

manded not less than twenty-five per cent of chloroform as a standard for this product, basing this requirement upon the present formula. Such an act would have given official recognition to the volatile nature of the compound, and would also have set a limit of deviation. The Pharmacopœia sets no standard for this product other than the quantities in the formula, and the matter of legality is left to the judgment of the supervising agency. At all events, in preparations such as Chloroform Liniment, the customary toleration of ten per cent limitations, is manifestly impossible to maintain. Another point of interest in this product is found in the fact that, in making Chloroform Liniment from chloroform and soap liniment, an opportunity is afforded to gage the composition of the soap liniment so far as its alcoholic content is concerned. If the resulting product is perfectly clear, it can be accepted as indicating that the soap liniment is up to standard in alcohol. Any reduction in the alcohol content of Soap Liniment is sure to affect the solubility of chloroform, especially in such proportions demanded in the official Chloroform Liniment. In the total number of Chloroform Liniments considered here only one spurious sample was found. In one case the product was shown to consist of cotton seed oil to which a few drops of chloroform had been added.

During the two years covered by this study, no sub-standard lots of Acetylsalicylic Acid Tablets or Spirit of Camphor have been found.

Confessedly, the matter as presented here is inadequately covered, and in a sense superficially studied, as I have made no attempt to go into exhaustive details. However, I feel satisfied that the figures submitted are such as to reflect much credit upon the retail practicing pharmacists of my State, and they are sufficient in my judgment, to refute the statement, all too frequently made, that the products dispensed by the retail pharmacists are grossly adulterated or carelessly prepared. My observations are based upon an experience covering the past four years, during which I have had unusual opportunity to study this matter, and I respectfully submit this brief study of several hundred drug products as showing that the official standards are met to an extent quite remarkable.

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#### THEORETICAL STRUCTURE OF THE CORRECTION FACTOR AS APPLIED IN THE MENTHOL ASSAY OF PEPPERMINT OIL—WITH A NOTE ON THE ASSAY OF OIL OF ROSEMARY.

BY SIMON MENDELSON.

The present official assay procedure for the valuation of peppermint oil is a modification of the method originally proposed by Power and Kleber<sup>1</sup> in 1894. The formula for the final reduction of the results of an assay has in the U. S. P. X been rendered more complicated by the application of the correction factor  $[1 - E \times 0.0021]$  in accord with the newer requirements therein specified.

Example: (Specified indication of analytical results in the assay of oil of peppermint).

$$\text{U. S. P. IX } \frac{A \times 0.07808 \times 100}{B - (A \times 0.021)} = \frac{A \times 7.808}{B - (A \times 0.021)} = \text{percentage of menthol.}$$

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<sup>1</sup> *Pharm. Rund.*, 157 (1894); *Z. anal. Chem.*, 33, 762 (1894).

$$\text{U. S. P. X } \frac{A \times 7.811}{B - (A \times 0.021)} \times [1 - (E \times 0.0021)] = \text{percentage of total menthol,}$$

where  $A^1$  = quantity of  $N/2$  alcoholic KOH required for saponification of the ester (menthyl acetate,  $C_{10}H_{18}C_2H_3O_2$ ),

$B$  = weight of acetylated oil used for the actual test,

$E$  = percentage of esters calculated as menthyl acetate,

0.021 = correction for the increase in weight of the oil due to acetylation, in terms of  $N/2$  alkali. In other words, this factor represents the equivalent of 1.0 cc., of  $N/2$  alkali in terms of the acyl radicle ( $CH_3C:O$ ) in combination with the menthol to form menthyl acetate (m. w. of acyl radicle = 43).

Equivalent in terms of  $N/2$  KOH =  $\frac{43}{2} = 21$  Gm. per L; therefore equivalent of 1.0

$$\text{cc. of } N/2 \text{ KOH} = \frac{21}{1000} = 0.021 \text{ Gm.,}$$

7.811 =  $100 \times 0.07811$ , where the latter term = the equivalent of 1.0 cc. of  $N/2$  KOH in terms of menthol; 1 molecule of menthyl acetate = 1 molecule of menthol; M. w. = 156.21.

Equivalent of 1 L  $N/2$  KOH =  $\frac{156.21}{2} = 78.11$  Gm.; hence equivalent of 1.0 cc.,  $N/2$

$$\text{KOH} = \frac{78.11}{1000} = 0.07811 \text{ Gm.}$$

N. B. The disparity between the values 7.808 and 7.811 is due to differences in the atomic weights of the elements comprising the molecular constitution of menthol—as included in the respective Pharmacopœias.

A comprehensive survey of pharmaceutical treatises published or revised since the advent of the U. S. P. X disclosed the failure of these texts to elucidate the principles or manner of calculating the correction factor as specified in the official monograph.

The formula as stated in the U. S. P. IX disregarded the presence of the small amount of menthyl acetate invariably associated with oil of peppermint and was derived on the assumption that all of the menthol was present in a free or uncombined state. The presence of ester up to 10.0 per cent produces an appreciable error which, however, is now compensated for by the modified formula in U. S. P. X as originally recommended by F. D. Dodge<sup>2</sup> and others.

The derivation of the new formula is demonstrated in detail as follows:

Lct  $X$  = per cent of total menthol in the oil,

$e$  = per cent of menthyl acetate,

$\left. \begin{array}{l} A \\ B \end{array} \right\} = \text{as in U. S. P., or as previously above cited;}$

then noting that menthyl acetate contains 78.0 per cent of menthol and the latter in turn yields 127.0 per cent of the ester, it becomes evident that

$$(1) \quad X - 0.78e = \text{free menthol;}$$

the acetylated oil from 1 part of original oil will, accordingly, amount to

$$(2) \quad 1 + 0.27(x - 0.78e) \text{ Gm.,}$$

representing all of the original menthol, plus 27.0 per cent of the free menthol as ester.

