THE ASSAY OF SODIUM SALICYLATE.

BY H. W. JONES.

The method for the assay of alkali salts of organic acids given in the 9th revision of the Pharmacopoeia, while giving satisfactory results in general, is open to several objections, not the least of which is the fact that it is time-consuming and requires the most careful manipulation to secure accurate results. Again, owing to the fact that these salts are usually made by neutralizing the respective acids with alkali carbonates or bicarbonates, it is easy to conceive of a case where the method would show a salt to be of standard quality when in fact it was substandard because of an excess of carbonate. Hence, any method giving accurate results in the assay of any one of these salts would be welcome, if not open to the above objections.

Use has been made in the Pharmacopoeia of Koppeschaar's solution for the assay of certain phenols and phenolic salts. The same method is available for the assay of sodium salicylate, since salicylic acid will react with bromine and eventually form a tribromophenol; one molecule of salicylic acid absorbing in this way six atoms of bromine.

The method as applied to sodium salicylate is as follows: Dissolve 1 Gm. of sodium salicylate, previously dried at 100° C. to constant weight, in a sufficient quantity of distilled water to make the solution measure 100 mils. By means of a pipette measure 10 mils of this solution into a glass-stoppered flask of about 250 mils capacity. Add 75 mils of distilled water and 50 mils of tenth-normal bromine V. S., followed by 5 mils of hydrochloric acid. Stopper the flask and allow it to stand for fifteen minutes, shaking occasionally. Then add 10 mils of potassium iodide T. S. and titrate the liberated iodine with tenth-normal sodium thiosulphate V. S., using starch T. S. as indicator. The difference between the amounts of bromine V. S. and sodium thiosulphate V. S. multiplied by 2.667 gives the percentage purity of the sodium salicylate.

Each mil of a tenth-normal bromine V. S. used corresponds to 0.002667 Gm. of sodium salicylate.

The method is often useful for the estimation of salicylic acid or sodium salicylate in certain mixtures. It is especially of use in the presence of benzoic acid, which does not react with bromine in aqueous solution.

It is suggested that the method be included in the next revision of the Pharmacopoeia.

ON THE SOLUBILITY OF VOLATILE OILS IN MIXTURES OF ALCOHOL AND WATER.*

BY HORATIO C. WOOD, JR.

In connection with some researches concerning the antiseptic properties of the volatile oils, it became desirable to prepare solutions of these oils in the lowest possible concentration of alcohol. In the effort to accomplish this desideratum, I made some experiments on the solubility of the essential oils in different propor-

*Read before Scientific Section, A. Ph. A., City of Washington meeting, 1920.

tions of alcohol and water. Although I have tested so far only five oils, the results offer certain points of interest which have led me to present this communication.

Method.—It is apparent that the ordinary methods of determining the solubility of solids or non-volatile liquids are not applicable to the essential oils for the reason that one cannot dry the residue to be weighed, without the danger of an unknown amount of loss of the volatile oil through evaporation. I therefore, had recourse to a determination of the amount of water necessary to cause separation of the volatile oil from its alcoholic solution. There is in this method a considerable possibility of personal error, owing to the fact that, especially with very dilute solutions, the first precipitation of the oil from its alcoholic solution produces an almost imperceptible degree of opalescence. It requires considerable practice and the use of varying intensities and directions of illumination to achieve even approximate accuracy. With concentrated solutions there was relatively little difficulty in determining the point of precipitation of the oil. Fortunately, at the low concentrations of the oil which made accuracy difficult, small discrepancies in the end-point were of lesser import, for the reason that at these concentrations the solubility of the oil diminished at a rate more or less parallel with the strength of the alcohol. While the method would scarcely satisfy the fastidiousness of the analytical chemist, it has yielded some interesting results.

Various modifications, based upon the same principle, were tried. For dilutions of alcohol above 25 or 30 percent, the best results were obtained by the following:

A fairly concentrated solution (from two to ten percent) in strong alcohol (93 percent at 15.56° C.) was used as a stock solution for the experiment. To one mil of this was added a measured quantity of strong alcohol. Water was then added from a burette until the appearance of the first slight opalescence. The volume of water employed is then read, and by a simple arithmetical calculation the percentage of oil and alcohol in this mixture made. For example, suppose that one mil of 5 percent solution plus 5 mils of alcohol required three mils of water to cause turbidity. To find the percentage of oil, divide 5 (the percentage of oil originally taken) by 9 (the final number of mils); to find the percentage of alcohol, multiply the total quantity (6 mils) of alcohol by 93 (the percentage of alcohol employed) and divide this product by nine; the result of these two calculations shows that 0.555 percent of the oil saturates 62 percent of alcohol. To this percentage of alcohol corrections must be made for the shrinkage which takes place when water is added to alcohol. I have commented on the shrinkage of alcohol-water mixtures in another place. (JOURNAL A. PH. A., 1919, p. 730.) I give here a table of the corrections which must be added to the apparent percentage of alcohol.[1]

TABLE I.—SHOWING CHANGE IN VOLUME PERCENT OF MIXTURES OF 93 PERCENT ALCOHOL WITH WATER.

Expected percent alcohol.	Shrinkage percent.	True percent alcohol.
20	1.42	20.28
30	2.38	30.73
40	2.79	41.15
50	2.90	51.49
60	2.69	61.66
70	2.24	71.60
80	1.51	81.23

Since each volatile oil is a mixture of several ingredients in more or less uncertain proportions, and since it is highly improbable that all of these ingredients

[1] In all cases the strength of alcohol is expressed by *volume* percent.

will have the same solubility relations, it is manifest, first, that two samples of volatile oils may show different solubilities by this method of study, and second, that in case a volatile oil should contain small amounts of some highly insoluble substance, it would show precipitation with comparatively high percentage of alcohol, although the great bulk of the oil would be soluble in much lower proportions of alcohol. This latter fact is strikingly illustrated in the case of Oil of Cloves.

