SOLUBILITY DETERMINATIONS OF U. S. P. CHEMICALS.

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SOLUBILITY OF SODIUM BIPHOSPHATE IN WATER AT 25° C.

The sodium biphosphate (sodium phosphate monobasic) used in this determination was of U. S. P. quality. Solutions were prepared by the undersaturation and the supersaturation method. The amount of salt dissolved was determined first by evaporating the solution and drying the residue at 110° C. to constant weight, and, second, after the residue was dried to constant weight, by igniting it to metaphosphate. When the residue was dried at 110° C. a crust was formed which prevented the complete evaporation of the adhering water. Even after drying for several weeks, the results were still somewhat higher than those obtained on ignition.

A check test was run to determine the loss of weight of the official salt on drying at 110° C. The U. S. P. requires that the sodium biphosphate loses not more than 15% of weight on drying at 100° C. This corresponds to approximately one mol of water of crystallization. Theoretically this monohydrated salt contains 13.05% water of crystallization, the U. S. P. giving a leeway of about 2% more moisture. The anhydrous salt should lose upon ignition an additional mol of water of constitution, making a total of 26.10%. The sample used for the experiment lost at 110° C. 13.6% and upon ignition suffered a further loss of 14.9%, making a total of 28.5%.

Sodium biphosphate crystallizes also with two mols of water (23.09%). It was of interest to know which of the hydrates is in equilibrium with water at 25° C. The excess of solute in the saturated solution was collected on cotton, separated from the main part of the adhering water by suction and dried over sulphuric acid for two hours. The dried samples were finely powdered, accurately weighed and fused. The excess remaining from the solution prepared by undersaturation method lost 35.34% and that from the solution prepared by supersaturation method lost 34.89% of weight. Theory is 34.64%. This indicated that sodium biphosphate with two mols of water of crystallization is in equilibrium with water at 25° C.

The results are stated as anhydrous sodium phosphate monobasic.

TABLE I.—RESULTS OF SOLUBILITY DETERMINATION OF SODIUM BIPHOSPHATE U. S. P. IN WATER AT 25° C.

Experiments.	Method of analysis.	Time of preparing solutions, days. 3.	7.	10.	23.
I	Dried at 110° C.	...	48.82	...	...
Prepared by under-		...	48.84	...	...
saturation method	Fused	...	...	...	48.49
		...	...	...	...
II					
Prepared by under-	Dried at 110° C.	...	...	48.61	...
saturation method	Fused	...	...	48.66	...
III					
Prepared by super-	Dried at 110° C.	48.72	...	...	...
saturation method	Fused	48.69	...	...	...

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[1] Continued from JOUR. A. PH. A., 18 (1929), 1230.

The average of the above results is 48.69. *Conclusion: 48.69 Gm. of anhydrous sodium biphosphate is present in 100 Gm. of the aqueous solution saturated at 25° C.*

Therefore: One gram of anhydrous sodium biphosphate is soluble in 1.05 cc. of water, or 1 Gm. of the monohydrate is soluble in 0.79 cc. of water, or 1 Gm. of the dihydrate is soluble in 0.58 cc. of water at 25° C.

SOLUBILITY OF POTASSIUM CHLORATE IN GLYCERIN AT 25° C.

The potassium chlorate and the glycerin used for the solubility determination were both of U. S. P. quality. The potassium chlorate was very finely powdered before mixing with glycerin. Solutions were prepared by the undersaturation and the supersaturation method.

For the analysis of the solutions the U. S. P. assay method for potassium chlorate is not suitable, as glycerin is rapidly oxidized by permanganate solution. The chlorate was, therefore, reduced to chloride and the resulting chloride determined volumetrically by Volhard's method, or gravimetrically by precipitation as silver chloride. The reduction was effected by diluting a weighed quantity of the solution with water in an Erlenmeyer flask provided with a Bunsen valve. A moderate excess of acidulated ferrous sulfate solution was added and the mixture heated. The solution after cooling was treated with nitric acid, an excess of *N*/10 silver nitrate added and the excess titrated with *N*/10 sulfocyanate. Or, for gravimetric determination, the reduced solution after treating with nitric acid was treated with silver nitrate, etc., and the resulting silver chloride weighed.

