close approximation to the truth in samples containing a proportion of menthol not varying greatly from the pharmacopoeial standard:

Determine total menthol by the percent U. S. P. formula, then multiply the percent thus determined by $\frac{100 - (P \times 0.212)}{100}$, the symbol P standing for the percent of menthol present in the oil as ester. The full expression will read:

$$\text{Percentage of total menthol} = \frac{A \times 7.808}{B - (A \times 0.021)} \times \frac{100 - (P \times 0.212)}{100}.$$

Example: Ten Gm. of a given sample of oil consume in saponification 7 mils of half-normal alcoholic alkali, while 5 Gm. of the acetylized oil consume 30 mils. By the U. S. P. formula, the sample contains 53.48 percent total menthol. By either of the modified formulas here proposed the percentage is reduced to a little less than 52.9 percent.

All that has been said in criticism of the U. S. P. assay for oil of peppermint applies, *mutalis mutandis*, to that for oil of rosemary. The second of the two modified formulas given above requires only the change in the numerator from 7.808 to 7.707 when borneol instead of menthol is to be determined.

SOME VARIATIONS IN CINCHONA BARK AND ITS PREPARATIONS.*

BY HUGO H. SCHAEFER.

Ever since the outbreak of this great war much has been said of the low grade cinchona barks on the market. Numerous samples have been brought to the author's attention which failed to pass the U. S. P. requirements. This, of course, is largely due to the fact that owing to the derangement of shipping facilities the regular supply of Java Cinchona has been interfered with, thereby resulting in a shortage of this high grade bark. The result is that the price of bark has increased considerably and new sources of cinchona are being sought all over the world. Many of these barks have not been investigated and upon analysis are found to be very low in alkaloidal content. This, of course, is supposed to be taken care of in the U. S. P. IX by its requirement of 5% total alkaloids. Quinine, however, as we know is the most important alkaloid in cinchona bark. The U. S. P. VIII required 5% total alkaloids, and 4% ether-soluble, the latter representing an approximation of the quinine content. In the latest revision, however, this ether-soluble requirement was omitted, possibly due to the fact that in the usual cinchona barks the proportions of the various alkaloids do not vary greatly. In the last few years, however, the author has had occasion to assay a number of samples of cinchona bark and its preparations containing 5% or more of total alkaloids but comparatively little quinine or ether-soluble alkaloids. These barks, after being reduced to a No. 60 powder, were assayed according to the U. S. P. IX for total alkaloids using, however, double quantity of bark solvents, etc. The bark was extracted with the ether-chloroform mixture, the latter made alkaline with ammonia, the water added to cause the drug to settle and the aliquot portion of the solvent decanted. This was completely shaken out with weak sulphuric acid and the volume of this acid extract made up to exactly 100 mils with water. This then contained the alkaloids of 8 Gm. of drug. One-

* Read before Scientific Section, A. Ph. A., Chicago meeting, 1918.

half, or exactly 50 mils of it, representing 4 Gm. of drug was used for determining the total alkaloids by extracting with chloroform, evaporating the solvent, drying, and weighing the residue, the other half was extracted with ether in accordance with U. S. P. VIII to determine ether-soluble alkaloids. Following are the results of five samples found to contain more than 5% total alkaloids but less than 4% ether-soluble:

U. S. P. IX = Not less than 5 percent total alkaloid.
U. S. P. VIII = At least 5 percent total and 4 percent ether-soluble alkaloids.

	Total alkaloids.	Ether-soluble alkaloids.
1	5.32	3.42
2	5.83	2.92
3	6.01	3.01
4	5.52	2.98
5	5.08	2.67

The question at once arose as to whether any of such barks had been used in making preparations and with this in view a number of tinctures obtained on the open market were analyzed in accordance with U. S. P. IX for total alkaloids by evaporating 25 mils of the sample, incorporating with sawdust, drying and proceeding as directed under Cinchona. The residue of total alkaloids so obtained was then redissolved in dilute sulphuric acid and assayed for ether-soluble alkaloids in accordance with directions given under Fluid Extract of Cinchona of the U. S. P. VIII, which was also the method used for assaying the tincture.

