

digestions. This suggests that the enzyme digests itself or its carrier and so loses its activity.

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A SUGGESTED CHANGE IN THE OFFICIAL METHOD OF ASSAY OF CRESOL IN LIQUOR CRESOLIS COMPOSITUS.

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The Pharmacopœia of the United States, tenth decennial revision, provides under **Liquor Cresolis Compositus**, page 210, a method for the assay of cresol. In this method the cresol is determined as the increase in volume of the aqueous layer, which results when the kerosene and cresol mixture, obtained by distilling 50 cc. of liquor cresolis compositus with kerosene after the addition of sodium bicarbonate, is shaken with 15 per cent sodium hydroxide solution. The cresol is separated from this solution by treatment with hydrochloric acid and washed with a saturated solution of sodium chloride. Five grams of freshly ignited potassium carbonate is then added to the washed cresol, after which the mixture is shaken gently at frequent intervals during three hours and allowed to stand over night. The cresol, decanted from the potassium carbonate, must meet the U. S. P. distillation requirements for cresol. In short, the pharmacopœial requirements for this product are twofold: (1) The proportion of cresol present in 50 cc. must be such as to produce a 23- to 26-cc. volume increase in the sodium hydroxide solution in which it is dissolved. (2) The liberated cresols, when dry, must come within the definite distillation requirements; 90 per cent should distil between 195° and 205° C. as described.

This method of assay was applied to several samples of liquor cresolis compositus of known composition. In all cases the increase in volume of the sodium hydroxide solution, due to cresols, was within the prescribed limits. When the cresol was separated, washed, treated with 5 grams of freshly ignited potassium carbonate, and decanted as directed, the resulting product had become viscous, almost syrupy, and on distillation left a rather large residue. When ashed the residue showed the presence of potassium. When the distillation residue was treated with hydrochloric acid very little effervescence resulted, indicating that little or no carbonate was present. This suggested that the potassium carbonate had reacted to some extent with the cresol to form potassium cresylate. More detailed experiments were, therefore, undertaken.

Liquor cresolis compositus was made from a cresol of which 98 per cent came over between 195° and 205° C. when distilled according to Method II of the Pharmacopœia. This solution was then assayed according to the Pharmacopœia method. The dried cresol was decanted through cotton and no suspended potassium carbonate was carried with it. The residue after distillation at 205° was washed out of the flask with alcohol into a weighed platinum dish, evaporated on

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the steam-bath, cooled, and weighed. This residue was then ashed and the ash titrated with normal sulphuric acid, using methyl orange as an indicator. From the titration the percentage of potassium cresylate was calculated. The results follow.

Increase in volume of NaOH solution. Cc.	Decanted dry cresol. Cc.	Distillation of cresols.			Residue at 205° C. Per cent.	Calculated potassium cresylate.
		To 195° C. Water. Per cent.	Phenols.	195° to 205° C.		
26.0	13.0	2	5	63	28	17
25.3	13.5	2	3	65	30	..
25.8	14	3	2	68	21	12

In the first two analyses granular, analytical grade, potassium carbonate, which had been freshly ignited, was used. In the third case the potassium carbonate was made in the laboratory by the ignition of granular, C. P. potassium bicarbonate to insure the absence of hydroxide. The potassium present in the residue of the first assay amounted to more than one-fifth of that in the 5 grams of potassium carbonate used in the assay. The quantity was also large in both of the other cases. With such a large quantity of material held in the residue, the distillate between 195° and 205° C. fell far below the required 90 per cent. Ignited potassium carbonate, therefore, is not suitable as a dehydrating agent for cresol.

Other drying agents, including dehydrated sodium sulphate, silica gel, and dehydrated copper sulphate, were tested. The first two were not effective in removing the water. Dehydrated copper sulphate was the best material tested. It removed most of the water and did not react with the cresol or dissolve in it in appreciable quantities. If a somewhat granular dehydrated copper sulphate was used, more dried cresol was obtained for distillation than when potassium carbonate was used.