TABLE II.—RESULTS OF SOLUBILITY DETERMINATION OF POTASSIUM CHLORATE IN GLYCERIN AT 25° C.

	Time of preparing solution, days.					
Experiments.	5.	12.	13.	14.	21.	42.
I						
Prepared by under-	1.04	..	..	..	..	..
saturation method	..	..	..	..	..	..
II						
Prepared by under-	..	..	..	1.06	1.04	..
saturation method	..	..	..	..	1.02	..
III						
Prepared by super-	..	..	1.07	..	..	1.07
saturation method	..	..	1.06	..	..	1.07
IV	..	1.10	..	..	..	1.06
Prepared by super-	..	1.11	..	..	..	..
saturation method	..	1.12	..	..	..	1.06

The average of these results, excluding those of Experiment IV after 12 days which indicate supersaturation, is 1.055. *Conclusion: 1.055 Gm. of potassium chlorate is present in 100 Gm. of a U. S. P.-glycerin solution saturated at 25° C.*

Therefore: One gram of potassium chlorate is soluble in 75.26 cc. (= 93.79 Gm.) of U. S. P. glycerin at 25° C.

SOLUBILITY OF POTASSIUM CITRATE IN GLYCERIN AT 25° C.

When potassium citrate is dissolved in glycerin a thick and viscous solution results. The saturation of the solution prepared by undersaturation method and the separation of excess solute in the solution prepared by supersaturation method have taken place very slowly on account of the viscosity of the solution. The viscosity of the solution also caused difficulties in filtering. When cotton was used as a filtering fibre with the aid of strong suction applied over a period of several hours, a few cc. of a clear filtrate, enough to make an analysis, could be obtained. It was not, however, always possible to obtain a clear filtrate. Slightly turbid solutions yielded, as a matter of course, slightly higher results. Illustrative in this respect are the results of the Experiments I and II. The filtrate in Experiment II was clear and, though having been in contact with the solute three times as long as in Experiment I, it showed a lower concentration. The average result may therefore be slightly too high.

For analysis the assay method of the U. S. P. for benzoates and salicylates was used. About 0.5 Gm. of the solution was heated to the flashing point of glycerin and allowed to burn. The residue was finally ignited and the resulting potassium carbonate dissolved in $N/10$ hydrochloric acid and the excess titrated with $N/10$ sodium hydroxide, using methylorange indicator.

TABLE III.—RESULTS OF THE SOLUBILITY DETERMINATION OF POTASSIUM CITRATE IN GLYCERIN AT 25° C.

	Time of preparing solutions, days.					
Experiments.	9.	13.	24.	27.	40.	135.
I	...	...	...	...	28.73	...
Prepared by under-	...	27.27	27.62	28.40	28.79	...
saturation method	...	...	...	...	28.83	...
II						
Prepared by under-	...	...	...	...	...	27.23
saturation method	...	...	...	...	...	27.99
III						
Prepared by super-	29.01	...	...	28.86	...	...
saturation method	29.03	...	...	28.33	...	...

The average of all the results, except those of Experiment III after 9 days which, at this time, still indicated supersaturation of the solution, is 28.20. *Conclusion: 28.20 Gm. of potassium citrate is present in 100 Gm. of a U. S. P.-glycerin solution saturated at 25° C.*

Therefore: One gram of potassium citrate is soluble in 2.02 cc. (= 2.55 Gm.) U. S. P. glycerin at 25° C. (glycerin 1.246 at 25°/4° C.).

SOLUBILITY OF FERRIC CHLORIDE IN ALCOHOL AT 25° C.

Crystallized iron chloride U. S. P. was crushed and mixed with U. S. P. alcohol. It dissolved rapidly and to a large extent. A sample of the clear supernatant solution was taken out after various periods of time and the chloride-ion determined volumetrically. As is evident from the table saturation was attained in six days.

TABLE IV.—RESULTS OF SOLUBILITY DETERMINATION OF FERRIC CHLORIDE IN ALCOHOL AT 25° C.

