noticeable symptoms until a considerable time has elapsed after the administration of the dose. Death is preceded by intermittent convulsions. The following table gives the details of the toxicity determinations:

Weight of guinea pig, Gm.	Weight of seed containing 23% oil, Gm.	Equivalent weight of unpressed seed, Gm.	Elapsed time between administration of the material and death, hours
No. 1—520	0.2	0.308	About 12
No. 2—540	0.15	0.231	About 23
No. 3—450	0.10	0.154	About 25
No. 4—400	0.07	0.108	About 45
No. 5—429	0.05	0.077	About 52
No. 6—510	0.03	0.046	Did not die

No. 6 pig was alive and active after several weeks. The toxicity of castor seed is evidently about 0.077 Gm. per 429 grams of guinea pig or 0.179 Gm. per kilo. If the toxicity is in the same proportion about 12.2 grams of castor seed would prove fatal to a man weighing 150 pounds.

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LABORATORY NOTES.

BY PETER MASUCCI AND MARGARET I. MOFFAT.

I. THE DIFFUSION OF PHENOL AND TRI-CRESOL THROUGH RUBBER.

A large percentage of bacterial vaccines intended for industrial, hospital, or community practice are marketed in 5, 10 and 20 cc rubber-capped vials. These vials have as a stopper a puncturable rubber cap which permits the removal of the bacterin without exposure to outside contamination. The dimensions of the cap are about $^{7}/_{8}$ inch in diameter and $^{1}/_{16}$ inch in thickness.

Bacterial vaccines as well as most biological products are generally preserved with 0.5% phenol or 0.3% tri-cresol. During the course of a certain investigation it was shown that on determining quantitatively the amount of tri-cresol in certain lots of bacterial vaccines, the amount found was only about one-third of what had been added as shown by the records. We were at a loss to explain the discrepancy. After much speculation, it was decided to do some experimental work in order to determine whether the loss had occurred by the diffusion of the tri-cresol vapor through the rubber cap.*

A review of the literature showed that much work has been done on the penetration of gases through rubber and the factors that influence penetration. Edwards and Pickering[1] have shown that the rate of penetration of a gas through a given sample of rubber is proportional to the partial pressure difference and increases with temperature. Graham[2] advanced the theory that the penetration consisted in the solution of the gas on one side of the rubber, with a subsequent diffusion of the dissolved gas through the rubber and vaporization on the other side. Recently Venable and Fuwa[3] have found that rubber holds a gas in true solution and not by adsorption; that there is a general relationship between the solubility and density of a gas and degree of penetration through rubber.

* This theory was advanced by Mr. S. S. Sadtler, of the S. P. Sadtler Laboratories.

We found nothing in literature bearing upon the diffusion or penetration of phenol or tri-cresol vapors through rubber. In view of the work on gases, quoted above, we were inclined to believe that phenol and tri-cresol vapors behaved somewhat similarly.

Normal horse serum, physiological salt solution, plain typhoid bacterin, and sensitized typhoid bacterin, all containing 0.3% tri-cresol, were filled in 20-cc rubber-capped vials on 4/18/21. A similar set of products, containing 0.5% phenol, was also filled in 20-cc rubber-capped vials. Simultaneously a small quantity of each product was filled in flame-sealed ampuls.

It was our intention to test each material once a month, but owing to the pressure of other work this was not possible. The materials, therefore, were tested quantitatively for phenol or tri-cresol content only immediately after filling and again on 10/10/22, or approximately 18 months from the date of filling.

The vials and ampuls were kept at room temperature which varied from 20° C. to 30° C. The method used for the quantitative determination of phenol and tri-cresol was that of Elias Elvove[4] which in our experience we have found to be reliable and accurate to ±0.02%.

RESULTS.

TABLE I.

Date of test.	Substance.	Container.	Preservative added.	Preservative found.	Remarks.
4/ 8/21	Normal horse serum	20 cc vial	0.30% tri-cresol	0.30% cresol	
10/10/22		20 cc vial		0.15% cresol	
4/ 8/21		10 cc amp.	0.30% tri-cresol	Not tested	
10/10/22		10 cc amp.		0.28% cresol	
4/ 8/21	Salt soln.	20 cc vial	0.30% tri-cresol	0.29% cresol	
10/10/22		20 cc vial		0.12% cresol	
4/ 8/21		10 cc amp.	0.30% tri-cresol	Not tested	
10/10/22		10 cc amp.		0.29% cresol	
4/ 8/21	Typh. bac. plain	20 cc vial	0.30% tri-cresol	0.26% cresol	
10/10/22		20 cc vial		0.08% cresol	
4/ 8/21		10 cc amp.	0.30% tri-cresol	No ampuls were filled through oversight	
10/10/22		10 cc amp.			
4/ 8/21	Typh. bac. sensitized	20 cc vial	0.30% tri-cresol	0.29% cresol	Vial had no gelatin seal
10/10/22		20 cc vial		0.08% cresol	
4/ 8/21		10 cc amp.	0.30% tri-cresol	Not tested	
10/10/22		10 cc amp.		0.28% cresol	

TABLE II.

