

one temperature as was obtained before. An increase in the temperature results in a slight increase in volume of gas as well as a slight increase in amount of impurity.

We also used commercial aluminium oxide but in no case got gas of a higher purity than 85% propylene.

#### SUMMARY.

1. The most favorable temperature for the production of propylene from propyl alcohol with alumina catalysts lies at about 360–370° C.

2. The catalyst can be regenerated by burning off the carbon deposit.

3. Propylene of a high grade of purity can be readily prepared by this method.

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## THE SYNERGISTIC ACTION OF CAMPHOR IN PHENOL POISONING.

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Poisoning by Phenol is still sufficiently frequent to render a knowledge of appropriate measures of treatment important. Here, as with practically every other orally administered poison, evacuation of the stomach is probably the most valuable therapeutic measure. Emetics may be unsatisfactory for this purpose; either because of the anesthetic action of the poison on the mucous membrane of the alimentary tract rendering reflex emetics ineffective; or because of the depression of the central nervous system which occurs after sufficient absorption of the phenol has taken place. The services of a physician are often obtained only after the lapse of much valuable time and the average pharmacist is unfamiliar with the simple technic of gastric lavage. Therefore, the announcement by E. D. Wilson<sup>1</sup> that in Spirit of Camphor we have a valuable antidote for phenol is deserving of especial attention.

Apparently, Wilson's recommendation is unsupported by experimental evidence. He reasons that, since phenol-camphor mixtures are relatively free from irritant properties, the camphor must combine with and neutralize the phenol. Similar theorizing was responsible for the former belief that alcohol is an antidote for phenol, but it has been conclusively shown that alcohol is in no sense an antidote for the systemic toxic action of phenol. A clear distinction should be made between the purely local action of phenol, elicited when the drug comes into contact with the tissues, and the systemic action, manifest only after absorption from the alimentary tract or other sites. It is true that alcohol renders phenol much less irritant locally and may be used successfully in the treatment of local burns by the poison, but this is simply due to the great solvent power of alcohol for phenol. Systemically, alcohol and phenol resemble each other in their power to depress the central nervous system, and it is a simple matter to show that alcoholic solutions

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<sup>1</sup> *Practical Druggist*, May, 1924, p. 18.

of phenol are fully as toxic as aqueous solutions when they are injected intravenously or administered orally to animals, prevented from vomiting by the previous administration of morphine. The observation that drunken persons seem to be more resistant to the action of phenol than normal individuals, is explained by the fact that alcoholic intoxication retards absorption from the alimentary tract, and, of course, has no practical application in the therapy of poisoning. Indeed experiments carried out in this laboratory several years ago seem to indicate that dogs rendered drunk with ethyl alcohol are actually more susceptible than are the control animals to the toxic action of phenol injected intravenously.

The comparative freedom from irritant action shown by phenol-camphor mixtures in no way proves that camphor is an effective antidote for the systemic action of phenol. Indeed, there is little in the action of camphor that would incline one to use it in an attempt to combat the systemic action of phenol. Though credited by some with having a favorable action on the circulation, accurate investigations have failed to show that camphor, in safe doses, affects the heart or the blood vessels in any beneficial way. Moreover, any stimulation of the respiration following the administration of such doses of camphor is to be ascribed to a reflex action, arising from local irritation, especially after the subcutaneous injection of the oily solution. In very large doses, camphor stimulates the central nervous system, leading to the production of convulsions and then to a depression. Certainly, in these features of its systemic action, camphor resembles phenol rather than seeming capable of acting as an antagonist. It seemed desirable, therefore, and advisable to determine by animal experimentation whether there is any basis for the recommendation of camphor as an antidote for phenol.

An effective antidote for a poison should save the great majority of animals from death following a dose of the poison which proves fatal in the untreated controls. Obviously, it is necessary to make at least an approximate determination of the minimum fatal dose (M.F.D.); it would scarcely be fair to employ a dose of the poison much in excess of this. It previously has been determined in this laboratory that the M.F.D. for liquefied phenol injected intravenously into dogs is from 0.125 to 0.130 cc. per kilogram body weight. Since, however, most cases of clinical phenol poisoning are due to the oral administration of the drug, it was necessary to determine the M.F.D. for the dog by this method of administration.

In the experiments carried out for this purpose, apparently healthy dogs were employed. The animals were weighed and given twenty-five cubic centimeters of tap water per kilogram weight through a tube, and were then placed in metabolism cages. At the end of twenty-four hours, the dogs, having been given no food or additional water in the meantime, were again weighed and a dose of twenty milligrams of morphine sulphate per kilogram body weight was injected subcutaneously. When marked depression had occurred (usually about thirty minutes), the desirable dose of liquefied phenol was administered orally through a tube and washed down with a small quantity of water. Fourteen dogs were used in these experiments, and it appeared that the M.F.D. of liquefied phenol when administered in this way to dogs is in the neighborhood of 0.4 cc. per kilogram body weight. The condensed protocols are given in Table I.

An antidote should be used in a sufficiently large dose, but care must be taken that it is not used in an amount sufficient in itself to cause poisoning. It is necessary,

TABLE NO. I.

Phenol x Kgm.	1 cc.	2 cc.	3 cc.	4 cc.	5 cc.	6 cc.	7 cc.	8 cc.
Series No. 1					+	+	+	+
Series No. 2		+	—	+	+			
Series No. 3				+	+			
Series No. 4	—	—	+	+				

Died = +. Survived = —.

therefore, to ascertain the toxicity of camphor for dogs also. Sollman<sup>1</sup> states that in the dose of 0.5 gram per kilogram, camphor causes convulsions with recovery in the dog. It was felt that 0.3 gram of camphor would not, in itself, cause marked injury and, on the other hand, would be sufficiently large to ensure an abundance of the supposed antidote. Consequently a second series, consisting of seven dogs, was used to determine the value of this amount of camphor as a protective against phenol. The animals were weighed and starved as previously described, and then given the 20 mg. dose of morphine sulphate per kilogram subcutaneously. Six of the seven animals then were given 0.3 cc. of liquefied phenol per kilogram body weight orally; of these six, three were allowed to serve as controls, receiving no treatment; while the other three were given 0.3 gram of camphor (in the form of the spirit) per kilogram body weight orally, immediately after the phenol had been administered. The seventh dog was given camphor alone. The results of these experiments are given in Table II.

TABLE NO. II.

Dog no.	Wt., Kg.	Phenol, mls.	Camphor, Gm.	Result.
23	5.0	0.3	0.3	Died
3	5.9	0.3	0.3	Died
6	5.02	0.3	0.3	Died
22	5.02	0.3	0	Survived
5	3.86	0.3	0	Survived
17	8.63	0.3	0	Survived
10	5.0	0	0.3	Survived

It is obvious from these experiments that spirit of camphor is not only of no value as an antidote for phenol poisoning but actually appears to increase the toxicity of the poison, as would be inferred from a consideration of the systemic action of the two drugs. The three dogs receiving the phenol alone in a dose about 25% less than the M.F.D. survived, whereas when camphor was given in an amount which, alone, should cause no injury, death resulted in every instance.

The search for effective antidotes has too often resembled the chase of the Will-o'-the-Wisp; and, unfortunately, both quests may lead to disaster. Impressed by positive statements, even though unsupported by proof, the untrained layman or even the pharmacist may place implicit confidence in the use of an antidote which, even if it does not itself directly lessen the patient's chance of recovery, leads to the same result through encouraging the neglect of measures, such as gastric lavage, which are of real value.

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<sup>1</sup> Sollman, "A Laboratory Guide in Pharmacology."