	Time of preparing solutions, days.		
Experiments.	3.	6.	13.
Prepared by under-	50.77	51.52	51.37
saturation method	50.44	51.51	51.40

The average of Experiments II and III is 51.45. *Conclusion: 51.45 Gm. of ferric chloride is present in 100 Gm. of a U. S. P.-alcohol solution saturated at 25° C.*

Therefore: One gram of Ferric Chloride is soluble in 1.17 cc. (= 0.94 Gm.) U. S. P. alcohol at 25° C. (Density of alcohol used in the experiments was 0.8063 at 25°/4° C.)

SOLUBILITY OF METHYLENE BLUE IN WATER AND ALCOHOL AT 25° C.

The solutions of methylene blue U. S. P. in water or alcohol were prepared either by the undersaturation or the supersaturation method. They were analyzed by evaporating the solvent and drying the residue at 110° C. The iodometric method of Sabalitschka (*Chem.-Ztg.*, 49 (1925), 561) was used in several experiments but the results were not satisfactory.

The results shown in the tables refer to the residue obtained on drying at 110° C., that is to anhydrous methylene blue. The sample of methylene blue used for the experiments lost on drying at 110° C. about 12% of its weight. The water content of commercial methylene blue varies within a few per cent. It seldom corresponds to a definite number of mols of water of crystallization. The U. S. P. allows not more than 15% of water. Three mols of water of crystallization correspond to 14.5 %. The German Pharmacopœia concedes 18 to 22% which corresponds to from four to five mols. It was of interest to know whether the water content of methylene blue is changed during the solubility determination where it is in contact with water or alcohol. For this purpose some of the excess solute from the aqueous and alcoholic solutions was collected on a filter, dried in air for about one hour, then over sulphuric acid for two hours to remove the adhering solvent. An accurately weighed amount was then dried at 110° C. to constant weight. All samples, either taken from the aqueous or the alcoholic solution, or either from the solution prepared by undersaturation or supersaturation method, lost approximately 17%. This would indicate that methylene blue with four mols of water of crystallization is in equilibrium with water or aqueous alcohol at 25° C.

The excess of solute present at the beginning in the aqueous or alcoholic solution prepared by supersaturation method separated very slowly. After 39 days the alcohol solution had reached the concentration of the solution prepared by undersaturation method, which was saturated after 12 days. The solution in water prepared by supersaturation method, however, did not read the concentration of that prepared by undersaturation method during the observation period of 38 days. It shows a continuous decrease of concentration during that time. The results of this experiment are, therefore, not included in the calculation of solubility.

TABLE V.—RESULTS OF THE SOLUBILITY DETERMINATION OF METHYLENE BLUE IN WATER AT 25° C.

	Time of preparing solutions, days.						
Experiments.	4.	6.	9.	12.	22.	28.	38.
I							
Prepared by under-	2.32	..	2.28	2.32	..	..	..
saturation method	2.32	..	2.28	2.28	..	..	..
II							
Prepared by super-	..	3.95	..	3.84	3.67	3.50	3.25
saturation method	..	4.00	..	3.85	..	3.60	..

The average of Experiment I is 2.30. *Conclusion: 2.30 Gm. of anhydrous methylene blue is present in 100 Gm. of an aqueous solution saturated at 25° C.*

Therefore: One gram of anhydrous methylene blue is soluble in 42.81 cc. (= 42.48 Gm.) of water at 25° C.

Calculated for methylene blue with water of crystallization:

One gram of methylene blue with three mols (14.46%) of water of crystallization is soluble in 37.3 cc. (= 37.0 Gm.) of water at 25° C.

One gram of methylene blue with four mols (18.39%) of water of crystallization is soluble in 35.7 cc. (= 35.5 Gm.) of water at 25° C.

TABLE VI.—RESULTS OF THE SOLUBILITY DETERMINATION OF METHYLENE BLUE IN ALCOHOL AT 25° C.

