

THE STABILIZATION OF SOLUTION OF ARSENOUS AND MERCURIC IODIDE, U. S. P. X.\* \*\*

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Solution of Arsenous and Mercuric Iodide, U. S. P. X, commonly known as Donovan's Solution, is notably poor in keeping qualities, the trivalent arsenic being gradually oxidized to pentavalent arsenic on storage under ordinary conditions. In a previous paper by the present authors (1) it was shown that the stability of Donovan's Solution is increased by the following factors: (a) storage in amber-colored bottles, (b) storage in well-filled bottles, (c) storage in a refrigerator, (d) replacement of the air in the bottle by an inert gas, (e) replacement of 25% of the water by honey or syrup, (f) by neutralization of the solution with KOH, (g) by use of a modified formula proposed by the authors and (h) by the addition of stabilizers, of which the most effective were calcium carbonate, oxalic acid, methenamine and terpin hydrate.

The usual method of procedure for comparing the stability of the various solutions was to expose 50-cc. samples, contained in ordinary 2-oz. prescription bottles, in diffused light and sunlight. The deterioration under these conditions was more rapid than in well-filled, amber-colored bottles and it was thus possible to secure quicker results. At the conclusion of the previously reported work outlined above, other experiments were started to throw further light on the comparative value of the various methods of stabilization under drug store conditions,

TABLE I.—DETERIORATION OF DONOVAN'S SOLUTION STABILIZED IN VARIOUS WAYS, WHEN STORED IN PINT AMBER-COLORED BOTTLES IN DIFFUSED LIGHT.

Solution No.	Description of solution.	Date of preparation.	Gm. AsI <sub>2</sub> in 100 cc. originally.	Gm. AsI <sub>2</sub> in 100 cc. after 10 months.*	Deterioration after 10 months.
I	Modified formula proposed by authors	5-21-29	1.005	0.996	0.9%
II	Same as I, but separately neutralized	5-21-29	1.005	0.999	0.6%
III	Donovan's Solution (control)	5-22-29	0.991	0.868	12.4%
IV	Neutralized with KOH	5-22-29	0.940	0.845	10.1%
V	Saturated with CO <sub>2</sub>	5-22-29	0.976	0.891	8.7%
VI	Neutralized with KOH and saturated with CO <sub>2</sub>	5-22-29	0.940	0.883	6.1%
VII	Air replaced by H <sub>2</sub>	5-22-29	0.991	0.867	12.5%
VIII	Neutralized with KOH and air replaced by H <sub>2</sub>	5-22-29	0.940	0.871	7.3%
IX	CaCO <sub>3</sub> added (1.4 Gm. per pint)	5-22-29	0.991	0.932	6.0%
X	Terpin hydrate added (1.9 Gm. per pint)	5-22-29	0.993	0.911	8.3%

\* Exact date of analysis: 3 13-30.

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*i. e.*, starting with well-filled amber-colored bottles stored in diffused light, portions of the contents being withdrawn from time to time. Pint amber-colored bottles, fitted with rubber stoppers, were used. The results are summarized in Table I.

Amounts withdrawn: 30 cc. on 12-14-29, 35 cc. on 3-5-30, 30 cc. on 3-13-30, 30 cc. on 3-25-30.

A test was also made to determine the effect of replacing 15% of the water by syrup. It was found that the U. S. P. method of analysis for trivalent arsenic was not reliable in this case, due to the fact that some iodine was used up in oxidizing glucose formed by hydrolysis of the sucrose.

#### DISCUSSION OF RESULTS.

*Replacement of Air by Inert Gases.*—The method of replacing the air in the bottle by an inert gas was partially effective using carbon dioxide but ineffective with hydrogen. This method might be applicable to small bottles which would be dispensed as soon as opened, but is not very effective for stock bottles, due to escape of the gas and entry of air each time the bottle is opened. As would be expected under these conditions, a gas heavier than air, such as carbon dioxide, is superior to a light, fugitive gas such as hydrogen.

