water (*Fig. 20*). In all these cases, however, equilibria are not attained; the phenomena are those of non-stability.[1]

SUMMARY.

The physical conditions under which pendant and wetting drops are formed, are discussed in detail. From theoretical considerations, we conclude that these formations are stable only if the various interface tensions involved satisfy definite conditions. Of especial importance is the magnitude of the wetting tensions.

In order to test the correctness of the theoretical conclusions, the subject of wetting is investigated in some detail. The known methods of measuring the wetting tension are discussed, and a new method is described, which overcomes certain difficulties of the methods heretofore in use. A few results of the measurements by this method are recorded.

The study of the wetting phenomena invariably shows that wetting is a complicated process, which cannot be characterized by the magnitude of wetting tensions alone. For this reason, wetting was studied more in detail, from its experimental aspect as a phenomenon.

To this end, a special optical arrangement was worked out, by the aid of which, wetting in glass tubes may be rendered very plainly visible. The method also permits proving the existence of very thin wetting films which otherwise could not be seen. The origin of pendant and wetting drops is very closely bound up with the behavior of these wetting films, which is shown in a series of photographs.

The earlier published observations of the senior author were confirmed in every respect.

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

BY WILLIAM J. HUSA.**

RELATION BETWEEN STABILITY AND p_H.

Historical Review.—In 1903, William Duncan (1) reported that the tendency of Donovan's Solution to liberate iodine could be checked by adding sufficient alkali to neutralize the free hydriodic acid, and suggested this method for adoption in the British Pharmacopœia. His suggestion did not receive favorable consideration. Guyot (2) offered this same suggestion for checking the deterioration of a solution of arsenous iodide. In confirmation of these reports, Husa and Enz (3) found that Donovan's Solution was more stable near the neutral point, the rate of deterioration increasing with increasing acidity or basicity.

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[1] The contrast between these exceptions and the regular phenomenon may probably be characterized as follows:

The normal phenomena depend solely on the values of the interface tensions, regardless of the order in which the two liquids are mixed. With the 2 anomalies described, exactly the same order of superposition must be observed in order to be successful. Contact of the pendant drop with the glass wall must be especially avoided, because as soon as contact takes place, the laws we derived concerning the magnitudes of interface tensions will go into effect, tending to stability.

* Presented before the Scientific Section, A. PH. A., Miami, Fla., 1931.

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Experimental Data.—As the literature contains no data on the exact relation between the stability and p_H of this solution, experiments were carried out to supply this information. Tests were made of the stability of a series of solutions adjusted to different p_H values by the addition of KOH. In order to have the Donovan's Solution of U. S. P. strength after the addition of the base, the solution was first made up of double strength. In each case, 250 cc. of double strength solution was placed in an 800-cc. beaker fitted with a mechanical stirrer, and the specified number of cc. of approximately $N/2$ KOH was slowly run in from a burette with vigorous stirring. Then distilled water was added q. s. 500 cc. The tests were carried out in dark amber-colored, cork-stoppered bottles in diffused light, each bottle containing 400 cc. of solution. It was found essential to add the base slowly and with vigorous agitation as described, for otherwise the KOH caused the solution to become cloudy, due apparently to precipitation of a basic mercury salt.

The p_H was determined colorimetrically and the assay for arsenous iodide was carried out by the U. S. P. method. After a period of approximately six months, the solutions were again analyzed for trivalent arsenic with results as follows:

TABLE I.—RELATION BETWEEN STABILITY AND p_H.

No. of Cc. of Approx. $N/2$ KOH Used in 500 Cc. of Solution.	p_H Determined Colorimetrically.	Deterioration after 177 Days (% of As^{III} Oxidized to As^V).
None (control)	1.2	46.9%
50.0 cc.	1.5	27.2%
75.0 cc.	2.0	21.5%
88.3 cc.	3.4	12.2%
88.8 cc.	4.8	9.4%
89.1 cc.	5.6	5.9%
89.3 cc.	6.3	0%
89.5 cc.	6.9	0%
90.0 cc.	7.5	0%
91.2 cc.	7.8	0%

The results in Table I indicate that with increasing p_H values (decreasing concentration of H ions) the stability increased and that in the p_H range from 6.3 to 7.8 there was no deterioration whatever in approximately six months. These results were verified by another similar experiment in which there was no deterioration in seven months in solutions adjusted to a p_H of between 6.0 and 8.0.

