

rats is 15.7 and 23.1 Gm. per Kg., respectively, as compared to corresponding values of 7.6 and 15.1 Gm. per Kg., respectively, for glycerol.

In rabbits, the acutely fatal dose of propylene glycol by oral administration is 20 Gm. per Kg. Daily oral doses up to 8 cc. per Kg. administered for 50 days are tolerated by rabbits with no observed cumulative effects.

The low systemic toxicity of propylene glycol would recommend it as a solvent for certain medicinals. However, the severe, although transient, local irritation produced by its subcutaneous injection would appear to preclude its use in hypodermic preparations in undiluted form.

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## DETECTION OF DIETHYLPHTHALATE IN WHISKIES AND OTHER ALCOHOLIC PRODUCTS.

(ELIMINATING SOURCES OF ERROR DUE TO FALSE POSITIVES AND THE 24-HOUR REQUIREMENT.)\*

BY ISRAEL SCHWARTZ.<sup>1</sup>

Within the last years, mainly during prohibition, much has been published upon detection of diethylphthalate in alcoholic products. Its presence in a spirituous product was proof that industrial grade of alcohol was diverted for illicit use. Under Spiritus Frumenti U. S. P. X, listed among tests for denaturants, also was included the test for diethylphthalate. The U. S. P. XI now omits the test for diethylphthalate but retains the test for other denaturants. Apparently, the test for diethylphthalate was deleted because it was unreliable and therefore subject to criticism. Handy and Hoyt pointed out that many organic substances yield fluorescences, but those not due to diethylphthalate fade after 24 hours. It now is known that with such products as old bonded whiskies, rums, brandies, etc., fluorescent reactions are obtained with the U. S. P. X test which last more than 24 hours, sometimes a week or longer.

Denaturants still are a problem to be dealt with in testing alcoholic products, and routine tests for diethylphthalate should be included along with tests for other denaturants listed in U. S. P. XI. Ending of prohibition did not eliminate illicit practices, and products offered for consumption and containing denaturants are still with us. Such spurious products may represent prohibition left-overs brought out from concealment, or those due to diversion and "cleaning" of denatured alcohol, contamination, etc. Since the repeal, we found diethylphthalate in an imported rum offered through a very dependable concern. Investigation showed that its presence was due to filling machines previously used for bay rum, the latter legally containing diethylphthalate alcohol.

In certain types of cordials, diethylphthalate was found to be added as a "fixative." In this country such finding would be wrongly construed and injure

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the dealer's reputation. Diethylphthalate was found also in samples of bonded liquor obtained from licensed liquor stores. Samples submitted by State Liquor Commissions also showed the presence of denaturants in some of the tested liquors. These and other reasons indicate the need for testing for diethylphthalate in spirituous products along with other denaturants listed in the U. S. P. XI. In view of the fact that the former U. S. P. test for diethylphthalate was not dependable, and since the U. S. P. XI omits the test, we offer the test here described as trustworthy, giving no false positives, and in our hands has proven successful for more than twelve years.

On several occasions, diethylphthalate was added to liquors and sent to other laboratories as unknowns. In each case negative reports were received, yet, by this method it was detected. In one case in which diethylphthalate was found in bonded liquor and so reported, other laboratories could not establish its presence. Dr. Goettler who reported it did not employ the U. S. P. test. The author's test has been successfully used by Dr. Joseph L. Mayer of the Brooklyn College of Pharmacy, by E. Freedman, Macy's Director of Bureau of Standards, and several others.