	Time of preparing solutions, days.						
Experiments.	5.	9.	12.	18.	22.	28.	39
I							
Solution prepared by undersaturation method	..	1.45	1.48	1.49	..	..	..
	..	1.44	..	..	..	..	..
II							
Solution prepared by supersaturation method	1.64	..	1.63	..	1.59	1.55	1.48
	1.64	..	1.64	..	..	..	..

The average of all the results of Experiment I and of the results of Experiment II after 39 days, is 1.47. *Conclusion: 1.47 Gm. of anhydrous methylene blue is present in 100 Gm. of a U. S. P.-alcohol solution saturated at 25° C.*

Therefore: One gram of anhydrous methylene blue is soluble in 83.10 cc. (= 67.00 Gm.) of U. S. P. alcohol at 25° C. (Density of alcohol used 0.8063 at 25°/4° C.)

Calculated for methylene blue with water of crystallization:

One gram of methylene blue with three mols (14.46%) of water of crystallization is soluble in 72.4 cc. (= 58.4 Gm.) of U. S. P. alcohol at 25° C.

One gram of methylene blue with four mols (18.39%) of water of crystallization is soluble in 64.5 cc. (= 56.0 Gm.) of U. S. P. alcohol at 25° C.

SOLUBILITY OF BARBITAL SODIUM IN ALCOHOL AT 25° C.

Solutions of barbital sodium were prepared by the undersaturation and the supersaturation method. They were analyzed by the residue method. The alcohol was evaporated and the residue dried at 110° C. to constant weight. Due to the small solubility of this chemical in alcohol the results varied within about ±3% from each other. Variation of strength of the alcohol also has a considerable influence on the solubility. For some reason, which due to lack of time could not be investigated, the solution prepared by supersaturation method yielded a considerably lower concentration. The results of Experiment II are, therefore, not included in the calculation of solubility.

TABLE VII.—RESULTS OF THE SOLUBILITY DETERMINATION OF BARBITAL SODIUM IN ALCOHOL AT 25° C.

	Time of preparing solution, days.						
Experiments.	2.	4.	9.	12.	18.	24.	44.
I							
Solution prepared by undersaturation method	...	...	...	0.319	0.301	0.321	0.318
	...	...	...	0.300	...	0.318	...
II							
Solution prepared by supersaturation method	0.282	0.284	0.281	...	...	...	...
	...	...	...	...	...	...	...

The average of all the results of the solution prepared by the undersaturation method is 0.313. *Conclusion: 0.313 Gm. of barbital sodium is present in 100 Gm. of the U. S. P.-alcohol solution saturated at 25° C.*

Therefore: One gram of Barbital Soluble is soluble in 395.0 cc. (= 318.5 Gm.) of U. S. P.-alcohol at 25° C. (Density of alcohol used 0.8063 at 25°/4° C.)

SOLUBILITY OF SULPHONETHYLMETHANE IN ALCOHOL AT 25° C.

The solutions for the determination of the solubility of sulphonethylmethane in alcohol were prepared either by the undersaturation or the supersaturation method. They were analyzed by evaporating the alcohol at 60° C. and fusing the residue at 80° C. By this procedure constant weight was attained after a short time as may be seen from the following experimental data.

	I.	II.
Residue after 20 minutes at 80° C.	1.0244;	0.9438
Residue after 50 minutes at 80° C.	1.0240;	0.9432
Residue after 70 minutes at 80° C.	1.0240;	0.9432

The alcohol used for Experiments I, II and III, had a strength of 95.2% (by volume), that used for Experiments IV and V, 94.9%. This causes a slight difference in the results of the two groups of experiments performed with these two lots of alcohol.

TABLE VIII.—RESULTS OF SOLUBILITY DETERMINATION OF SULPHONETHYLMETHANE IN ALCOHOL.—ALCOHOL OF 95.2% BY VOLUME.

	Time of preparing solutions, days.								
Experiments.	1.	4.	6.	8.	12.	16.	32.	39.	41.
I									
Prepared by under-	...	13.67	...	...	14.02	...	...	14.33	14.21
saturation method	...	13.26	...	...	14.06	...	...	...	...
II									
Prepared by under-	...	...	14.01	...	...	...	14.36	...	...
saturation method	...	...	...	...	...	...	14.40	...	...
III									
Prepared by super-	14.83	...	...	14.64	...	14.77	...	...	...
saturation method	...	...	...	...	...	14.76	...	...	...