The fact that the hydriodic acid in Donovan's Solution need not be completely neutralized to assure stability is in accord with the results obtained by Husa and Shattuck on solutions of pure hydriodic acid. These results, which are being reported in another paper, indicate that when HI is diluted to $N/100$ and $N/1000$, it becomes unusually stable. On the alkaline side, the present tests did not go beyond a p_H of 8.0, but in more alkaline solutions the stability would be poorer as the oxidation of trivalent arsenic by atmospheric oxygen becomes a factor in alkaline solutions; the earlier results of Husa and Enz (3) bear this out.

Since by adjusting the p_H the deterioration was reduced from about 50% to 0%, the advisability of changing the p_H of this solution should be seriously considered for adoption in the U. S. P. XI. A suitable p_H range for official adoption would be from p_H 6.5 to 7.5. This would allow for minor variations and would still be within the p_H range in which Donovan's Solution is stable.

Adjustment of p_H by a Simple Method.—Since the exact adjustment of p_H by addition of KOH solution, using the colorimetric method, is a rather tedious process which is not very well suited for use in the retail pharmacy, an effort was made to devise a simpler process. It was evident that the use of a strong base, such as KOH, would necessarily require extreme care in manipulation, since a small quantity of strong base causes a great change in p_H near the neutral point, and since a local excess of KOH in the solution causes precipitation. This method could easily be used on a factory scale with adequate chemical control but would hardly be suitable for the average retail pharmacist under present conditions.

It was concluded that the best possibility for a reliable extemporaneous method of adjusting the p_H would be a method of neutralizing the solution by the mere addition of a weighed quantity of some commonly available substance of low cost, of adequate neutralizing power yet of feeble alkalinity (so that a slight inaccuracy in weighing would not vitiate the results, and a local excess would not cause precipitation); furthermore such a substance should be unobjectionable therapeutically. When the problem was once visualized from this standpoint, the only step remaining was to find a substance having this combination of desirable properties, and to establish the proper conditions for its use.

In approaching the problem of finding a substance having the desired combination of properties, some alkaline substances such as hydroxides, and certain borates and phosphates were eliminated from consideration for obvious reasons. In considering the relative value of carbonates and bicarbonates, particularly those of sodium and potassium, it was apparent that the bicarbonates would require less accurate weighing, both on account of the feebler alkalinity and because of the larger quantity required to neutralize a given amount of acid.

Tests were made of the use of sodium bicarbonate, U. S. P. X, powder, and potassium bicarbonate, U. S. P. X, granular, as materials for adjusting the p_H of Donovan's Solution. The p_H of solutions of these compounds was determined colorimetrically to see whether there was any difference in alkalinity. The solutions were made up on a weight to volume percentage basis and the results were as follows:

TABLE II.—p_H OF SOLUTIONS OF $NaHCO_3$ AND $KHCO_3$.

Percentage Strength of Solution.	p_H Values of $NaHCO_3$ Solutions.	p_H Values of $KHCO_3$ Solutions.
4.0	8.6	8.1
2.0	8.6	8.1
0.1	8.6	8.0
0.01	7.8	7.3
0.001	6.3	

NOTE: The distilled water used had a p_H of 5.6.

The results in Table II indicate that $KHCO_3$ is slightly less alkaline, weight for weight, than $NaHCO_3$.

After some preliminary tests, a series of solutions was prepared as follows: The specified amount of $NaHCO_3$ or $KHCO_3$ was added to 250 cc. of double strength Donovan's Solution in a beaker; after effervescence ceased, distilled water was added q. s. 500 cc. The tests were carried out in 500-cc. dark amber-colored bottles in diffused light, each bottle containing 430 cc. of solution at the start of the experiment; 50-cc. portions were withdrawn for analysis after 101 days and 174 days. The results were as follows:

Table III.—Stability and p_H of Donovan's Solution with Addition of $NaHCO_3$ and $KHCO_3$.

