

SULPHUROUS ACID, ITS EXTEMPORANEOUS PREPARATION.*

BY OTTO RAUBENHEIMER.

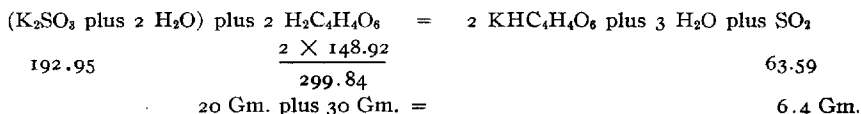
Acidum Sulphurosum, U. S. P. VIII, although it has been deleted from the Pharmacopoeia and has *not* been admitted into N. F. IV, but will be relegated to the A. Ph. A. Recipe Book, is occasionally prescribed owing to its antiseptic and germicidal properties, both for internal and external use.

The principal trouble with this acid is that it is very unstable, and, when the pharmacist is called upon to dispense it, he finds, to his sorrow, that his stock has deteriorated and has oxidized to a diluted sulphuric acid. Such was the case when I received a prescription sometime ago for Acidum Sulphurosum. The U. S. P. VIII gives a most excellent process together with minutest details, occupying a total of one and a half pages, for this preparation of this acid by the reduction of sulphuric acid with charcoal. However, for the preparation of a small amount, for instance, 50 or 100 mls, it is hardly practicable for the pharmacist to put together the apparatus required by the U. S. P.

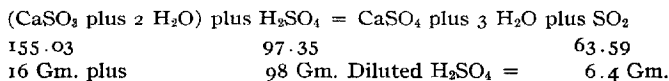
It, therefore, occurred to me that a method for the extemporaneous preparation of sulphurous acid would be of help to the pharmaceutical profession.

EXPERIMENTS AND STOICHIOMETRY.

Process No. I.—A modification of the Fothergill process, namely, liberation of SO_2 and precipitation of potassium bitartrate by the double decomposition of solutions of potassium sulphite and tartaric acid. In the reaction, which I present, the first line gives the chemical equation, the second line contains the molecular weights of U. S. P. VIII, as the work was commenced and finished before the ninth revision was published, and the third line contains the number of grammes and sufficient distilled water to produce 100 Gm. of Acidum Sulphurosum.



Process No. II.—Decomposition of calcium sulphite with diluted sulphuric acid.



Filtering is required in both these processes. The chief objection, however, is, that neither potassium nor calcium sulphite are generally in stock in most pharmacies.

Process No. III.—Sodium sulphite, both crystallized, as well as anhydrous, is practically in every drug store and my efforts were directed to use this chemical in the extemporaneous preparation of sulphurous acid.

In examining the excellent Index of Chemical Abstracts for 1915, I find under "Sulfur Dioxide"—"Preparation of Solutions," the very thing I have been looking for, although hidden in such a way that it is rather difficult to find.

* Read before Scientific Section, A. Ph. A., Atlantic City meeting, 1916.

The Abstract in Chemical Abstracts of August 20, 1915, p. 2286, is entitled: *Extemporaneous Preparation of Solutions of Sulfur Dioxide*. Cheney, Boll. chim. farm., vol. 54 (1915), 359:

In a bottle of 250 Cc. capacity, provided with a ground glass stopper, are placed 5.7 Gm. dry Na_2SO_3 and 18 Cc. diluted HCl. The bottle is then quickly stoppered and set in a cool place. The contents are shaken cautiously so as to facilitate solution of the salt. When effervescence has ceased, 25 Cc. H_2O are added and the mixture is shaken for several minutes. The volume of the final solution is 40 Cc. and the SO_2 content is 6 to 6.4 percent.

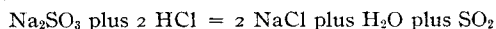
FALLACIES IN ABSTRACTS.

In glancing over this abstract my suspicion about its correctness was aroused when I added the given quantities, *i. e.*, 5.7 Gm., 18 Cc. and 25 Cc. are supposed to produce a total of 40 Cc.

Not having the latest edition of the Italian Pharmacopoeia on hand, I learned from my friend, Martin I. Wilbert of the Hygienic Laboratory, Public Health Service, Washington, D. C., that the Diluted Hydrochloric Acid in that standard contained 8.07 percent by weight of HCl. I prepared this strength acid and then made a number of experiments, based on a total volume of both 40 and 100 mls, with the following results:

Na_2SO_3 .	8% HCl.	Volume.	Add H_2O .	Total volume.
5.7 Gm.	18 mls	20 mls	20 mls	40 mls
14.25 Gm.	45 mls	50 mls	50 mls	100 mls

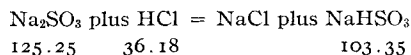
I noticed that this reaction was accompanied by the generating of *heat*, while the generation and particularly the absorption of gases produces *cold*, and my suspicion was again aroused. The chemical reaction and molecular proportion is as follows:



$$\begin{array}{r} 125.25 \quad \quad \quad \frac{2 \times 36.18}{72.36} \quad \quad \quad 63 \end{array}$$

or $\begin{array}{r} 14 \text{ Gm. plus } 72.36 \text{ Gm. Diluted HCl} = 6.3 \text{ Gm. in } 100 \text{ mls} \\ 90\% \quad \quad \quad 10\% \end{array}$

Sodii Sulphis Exsiccatus has been admitted into U. S. P. IX in place of the crystallized salt, with a purity rubric of not less than 90 percent of Na_2SO_3 . The Italian formula calls for 45 mls of 8 percent HCl which is the equivalent of just 36 mls of 10 percent HCl, which is exactly one-half of the requirement. The Italian chemist consequently gets the following reaction:



The SO_2 which is evolved combines with the sodium sulphite to form a bisulphite. Instead of calculating his result as NaHSO_3 , the Italian author reports that the finished product contains from 6 to 6.4 percent of *free* SO_2 . Another proof that it is absolutely necessary to base the calculation upon the chemical reaction which actually takes place!