In other instances certain whiskies, some bonded, in which diethylphthalate was reported, were submitted to us for analysis. Our tests showed no diethylphthalate. This discrepancy was due to unfamiliarity with the U. S. P. test which, as stated, yields very strong fluorescent reactions which are misleading, particularly in aged and bonded whisky. Blended whiskies reported as containing diethylphthalate also were tested with this method along with various ingredients used in making blends—alcohol, sherry wine, caramel and whisky. Except the alcohol, these substances, when tested, gave very strong and lasting fluorescence which could be mistaken for diethylphthalate. The wine and caramel, distilled separately with 50% alcohol, yielded very strong fluorescent reactions which lasted for several days. Employing the described test, we were able quickly to determine the absence of diethylphthalate. Experimenting with fluorescence dye, we found that very small amounts very easily could be extracted from acid solution with ethyl-ether. Even 1 part in 40,000,000 could be extracted and identified. Upon this fact is based the modification forming the subject of this paper. The following method, therefore, is offered.

#### METHOD.

Twenty-five cubic centimeters of sample diluted with 50 cc. of water are distilled and 50 cc. of distillate collected. Ten to 12 cc. (with low proof products more distillate is used to correspond to about 5 cc. of absolute alcohol) of distillate are evaporated over a steam-bath with from 5 to 6 drops of 5% sodium hydroxide. When dry, moisten with 5 or 6 drops of 10% sulphuric acid to dissolve the sodium salts. Add 1.2 cc. of concentrated sulphuric acid and thoroughly rub it up with a glass rod, being sure to effect solution, using a little heat if necessary. In a long, narrow test-tube, containing 0.05 Gm. of resorcin, add all of the sulphuric acid solution.

In an oil-bath in which a stationary thermometer is immersed, place the tube containing the resorcin-acid mixture and heat to 165° to 175° C., for from 3.5 to 4 minutes, thoroughly agitating the bath to maintain even temperature. Withdraw and cool the tube, place about 0.2 to 0.5 cc. of the acid concentration product in a separatory funnel of about 50 cc. capacity; add 5 to 10 cc. of water and shake thoroughly with 8 to 10 cc. ethyl-ether, U. S. P., for 30 seconds. Allow the liquids to separate, draw off and discard the lower portion. Wash the funnel contents 3 or 4 times (more if necessary) with 10 cc. of water, removing all traces of acid from the ether layer, especially that portion tending to cling to the bottom of the ether layer in the form of a collar or

emulsion. Discard all aqueous washings through the stem of the separatory funnel. This is done to assure that none of the acid washings contaminate the ether. Pour off the ether extract into a long, narrow dry test-tube (do not drain), allowing about 0.5 cc. of liquid to remain.

To the ether extract in the test-tube (which never should be more than 3 to 4 cc.) add down the side 2 cc. of 5% sodium hydroxide solution, and let stand for 15 minutes without agitation. If any diethylphthalate then is present, a yellowish green fluorescence will appear, extending into the hydroxide stratum. If an appreciable amount of diethylphthalate is present—now fluorescence dye—the characteristic yellow-green fluorescence almost immediately will appear at the junction of the liquids. Where the sodium hydroxide solution has passed down the side of the tube and through the ether layer, a filmy yellow-green fluorescence also will appear, sometimes in spotted form, if positive. Slight rotation of the test-tube will intensify the color at the junction of the liquids. Bluish, reddish, brownish and ocean-blue and ocean-green colorings were obtained in less than 1% of samples tested; but these disappear on agitation of the liquids and are so uncharacteristic as to leave no doubt as to results. In the absence of diethylphthalate, the liquids show no or little color changes at the junction.

The U. S. P. X test for diethylphthalate in alcohol and whisky directed that the alcoholic product be shaken with petroleic ether, the latter transferred to a dish containing 1 cc. of sodium hydroxide, and evaporated to dryness on a water-bath. To the residue, 2 cc. of sulphuric acid are added and the dish rotated until the residue is completely moistened. This is heated on a water-bath for a few minutes at 160°–170° C. The solution then is poured into a mixture of water containing sufficient sodium hydroxide to render it distinctly alkaline. It then is directed that this be permitted to stand for 24 hours.