Material Added per Liter.	Original p_H.	p_H After 101 Days.	p_H After 174 Days.	Percentage Deterioration	
				101 Days.	174 Days.
6.0 Gm. $NaHCO_3$	5.9	5.9	6.0	0	1.0
8.0 Gm. $NaHCO_3$	6.7	6.7	6.9	0	0
10.0 Gm. $NaHCO_3$	6.9	6.9	7.1	0	0
Control (no addition)	1.2	1.2	1.2	18.6	36.8
7.2 Gm. $KHCO_3$	5.8	5.9	5.9	0	0.03
9.6 Gm. $KHCO_3$	6.6	6.6	6.7	0	0
12.0 Gm. $KHCO_3$	6.8	7.0	7.2	0	0

The results in Table III indicate that both $NaHCO_3$ and $KHCO_3$ are suitable agents for adjusting the p_H of Donovan's Solution to the range of stability. The slight rise in p_H values which occurs on standing is doubtless caused by loss of CO_2. It is thus apparent that the p_H of the solution may be adjusted by simply weighing out and adding a portion of $NaHCO_3$. For a liter of Donovan's Solution, 9.0 Gm. of $NaHCO_3$ will give proper results, and if as low as 8.0 Gm. or as much as 10.0 Gm. were used the p_H would still be within the recommended range of p_H 6.5 to 7.5. We thus have an extemporaneous, fool-proof method suitable for adoption in the U. S. P. XI. The formula and directions for the preparation of a liter of Donovan's Solution of adjusted p_H would be as follows:

Arsenous iodide		10 Gm.
Red mercuric iodide		10 Gm.
Sodium bicarbonate		9 Gm.
Distilled water	q. s.	1000 cc.

Triturate the arsenous iodide and red mercuric iodide in a mortar, add 150 cc. of distilled water, and continue the trituration until solution is effected. Filter the solution, and pass sufficient distilled water through the filter to make the filtrate measure 500 cc. Place the filtrate in an open vessel, and add the sodium bicarbonate. When effervescence has ceased, filter if necessary, and add sufficient distilled water to make the product measure 1000 cc. Mix thoroughly.

The results by the above method were distinctly better than could be obtained by triturating all three solids with water.

EFFECT OF COLOR OF GLASS CONTAINER ON STABILITY.

The U. S. P. X directs that Donovan's Solution be preserved in well-filled, amber-colored bottles. Husa and Enz (3) reported that the stability was increased by: (*a*) storage in amber bottles; (*b*) storage in well-filled bottles; (*c*) storage in a refrigerator; (*d*) replacement of the air in the bottle by an inert gas. Contrary to these statements, however, Acton (4) determined the rates of deterioration in bottles of amber-colored glass and colorless glass under conditions of exposure to sunlight and protection from sunlight, and came to the conclusion that there was not sufficient difference in these rates of deterioration to warrant any unusual care in the storage of the solution.

On account of these conflicting statements, further experiments were carried out on this point in the present investigation. The results with Donovan's Solution stored under various conditions were as follows:

TABLE IV.—PERCENTAGE DETERIORATION AFTER 8 WEEKS. 200 CC. DONOVAN'S SOLUTION IN EACH BOTTLE.

Conditions of Storage.	Percentage Deterioration in Following Kinds of Bottles: Amber-colored, 240 cc. capacity.	Colorless, 293 cc. capacity.	Greenish tint, 267 cc. capacity.
Diffused light	15.9	17.0	14.7
Sunlight (inside of window)	19.2	44.4	34.0
Sunlight (on roof)	16.5	64.9	56.8

In experiments of this character the amount of air in the bottles is an important factor. In the results given in Table IV, the different colored bottles cannot be compared directly because of the differences in capacity, but the results with each kind of bottle should be compared under the different conditions. Thus in amber bottles the rate of decomposition in sunlight was only slightly greater than in diffused light, while with colorless or greenish bottles the rate of deterioration in direct sunlight was about four times as great as in diffused light. These tests show clearly and conclusively that amber-colored bottles of proper quality offer great protection to Donovan's Solution. The U. S. P. is therefore justified in continuing to direct storage of Donovan's Solution in amber-colored bottles. The words "proper quality" are used advisedly since it is known that some amber-colored bottles are no better than colorless bottles in keeping out the deleterious shorter light waves. It should not be expected that amber-colored bottles should show any particular advantage in diffused light, nor is it assumed that pharmacists would ordinarily place the solution where it would be exposed to direct sunlight. But when it does happen that the solution is exposed to shorter light waves, the amber-colored bottle will give protection. In other words the amber-colored bottle gives protection when protection is needed, which is as it should be.

