1910 Cohn.
Pharm. Zentralhalle, 51, 265.
Year Book Pharm., 12 (1910).
Method for manufacture.

1911 May.
Chem. Syn. Drugs, 84 (1911).
Mentions that quinine tannate is but slowly split up in the intestine and for this reason it is lacking in therapeutic promptitude and certainty.

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PROPOSED STANDARDS FOR CAMPHOR AND SPIRIT OF CAMPHOR.

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Spirit of Camphor and Camphor were made official in 1820. The Spirit has for many years been a very popular household remedy and in view of the fact that it has been reported as extremely variable in strength and quality by analysts in various parts of the country, it would seem desirable to introduce into the forthcoming Pharmacopoeia some special tests for determining its strength and purity. In the years that this preparation has been official, it, like many other official preparations, has been subjected several times to fancied improvements.

In general, changes of formula lead to confusion, and as these changes have many times been shown to have been ill advised, criticism has thus arisen to the effect that the committees of revision often do not give sufficient attention to them. The decennial revisions have sometimes seemed to be somewhat lacking in that definiteness of purpose which is conducive to confidence and healthy growth.

In tracing the evolution of Spirit of Camphor, several interesting changes are noted. It was official in 1820 as Tincture of Camphor, the title by which it is still known in the French Pharmacopœia. It was made by dissolving one Troy ounce of Camphor in one pint of Alcohol. This is the equivalent of about 6.14 gm. of Camphor dissolved in enough Alcohol (89.7%) to make 100 cc. There were two Pharmacopœias in 1830. That which resulted from the New York convention changed the title to Spirit of Camphor, the title by which it is known in the latest editions of the German, Swiss, British and Japanese Pharmacopœias. The Pharmacopœia which resulted from the Washington convention retained the title of Tincture. In both pharmacopœias the formula was changed to a strength of four Troy ounces of Camphor dissolved in two pints of Alcohol. This is the equivalent of about 11.54 gm. of Camphor dissolved in sufficient Alcohol (89.7%) to make 100 cc. In 1840 the Washington convention disregarded the timely change in the New York convention ten years before and continued the preparation without change until 1860. Then the title was changed to Spirit. No additional change was made in 1870 but in 1880 the formula was materially altered and the Spirit as then prepared consisted of Camphor, 10 parts, Alcohol (94%) 70 parts, and water 20 parts. This is the equivalent of about 8.72 gm. of camphor dissolved in sufficient Alcohol (80.56%) to make 100 cc.

In the light of subsequent revisions this weakening of the alcoholic strength was ill advised. In 1890 the formula was again changed and the preparation was made by dissolving 10 gm. of Camphor in sufficient Alcohol (94%) to make 100 cc. The manufacture by weight directed ten years before was discontinued. It is to be noted in this connection that of the Pharmacopœias before mentioned, the British is the only one in which this preparation is not directed to be made by weight at the present time. It has been claimed in defense of this change that the manufacture of Galenicals by weight was not popular with the Americans. This may have been so but we are inclined to the belief that this method of compounding was and is still popular with many manufacturing pharmacists, and, that it would have been desirable to have retained the formulas for compounding by weight at least as alternative ones. The diluting of the alcohol was not only discontinued but the alcoholic strength was increased beyond that of any previous formula. In the Pharmacopæia of 1900 the formula again underwent a slight change by reason of the increase in strength of Alcohol from 94 to 94.9%.

A comparison of the formulas for Spirit of Camphor as found in the foreign Pharmacopæias shows that the English method of manipulation is similar to ours, but that alcohol of 90% is used. In the German, Swiss and Japanese Pharmacopœias the compounding is by weight and the finished preparation is practically identical and approximates the formula of the 1800 Pharmacopœia. The formula of the French Pharmacopœia is composed by weight, but the alcohol used is of the same strength (90%) as that of the British Pharmacopœia.

We believe that the present U. S. P. formula is suited to the needs of the American physicians and that further tampering with it is unnecessary. All of the recent foreign Pharmacopœias give either the specific gravity or density of this preparation and this data should be included in ours. This data will enable those who so desire to manufacture Spirit of Camphor by weight. The specific gravity, however, does not seem sensitive enough to serve as a suitable standard as shown by the following: The apparent specific gravity at 20° C. of this Spirit when made with 90% alcohol would be about 0.8449, when made with 94.9% alcohol about 0.8296 and when made with alsolute alcohol about 0.8133. These figures indicate that a variation in specific gravity of about 0.003 would indicate a variation in alcoholic strength of about 1%. With a constant Camphor content the specific gravity would serve as a satisfactory measure of the alcoholic strength. The apparent specific gravity of a spirit containing 8 grammes of Camphor in each 100 cc., when made with 94.9% alcohol is about 0.8263 and for one containing 12 gm. of camphor in each 100 cc., about 0.8324. It is thus seen that here a variation of 0.003 in specific gravity would indicate a variation of about 2 gm. or 20% in the Camphor content, a variation which is in our opinion too great. For this reason we would recommend that the approximate specific gravity be given instead of a limiting range. In view of the above facts it seems to us desirable to have some recognized method for the direct determination of water in this spirit as well as a specific method for determining the allowable variation in camphor

[1]Seymour: A simple method of estimating Camphor and Alcohol in Spirit of Camphor. Proc. A. Ph. A. (1907), Vol. 55, page 443.

content. We have found that the use of anhydrous Potassium Carbonate as proposed by Seymour[1] answers very well for the detection of water.