Alcohol of 94.9% by Volume.

	Time of preparing solutions, days.						
Experiments.	1.	6.	14.				
IV				V			
Prepared by under-	...	...	13.38	Prepared by super-	13.80	13.33	...
saturation method	...	...	13.42	saturation method	13.55	13.32	...

The average of the results of Experiment I, 39 and 41 days; Experiment II, 32 days and of Experiment III, is 14.41. The average of the results of Experiment IV, 14 days and Experiment V, 6 days, is 13.36.

The mean of both these averages is 13.9. *Conclusion: 13.9 Gm. of sulphonethylmethane is present in 100 Gm. of a U. S. P.-alcohol solution saturated at 25° C.*

Therefore: One gram of sulphonethylmethane is soluble in 7.7 cc. (= 6.2 Gm.) of U. S. P. alcohol at 25° C.

SOLUBILITY OF EMETINE HYDROCHLORIDE IN WATER AT 25° C.

The solubility of emetine hydrochloride was determined in the usual way. The solution was prepared by the undersaturation method only. In shaking the solute with water at room temperature quite a large amount dissolved. Very soon, however, the solution formed a thick mass of fine crystals. There seems to occur the formation of a hydrate which possesses a different solubility. From the crystalline mass the solution was separated by suction and the clear filtrate evaporated on a water-bath and the residue dried at 100° C. The results are stated as anhydrous emetine hydrochloride.

It was also intended to determine the emetine hydrochloride in solution by shaking out the base with ether after making alkaline with ammonia, but, due to lack of time, this could not be accomplished.

TABLE IX.—RESULTS OF SOLUBILITY DETERMINATION OF EMETINE HYDROCHLORIDE IN WATER AT 25° C.

Experiments.	Time of preparing solutions, days. 8.	18.
Solution prepared by undersaturation method	16.56	16.51
	...	16.51

The average of these results is 16.53. *Conclusion: 16.53 Gm. of anhydrous emetine hydrochloride is present in 100 Gm. of an aqueous solution saturated at 25° C.*

Therefore: One gram of anhydrous emetine hydrochloride is soluble in 5.05 cc. of water at 25° C.

Calculated for emetine hydrochloride with two mols (or 11.23%) of water of crystallization:

One gram of emetine hydrochloride with 2 mols of water of crystallization is soluble in 4.37 cc. of water.

Calculated for emetine hydrochloride with four mols (or 20.20%) of water of crystallization:

One gram of emetine hydrochloride with 4 mols of water of crystallization is soluble in 3.83 cc. of water at 25° C.

Calculated for emetine hydrochloride with $3^1/_2$ mols (or 18.13%) of water of crystallization. This value is included as the Pharmacopœia allows a loss of not more than 19% on drying Emetinae Hydrochloridum at 100° C.

One gram of emetine hydrochloride with three and one-half mols of water of crystallization is soluble in 3.95 cc. of water at 25° C.

SOLUBILITY OF VANILLIN IN ALCOHOL AT 25° C.

The solution for the solubility determination of vanillin in alcohol was prepared by the undersaturation method. It was analyzed by evaporating the solvent and drying the residue at 60° C. to constant weight. The loss of weight on drying the original vanillin at this temperature was so small as to be safely ignored. The density of the alcohol used was 0.8063 at 25° C. which corresponds to 95.2% by volume.

TABLE X.—RESULTS OF SOLUBILITY DETERMINATION OF VANILLIN IN ALCOHOL AT 25° C.

Experiment.	Time of preparing solution, days. 10.	15.
Solution prepared by undersaturation method	48.38	48.46

The average of the results is 48.42. *Conclusion: 48.42 Gm. of vanillin is present in 100 Gm. of the U. S. P.-alcohol solution saturated at 25° C.*

Therefore: One gram of vanillin is soluble in 1.31 cc. (= 1.06 Gm.) U. S. P. alcohol at 25° C.