COMMENTS ON ASSAY FOR TOTAL ARSENIC.

In connection with various arsenical solutions which undergo oxidation, it has frequently been suggested that the assays for trivalent arsenic be replaced by assays for total arsenic. The Pharmaceutical Chemistry Sub-Committee has recommended (5) that in the next British Pharmacopœia, Donovan's Solution should be assayed for total arsenic.

The objection to such assays for total arsenic lies in the great variability which such an assay would allow. If we grant that the relative therapeutic value of trivalent and pentavalent arsenic is a problem for the clinician to decide, yet it may be questioned whether it is good pharmacy to officially approve solutions in which the total arsenic may be in from 0 to 100% in the trivalent form and from 0 to 100% in the pentavalent form.

FURTHER TESTS OF NEW METHOD OF PREPARATION.

Husa and Enz (3), (6) devised a new method for the preparation of a neutral modified Donovan's Solution in which As_2O_3 was dissolved in HCl, and the solution then neutralized; the HgI_2 was dissolved in KI solution and the two solutions were mixed. This solution was much more stable than U. S. P. Donovan's

Solution. In the present investigation, a further study was made of this method to determine its general suitability and also particularly to determine how its stability compared with that of carefully neutralized Donovan's Solution made from AsI_3 and HgI_2. The details for the preparation of the modified solution are given in an earlier paper (3).

TABLE V.—COMPARATIVE STABILITY OF DONOVAN'S SOLUTION, MODIFIED DONOVAN'S SOLUTION AND NEUTRALIZED DONOVAN'S SOLUTION.

Solution Stored in Diffused Light.	p_H.	Per cent Deterioration After 35 Days.	After 224 Days.
Donovan's Solution in colorless g.s. bottle	1.2	1.9	20.1
Donovan's Solution in amber-colored g.s. bottle	1.2	1.9	18.7
Neutralized Donovan's Solution in colorless g.s. bottle	6.9	0	0
Neutralized Donovan's Solution in amber-colored g.s. bottle	6.9	0	0
Modified Donovan's Solution in colorless g.s. bottle	7.1	0	0
Modified Donovan's Solution in amber-colored g.s. bottle	7.1	0	0

The results in Table V indicate that both the neutralized Donovan's Solution of p_H 6.9 and the modified solution of p_H 7.1 prepared by the method of Husa and Enz are stable, no deterioration having been observed after about seven months. The neutralized solution has the advantage of being a little easier to prepare, while the modified solution of Husa and Enz has the advantage of avoiding the use of arsenous iodide, which is variable in composition and difficult to preserve.

SUMMARY.

1. The stability of Donovan's Solution is greatly increased by neutralizing with KOH to a p_H of 6.0 to 8.0. A suitable p_H range for adoption by the U. S. P. XI is from p_H 6.5 to 7.5.
2. Since the exact adjustment of p_H by addition of KOH solution, using the colorimetric method, is a rather tedious process which is not very well suited for use in the retail pharmacy, an effort was made to devise a simpler process. It was found that the addition of 9.0 Gm. of $NaHCO_3$ per liter will give the proper p_H. This method could readily be carried out by the average retail pharmacist and is therefore recommended for adoption by the U. S. P. XI.
3. Contrary to the report of Acton, the U. S. P. is justified in directing storage in well-filled, amber-colored bottles in the case of this solution.
4. An assay for total arsenic rather than for trivalent arsenic is deemed inadvisable.
5. Modified Donovan's Solution made by the method of Husa and Enz is stable and avoids the use of arsenous iodide, which is variable and difficult to preserve.

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