

Four portions of 500 Gm. each of nux vomica in No. 40 powder (assaying 2.35% alkaloids) were percolated using Type Process B except for variations in maceration and rate of flow. The following menstrua were employed: Menstruum I: acetic acid 100 cc., water 150 cc., alcohol 750 cc.; Menstruum II: alcohol 3 volumes—water 1 volume. Each portion of drug was moistened with 300 cc. of Menstruum I and macerated for 15 minutes before packing.

TABLE V.—ASSAY RESULTS ON RESERVE PORTION.

Rate of Flow.	Gm. Total Alkaloids in Reserve Portion.		Gm. Total Extractive in Reserve Portion.	
	No Macera- tion.	48 Hours' Maceration after Packing.	No Macera- tion.	48 Hours' Maceration after Packing.
0.5 cc. per minute	8.95	9.97	53.0	54.8
1.5 to 2.5 cc. per minute	8.77	9.30	53.7	50.2

The efficiency of extraction of the alkaloids of nux vomica was increased slightly by the 48-hour period of maceration after packing and also by percolating at the slower rate.

SUMMARY.

Maceration before packing is of no importance in increasing the efficiency of extraction of belladonna root in a percolation process; maceration after packing causes a slight increase in efficiency of extraction of total alkaloids and total extractive. Experiments on yellow cinchona and nux vomica also tend to show that maceration after packing increases the efficiency of extraction to a slight extent.

Slow percolation gave slightly more concentrated percolates than rapid percolation in case of nux vomica and yellow cinchona. Percolation of belladonna root at a moderate rate gave just as efficient extraction as the slower rates tested.

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THE DETERMINATION OF ALCOHOL IN PHARMACEUTICAL LIQUIDS. I. A STUDY OF THE U. S. P. X AND U. S. P. XI METHODS.

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The United States Pharmacopoeia IX (2) was the first edition to carry a method for the determination of alcohol in liquids, and the method stated there was repeated without significant changes in the U. S. P. X (3). The method is based upon the well-known procedure of distilling the alcohol from the sample and determining the specific gravity of the distillate. Then by reference to the proper tables the alcohol percentage of the original sample can be found. Volatile substances other than alcohol and water which would affect the specific gravity are directed to be removed in so far as possible by saturating the distillate with sodium chloride, shaking it with petroleum benzin, and then redistilling the aqueous portion. This procedure is definitely time-consuming and the new U. S. P. XI method (4) is somewhat shorter and simpler, consisting of adding saturated sodium chloride solution to the sample, shaking it with petroleum benzin, and distilling the aqueous portion.

It is similar to the A. O. A. C. method (1). When troublesome emulsions are formed in the shakeout a double distillation very similar to the U. S. P. X method is used.

The authors have long questioned the accuracy of the methods when interfering volatile substances are present, and have felt that the procedures are unduly time-consuming for routine work. An analytical method is at a double disadvantage when, in addition to being lengthy, it is not particularly accurate, and therefore a speedy, reliable official method is badly needed.

EXPERIMENTAL.

In order to test the accuracy of the methods, measured samples of known alcohol-water mixtures were contaminated with various volatile substances commonly found in official products and attempts were then made to determine the alcohol content of the original alcohols by the U. S. P. X and U. S. P. XI methods. The details of the procedures follow:

The specific gravities of the alcohol-water mixtures were carefully determined by the pycnometer and the alcohol contents found by reference to the proper tables. Certain quantities of chloroform, volatile oils, or soap were added to measured samples of these known alcoholic mixtures. In case the U. S. P. X method was to be followed, the sample containing the contaminating substance was distilled, the distillate saturated with sodium chloride, shaken with petroleum benzin and redistilled, and the specific gravity of the second distillate was determined. In case the U. S. P. XI method was to be followed the sample of the known alcohol was measured directly into a separatory funnel, the contaminant added, and then the shakeout and distillation were completed. In every case the official instructions were followed exactly, using the prescribed quantities of water, petroleum benzin and saturated sodium chloride solution.

Samples of known alcohols were also distilled directly in order to test the efficiency of the distillation apparatus, which consisted of a 500-cc. short-neck Kjeldahl flask, a Kjeldahl trap, and a 12" spiral condenser. City water at a temperature of 20-25° C. was used in the condenser.

TABLE I.

Contaminant.	Sample of Known Alcohol. Cc.	Correct Alcohol Content %.	Alcohol Content Found.	
			U. S. P. X Method %.	U. S. P. XI Method %.
0.5 cc. oils for Flexit. Cascara Aromatic (anise, cinnamon, coriander, methyl salicylate)	50	17.5	16.9	17.0
			16.6	16.7
1 cc. Chloroform	50	17.5	16.8	16.7
			17.1	16.6
0.15 cc. oils for Elixir Aromatic (orange, lemon, coriander, anise)	50	17.5	16.3	17.1
			16.5	16.8
1 cc. Chloroform	25	50.0	48.2	49.1
			48.4	48.7
1.5 Gm. Powdered Soap and 0.5 cc. Oil Rosemary (and excess sulphuric acid)	25	50.0	48.6	49.4
			48.6	49.2
0.12 cc. oils for Aromatic Spirit of Ammonia (lemon, lavender, myristica)	10	77.8	75.5	..
			75.0	..
0.3 cc. oils for Aromatic Spirit of Ammonia	25	77.8	..	76.2
			..	76.6
None, but using the petroleum benzin shakeout as if a contaminant were present	25	50.0	..	49.7
			..	77.2

TABLE II.

