AN EMPIRIC ASSAY FOR THE RESIN CONTENT OF COMPOUND PILLS OF MERCUROUS CHLORIDE.*

BY L. E. WARREN.[1]

Compound pills of mercurous chloride, U. S. P. X have essentially the same composition as the compound cathartic pills of the U. S. P. IX. The difference between the two preparations is that the U. S. P. X formula contains resin of ipomea and the U. S. P. IX resin of scammony. Ipomea and scammony are closely related botanically. Their respective resins, although not chemically identical, have practically the same therapeutic properties. The preparation is a complex mixture containing calomel, resin of jalap, gamboge and compound extract of colocynth. The last-named preparation contains aloes, extract of colocynth, cardamom seed, resin of ipomea and soap. The Pharmacopœia directs the use of diluted alcohol as an excipient in compounding pills but most manufacturers use water instead. Also they frequently employ powdered licorice root or powdered extract of licorice as a binder or mass-maker.

Examination of the literature and consultation with manufacturers revealed no method for the assay of compound cathartic pills, except that some attempts had been made to determine calomel. It occurred to the writer, that since nearly all of the ingredients contained resinous material or vegetable acids, a method which would evaluate these constituents taken as a whole would be of empiric value and might serve for the detection of gross adulteration. The method which seemed to offer the greatest possibilities was a modification of the Jenkins' method for the assay of podophyllum.[2] Accordingly this method was tried. As used the method is as follows:

Weigh 20 pills individually and calculate the average weight and the maximum deviations from the average. Pulverize the pills in a mortar and pass the powder through a No. 40 sieve. Mix the pulverized material well.

ALCOHOL SOLUBLE.

Weigh a quantity of the powdered material, equivalent to ten pills, into a Gooch crucible or fat-free thimble. Place the container in a Wiley or a Bailey extractor and extract with alcohol until the material is completely exhausted of alcohol-soluble material. Transfer the alcoholic solution to a 100-cc. graduated flask, cool the solution to room temperature and make up to the mark with alcohol. Mix the solution well. Evaporate 10 cc. of the solution, equivalent to one pill, to dryness on the steam-bath in a weighed beaker and dry the residue at 100° C. for 30 minutes.

TOTAL RESINS.

Measure 10 cc. of the tincture of the material prepared as above described into a separator and add 10 cc. of chloroform and 10 cc. of 0.6 per cent hydrochloric acid (2 cc. of hydrochloric acid in 100 cc. of water). Shake the mixture and allow it to separate. Draw off the lower layer into another separator and repeat the extraction of the liquid in the first separator three times, using 15 cc. of a mixture of one volume of alcohol and two volumes of chloroform, each time, and adding these extractions to the extract in the second separator. Shake the combined extract with 10 cc. of 0.6 per cent hydrochloric acid and allow the mixture to separate. Draw off the lower layer, through a pledget of cotton placed in the stem of the separator, into a weighed flask

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[1] Food, Drug & Insecticide Administration, Washington, D. C.

[2] *Ind. & Eng. Chem.*, 6 (1914), 671.

and repeat the extraction of the acid liquid three times, using 15 cc. of fresh alcohol-chloroform mixture each time and passing the chloroform layer through the cotton. Evaporate the combined chloroform extracts to dryness, taking care to hold the container in an inclined position as the last portions of solvent are dissipated. Dry the residue to constant weight at 100° C.

Several commercial brands of compound cathartic pills were subjected to these tests. Such uniform results were obtained that it was deemed worth while to apply the method to a number of specimens. Consequently a specimen of the product was obtained from each of ten manufacturers. In addition, a laboratory specimen of unknown age and manufacture was included. Each product was assayed by the method heretofore described. The results obtained are given in Table I.

TABLE I.—RESIN CONTENT OF SEVERAL BRANDS OF COMPOUND CATHARTIC PILLS.

Specimen	Alcohol-Soluble. Solids.	Alcohol-Soluble. Per cent.	Total Resins. Per cent.		Total Resins. Grains per pill.	
A	31.63	31.66	19.79	20.03	1.14	1.16
B	38.12	37.88	22.45	22.17	1.11	1.10
C	44.58	44.55	25.60	25.21	1.23	1.21
D	46.82	46.92	24.38	23.73	1.10	1.07
E	50.25	50.29	26.53	26.53	1.17	1.17
F	45.42	45.59	27.57	27.21	1.26	1.25
G	48.93	49.09	18.71	18.74	1.08	1.08
H	40.98	40.97	22.98	22.94	1.15	1.15
I	39.73	39.77	25.42	26.09	1.17	1.19
			25.19	25.67	1.17	1.13
J	51.54	51.13	18.07	18.01	1.05	1.02
K	46.96	47.05	37.57	38.00	1.34	1.35

Origin unknown

If the results from the specimen of unknown origin be excluded, the alcohol-soluble material ranged from about 32 per cent to 51.5 per cent and the total resins from about 18 per cent to 27.5 per cent. The total resins in each pill ranged from 0.066 Gm. to 0.080 Gm. equivalent to from 1.05 grain to 1.26 grain. The average weight of the several brands of pills varies greatly, probably owing to the fact that each manufacturer uses different quantities of excipient or a different excipient. Therefore the determination of the alcohol-soluble matter is not of much value to regulatory officials. In like manner the *percentage* of total resins is not a standard of importance. However, these factors should be valuable checks in the control of manufacturing processes in which the weight and nature of the excipients are known. The criterion of greatest value is the quantity of resins per pill.

