

## THE OFFICIAL MENSTRUUA.\*

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For the exhaustion of vegetable drugs in making extracts, fluidextracts and tinctures—a total of 233 of these preparations—the U. S. Pharmacopœia and National Formulary use 20 different alcoholic strengths of menstrua, besides water, the menstrua which contain acid or glycerine, and aromatic spirit of ammonia.

These alcoholic menstrua are as follows:

MENSTRUUM.				
Alcohol.	Water.	Sp. gr.	Strength.	No. of preparations used in.
1	0	0.8095	95.0%	34
95	5	0.8243	90.9%	1
9	1	0.8384	86.5%	1
8	1	0.8413	85.6%	1
85	15	0.8516	82.0%	1
5	1	0.8569	80.2%	3
4	1	0.8645	77.4%	15
3	1	0.8768	72.8%	36
7	3	0.8886	68.1%	1
675	325	0.8943	65.7%	1
2	1	0.8977	64.3%	25
65	35	0.9016	62.6%	1
5	3	0.9053	61.0%	1
3	2	0.9110	58.4%	10
1	1	0.9311	49.0%	69
3	4	0.9441	42.0%	1
2	3	0.9490	39.0%	2
1	2	0.9582	32.8%	7
1	3	0.9696	24.0%	5
1	7	0.9838	11.8%	1
0	1	1.0000	0.0%	17

(Glycerin is used in many of the above, but is ignored here for reasons which will be explained later.)

If these menstrua were divided between the drugs and preparations with any degree of uniformity, it would mean an average of about 11 preparations to each menstruum, and an average variation of 5 per cent of alcohol in the menstrua. But the table discloses a different condition. Of the 233 preparations, 206, or 88+ per cent of all are made with seven different strengths of menstrua.

Thus, 95% alcohol is used for 34 preparations, 77.4% alcohol for 15, 72.8% alcohol for 36, 64.3% alcohol for 25, 58.4% alcohol for 10, 49% alcohol for 69, and water for 17 preparations. (The last have alcohol added, except extracts, but water is the menstruum used.) And 10 of the menstrua are used for one preparation each, while, four are employed in 17 preparations, there being 2, 3, 5 and 7 respectively for each.

In other words, 7 different strengths of alcohol, or water are sufficient for 88 per cent of all the preparations, four others are used in a remaining 7 per cent, and ten different menstrua are used for the remaining 4 per cent of preparations.

\* Section on Practical Pharmacy and Dispensing, A. PH. A., Philadelphia meeting, 1926.

If the smaller 12 per cent of the preparations possess peculiarities which require a variety of individual menstrua, they are scientifically sound, but if these menstrua are the result of accident in experimental research, of tradition, or of isolated consideration, then they need revision.

Most of the menstrua used in extraction of drugs are the result of empirical work, and are adopted independently. As an instance of how discrepancies will occur take the Fluidextract and Tincture of Calendula of the N. F. V. This drug has usually been extracted with 95% alcohol, but the sub-committee on Fluidextracts recommended a change to 64% alcohol for the fluidextract. The sub-committee on tinctures did not agree with this, and retained the 95% alcohol for the tincture. Thus the official Fluidextract of Calendula is made with 64% alcohol, and the Tincture is made with 95% alcohol. Obviously one of these sub-committees is mistaken in its judgment. A series of experiments on different lots of Calendula is needed to determine which is right.

With some of the menstrua, the authority evidently had only one preparation in mind. Thus Tincture of Cinnamon, made with a mixture of 675 cc. of alcohol and 325 cc. of water is obviously designed as a menstruum for 1000 cc. of tincture only. (The present menstruum contains some glycerin in place of water.) Tincture of Gelsemium, with a menstruum of 650 cc. of alcohol and 350 cc. of water is designed similarly—for 1000 cc. of tincture, though the mixtures stated are not sufficient in either case for the required yield. Furthermore the menstrua for the Fluidextract and for the Tincture of Gelsemium are not the same—one being 77 per cent and the other 62.5 per cent alcohol.

Again it seems very probable that the experimenters in either case did not realize that a simple mixture of two volumes of alcohol and one of water contains within 1.5 per cent as much alcohol as either of the two large-figured menstrua. This factor seems to have been overlooked in many cases. The table has been a revelation in that respect, and a surprise also. Thus one would not have guessed that a mixture of 8 volumes of alcohol and 1 volume of water is practically the same as that of 9 volumes of alcohol and 1 of water, but the actual difference is less than 1 per cent of strength. It is noticeable that most of the separate menstrua are close enough to one of the six or eight leading menstrua to warrant a suspicion, at least, that most of them could be merged into the more common or simpler mixtures without any sacrifice of value. A brief study of the table suggests that the 21 menstrua there listed might well be cut to 8 or 10.

At least some corresponding preparations might be unified. For instance, no good reason is apparent for having three individual and different menstrua for such similar tinctures as Tincture of Capsicum (U. S. P. 90.9%), Tincture of Capsicum and Myrrh (N. F. 85.6%) and Tincture of Ginger (U. S. P. 82.0%). If 95% alcohol is too strong, a single 80 per cent or 85 per cent should be satisfactory for all these.

Also why should Tincture of Ignatia be made with 85.6% alcohol, and the Extract with 72.8%, particularly when the last menstruum is satisfactory for Tincture of Nux Vomica?