	Size of Sample. Cc.	Correct Alcohol Content %	Alcohol Content Found %
Single, direct distillation, without shakeout	25	77.8	77.6 77.8
Distilled twice, without shakeout	25	77.8	77.6 77.5

DISCUSSION.

It is clear that the U. S. P. X and U. S. P. XI methods of determining alcohol in pharmaceutical preparations when volatile substances are present give low results and that only slight loss occurs due to the shakeout alone (Table I). It has been shown (Table II) that even with non-chilled condenser water the loss on simple double-distillation is slight. In addition to being inaccurate the methods consume considerable manipulative time; the U. S. P. X procedure is the worst in this respect.

The U. S. P. X required that a 10-cc. sample be taken with alcohol percentages above 50%; since the final distillate had a volume of 50 cc., this meant that the alcohol percentage of the distillate was multiplied by five in order to get the alcohol content of the sample. This, of course, introduced a large factor with which to multiply the already noticeable errors. The U. S. P. XI method is an improvement in this case, since it requires that a 25-cc. sample be taken for all alcohols above 30%. However, it would have been more consistent to have stipulated that a 25-cc. sample be taken for all alcohols above 40%, since a 50-cc. sample of a 40% alcohol contains the same quantity of ethyl alcohol as a 25-cc. sample of an 80% alcohol. If the U. S. P. XI method works with 25 cc. of an 80% alcohol, surely it should work with 50 cc. of a 40% alcohol. This has been checked experimentally, and it was found that no detectable loss occurred when a 50-cc. sample of a 40% alcohol was distilled into a 50-cc. flask.

The U. S. P. XI directions state,

"If volatile oils are present in small proportions only, and a cloudy distillate is obtained, the benzin treatment not having been employed, the distillate may be clarified and rendered suitable for the specific gravity determination by shaking it with about one-fifth its volume of purified petroleum benzin, or by filtering it through a thin layer of purified talc."

Shaking the distillate with benzin or filtering it through talc *after it has been made to volume* and just before the specific gravity determination should not be permitted. It is contrary to any good analytical technique; the objections to it so far as correct analytical procedures are concerned are so obvious that they need not be mentioned here. In addition, we have tried filtering certain cloudy distillates and frequently the results are far from correct. In the case of Fluidextract Cascara Sagrada Aromatic, for instance, our results have been low; in some other cases the results have been high. If the portion of the volatile substance soluble in the distillate has a high specific gravity, of course the apparent alcohol percentage will be low. In the interest of good analytical procedures, both theoretically correct and giving accurate results, the authors are definitely opposed to the inclusion of this paragraph in the description of the official method.

We do not wish to give the impression that this study has resulted in destructive criticism only, and that we have nothing constructive to offer. The authors have worked out a new method of determining alcohol in pharmaceutical preparations which is based upon the distillation being carried out in a simple, special apparatus in such a way that all volatile substances which would otherwise have to be shaken into petroleum benzin are automatically removed in the distillation. The method gives correct results in all of the cases listed in this paper where the official method gave inaccurate results. The procedure will be described in a later issue of *THIS JOURNAL*.

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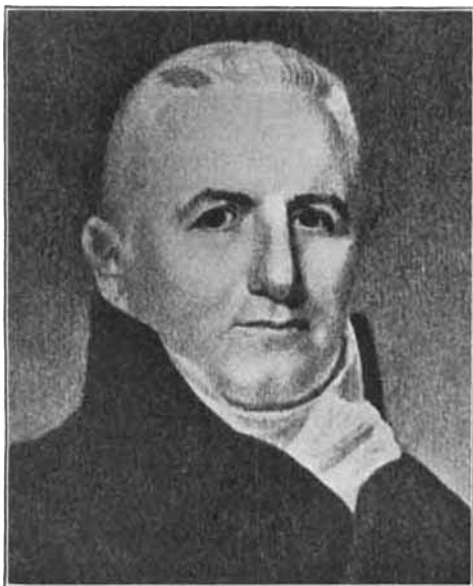
SUMMARY.

The U. S. P. X and U. S. P. XI methods for the determination of alcohol in pharmaceutical liquids when other volatile substances are present are both time-consuming and inaccurate. In some respects the U. S. P. XI method is an improvement over that of the U. S. P. X but both methods tend to give low results.

A new method of assaying for alcohol has been worked out which is rapid and accurate; it will be reported later.

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- (4) *United States Pharmacopœia XI*, 436 (1936).



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