Oil of cloves requires at least 200 parts of 50% alcohol to give a clear solution, but eugenol, which constitutes 82 percent of the oil of cloves, is dissolved by less than 20 volumes of 50% alcohol. The U. S. Pharmacopoeia gives the solubility in diluted alcohol of only one oil, that of peppermint, which it states "is soluble in 4 volumes of 70% alcohol, showing not more than slight opalescence and no separation of oil globules." In my experiments two-tenths of one percent was the limit of oil of peppermint which could be dissolved in 70% alcohol without some opalescence.[1] I have been unable to find in the British Pharmacopoeia any precise definition of what is meant by the statement, for example, that oil of cinnamon is "soluble in three or four parts of alcohol (70%);" according to my results fifty to one hundred parts is nearer the truth; nor any information how this solubility is to be determined. If, however, the statements of the British Pharmacopoeia on the solubility of the volatile oils are in the same sense as that of the U. S. Pharmacopoeia concerning peppermint, then no comparison should be made with my results.

A very interesting practical problem suggests itself in this connection, namely, as to which of its ingredients the therapeutic virtues of a given oil are owing. It is very evident, for example, that if we were to make an aromatic water from oil of clove, it would contain a much larger proportion of eugenol than the oil from which it was prepared. It is not safe to take for granted that the ingredient present in the largest proportion is the most important ingredient of a volatile oil. Martindale (*Perf. and Ess. Oil Rec.*, 1910, p. 266) has found that the germicidal power of oil of cinnamon is higher than that of cinnaldehyde, and my own studies indicate that oil of clove is more antiseptic than eugenol.

The result of these studies which has struck me the most forcibly is the complete inefficiency of even relatively concentrated alcohol as a solvent for the volatile oils. None of the oils tested yielded clear solutions with one hundred volumes of 55% alcohol, while proof spirit dissolved only one or two parts per thousand. There is a sort of "critical" strength of alcohol; a certain point at which the solubility of the oil increases very markedly with only slight variations in the concentration of the alcohol; this critical point ranged between 60 percent in the case of oil of clove and 90 percent with oil of peppermint. In general, I may add, that contrary to previous assumptions, alcohol of 70 percent is not a good solvent for the majority of the volatile oils.

The results of my experiments are summed up in the following table, which shows the percentage of volatile oil required to saturate different dilutions of alcohol.

[1] Gildermeister and Hoffman state that there is a difference between the solubilities of Japanese and American peppermint oil, the latter not forming clear solutions with 70% alcohol, although both the English and Japanese do.

TABLE II.

SHOWING THE NUMBER OF MILS OF SOME VOLATILE OILS SOLUBLE IN 100 MILS OF ALCOHOL OF VARIOUS CONCENTRATIONS.

Alcohol. Percent.	Anise.	Cinnamon	Clove.	Eugenol.	Peppermint.	Sassafras.
30	0.05	....	0.02	...	0.02	0.07
40	0.08	....	0.10	0.30	0.02	0.10
50	0.10	0.20	0.40	5.80	0.03	0.20
60	0.25	0.40	2.00	16.00	0.06	1.30
65	0.80	1.10	10.00	...	0.07	2.30
70	1.50	2.20	21.75	...	0.10	4.00
75	4.00	7.00	...	...	0.17	7.00
80	7.50	....	...	...	0.35	11.00

ABSTRACT OF DISCUSSION.

In response to a question by C. E. Caspari, Dr. Wood stated that as an antiseptic, Oil of Clove was more efficient than eugenol. Answering Mr. Scoville, relative to effect of temperature on solubility, the author replied, that there was a marked difference in solubilities of oils at different temperatures. The temperatures were not accurately observed, however, within two degrees; the tests were made at temperatures between 22–25° C.

H. C. Hamilton asked relative to methods used in the germicidal tests, and results obtained. Dr. Wood replied that this work had not proceeded far enough to give definite figures, only seven oils had been determined. The phenol coefficient of oil of cinnamon is about 12, cloves about 18, eucalyptol about 1. Oil of sassafras stands very high as an antiseptic, in dilutions of from 1000 to 7000 it inhibits the growth of all organisms tested. Oil of clove is effective in dilutions of about 1000 to 6000; oil of cinnamon about the same; oil of peppermint is comparatively feeble and oil of lemon has practically no effect. The oils can be grouped, but there is a marked difference in the individual volatile oils relative to their antiseptic value.

E. H. Grant thought that different solubility results would have been obtained if the tests had been started with 70% alcohol instead of 93% alcohol. Higher results would probably have been obtained.

EXPERIENCES IN THE MANUFACTURE AND STANDARDIZATION OF DAKIN'S SOLUTION.

BY A. J. SELLS.

The early months of my services in the army were spent with Base Hospital No. 50, as bacteriologist and chemist, and in such capacity I found that the Army method for the preparation of Dakin's solution was at fault because of the materials furnished.

After a preliminary training of three months at Camp Fremont, California, the unit left for France and arrived at Mesves-Bulcy Hospital Center on August 6, 1918. This hospital center was located about one hundred and fifty miles south of Paris and was the largest hospital center in the world.

As our unit was designated a surgical unit by the Army, at least one-half of the cases were surgical and the remainder medical. These surgical cases called for a large quantity of Dakin's solution each day.

The Army method for the preparation of Dakin's solution was as follows:

Sodium carbonate (dry)	140 grammes
Calcium hypochlorite (25 percent Cl)	200 grammes
Boric acid	40 grammes
Water	8 liters