

to form solutions which are slightly alkaline to litmus. Their bismuth content is low. Others appear for the most part to be basic bismuth tartrates of unknown constitution but containing small amounts of sodium and potassium salts probably as impurities. Their bismuth content is relatively high and they are insoluble in water.

It is a reflection on manufacturing pharmacy that the error of Sazerac and Levaditi in calling the Cowley product potassium sodium bismuth tartrate has been allowed to remain in the literature for several years without challenge, whereas proper chemical control by the makers of Trepol would have revealed the error before any of the first batch of material had been marketed. The fact that some of these compounds have been used in so-called scientific research without their composition being known to the users is a reflection on research.

THE DISINFECTANT ACTION AND TOXICITY OF TRICHLOR-ISOPROPYL ALCOHOL.*

BY J. W. HOWARD AND F. D. STIMPERT.

INTRODUCTION.

A number of compounds containing the trichlor-methyl group have proven of interest because of their physiological action. One of these, trichlor-isopropyl alcohol (often called "isoprol" for practical purposes) has been investigated only to a limited extent. Impens¹ has found it to be a hypnotic. He also states that 0.10% solution of isoprol inhibits the fermenting action of the yeast cell.

It was the object of this investigation to add to this data a study of its disinfectant action and toxicity.

For this purpose we have compared it with isopropyl alcohol as this shows the effect of replacing a methyl by a tri-chlor-methyl group.

The toxicity of isopropyl alcohol has been studied by Macht² who found it to be less toxic than propyl alcohol but twice as toxic as ethyl alcohol. His study was made by intravenous injection in the cat. A different method and animal was used by us. Our study of its disinfectant action, however, is entirely new.

EXPERIMENTAL PART.

Preparation of Materials.—The isopropyl alcohol was obtained from the Research Laboratories of the Eastman Kodak Company.

The trichlor-isopropyl alcohol has previously been prepared by the combination of chloral and zinc dimethyl³ or methyl magnesium salts.⁴ The latter method

* Contribution from the Departments of Chemistry and Biology of the State University of Montana.

¹ *Therapeutische Monatshefte*, 17, 533 (1903).

² *J. Pharm. and Expt. Therapeutics*, 16, 1 (1921).

³ Garzarolli-Thurnlockh, *Ann.*, 210, 77 (1881).

⁴ Henry, *Compt. rend.*, 138, 205 (1904); *Rec. Trav. Chim.*, 24, 331 (1905); *Victoria Rec. trav. Chim.*, 24, 265 (1905).

was used in this study. The usual procedure of the Grignard reaction was used in combining 36 grams of methyl iodide, 6 grams of magnesium turnings and 37 grams of chloral. On completion of the reaction 2*N* HCl was added to the reaction mixture until the whole of the solid matter was dissolved. The ethereal layer was then removed, washed with NaHCO₃ solution, then with NaHSO₃ solution and again with NaHCO₃. It was dehydrated over K₂CO₃ and the ether removed by distillation and the alcohol distilled *in vacuo*. It boils at 85° C. at 240 mm. As the product was still somewhat dark, it was dissolved in ether and decolorized by boiling with animal charcoal. Yield 18 grams, m. p. = 49° C.

It has a camphor-like odor and sublimes quite readily at ordinary temperature.

In making up the solutions for the later tests it was found that it was soluble only *slightly* in excess of 2.5 grams in 100 cc. of water at 20° C.

It is readily soluble in acetone, chloroform, ether, benzene, carbon-bisulphide, methyl alcohol, 95% ethyl alcohol, and carbon tetrachloride.

Bactericidal Studies.—The solutions of the alcohols were so diluted as to make 5 cc. in each case. To each of these 5-cc. portions was added 0.1 cc. of a 24-hour broth culture of *Eberthella typhi* (Hopkins) that had been transplanted on 2 successive days. At 2½-minute intervals a 5-mm. loop was transplanted from these solutions in 10 cc. of broth and incubated for 48 hours. An examination was made of the broth for positive and negative cultures by cloudiness. The results are summarized in the following tables:

TABLE I.