Before addition of the resorcinol-sulphuric acid mixture to the sodium hydroxide solution, the method here suggested is to remove a portion of this acid mixture which is placed in a separatory funnel, shaken with ethyl-ether, the extract washed free of acid as before into a test-tube, followed by sodium hydroxide as above described. This modification, added to the U. S. P. X test, will eliminate false positives, which have proven to be so greatly annoying since this test was published in the U. S. P. X. We were able to get stronger fluorescent reactions on the distillates than with the petroleic-ether shake-out procedure, and therefore it is recommended that the test be made on the distillate.

Diethylphthalate in perfumes, toilet articles, pharmaceutical and other spirituous products readily can be detected by this method, modifying the procedure according to the nature of the product. Pharmaceutical and spirituous products first are distilled. Oily and perfume products can be tested direct, employing 5 to 10 drops evaporated with sodium hydroxide and treated as above.

Alcohol derived from 39B or 39C in the following products:

Witch Hazel: This can be evaporated directly with sodium hydroxide.

Spirit of Peppermint: Add water and evaporate. Repeat the addition of water and evaporate until all or most of the oil is removed, previously adding sodium hydroxide.

Soap Tincture: Add dilute sulphuric acid, distil and test distillate.

Tincture of Iodine: Add water and evaporate. Repeat until free iodine is removed. Add sodium hydroxide and evaporate.

Spirit of Camphor: Evaporate to near dryness; add sodium hydroxide and water; evaporate until all or most of the camphor is removed.

Chloroform Liniment: Add water and evaporate to near dryness; add sodium hydroxide and evaporate.

Fluid Extracts: Distil. If distillate is cloudy, filter with magnesium carbonate and test filtrate, using the equivalent of 5 cc. of alcohol.

Aromatic Spirit of Ammonia: Evaporate to near dryness, adding sodium hydroxide near the end.

Tincture of Ginger: Distil and filter the distillate through magnesium carbonate.

After the final evaporation steps with sodium hydroxide, the above products can be tested according to the method given.

#### SUMMARY.

A test is described for diethylphthalate detection in alcohol and spirituous products. False positives and negative blanks are obviated where previously, with the U. S. P. X test, such false reactions could not be entirely excluded. After completion of the test, results can be read in fifteen minutes or less. The host of organic substances giving false positives are eliminated by the ethyl-ether shake-out of the acid resorcinol mixture, retaining only the fluorescence dye formed. This new modification is offered for review by the Revision Committee of the U. S. Pharmacopœia.

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## PHENYLMERCURY NITRATE AND SOME OTHER PHENYLMERCURY SALTS.\*

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Phenylmercury nitrate was first prepared by Otto in 1870 (1). Renewed interest has been aroused recently by Weed and Ecker (2, 3, 4), who have studied its use as a non-toxic, non-irritating germicide.

The authors of the above papers have all assumed that the compound was of the normal constitution  $C_6H_5HgNO_3$ . Studies in these laboratories begun early in 1932 showed that this could not be correct. The average of eighteen analyses for mercury was 63.6%, with 64.1% as the upper, and 63.0% the lower, limit. This result suggested a basic phenylmercury nitrate,  $C_6H_5.HgOH.C_6H_5.HgNO_3$ , which requires 63.3% mercury. The compound is not, however, a basic salt analogous to bismuth subnitrate, for example. Not only is the composition unaffected by boiling tenth-normal nitric acid but the  $p_H$  of an aqueous solution is 4.3. Confirmation of the basic formula for phenylmercury nitrate was obtained by the behavior of phenylmercury hydroxide on titration. The hydroxide behaves as a moderately strong base toward acetic, lactic, hydroxybutyric, and the halogen acids yielding normal salts but behaves as a semi-acid base toward nitric, sulphuric, gluconic and phenol sulphonic acids, yielding basic salts. The remaining hydroxy group in the basic salts cannot therefore be ionized but must be firmly bound in a complex radicle such as  $[C_6H_5.HgOH.C_6H_5.Hg.]^+$ . Even assuming the presence of a complex ion in aqueous solutions of phenyl mercury nitrate certain anomalies still confront us.

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