THE HEAVY METALS TEST OF THE U. S. P.*

BY M. W. CAREY AND R. E. SCHOETZOW.[1]

The United States Pharmacopœia makes no distinction between inorganic substances and organic ones, with the exception of the volatile oils, in testing for heavy metal impurities. It is known that in many organic compounds the heavy metal impurities may be so firmly combined chemically with organic matter that the sensitivity of the test with hydrogen sulfide is impaired. The possibility is also recognized that the organic matter, even if not in chemical combination with the metal, may be of such a nature as to inhibit the formation of visible sulfides.

We find the following instances where traces of heavy metals present have not been detected by the U. S. P. XI heavy metal test, but have been detected by first destroying the organic matter by digestion with sulfuric and nitric acids and then applying the U. S. P. XI test:

	Organic Matter Destroyed.		Organic Matter Not Destroyed.	
Sample	Acid Solution.	Alkaline Solution.	Acid Solution.	Alkaline Solution.
Calcium mandelate				
85658	Slight color	Green color	None found	Slight green color
85659	Slight color	Green color	None found	Slight green color
85660	Slight color	Green color	None found	Slight green color
86068	Slight color	Green color	None found	Slight green color
Acid dehydrocholic				
88308	Faint color	Green color	None found	Slight green color
90056	Faint color	Dark green color	None found	Slight green color
90058	Faint color	Dark green color	None found	Slight green color
90059	Faint color	Dark green color	None found	Slight green color
Sulfanilamide				
87205	Slight color	None found	None found	Slight green color
87207	Slight color	None found	None found	Slight green color
Calcium gluconate				
87373	Slight color	Slight green color	None found	None found
Yeast				
87288	Slight color	Dark green color	None found	Faint color
Acid Mandelic				
87285	Faint color	Slight color	None found	Faint color
Triisopropanolamine				
86948	Definite color	None found	None found	None found

From the above it seems obvious that if one desires to know whether there are any traces of heavy metals present in organic compounds or samples containing organic material it is necessary to first destroy the organic matter. But, since the destruction of organic matter presents difficulties such as liberation of disagreeable fumes, consumption of time and, more important, the possibility that metals may

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be lost during the ashing or the destruction of the organic material by other means, we urge that the question be studied, especially as to how best to destroy the organic material, if it is desired that organic medicinals be as free from metallic contamination as the inorganic medicinals, and that the prior destruction of organic materials be made a part of the U. S. P. heavy metals test. Further we suggest that, if it should be found difficult to prevent the presence of some traces of metallic impurities in organic medicinals, it would be advisable to further amplify the U. S. P. tests to show the identity of the metal present and indicate the amount permissible. A toxic metal such as mercury or lead should be strictly limited in concentration, while more leniency might be shown to less toxic or harmless ones.

DRUG EXTRACTION. XXII. THE EXTRACTION OF PODOPHYLLUM.*,[1]

BY WILLIAM J. HUSA[2] AND D. W. LEE.[3]

In a previous study (1) it was found that alcohol was preferable to alcohol-water mixture (9:1) for the preparation of resin of podophyllum. Further research has been carried out to determine the relative efficiency of various methods of extraction as applied to podophyllum.

EXPERIMENTAL PART.

Materials Used.—Podophyllum, U. S. P. in fine powder (No. 60) obtained from two different sources was used. Drug A contained 7.35% resin and 7.24% moisture. Drug B contained 5.69% resin and 7.66% moisture. Alcohol was used as the menstruum.

Analytical Methods.—Resin determinations were made by the U. S. P. XI method. Moisture was determined by the U. S. P. XI method for drugs containing no constituents volatile at 100° C. To determine total extractive, 10 cc. of liquid were evaporated to apparent dryness on a water-bath, the residue treated with 1 cc. of absolute alcohol and again evaporated to dryness on a water-bath; the residue was then heated in an oven at 105° C. until the loss in weight between two successive weighings did not exceed 5 mg. Due to the hygroscopic nature of the resin, the balances were equipped with balance desiccators.

Experiment 1. Maceration with an Excess of Alcohol.—An experiment was conducted to determine the time necessary for the establishment of equilibrium in the maceration of podophyllum with an excess of alcohol, using the centrifuge method developed by Husa and Magid (2).

Into each tared, wide-mouth bottle of about 250-cc. capacity were placed 10 Gm. of drug and 90 Gm. of alcohol. The bottles were then placed in a cabinet at 22–25° C. for 15 minutes, during which time the bottles were gently shaken every 5 minutes. The bottles were then centrifuged at about 1000 r. p. m. for ten minutes and allowed to stand 5 minutes. The clear supernatant liquid was decanted into tared, glass-stoppered bottles and weighed; the bottles containing the wet marc were also weighed. The macerate was adjusted to 20° C. before withdrawing samples for assay. The same technique was used for 12-hour, 24-hour and 36-hour maceration periods except that the bottles were shaken at convenient irregular intervals.

Calculations were made as follows: (Weight of drug) minus (weight of moisture in drug) minus (weight of total extractive in macerate) = (weight of dry marc). (Weight of wet marc) minus (weight of dry marc) = (weight of liquid imbibed by the marc). The loss of menstruum

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