3. A number of salts of amines and phthalamidic acids have been prepared.

4. Some of these salts when heated above their melting points evolve the amine and water and yield the imide,

$$RNHCOC_6H_4CO_2NH_3R' \longrightarrow C_6H_4\begin{matrix}CO\\ \diagup\\ \diagdown\\ CO\end{matrix}NR.$$

5. The remaining salts, when heated, form unsymmetrical phthaldiamides, $RNHCOC_6H_4CONHR'$, or the symmetrical compounds in which R is derived from the ammonium complex, thus,

$$R'NHCOC_6H_4CO_2NH_3R \longrightarrow C_6H_4(CONHR)_2.$$

Dibenzylammonium phthalate gave phthalbenzylimide.

6. The action of a number of amines on phthal-*p*-chlorphenylamidic acid has been studied; they lead to the formation of the *p*-chlorphenylimide.

After the manuscript of this paper had been prepared, our attention was called to a communication by Shigeru Komatsu, on the "Amine Salts of Phthalamic, Phenylphthalamic, and Phenylsuccinamic Acids."[1] His work was carried out in Prof. M. Kuhara's laboratory, the problem being to show that salts of amines and of the acids mentioned could exist. Komatsu mentions the paper of Bishop Tingle and Lovelace, but, unfortunately for himself, has remained in ignorance of the later work on the subject. Had he been better informed he would have been aware that *his* problem was solved by Bishop Tingle and Rolker more than a year ago. A slight acquaintance with more recent literature would also have saved Mr. Komatsu from being guilty of the discourtesy of intruding on a field of work concerning which the senior author has published four papers in the space of two years. In each of these papers a request was made for the subject to be reserved; it was mentioned that work was proceeding and special stress was laid on the question of the formation of ammonium salts of amines and the amidic acids which were under investigation.

McMASTER UNIVERSITY, TORONTO, CANADA,
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[DIVISION OF PHARMACOLOGY, HYGIENIC LABORATORY, U. S. PUBLIC HEALTH AND MARINE-HOSPITAL SERVICE, WASHINGTON, D. C.]

SOLUBILITIES OF THE SALICYLATES OF THE UNITED STATES PHARMACOPOEIA IN AQUEOUS ALCOHOL SOLUTIONS AT 25°.

BY ATHERTON SEIDELL.

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The following results upon the salicylates of the United States Pharmacopoeia are a part of an extended series of determinations which are now

[1] *Mem. Col. Sci. and Eng., Kyoto*, 1, 431.

being made in this laboratory upon those pharmacopoeial compounds for which the published data are of more or less uncertain reliability. More detailed descriptions of the experiments will appear in the laboratory bulletin which, it is expected, will be prepared as soon as the determinations upon the metallic salts of the remaining United States Pharmacopoeial organic acids are completed.

Experimental Method.—The saturation of the solutions was effected by moderate agitation of the mixtures of solute and solvent enclosed in tubes immersed in a constant temperature water bath maintained at 25°. The attainment of equilibrium was insured by analyzing solutions shaken different lengths of time. All the alcoholic solvents were prepared and analyzed in advance. The dissolved material was determined usually by evaporation and weighing the residues after careful drying at room temperature in vacuum desiccators. The results in all cases were calculated to the grams of salt dissolved in 100 grams of the saturated solution. These figures were plotted as the abscissae and the weight percents of C_2H_5OH in the several solvents plotted as ordinates on cross section paper. The curve drawn through the points thus determined represented the curve of solubility of the particular salt in aqueous alcoholic solvents of increasing content of alcohol. From this curve the figures corresponding to regular intervals of alcoholic strengths of the solvent were read.

Material Employed.—The samples of the several salicylates used for the solubility determinations were purified as thoroughly as possible by recrystallization and analyses made in those cases where satisfactory methods were available. The *ammonium salicylate* sample was practically neutral to litmus paper and contained 98.7 per cent. $C_6H_4OHCOONH_4$ calculated from ammonia determinations made by the Kjeldahl method. Solubility determinations also made with a sample which contained 96.8 per cent. agreed satisfactorily with those made with the above sample and no irregularities could be traced to this variation in content of salicylate. The very carefully recrystallized *lithium salicylate* sample contained, when analyzed by the United States Pharmacopoeia method, 95.5 per cent. $C_6H_4OHCOOLi$. If the presence of one-half a molecule of water of crystallization be assumed, the calculated amount of the hydrated salt is 101.5 per cent. This variation from the theoretical composition may possibly be ascribed to the presence of a very small amount of other alkalies than lithium which could not be removed by recrystallization. The *sodium salicylate* was very carefully recrystallized and dried. No analytical results for its composition can be given, however, since none of the methods of analysis was found trustworthy. The *salicylic acid* showed a purity of 100 per cent. determined by titrations with standard alkali. The *phenyl salicylate* was also of practically 100 per cent. purity when analyzed by saponification in a closed flask

at 100° and titrating the excess of alkali. The *strontium salicylate* samples were analyzed by the United States Pharmacopoeia method and contained 99.04 and 99.55 per cent. $(C_6H_4OHCOO)_2Sr + 2H_2O$ respectively. The *quinine salicylate* was the Merck product and had a melting point of approximately 195° instead of 183–187° with decomposition, as stated by the United States Pharmacopoeia.