The experimental results obtained, using the same liquor cresolis compositus as before, and the same procedure, except that 5 grams of granular, dehydrated copper sulphate (dehydrated by ignition at a low temperature) were used in place of the potassium carbonate, were as follows.

Increase in volume of NaOH solution. Cc.	Decanted dry cresol. Cc.	Distillation of cresols.			Residue at 205° C. Per cent.	Ash.
		To 195° C. Water. Per cent.	Phenols.	195° to 205° C.		
25.4	18	0.6	0.6	92	dry*	nil
25.4	17	0.6	1	91	dry*	...

* The flask was dry at 205° C., but, of course, a little cresol condensed in it when it cooled.

These distillations indicate that material used was U. S. P. cresol. The 195° to 205° fraction, however, was somewhat below that obtained with the original cresol. This is due to the large proportionate losses in distilling 18 cc. from a 200-cc. flask.

Dehydrated copper sulphate as a drying agent in the assay of liquor cresolis compositus was tested by W. A. Gersdorff of this laboratory on two samples of known composition. The dehydrated copper sulphate used was somewhat less

Decanted dried cresols. Cc.	Distillate 195° to 205° C. Cc.	Distillate 195° to 205° C. Per cent.	Original cresol. 195° to 205° C. Per cent.	Distillate 195° to 205° C. Per cent.
12	11*	92	98	
13	12*	92	97.5	

* In these samples the dry point was below 205° C.

granular than that used in the experiments just reported, and he was able to decant less cresol for distillation. He obtained the above results.

These results check those obtained by the writer and the variation from the results with the original cresol are again to be explained by proportionately high losses in such a large distillation apparatus.

Since it had been shown that the use of copper sulphate as a dehydrating agent gave distillation results which agree reasonably well with the known values for the original cresol, it seemed desirable to determine what results would be obtained when a tar acid not of the grade of U. S. P. cresol was used. Therefore, mixtures were made in which the formula for liquor cresolis compositus was followed except that the cresol was replaced by other commercial "tar acids." The procedure for assay in every case was the same as that provided by the Pharmacopœia method except that granular dehydrated copper sulphate (5 Gms.) was used in place of the ignited potassium carbonate. Some of the results follow.

Brand.	Decanted dry phenols. Cc.	Distillation of phenols to 195° C.			Distillation on original phenols (Method II)*.	
		Water. Per cent.	Phenols. Per cent.	195° to 205° C.	to 195° C.	195° to 205° C. Per cent.
A	18	Trace	0	14	0	11
B	17	0.5	12	76	28	71
C	17.2	0.5	28	66	43	55

* Acknowledgment is made to W. A. Gersdorff for making these distillations.

These results, although not exactly duplicates of those obtained in the distillation of the original phenols, are as close as can be expected, in view of the fact that the method is empirical and that different quantities of material are used in the same apparatus. Manifestly, distilling 18 cc. from a 200-cc. bulb will not give the same results as distilling 100 cc. from the same bulb. The results certainly give a reasonably accurate idea of the material used in the supposed liquor cresolis compositus.

SUMMARY.

The cresols recovered by assaying U. S. P. liquor cresolis compositus according to the method given in the U. S. Pharmacopœia, tenth decennial revision, do not give distillation results which come within the requirements for U. S. P. cresol. The recovered cresol contains a large amount of potassium, probably as potassium cresylate. This accounts for the erroneous results.

It was found that when 5 grams of granular, dehydrated copper sulphate was used in place of the equal weight of ignited potassium carbonate prescribed by the official method (the remainder of the procedure being the same) the results obtained by distillation of the recovered cresols were comparable with those obtained on the original cresol. The loss in the apparatus is about the same whether 18 cc. of recovered cresol or 100 cc. of original cresol is used. On a percentage basis, however, it is higher when 18 cc. of recovered cresol is used. This might be corrected either by changing the distillation procedure or by using a larger sample of recovered cresol.