By far the greater number of samples passed both the requirements of the old as well as of the new Pharmacopoeia, but the following results were obtained from three of the tinctures:

U. S. P. IX = not less than 0.8 Gm. nor more than 1 Gm. total alkaloids in 100 mils.
U. S. P. VIII = 0.75 Gm. ether-soluble alkaloids in 100 mils.

	Total alkaloids. Gm. in each 100 mils.	Ether-soluble alkaloids Gm. in each 100 mils
A	0.912	0.64
B	0.954	0.59
C	0.983	0.49

It is interesting to note in U. S. P. VIII the directions for making Tincture of Cinchona called for the use of Cinchona yielding not less than 4% of anhydrous ether-soluble alkaloids and in the finished product the requirement was 0.75 Gm. anhydrous ether-soluble alkaloids in each 100 mils. Nothing at all is said of total alkaloids, but the ether-soluble requirement was the one considered of prime importance. In the U. S. P. IX, however, only the total alkaloidal percentage is considered irrespective of the kind of alkaloid present.

A number of samples of fluidextracts of cinchona were assayed in similar manner for both total and ether-soluble alkaloids, with the following results obtained from three of the samples:

U. S. P. IX = Not less than 4 nor more than 5 Gm. total alkaloids of cinchona in each 100 mils.
U. S. P. VIII = 4 Gm. ether-soluble anhydrous alkaloids in each 100 mils.

	Total alkaloid. Gm. in each 100 mils.	Ether-soluble alkaloids. Gm. in eaeh 100 mils.
A	4.61	3.20
B	4.23	3.01
C	4.01	2.92

Here also the U. S. P. VIII simply considered ether-soluble alkaloids and the U. S. P. IX only total alkaloids. All these facts seem to show that the requirements of the new Pharmacopoeia are lower than those of the old. For example, a fluidextract of cinchona according to U. S. P. IX may pass with 4 Gm. total alkaloids in 100 mils while the U. S. P. VIII required at least 4% ether-soluble alkaloids.

In the opinion of the author it would be much better to have requirements for both total and ether-soluble alkaloids for Cinchona and its preparations. Quinine is, of course, the most important and active alkaloid present and the ether-soluble alkaloidal factor is a fairly good check on the percentage of quinine present. Especially, at present, when such a large variety of cinchona barks are being placed on the market, a close check on the quality should be kept.

RESEARCH AND THE UNITED STATES PHARMACOPOEIA.*

BY A. H. CLARK.

The question of Pharmacopoeial Revision is now a very live one. Much has been published within the past year regarding the present plan of revision. Many suggestions have also been made as to changes which might lead to an improvement in the present arrangements. In this paper only one phase of this important subject is discussed—research in connection with the scientific problems involved. Only by thorough and accurate research can any of the objectionable features of the present scientific work of the Pharmacopoeia be overcome.

When I became a member of the present Committee I was a stranger to revision methods, and also somewhat younger and much less experienced. Both of these factors operated to give me abundant enthusiasm. I immediately set out to demonstrate by a thorough investigation of the literature the correctness of all statements made in the Book and, if necessary, confirm them by experiments conducted by myself or under my directions. Alas! Before proceeding very far along this path I was hopelessly lost in the wilderness. Some of the statements made did not seem to have any source in the literature. Effort was then made to demonstrate by actual experiment whether or not these statements were true. Again, disappointment! In some cases the experiments led so far into the maze of scientific thought that I was completely lost. Other statements, while involving apparently simple question of theory, were found to be so complicated in fact that experiments undertaken to decide them seemed to involve work without end. Finally nearly all of my dreams vanished in the mists of reality, for it was found to be physically impossible to accomplish even a small portion of the things I had hoped to do. It is not unlikely that others have had the same dreams and disappointments.

The instructions for the last revision were to change only those things that had been criticized or about which something new had been published. In other words, to base all revision upon published criticisms and to attempt no extended investigations. This has been the policy to a greater or less extent from the very beginning. It has resulted, I am sure, in some statements being handed down

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