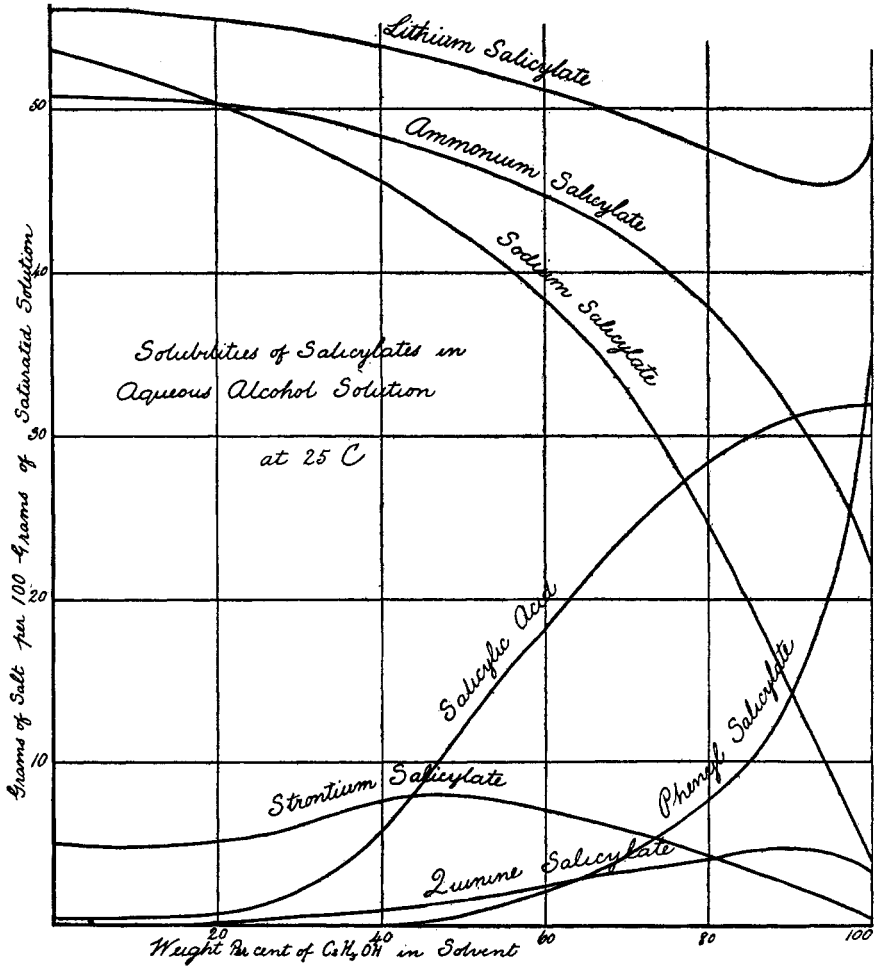
TABLE SHOWING THE SOLUBILITIES OF SALICYLATES IN AQUEOUS ALCOHOL SOLUTIONS AT 25°.

Wt. per cent. of C_2H_5OH in solvent.	Lithium salicylate.		Ammonium salicylate.		Sodium salicylate.		Salicylic acid.	
	Sp. gr. of sat. solution at 25°.	Gms. $C_6H_4OHCOOLi + \frac{1}{2}H_2O$ per 100 grams sat. solution.	Sp. gr. of sat. solution at 25°.	Grams $C_6H_4OHCOONH_4$ per 100 grams sat. solution.	Sp. gr. of sat. solution at 25°.	Gms. $C_6H_4OHCOONa$ per 100 grams sat. solution.	Sp. gr. of sat. solution at 25°.	Gms. $C_6H_4OHCOOH(o)$ per 100 grams sat. solution.
0	1.209	56.0	1.148	50.8	1.256	53.6	1.001	0.22
10	1.195	55.9	.....	....	1.235	52.1	0.984	0.38
20	1.180	55.4	1.122	50.3	1.205	50.2	0.970	0.80
30	1.163	54.5	.....	....	1.176	48.0	0.959	2.20
40	1.144	53.7	1.088	48.3	1.142	45.5	0.951	5.90
50	1.124	52.5	1.067	46.7	1.106	42.2	0.945	12.20
60	1.104	51.1	1.042	44.7	1.066	38.4	0.943	18.30
70	1.083	49.5	1.015	42.0	1.016	33.0	0.941	24.00
80	1.056	47.5	0.979	38.0	0.957	25.0	0.937	28.30
85	.....	....	0.958	35.0	.....	....	.....	.....
90	1.026	45.8	0.936	31.6	0.885	15.0	0.930	31.40
92.3[1]	1.020	45.6	0.925	30.0	0.864	12.0	0.928	31.90
95	.....	....	0.907	27.8	.....	....	.....	.....
100	1.027	48.2	0.875	22.3	0.805	3.82	0.919	33.20