The test for limiting the camphor content as proposed by the German and Swiss Pharmacopœias is based upon the volume of water necessary to cause a precipitation of camphor in 10 gm. of the Spirit under stated conditions. The German standard seems to us to be too lax as it seemingly allows a range of approximately 2 gm. or 20% in camphor. This is however closely in accord with their allowable range in specific gravity, 0.885 to 0.889. On the other hand the standard of the Swiss Pharmacopœia accords more closely with our ideas as it allows a variation of about ½ gm. or 5% in camphor content. This, however, is not in accord with the range allowed by the specific gravity which is the same as that of the German Pharmacopœia. The French Pharmacopœia gives the approximate density and the optical rotation but does not define the allowable variation. The precipitation method is very satisfactory when the percentage of water and the temperature are kept constant. We have ascertained at 20° C. the number of cc. of water which are necessary to cause a precipitate on 5cc. of Spirit of various strengths in U. S. P. Alcohol to be as follows:

5 cc. spirit of strength 4 gm.: 100 cc. requires 7.90 cc. of water.
5 cc. spirit of strength 5 gm.: 100 cc. requires 6.95 cc. of water.
5 cc. spirit of strength 6 gm.: 100 cc. requires 6.4 cc. of water.
5 cc. spirit of strength 8 gm.: 100 cc. requires 5.45 cc. of water.
5 cc. spirit of strength 10 gm.: 100 cc. requires 4.7 cc. of water.
5 cc. spirit of strength 12 gm.: 100 cc. requires 4.15 cc. of water.
5 cc. spirit of strength 14 gm.: 100 cc. requires 3.7 cc. of water.
5 cc. spirit of strength 15 gm.: 100 cc. requires 3.5 cc. of water.

The importance of fixing the alcoholic strength is shown by the fact that 5 cc. of a spirit made by dissolving 7.5 gm. of camphor in sufficient alcohol (90%) to make 100 cc. has the same precipitating value as 5 cc. of the official Spirit.

The description and tests which we would propose for Spirit of Camphor are as follows:

Keep in a closely stoppered bottle in a cool place.

A clear, colorless liquid, neutral to litmus paper and containing about 85 % of alcohol by volume (84.9%).

Specific gravity about 0.8296 20°/20° C.

Five cc. of the Spirit vigorously shaken in a dry, stoppered test tube with 0.5 gm. of anhydrous Potassium Carbonate should not moisten the latter within one-half hour. (Limit of water.)

Five cc. of the Spirit when cooled to 20° C. and quickly mixed with distilled water of the same temperature should require not more than 4.8 cc. nor less than 4.6 cc. of the later to produce a slight permanent precipitate of Camphor. (Indicating from 9.7% to 10.3 gm. of camphor in each 100 cc. of the Spirit.)

The alcohol and the Camphor should correspond in other respects to their respective tests.

CAMPHOR.

Camphor at the time that it was admitted to the Pharmacopœia had none of its properties mentioned and it is doubtful if standards are contemplated, but as revision succeeded revision useful pharmaceutical knowledge and tests have from

time to time been supplied until in the VIII rev. this has reached a state of approximate completeness. To what additional extent this may carried is a matter worthy of careful attention. The limit has not been reached, however, and we would suggest the following extentions.

Our experiments lead us to believe that the optical rotation of Camphor should be given in the U. S. P. IX. We have examined refined Camphor from the American Camphor Refining Company, Charles H. Phillips Chemical Company, Charles Pfizer and Company, and H. J. Baker and Brothers, as well as from several Japanese refineries and have in every case found that the rotation when observed in the form of U. S. P. Spirit in a 200 mm. tube at 20° C. with sodium light was within the limits of +8.20° and +8.26°. This would correspond, in absolute alcohol, to (a)d 15°+42.9° to +43.2°, which corresponds very closely with the figure given in the French Pharmacopœia, (a)d 15°+43°. It should be noted that the highest figure obtained by us is considerably lower than the figure given in the German Pharmacopœia (a)d 20° +44° 22°.

We would suggest that instead of the redundant words of the present U. S. P., "it is optically active, being dextrogyrate," that the angular rotation be given at not less than +8.20° when dissolved in alcohol 10 gm.; 100 cc. and observed in a 200 mm. tube at 20° C. with sodium light.

It seems to us desirable to introduce the statement that camphor is insoluble in glycerin and to extend to list of solubilities to include at least Acetone and Glacial Acetic Acid. We think that it would be also appropriate to extend the list of liquefiable substances so as to include Salol, Naphthol, Pyrogallol and Resorcin. (Antipyrine and Salicylic Acid are not included in this list because they do not liquify under ordinary conditions.)

The permissible amount of non-volatile matter at a given temperature should also be stated. We have found no samples that completely volatilized at 110° C. The usual residue is approximately 0.025%.

DISCUSSION.

Dr. A. R. L. Dohme inquired as to the reason for making the requirements for Camphor such as to eliminate the synthetic product. While synthetic camphor was not on the market in such quantity as to make it an appreciable element, it would likely become an important factor in time. It is free from oil and, personally, he could see no good reason why the pharmacopœial requirement should be such as to practically eliminate it.

Prof. L. D. Havenhill replied that synthetic camphor had not been included because he did not know of any good reoson why it should be included. His recommendations had been guided by the countries where it was manufactured, and since the recent German Pharmacopœia had not recommended synthetic camphor for medicinal use, he could see no good reason why we should take it up.

Mr. M. I. Wilbert thought that before synthetic camphor is included it would be necessary, or at least very desirable, to show that it had the same physiological action as the natural product, since it is a well known fact that closely related compounds do not always produce the same physiological effect.

Prof. Virgil Coblentz gave it as his opinion that there was no difference between the physiological action of natural and synthetic camphor, and that whether one was used more than the other depended mainly upon the market price. Until a few years ago large quantities of crude synthetic camphor had been imported into this country for the making of celluloid, because it was possible to import it with little or no duty.