected by adding propylene oxide to dipropylene glycol. The alcoholysis of propylene oxide may take one of two courses, yielding either primary or secondary ethers of propylene glycol. Chitwood and Freure⁵ and also Reeve and Sadle⁶ have described the directive effect of catalysis on the cleavage of the epoxide ring and have shown that, with the simple primary alcohols, base-catalyzed reactions yield almost exclusively the primary mono-ethers of propylene glycol. Noncatalytic or acid-catalyzed alcoholyses yield mixtures of the isomeric ethers.

The materials used in the present investigation were commercial products of a base-catalyzed reaction. They are classified according to average molecular weight, the three available being 425, 1025, and 2025. Physically they are liquids of progressively increasing viscosity, with a specific gravity of practically 1. They are more oil-soluble and substantially less water-soluble than the liquid polyethylene glycols. Polypropylene glycol 425 is completely soluble in water at 20 C., but polypropylene glycol 1025 is soluble to the extent of only 1.5 per cent by weight, and polypropylene glycol 2025 to 0.15 per cent by weight at the same temperature.

PROCEDURE OF INVESTIGATION AND RESULTS

Acute Toxicity.—The acute toxicities of the polypropylene glycols orally and parenterally administered were determined on nonfasted, actively growing male albino rats of the Sherman strain, weighing between 90 and 120 Gm. These rats were maintained on Rockland rat diet (complete).

All toxicity data on dipropylene glycol were obtained with the undiluted compound. Aqueous solutions or suspensions of polypropylene glycols 425, 1025, and 2025 were used for oral doses, but the undiluted compounds were employed for intraperitoneal and intravenous injections. The

3. Procita, L., and Shideman, F. E.: Production of Auricular Fibrillation in the Dog by Dipropylene Glycol Methyl Ether, *Federation Proc.* **9**:309, 1950.

4. Berger, F. M.: Anticonvulsant Action of 2-Substituted-1, 3-Propanediols, *Proc. Soc. Exp. Biol. & Med.* **71**:270-271, 1949.

5. Chitwood, H. C., and Freure, B. T.: The Reaction of Propylene Oxide with Alcohols, *J. Am. Chem. Soc.* **68**:680-683, 1946.

6. Reeve, W., and Sadle, A.: The Reaction of Propylene Oxide with Methanol, *J. Am. Chem. Soc.* **72**:1251-1254, 1950.