Wt. per cent. of C_2H_5OH in solvent.	Phenyl salicylate.		Quinine salicylate		Strontium salicylate		Bismuth sub. salicylate.
	Sp. gr. of sat. solution at 25°.	Gms. $C_6H_4OHCOOC_6H_5$ per 100 grams sat solution.	Sp. gr. of sat. solution at 25°.	Gms. $C_6H_4OHCOOH.C_{20}H_{24}N_2O_2 + 2H_2O$ per 100 grams sat. solution.	Sp. gr. of sat. solution at 25°.	Gms. $(C_6H_4OHCOO)_2Sr + 2H_2O$ per 100 grams sat. solution.	Gms. $C_6H_4OHCOOBi$ per 100 grams of sat. solution.
0	0.999	0.015	0.999	0.065	1.022	5.04	0.010
10	.....	.....	0.982	0.080	1.006	4.88	.....
20	0.967	0.020	0.966	0.200	0.993	5.22	0.015
30	.....	.....	0.952	0.48	0.982	6.20	.....
40	0.934	0.22	0.935	1.00	0.966	7.70	0.022
50	0.914	0.76	0.916	1.70	0.948	8.08	.....
60	0.895	2.10	0.896	2.45	0.923	7.15	0.036
70	0.877	4.40	0.876	3.25	0.893	5.90	.....
80	0.863	7.70	0.854	4.20	0.859	4.40	0.065
90	0.865	14.00	0.832	4.71	0.824	2.56	0.095
92.3[1]	0.868	17.70	0.826	4.62	0.815	2.02	0.105
100	0.898	35.00	0.797	3.15	0.790	0.44	0.160

[1] United States Pharmacopoeial alcohol.

General Remarks.—The solubility curves plotted from the results shown in the accompanying table present several unexpected peculiarities. The lithium salicylate curve shows an unmistakable minimum point at a concentration of about 95 weight per cent. of alcohol. The solubility of the ammonium salicylate decreases regularly with increase of alcoholic strength, but at no point does the amount of salt dissolved correspond



to the sum of the amount dissolved by the quantity of water present plus the amount dissolved by the quantity of alcohol in the particular solvent. The quinine salicylate curve shows a maximum point at about 90 weight per cent. alcohol, and the strontium salicylate curve has both a minimum and a maximum point in the range of alcoholic concentration from 0 to 100 per cent. It will be noted that the three curves showing

the maximum or minimum points are each of salts containing water of crystallization. A simple calculation will show however that in no case is the amount of water introduced in this way enough to change the concentration of the solvent sufficiently to account for the irregularities. The connection between the water of crystallization and the maximum or minimum point of these three curves is still less noteworthy when it is considered that boric and camphoric acids which contain no water of crystallization show under similar circumstances minimum or maximum points respectively in their solubility curves.[1]

Of the determinations shown in the accompanying table, some agree fairly well with the results quoted by the United States Pharmacopoeia while others differ very considerably. In order to show such comparative values to better advantage they have been brought together in the following table and are given in the terms used for the pharmacopoeial data, that is, the part of solvent required to dissolve one part of salt.

TABLE SHOWING THE PRESENT DETERMINATIONS AS COMPARED WITH THOSE QUOTED BY THE U. S. PHARMACOPOEIA.

	Parts of solvent to dissolve 1 part of salicylate at 25°.			
	In water.		In 92.3 wt. per cent. alcohol.	
Salicylate.	Present results.	U. S. P. results.	Present results.	U. S. P. results.
Ammonium salicylate....	0.97	0.9	2.33	2.3
Lithium "	0.786	very soluble	1.193	very soluble
Phenyl "	6665.0	2333.0	4.65	5.0
Quinine "	1538.0	77.0	20.65	11.0
Salicylic acid.....	453.0	308.0	2.13	2.0
Sodium salicylate	0.867	0.8	7.33	5.5
Strontium "	18.85	18.0	48.51	66.0
Bismuth sub "	10,000.0	....	625.0	....

[DIVISION OF PHARMACOLOGY, HYGIENIC LABORATORY, UNITED STATES PUBLIC HEALTH AND MARINE-HOSPITAL SERVICE, WASHINGTON, D. C.]

METHODS FOR THE DETERMINATION OF SALICYLATES.

BY ATHERTON SEIDELL.

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In the course of the examination of the several salicylates used for the solubility determinations described in an accompanying paper it seemed desirable to base the analyses of the samples upon a determination of the salicylic radicle. The two methods which have so far been proposed for this purpose are the Messinger and Vortmann iodine method, and the Freyer bromate method. The experiments described in the present paper show that neither of these methods are dependable and that even with the most careful control of the conditions, accurate determinations are not obtained with certainty.

[1] Seidell, *Proc. Am. Electrochem. Soc.*, Albany Meeting, 1908.