<sup>1</sup> This represents the difference between the  $N/2$   $H_2SO_4$  V. S. used in titration, and the amount of  $N/2$  KOH V. S. originally used. (See U. S. P. X, p. 262.)

<sup>2</sup> Personal communication to the writer April 1926.

(3) Then,  $\frac{X}{1 + 0.27(X-0.78e)}$  = percentage of total menthol in the acetylated oil.

(4) But by assay,  $\frac{0.078A}{B}$  = percentage of menthol in the acidulated oil; also,

(5)  $\therefore \frac{X}{1 + 0.27(X-0.78e)} = \frac{0.078A}{B}$ , whence,

(6)  $X = \frac{0.078A + 0.021A(X-0.78e)}{B}$ . This equation through the indicated reduction assumes the following consecutive forms:

$$(7) \quad X = \frac{0.078A + 0.021AX - 0.0164Ae}{B} =$$

(8)  $X = \frac{A(0.078 + 0.021X - 0.0164e)}{B}$  which on transposing assumes the form

$$(9) \quad X - \frac{0.021AX}{B} = \frac{A(0.078 - 0.0164e)}{B}, \text{ whence,}$$

$$(10) \quad \frac{BX}{B} - \frac{0.021AX}{B} = \frac{A(0.078 - 0.0164e)}{B}.$$

Cancellation of B terms in the fraction  $\frac{BX}{B}$  and clearing of fractions,

$$(11) \quad = \frac{X(B - 0.021A)}{B} = \frac{A(0.078 - 0.0164e)}{B}.$$

Simplifying, equation (11) yields

(12)  $\frac{BX(B - 0.021A)}{B} = \frac{B.A(0.078 - 0.0164e)}{B}$  which on cancelling B terms outside of parentheses,

$$(13) \quad = X(B - 0.021A) = A(0.078 - 0.0164e) \text{ and}$$

$$(14) \quad X = \frac{A(0.078 - 0.0164e)}{(B - 0.021A)},$$

Multiplying equation (14) by 100 and substituting E for 100e =

$$(15) \quad X = \frac{A(7.8 - 0.0164E)}{(B - 0.021A)} = \text{percentage of total menthol in original oil. This formula}$$

in turn resolves itself to

$$(16) \quad X = \frac{A \times 7.8(1 - 0.0021E)}{(B - 0.021A)} \text{ which in turn resolves itself to}$$

$$(17) \quad \frac{A \times 7.8}{B - 0.021A} \times [1 - (E \times 0.0021)] \text{ as stated in the U. S. P. X.}$$

The same correction factor is applied to the analytical result in the assay of oil of rosemary, where, however, the object sought is the percentage of *total* borneol ( $C_{10}H_{17}OH$ ); E = esters calculated as bornyl acetate ( $C_{10}H_{17}C_2H_3O_2$ ), while the other symbols and constants retain similar significance as previously stated for the calculation of the menthol assay.

Summarily, the official assays for oils of peppermint and rosemary are based on the following assumptions; that

- (1) Menthol or borneol are the only alcohols present; that
- (2) Menthyl or bornyl acetates are the only esters present, and
- (3) That menthol or borneol are the only constituents reacting with acetic anhydride.

Inasmuch as none of these assumptions is strictly correct,<sup>1</sup> all of the calculations incident to correction of assay data could readily be obviated, by employing the simpler expedient as proposed by (E. J.) Parry.<sup>2</sup> Proceed in the following manner with an oil containing both esters and alcohols:

(I) Estimate the amount of combined alcohols by a preliminary saponification of the esters.

(II) Saponify 20.0 Gm. of the sample with alcoholic KOH solution, add H<sub>2</sub>O and wash the separated oil now free from esters, dry over KHSO<sub>4</sub> and

(III) Estimate the total alcohols (now all free) in 2.0 to 5.0 Gm. of (II).

(IV) The amount of alcohols as found in (III) refers to the *saponified* sample; to calculate the total alcohols in the original sample necessitates a correction by allowing for the reduction in weight by saponification of the original oil. This reduction can be ascertained by calculation from the amount of alkali used for saponification in (I).

(V) Deduct the combined alcohols found in I from the total alcohols determined in (IV); the difference represents the amount of free alcohols.

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## FURTHER STUDY OF THE TANNIN OF HEUCHERA AMERICANA, LINNE.\*

BY JOSIAH C. AND BERTHA L. D&G. PEACOCK.

This paper is intended to review, and will be found to revise in some particulars, the results of an investigation of the root of *Heuchera Americana*, published by one of us (J. C. P.) in *American Journal of Pharmacy*, April 1891.

Working then with the methods in general use for isolating and purifying tannins, as outlined in that paper, there was obtained a dark brown mass, which was but slowly and only partly soluble in cold water; and while readily soluble in hot water a large proportion of the dissolved matter separated when the solution was allowed to cool.

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<sup>1</sup> This is readily apparent on consideration of the complex character of American oil of peppermint in particular, which according to "Schimmel & Co.'s Report" (April 1897) consists essentially of the following:

Acetaldehyde,	Limonene,
Iso-valeric aldehyde,	Menthone (C <sub>10</sub> H <sub>18</sub> O),
Dimethyl sulphide,	Menthol,
Amyl alcohol,	Menthyl acetate,
Iso-valeric acid,	Menthyl iso-valerate,
Pinene,	a-lactone (C <sub>10</sub> H <sub>16</sub> O <sub>2</sub> ),
Phellandrene,	Cadinene.
Cineol,	

<sup>2</sup> "Allen's Commercial Org. Analysis," 5th edition, Vol. IV, p. 596.

\* Read before Pennsylvania Pharmaceutical Association, 1927.