*Effect of Neutralization.*—Donovan's Solution neutralized with KOH, using methyl orange as indicator, was somewhat more stable than the control. A more pronounced stabilization resulted when the solution was neutralized and the air replaced by carbon dioxide or hydrogen.

*Effect of Calcium Carbonate.*—The addition of 1.4 Gm. of calcium carbonate per pint of solution reduced the rate of deterioration by about 50%. The calcium carbonate reacts with the HI present in the solution; this results in a more favorable  $p_H$  and the carbon dioxide liberated replaces part of the air in the bottle. To avoid loss of carbon dioxide, the solution was not filtered after addition of the calcium carbonate; there was a slight sediment in the bottle after 10 months.

*Effect of Terpin Hydrate.*—Terpin hydrate had a slight preservative influence. After 10 months there was a very slight sediment and the solution had a terpene-like odor.

*Modified Formula.*—Details have already been published (1) for the preparation of Donovan's Solution by a modified formula proposed by the present authors, the change lying in the use of  $As_2O_3$ ,  $HgI_2$  and KI in place of  $AsI_3$  and  $HgI_2$ . This solution showed less than 1% deterioration after 10 months, as compared with a deterioration of 12.4% for the U. S. P. X solution. This modified formula appears worthy of serious consideration in connection with pharmacopœial revision. The method of preparation is somewhat longer and more complicated than the present official process and would thus seem to be better suited to large scale manufacture than to extemporaneous preparation. However, unless a change is made in the official formula, it seems desirable if not imperative that the next revision of the U. S. P. should require that Donovan's Solution be freshly prepared just before dispensing.

#### SUMMARY.

1. Experiments have been carried out to determine the comparative value under drug store conditions of various methods of stabilizing Donovan's Solution.

2. After 10 months, the % deterioration was as follows: modified formula proposed by authors, less than 1%; control, 12.4%; neutralized with KOH, 10.1%; saturated with CO<sub>2</sub>, 8.7%; neutralized with KOH and saturated with CO<sub>2</sub>, 6.1%; air replaced by H<sub>2</sub>, 12.5%; neutralized with KOH and air replaced by H<sub>2</sub>, 7.3%; CaCO<sub>3</sub> added, 6.0%; terpin hydrate added, 8.3%.

3. The modified formula proposed is worthy of serious consideration in connection with pharmacopœial revision.

4. It is recommended that in the next revision the U. S. P. should adopt a modified formula for Donovan's Solution, or require that the solution be freshly prepared just before dispensing.

#### REFERENCE.

- (1) William J. Husa and W. W. F. Enz, *JOUR. A. PH. A.*, 19 (1930), 328.

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### TEACHER-TRAINING IN PHARMACY.\*

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It is the chief aim, perhaps, of all of our schools and colleges of pharmacy to train young men and women to become practicing pharmacists, either as retail pharmacists, analysts or manufacturing pharmacists. Although this sort of training is, to be sure, very essential, I am inclined to believe that more emphasis should be placed upon the training for teachers in pharmacy in the future than has been done in the past. It seems to me that there is a demand, even to-day, for well-trained teachers in our schools and colleges. This belief was made more impressive during the past year in looking about for an additional member to our Teaching Staff. Some of the applicants for this position had apparently had no specialized training for qualifying them as teachers. A Dean of one of the larger schools also informed me that he had had seven or eight requests for positions to be filled during the past year, and that there never was a time, to his knowledge, when there were more opportunities for teachers of pharmacy. The recent advances in pharmaceutical education have naturally increased the demand for well-trained teachers of pharmacy.

The teaching profession is, doubtless, one of the least selfish and most poorly paid of all the professions. A teacher is required to give his time, knowledge, sympathy and understanding most freely and unselfishly. A paper, presented by Dean Rudd at the Portland meeting, entitled "Professors of Pharmacy" seems to confirm the above statement. In fact, I have long since concluded that all Pharmacy teachers should never expect to become over-burdened with wealth. However, there should come to all of us who profess to teach, a joy and satisfaction in knowing that we are training young men and women for an important and honorable profession.

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\* Section on Education and Legislation, *A. PH. A.*, Rapid City meeting, 1929.—No discussion.