DRUG EXTRACTION. XIV. THE EXTRACTION OF PODOPHYLLUM.*

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Although the N. F. VI has adopted a mixture of 9 volumes of alcohol and 1 volume of water in place of the alcohol of the U. S. P. X, as menstruum for the preparation of resins of jalap and ipomea, the U. S. P. XI has retained the U. S. P. X menstruum of alcohol for the preparation of resin of podophyllum. Husa and Fehder have shown that alcohol is a better menstruum than the hydro-alcoholic menstruum of the N. F. VI for the preparation of resin of jalap (1) and resin of ipomea (2). In the present paper a report is made of experiments which were conducted to determine the relative value of alcohol and alcohol-water mixture (9:1) as menstrua for the preparation of resin of podophyllum, from the standpoint of rate of extraction, purity and yield of resin.

EXPERIMENTAL DATA.

Effect of Alcohol and Alcohol-Water Mixture (9:1) on Rate of Extraction.—Podophyllum, U. S. P., in fine powder, containing 7.41 per cent of resin by the U. S. P. XI assay method, was percolated with alcohol and with a mixture of alcohol 9 volumes—water 1 volume. Two 500-Gm. portions were extracted with alcohol, using 250 cc. of moistening liquid and with a maceration period of 48 hours after packing. Two other percolations, employing the alcohol-water mixture, were carried out in the same manner. Percolation was conducted at the rate of 50 cc. per hour, the percolates being collected in successive fractions of 250 cc., 250 cc., 250 cc. and 500 cc. The various fractions of percolate were assayed for resin by the U. S. P. XI assay method and for total extractive. The assay procedure was modified by heating the resins in a Freas vacuum oven at a temperature of 75–80° C., at one-hour intervals, until the loss between two successive heating periods was not more than 0.8 mg. in the resin determinations and not more than 2 mg. in the total extractive determinations. The results, which are shown in Table I, are averages of duplicate experiments.

TABLE I.—PERCOLATION OF PODOPHYLLUM WITH ALCOHOL AND WITH ALCOHOL-WATER MIXTURE (9:1).

	Gm. of Resin in Various Fractions of Percolate.		Gm. of Total Extractive in Various Fractions of Percolate.	
Percolates.	Alcohol.	Alc. 9 Vol.—Water 1 Vol.	Alcohol.	Alc. 9 Vol.—Water 1 Vol.
250 cc.	26.6	27.1	31.1	36.6
250 cc.	5.8	6.0	9.4	13.1
250 cc.	1.1	1.4	3.0	6.6
500 cc.	0.8	1.1	3.5	7.6
Total	34.3	35.6	47.0	63.9

The results in Table I indicate that the two menstrua extract resin at practically the same rate. The alcohol-water mixture takes out more extractive matter in each fraction of percolate, the difference in the later fractions being relatively greater than in the first fraction. From 500 Gm. of drug, the more aqueous menstruum removed 1.3 Gm. more of resin and about 17 Gm. more of total extractive.

Comparison of the Effects of Alcohol and Alcohol-Water Mixture (9:1) on the Preparation of Resin of Podophyllum.—Experiments were conducted to determine how a mixture of alcohol 9

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volumes—water 1 volume would compare with alcohol as a menstruum for the preparation of resin of podophyllum.

Two different lots of resin of podophyllum were prepared from 500-Gm. portions of podophyllum, in fine powder, using alcohol as the menstruum; each 500-Gm. portion of drug was moistened with 250 cc. of menstruum before packing. A maceration period of 48 hours after packing was included in the extraction procedure. Percolation was carried out at an average rate of 50 cc. per hour, 1250 cc. of percolate being collected from each 500-Gm. portion of drug. Each percolate was concentrated to the consistency of a syrup (reached at a volume of about 150 cc.) by distillation under reduced pressure. The resins were precipitated from the concentrated percolates, according to the method of the U. S. P. XI. After washing, the precipitates were air-dried in a dark place, and were then transferred, as completely as possible, to tared evaporating dishes, in which they were heated to constant weight in a vacuum oven at 75–80° C., the weight being considered constant when the difference between two weighings was not more than 0.1 Gm. The dishes were kept in a dark place between heating periods to avoid decomposition of the resins by light.

Two portions of resin of podophyllum were also prepared from 500-Gm. portions of podophyllum, maintaining the same experimental details as before, except that a mixture of 9 volumes of alcohol and 1 volume of water was used as menstruum, and that the concentration of percolate was carried out by distilling the first 250-cc. fractions under reduced pressure, as described above, and then by concentrating the remainder of the percolates on a water-bath, exposed to the air, but in such a manner that the temperature of the liquid did not rise above 80–90° C. during the evaporation. The percolates were concentrated to a syrupy consistency (reached at a volume of about 250 cc.).

The average yield of resin of podophyllum obtained from the two 500-Gm. portions of podophyllum extracted with U. S. P. alcohol was 5.4 per cent, while from the two portions extracted with the alcohol-water mixture (9:1), the yield was 5.8 per cent. The various lots of resin were assayed by the U. S. P. XI assay method for determination of the percentage of resin in podophyllum. Taking the average of several determinations, the resin prepared with the U. S. P. alcohol was found to assay 99.7 per cent resin, while the resin prepared with a mixture of 9 volumes of alcohol and 1 volume of water assayed 98.2 per cent resin.

DISCUSSION OF RESULTS.

It was found that the two menstrua extract resin of podophyllum at practically the same rate. The alcohol-water mixture gave a slightly higher yield of resin, but according to assay results, the product was not as pure as that obtained by the use of the U. S. P. alcohol.

Since the yields of resin were 5.4% and 5.8%, respectively, while the drug assayed 7.41% resin, a loss of resin in the process of precipitation and washing is indicated.

The menstruum of alcohol 9 volumes—water 1 volume gave a slightly higher yield of resin, but the product was not as pure as that obtained by using alcohol as the menstruum. These results are in accord with the results of Husa and Fehder in similar investigations of the extraction of jalap and ipomea (1), (2).

SUMMARY.

Alcohol and alcohol-water mixture (9:1) extract the resin from podophyllum at practically the same rate. The alcohol-water mixture (9:1) gives a slightly higher yield of resin of podophyllum; however, the product is less pure than that obtained by use of alcohol. On the basis of purity of product, it is concluded that alcohol is preferable to alcohol-water mixture for the preparation of resin of podophyllum.

REFERENCES.

(1) Husa, W. J., and Fehder, P., JOUR. A. PH. A., 26, 121 (1937).
(2) Husa, W. J., and Fehder, P., *Ibid.*, 26, 319 (1937).