Date of test.	Substance.	Container.	Preservative added.	Preservative found.	Remarks.
4/ 8/21	Normal horse serum	20 cc vial	0.50% phenol	0.50% phenol	
10/10/22		20 cc vial		0.37% phenol	
4/ 8/21		10 cc amp.	0.50% phenol	Not tested	
10/10/22		10 cc amp.		0.48% phenol	
4/ 8/21	Salt soln.	20 cc vial	0.50% phenol	0.50% phenol	
10/10/22		20 cc vial		0.33% phenol	
4/ 8/21		10 cc amp.	0.50% phenol	Not tested	
10/10/22		10 cc amp.		0.50% phenol	
4/ 8/21	Typh. bac. plain	20 cc vial	0.50% phenol	0.47% phenol	No gelatin seal
10/10/22		20 cc vial		0.30% phenol	
4/ 8/21		10 cc amp.	0.50% phenol	Not tested	
10/10/22		10 cc amp.		0.48% phenol	
4/ 8/21	Typh. bac. sensitized	20 cc vial	0.50% phenol	0.48% phenol	No gelatin seal
10/10/22		20 cc vial		0.30% phenol	
4/ 8/21		10 cc amp.	0.50% phenol	Not tested	
10/10/22		10 cc amp.		0.50% phenol	

The rubber cap from the vial containing the cresolized salt solution was suspended in acidulated water, and the latter distilled. The tri-cresol recovered amounted to 0.0012 gram. The actual loss of tri-cresol from the vial was 0.034 gram. It is evident that only a very small fraction of the tri-cresol lost was retained by the cap. The conclusion, therefore, is that the loss of the tri-cresol from the vial occurred by the diffusion of its vapors through the rubber cap.

SUMMARY.

Aging experiments covering a period of eighteen months show in a remarkable way that biological products containing 0.3% tri-cresol or 0.5% phenol lose a portion of their preservative when such products are stored in rubber-capped vials at room temperature. The loss is 50 to 70% in tri-cresol, and 20 to 40% in phenol content. The loss can only be explained by the diffusion of tri-cresol or phenol vapors through the rubber cap.

REFERENCES.

1. Edwards and Pickering, *Chem. Met. Eng.*, 23, 17, 71, 1920.
2. Graham, *Phil. Trans.*, 156, 399, 1866.
3. Venable and Fuwa, *J. Ind. Eng. Chem.*, 14, 2, 139, 1922.
4. Elias Elvolve, "A Colorimetric Method for the Estimation of the Cresol or Phenol Preservative in Serums," *Hyg. Lab. Bull.*, 110, 25, 1917.

II. THE FORMATION OF A BLUE COLOR BY THE ACTION OF PHENOL ON CERTAIN RUBBER CAPS.

Our attention was called to the blue color of certain vials containing bacterins suspended in physiological salt solution to which 0.5% phenol had been added as a preservative. The cause of this blue color perplexed us for a while but on investigation we were able to show that there was a definite relationship between the phenol in the salt solution and some ingredient used in the vulcanization of the rubber caps.

By a process of elimination, we showed definitely that (1) the caps developed a blue color when immersed in physiological salt solution containing 0.5% phenol, (2) that phenol was necessary for the development of the color, because when the caps were immersed in distilled water or physiological salt solution no color developed, and (3) that a definite time element was necessary varying from three to thirty-six hours for the full development of the color.

The caps which gave this trouble were a lighter color than those used previously and which had not produced the blue color. Apparently some change had been made in the vulcanization process by the manufacturer of the caps.

On the addition of acid the blue color changed to violet and finally was totally discharged. When the solution was again neutralized with alkali the blue color appeared. Hydrogen sulphide also rendered the solution colorless, which again became blue on standing. Ether extracted the color from the aqueous solution; the ether layer assumed a beautiful purple color.

Of the known substances that give a blue or violet-blue color with phenol are (1) iron salts; (2) ammonia plus a hypochlorite, and (3) aniline plus a hypochlorite. We eliminated iron entirely. Since aniline is a widely used organic accelerator for fast curing purposes, we were inclined to believe that the blue color was due to the interaction of phenol with aniline.

On discussing the matter with the manufacturer, we were informed that a change had been made in the vulcanization process. Instead of the golden antimony previously used, a mixture of aniline and crimson antimony had been substituted as an accelerator. The evidence, therefore, seems to indicate that the use of aniline as an accelerator was responsible for the development of the blue color and thus our suspicions were confirmed.

SUMMARY.

Under certain conditions rubber caps coming into contact with a solution containing 0.5% phenol may give rise to the development of a blue color. The evidence is very strong that the blue color is due to the chemical interaction of phenol with the organic accelerator, aniline, used in the vulcanization of the caps.

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THE STATUS OF DRUG-PLANT GROWING IN THE UNITED STATES IN 1921.*

BY W. W. STOCKBERGER.[1]

The commercial production of drug plants under cultivation did not escape the general depression occasioned in almost every phase of agricultural activity by the sharp decline in prices which closely followed the ending of the World War. As was not unexpected the renewal of imported supplies brought about a competition that could not be met by domestic growers, many of whom discontinued entirely the cultivation of certain medicinals with which they had had considerable success during the war years.

With the year 1921 the effects of the artificial stimulus imparted to drug growing by the World War practically disappeared, leaving the general situation much the same as it was in pre-war years. Although this result might be taken as an indication that there is no further opportunity for drug growing in this country, there are on the contrary good reasons for regarding this apparently unfavorable outcome as actual progress toward the establishment of this industry on a sound economic basis. The situation in 1921 fully sustains the judgment of those who maintained a conservative attitude toward drug growing under war conditions and who realized that no permanency could be assured this industry except through its rational adjustment to approximately normal conditions of crop production and consumptive demand.

The experience of the past five years has greatly extended our knowledge in respect to localities in this country suitable for growing certain drug plants and concerning the labor and risks involved in the care and harvesting of drug crops. This experience has largely dispelled the illusions maintained for some years by a group of over-enthusiasts respecting the possibilities of deriving great monetary returns from drug growing and has brought about a general recognition of the fact that the demand for most of these crops is relatively small and that the suc-

* Read before Scientific Section, A. Ph. A., Cleveland meeting, 1922.

[1] Physiologist in charge of Drug, Poisonous and Oil Plant Investigations, Bureau of Plant Industry, U. S. Department of Agriculture.