Trichlor-isopropyl alcohol.

Dilutions.	Time in minutes.					
	2½.	5.	7½.	10.	12½.	15.
1 to 50	—	—	—	—	—	—
1 to 60	+	—	—	—	—	—
1 to 70	+	+	+	+	—	—
1 to 80	+	+	+	+	+	+
1 to 90	+	+	+	+	+	+

TABLE II.

Isopropyl alcohol.

Dilutions.	Time in minutes.					
	2½.	5.	7½.	10.	12½.	15.
1 to 4.76	—	—	—	—	—	—
1 to 4.87	+	—	—	—	—	—
1 to 5.00	+	+	—	—	—	—
1 to 5.12	+	+	+	—	—	—
1 to 5.71	+	+	+	—	—	—
1 to 5.88	+	+	+	+	—	—
1 to 6.25	+	+	+	+	+	+
1 to 6.66	+	+	+	+	+	+

This would indicate that trichlor-isopropyl alcohol has about twelve times the disinfectant power of isopropyl alcohol.

Toxicity Studies.—For these determinations the alcohols were dissolved in physiological salt solution and injected subcutaneously in the abdominal region of guinea pigs.

Trichlor-isopropyl alcohol was used as a 2½% solution. Doses of 0.045 gram per 100 grams of body weight caused death within 3 hours in all cases. This compound is absorbed very rapidly and causes complete loss of motor control in 5 minutes.

Doses of 0.035 gram per 100 grams of body weight caused the same loss of motor control as the lethal dose, but in the majority of cases the animals recovered and showed normal activity in 5 to 6 hours.

Isopropyl alcohol was injected in volumes per body weight corresponding to those used with trichlor-isopropyl alcohol. The dilutions were varied from 2½% to 50%. In none of these cases was a lethal dose obtained. This shows clearly that trichlor-isopropyl alcohol is much more toxic than isopropyl alcohol.

SUMMARY.

Trichlor-isopropyl alcohol has both a greater disinfectant action and toxicity than isopropyl alcohol.

CULTIVATION OF THE OPIUM POPPY IN NORTH CAROLINA.*

BY E. V. HOWELL.

In 1905, I began the cultivation of poppies. In 1909 at the Los Angeles meeting of the AMERICAN PHARMACEUTICAL ASSOCIATION I presented an historical sketch of opium production, with items of interest from my experiments. From translation of the work of Dioscorides about A.D. 77 and other authors, I found that the *μηκρώνιον* of Theophrastus was evidently an extract of the whole plant, while Dioscorides distinguishes *μηκρώνειον*, described as an extract of the entire herb, from *σπος*, the more active juice of the capsules. I found also that the ancients knew in a crude way almost as much as we now know of the plant. They stated that the young plants were harmless and could be eaten as a salad, the seeds were used in making bread (as to-day); could be fed to poultry, furnished oil, etc.

Dioscorides stated that the capsules had to be scarified to produce opium; methods were used to prevent the instruments from cutting too deep thus allowing internal bleeding. Discussion as to whether transverse or longitudinal cutting was the better was noticed. The plants were to be cut "advancing backwards lest the juice get on your raiment." The uses of the juice, the leaves and capsules, in various forms were enumerated.

Since 1909, I have grown annually poppies from the same strain of seed. I started with both white and black seeded varieties of the *Papaver somniferum*. The black variety evidently is the hardier as it has crowded out the white. In North Carolina, the poppy once started will seed itself, the problem becoming one of thinning or transplanting. Poppies should be sown in the fall, and may be sown by simply scattering on the top of snow, in the winter. They will mature the following spring. In transplanting, it is necessary that it should be done in cold weather, early in the spring. The poppy will survive a very considerable amount of cold, or even freezing.

* Scientific Section, A. P. H. A., Buffalo meeting, 1924.