In order to secure a preparation of undoubted authenticity the writer visited the laboratory of a pharmaceutical manufacturer and watched the preparation of a batch of compound cathartic pills. A sample of each constituent was taken and the weight of each ingredient was checked before the material was placed in the mixer. The formula used did not contain compound extract of colocynth but instead the several ingredients were added separately in the calculated amounts. Also powdered glycyrrhiza and water were used as excipients instead of diluted alcohol. A sample of the pill mass and a specimen of the uncoated pills as they come from the pill-making machine were also taken. Later a specimen of the coated pill was obtained. Each of these was subjected to the Jenkins' test. The

results are recorded in Table II. It might be expected that there would be slight differences between the results from the uncoated and from the coated pills owing to the fact that the uncoated pills are subjected to a certain amount of drying in starch powder before the coating is put on. However, the coating added tends to make up in weight for the loss in drying.

TABLE II.—COMPARISON OF PILL MASS, UNCOATED PILLS AND COATED PILLS.

Specimen.	Alcohol-Soluble. Solids.	Alcohol-Soluble. Per cent.	Total Resins. Per cent.		Grains per pill.	
Pill mass	40.2	40.7	27.6	28.5	..	..
Uncoated pill	34.12	34.47	24.42	24.80	1.19	1.21
Coated pill	33.52	33.25	24.68	25.14	1.23	1.26

It will be noted that the quantity of resins in the finished pill is approximately the same as the maximum values found for the ten commercial specimens as recorded in Table I.

Each constituent of the pill mass (except the calomel and water) was then subjected to the Jenkins' assay process in order to determine what proportion of resin or vegetable acid it contributed to the whole. The findings are given in Table III.

TABLE III —CONTRIBUTION (IN RESIN OR VEGETABLE ACID) OF EACH CONSTITUENT TO COMPOUND CATHARTIC PILL MASS.

Constituent.	Per cent of resin (or vegetable acid) by Jenkins' assay.		Per cent of constituent in pill mass.	Per cent resin (or vegetable acid) contributed.
Extract of colocynth	36.3	35.6	4.00	1.44
Aloe	42.50	44.3	12.50	5.42
Cardamom Seed	5.9	5.9	1.25	0.74
Resin of Ipomea	90.1	90.0	3.50	2.25
Soap	79.8	80.0	3.75	3.00
Resin of Jalap	95.3	95.2	6.84	6.52
Gamboge	79.8	79.0	5.00	3.97
Glycyrrhiza	13.50	13.63	31.25	4.28

Some manufacturers object to this general, empiric method on the ground that the normal variations in resin (and vegetable acid) content of the constituent drugs is so great that no dependence should be placed on any standards that might be suggested for the compound preparation. It is true that this objection has a certain degree of validity but, in the absence of any other method whatever for the assay of the resin content of the pills, it would seem that any method which would yield an approximate evaluation of the active constituents of the preparations (other than calomel) would be welcome. Other manufacturers considered the proposed method useful in absence of any other. This principle has been applied by Cocking[1] to the assay of compound tincture of benzoin B. P. He determines the acid number, ester number, saponification value, etc., of that preparation and, from the data so obtained, makes comparisons with the values obtained from known preparations.

SUMMARY.

A method has been devised for determining the total resins (including some vegetable acids) of Compound Cathartic pills. Ten commercial brands of the product and a specimen of authenticated origin were subjected to the test. The

[1] *Quar. Jour. Pharm.*, 1 (1928), 337.

resin content varied from 0.0660 Gm. to 0.0821 Gm. per pill, equivalent to from 1.05 to 1.26 grain per pill. The method should prove useful to control chemists.

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ASSAY OF OINTMENT OF YELLOW MERCURIC OXIDE.*

BY L. W. GREEN AND R. E. SCHOETZOW.

Notwithstanding the simple nature of this and similar preparations, their assay has offered difficulties. The following general methods were tried but yielded poor checks and low results.

(*a*) Removal of fats by various solvents and weighing the residual mercury oxide.
(*b*) Reduction to metallic mercury, separation and weighing of the same.
(*c*) Digestion with dilute nitric acid, filtration and titration with potassium sulphocyanate solution.

In the first case the difficulties were due to the fine state of subdivision of the mercury oxide which made quantitative filtration impossible. This verifies an observation made by Noel L. Allport (*Quarterly Journal of Pharmacy*, Vol. 1, No. 1, under date of Feb. 4, 1928).

Allport has devised a method in which the ointment is dissolved in a mixed solvent containing 13 parts of benzene, 2 parts of glacial acetic acid and 5 parts of 90% alcohol, and the mercury precipitated and weighed as mercuric sulphide. Sjöstrom (*Pharmazeutische Zeitung* (1915), 554) has given a method in which the ointment is dissolved in ether, the solution mixed with potassium iodide solution and a measured excess of tenth-normal hydrochloric acid added. This method depends upon the reaction $3KI + HgO + H_2O = KHgI_3 + 2KOH$. The excess hydrochloric acid is titrated with tenth-normal potassium hydroxide using phenolphthalein.

We have tried these methods on known ointments with the following results:

Ointment.	Method.	Per cent HgO.
No. 1	Sjöstrom	(*a*) 2.04% (*b*) 1.97%
No. 2	Allport	(*a*) 1.99% (*b*) 2.00%
	Sjöstrom	2.01%
No. 3	Allport	2.13%
	Sjöstrom	2.10%

Both methods have been found satisfactory. The Sjöstrom method is the easier and more rapid to perform.

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