WORKING FORMULA.

During the past few months I made over 50 experiments of 100 mls each, which were all checked by volumetric assays. In my work, I reached the following conclusions:

1. To bring up the finished preparation to a volume, namely, 100 mls, rather than weight.

2. To use the more permanent Exsiccated Sodium Sulphite, especially as same is now official in U. S. P. IX.

3. To pour the diluted hydrochloric acid on top of the sodium sulphite, as less SO_2 is lost, than when the reverse is done.

4. To keep the bottle cool during the process, as cold greatly helps the absorption of SO_2 .

The following working formula I have found to produce a full strength Sulphurous Acid:

Exsiccated Sodium Sulphite.....	14.5 Gm.
Diluted Hydrochloric Acid.....	75.0 mls
Distilled Water, a sufficient quantity,	

To make 100 mls

Place the salt in a 250 ml glass-stoppered cylinder, or bottle, which is graduated at 100 mls. Quickly add the acid, previously mixed with 20 mls of water, stopper and put in a cool place, for instance, under running water. Shake occasionally, and, if necessary, add water to make 100 mls.

Sulphurous Acid can, in this manner, be freshly prepared when wanted in a few minutes. This process produces a product which contains about 6 Gm. of SO_2 in 100 mls.

ASSAY.

The regular iodometric volumetric assay was employed as follows:

To 25 mls of tenth-normal iodine V. S. in a glass-stoppered flask, 1 ml of the sulphurous acid is added, the mixture agitated and allowed to stand a few minutes. This is then titrated with tenth-normal sodium thiosulphate V. S., using starch T. S. toward the end of the reaction. The number of mls of the iodine V. S. decomposed by the SO_2 are thus determined, and this figure multiplied by the factor gives the number of grammes of SO_2 in 1 ml of Acidum Sulphurosum. This multiplied by 100 gives the weight in volume percent.

The acid prepared without application of cold assayed from 5.1516 to 5.8512 w./v. percent of SO_2 . When cold or running water was used then it assayed from 6.042 to 6.678 w./v. percent of SO_2 , which proves beyond doubt the beneficial influence of cold in this reaction.

DETERIORATION.

Sulphurous Acid deteriorates very rapidly and within one month will assay only one-half the amount of SO_2 . For this reason it should be freshly prepared.

PRESENCE OF SODIUM CHLORIDE.

The acid prepared by this method will contain about 12 percent of sodium chloride, but I doubt if any serious objection can be made on account of this either for internal administration or for external application. Otherwise Process No. I or No. II can be used for the extemporaneous preparation of sulphuric acid.

As a result of the work on this subject, two points of great importance are noteworthy.

DANGER IN FOREIGN FORMULAS.

Whenever a formula is abstracted from a foreign source the careful investigator or experimenter should make sure of the strength of the ingredients, especially the chemicals, as they may differ considerably from the standards of the U. S. P., as again exemplified by the diluted hydrochloric acid of the Italian Pharmacopoeia which contains only 8 percent of HCl.

STANDARDS FOR ARTICLES DELETED FROM U. S. P. AND N. F.

A great many preparations, drugs and chemicals have been deleted from the U. S. P. and have been admitted into the N. F. Consequently their standards are taken care of. But how about a few articles, for instance, Sulphurous Acid, which have been completely deleted? It seems to me that the last standard should hold good. *I would suggest that the Preface of the U. S. P. should contain a statement to that effect.*

CONCLUSION.

I hope that this formula for the extemporaneous preparation of Acidum Sulphurosum will be of benefit to the pharmaceutical profession. If, however, the average pharmacist is too slow to use this process, then no doubt some up-to-date manufacturer will accommodate him by placing a package on the market containing a bottle of sodium sulphite and another of diluted hydrochloric acid together with directions. The author is not looking for any royalty!

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ABSTRACT OF DISCUSSION.

PHILIP ASHER: I am glad Professor Raubenheimer brought up this point. There is only one thing in my mind, and that is regarding the stability of the sodium sulphite. I have had a great deal of trouble in getting a sodium sulphite that would hold up, but he makes mention of the fact that the U. S. P. calls for an anhydrous salt. I would like to ask him if he has tried to find the strength of the sodium sulphite after it has stood for some time.

C. H. LAWALL: That has already been answered by Professor Clark's figures in which he says that the anhydrous salt is practically stable.

I. F. KEBLER: Dr. Raubenheimer referred to the use of sulphur dioxide. There are several proprietary products on the market that are sulphurous in character—namely, one that is called "Microbe Killer" and that is supposed to be good for everything on the face of the earth. I would just like to call attention, in this connection, to one point, and that is that some of the claims made by these people are substantiated by medical literature, and in fairly well recognized and accepted literature. This is due to the fact that this literature enumerates everything for which the particular article has ever been recommended and used, and it either places the authority in a very embarrassing position, and so also the practitioner. For instance, several books recommend sulphurous acid as a treatment for tuberculosis, and one of our well-known chemical friends said some years ago that it was an excellent agent for the treatment of tuberculosis. There is nothing in it. About the keeping of dry sodium sulphite. Sodium sulphite, on the market, is about 90 percent dry, and it does keep.