Why should Tincture of Aconite be made with 68.1% alcohol and the Fluidextract with 72.8%? Or Tincture of Gelsemium with 62.6% alcohol and the Fluidextract with 77.4%? And Tincture of Hop with 49% and the Fluidextract

with 61%? Experience has shown that in general the best menstruum for a tincture is the same as for the corresponding fluidextract, and in most of the cases in the Pharmacopœia and National Formulary the two correspond.

A menstruum serves three functions: (1) it extracts the active principles of the drug with as little extraneous matter as may be practicable, (2) it preserves the activity and usefulness of the drug or preparation under varying conditions of storage and exposure, and (3) it makes the preparation as economical as is consistent with the first two.

The first function is the simplest. It needs only a knowledge of the chemical and physical character of the drug, and of its active constituents to select the menstruum. If the active principle is resinous, a strongly alcoholic menstruum is needed. If the activity is due to alkaloids, glucosides or similar principles, weak alcohol or water may suffice. If sugars, gums, tannins, etc., are the main desired ingredients, water will extract these. But attention must be paid to the fact that while water or weak alcohol can extract the active constituents, they may also extract so much of gummy, saccharine, albuminoid, tannoid and coloring substances that the product is unduly dilute, and also more prone to deteriorate.

The second function is not as simple. Stability of the preparation now means not only freedom from fermentation or molding, or sedimentation, but it includes also the prevention of any change which would reduce the value of the preparation in any way. Until recent years, precipitation was the main criterion of stability, but recent work is recognizing that important and detrimental changes may occur without any precipitation.

The author showed in a previous paper<sup>1</sup> that some of the astringent preparations may entirely lose their value as astringents and yet show no evidence of change by precipitation.

Tincture of *Digitalis* has never been troublesome through precipitation, but we know that when made with diluted alcohol it soon loses its potency though remaining clear, while stronger alcohol preserves the activity. Tincture of *Gentian* is commonly made with stronger alcohol in Europe than here, because European pharmacists and physicians place more value upon an unchanged gentiopicrocin than do we.

This function is aided in many cases by the addition of acids to the menstruum, or by use of glycerin. While the addition of acid to a menstruum frequently increases its solvent power, thus aiding extraction, recent studies tend to show that acids play their most important part as stabilizers. Witness the recommended addition of acid to Tincture of *Aconite*, and to Tincture of *Digitalis*. Also the recent studies on  $p_H$  values in tinctures and fluidextracts. The value of hydrochloric acid in cinchona preparations is partly in facilitating extraction but more in stabilizing the preparations.

Glycerin is used in 17 of the official fluidextracts and in 10 tinctures. In all but two of these it is used in the menstruum. But it has been shown that in most cases glycerin hinders extraction, and the drugs are more rapidly exhausted by the aquo-alcoholic menstruum without glycerin, except in the case of the astringent drugs. Glycerin is a good solvent for tannin, and aids materially in extracting this principle. But in other drugs glycerin will serve its purpose

<sup>1</sup> "Permanence of Some Astringent Preparations," *JOUR. A. PH. A.*, p. 334 (1912).

better when added to the percolate. It serves well as a stabilizing agent,<sup>1</sup> but not as an extracting agent. Furthermore when dilutions are made of super-standard percolates of alkaloidal preparations, to bring them to standard, the dilution should be made with the mixture of alcohol, water and glycerin that is directed for the initial percolation, rather than with alcohol and water as is directed.

The full value of glycerin as a stabilizer would thus be secured in the adjusted product, which is not obtained under the present plan. Except for the astringent drugs—nearly all of the liquid preparations of which need better menstrua than are now used—it is better practice to add the glycerin to the percolate than to use it in the menstruum.

As for the third function—economy—it is scarcely necessary to point out that any reduction in costs at the expense of reliability or activity is not economy. Active and reliable preparations are the prime considerations and are always the most economical.

A tendency has been apparent to reduce the alcoholic strength of menstrua, partly to show a coöperative spirit with the prohibition enforcement, and partly to reduce costs. Both of these are laudable if made secondary to activity and reliability. But the tendency of recent studies is toward stronger alcoholic menstrua as needed for reliability in action.

Alcohol rejects more extraneous matter than does water, and an alcoholic solution retards hydrolysis and oxidation—two factors that make for deterioration. Aqueous and weakly alcoholic solutions are more prone to deteriorate through these actions as well as through fermentation. Thus while the active principles of a plant may be soluble in water or weak alcohol it does not follow that weakly alcoholic liquid preparations of the drug are suitable.

Aside from the larger amount of extraneous matter which water usually extracts from plants, and which may act as diluents in making solid or powdered extracts, the presence of an undue amount of extraneous matter invites changes which may precipitate or hydrolyze some of these, and some of the activity is very probably entangled in the reactions and thus lost. Experience has shown that when precipitation of inert matter occurs alkaloids are carried down with it, although the alkaloids are quite soluble in the menstruum.

The menstrua used in the majority of the official preparations seem to be satisfactory, but some certainly need revision. And a further unification of menstrua will help to prevent discrepancies, as well as simplifying the formulas.

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#### LABORATORY FIRST AID CHART.

The Committee on Safety and Safe Guards of the Department of Chemistry of the College of the City of New York has prepared a list of "First-Aids" for the treatment of laboratory accidents. This list deals with ordinary injuries likely to occur within the laboratories

and gives detailed directions for their treatment by various chemicals and products. The list has been amended and amplified by Dr. Alex O. Gettler, toxicologist for the Medical Examiners office of New York City. The list is to be published in chart form and copies are to be supplied laboratories throughout the country.

<sup>1</sup> "The Function of Glycerin in Tinctures and Fluidextracts," *JOUR. A. PH. A.*, p. 868, (1920).