

causing a great increase in total extracted matter, thus increasing the bulk of syrupy extract to be handled and greatly increasing the proportion of impurities to be removed during the precipitation and washing of the resin.

SUMMARY.

The N. F. VI menstruum for Resin of Ipomea (alcohol 9 volumes—water 1 volume) gives a slightly higher yield than that obtained with the U. S. P. X menstruum (alcohol). However, the N. F. VI product is less pure than that obtained by the U. S. P. X method. On the basis of the purity of the product, it is concluded that the U. S. P. X menstruum is preferable to the N. F. VI menstruum.

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METHODS USED IN THE DETERMINATION OF THE ALKALINITY IMPARTED TO WATER BY AMPUL GLASS.

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INTRODUCTION.

Chemists, perhaps, first used hermetically sealed glass containers for the preservation of materials sensitive to air and moisture.

Needham, 1759, and Spallanzani, 1769, mention the preservation of sterile putrescible liquids in flasks hermetically sealed by drawing out the necks of the flasks.

Limousin, inventor of the cachet, was the first to propose (1886) the method of dispensing sterile fluids in ampuls. French pharmacists were the first to offer injectable medicaments in such containers. Little change has been made during the subsequent years in the shape and appearance of ampuls.

The fact was noted rather early in the use of ampuls that certain solutions, notably the alkaloidal solutions, were visibly affected by the alkalinity produced by the glass during the sterilization and aging of the ampul solution.

AMPUL GLASSES.

The glass first used in ampuls was of the usual soda-lime type containing about 70% of SiO₂, 14% of Na₂O and 13% of CaO. Rather early in the present century glass was produced containing boric oxide. This Jena glass was found to be much more resistant to corrosion by reagents than was the ordinary soda-lime glass. Jena glass contained about 4% of B₂O₃, but in 1911 a new Jena glass was produced containing about 65% of SiO₂, 11% of B₂O₃, 4% of Al₂O₃, 11% of ZnO and 7.5% of Na₂O. Jena glass is harder to fuse than soda-lime glass and yet it can very nicely be used for ampuls, and has been widely introduced for this purpose.

A few years later, Pyrex glass was introduced for laboratory use. This glass contains about 80% of SiO₂, 12% of B₂O₃, 2% of Al₂O₃ and 4% of Na₂O. This glass is difficult to fuse, due to its low alkalinity and high content of silica. It is of high resistance to corrosion due to

* Scientific Section, A. PH. A., Dallas meeting, 1936.

¹ We wish to express our appreciation for advice and suggestions, as well as for the contributions of material which has aided this work, to: F. E. Bibbins, Eli Lilly & Co.; E. B. Carter, Abbott Laboratories; J. B. Fullerton, Upjohn Co.; C. C. Neal, Sharp & Dohme; F. O. Taylor, Parke, Davis & Co.

the high acidic oxide content (SiO_2 and B_2O_3 constitute more than 90% of the glass) and the low basic oxide content. Because of its high fusing point, requiring the oxy-acetylene torch, it is not practicable for ampuls.

In very recent years the Kimble Co. of New Jersey has introduced Non-Sol glass and Non-corrosive glass. Non-Sol glass contains about 67% of SiO_2 , 6% of B_2O_3 , 2.5% of Al_2O_3 , 8% of ZnO , 3.4% of MgO and 11% of Na_2O . The Kimble N. C. glass contains about 73.8% of SiO_2 , 9.6% of B_2O_3 , 5.5% of Al_2O_3 , 3.0% of BaO , 0.6% of ZnO , 0.5% of MgO , 0.6% of CaO , 6.5% of Na_2O , 0.1% of As_2O_3 . Its alkalinity and fusibility compare very favorably with the best Jena glass and it is now used extensively in America for ampuls.

THE ATTACK OF WATER ON GLASS.

It is incorrect to speak of the solubility of a glass as we would discuss the solubility of a salt. The action is one of diffusion and disintegration and not one of true solution. The mechanism of the attack of water upon an ordinary glass is not well known, but is highly selective. Sodium silicate is leached from the glass and this undergoes hydrolysis so that the solution contains essentially sodium hydroxide and colloidal silicic acid. Since calcium compounds and other earths are virtually insoluble in such a solution, we find in the filtered solution obtained by digesting powdered glass with water very little except soda and silica. Because of the insolubility of the lime or lime silicate and the relative insolubility of silica, these materials exert a protective action which causes the attack to proceed much more slowly as time goes on. It can be shown that the quantity of soda removed from the glass is approximately proportional to the square root of the time of exposure to the water.

The durability of a glass, or its fitness for use in various applications, is measured by estimating one special property—the quantity of alkali yielded to water under definite conditions.

THE ALKALINITY TESTS.

The Phenolphthalein Test, in which a dilute aqueous solution of the indicator is heated in the ampul, was the first test used to determine the alkalinity imparted to water by ampul glass. If the solution in the ampul becomes pink, the ampul is considered unfit for use. This test, standardized as to concentration of solution, length of heating period, and temperature was adopted in N. F. V (1926) when ampuls became official. The same test has been carried over into N. F. VI.

The N. F. VI Subcommittee on Ampuls recognized that the phenolphthalein test of the N. F. V was not sufficiently restrictive as regards ampul glass. Some attention was given to other tests for alkalinity in glass, but in the vast detail of preparing 28 new ampul monographs, an intensive study of these tests was postponed until this year.

The details of various methods employed for determining the alkalinity imparted to water by ampul glass are presented as follows:

N. F. VI Method.—Glass used for ampuls must be of high quality, particularly in regard to its resistance to water and heat. After cleansing, it shall pass the following test for solubility and reaction as a minimum requirement of quality: Mix 1 volume of a 1 per cent solution of phenolphthalein in neutral alcohol with 99 volumes of distilled water, and fill the ampuls to be tested; seal them, and immerse them in live steam or in boiling water for six hours; after cooling, the contents of the ampuls show no pink color, and no loose scales or flakes of glass.

NOTE: The spelling of "Ampul" is in accord with the Pharmacopœia quoted; British "Ampoule," U. S. P. "Ampul."

British Pharmacopœia Method (Whole Ampuls).—Not less than six ampoules are used, and each ampoule must comply with the test. The ampoules used must be from 0.5 cc. to 25 cc. in capacity.

Fill the ampoules to their prescribed capacity with acid solution of methyl red, seal by means of a blow-pipe, and heat in steam at a pressure of 15 lbs. per square inch for half an hour. Cool and examine the color of the solution. If necessary, when the ampoules are of colored glass, the solution is removed for examination on to a thoroughly washed white glazed tile. The glass passes the test if the color of the test solution has not changed from pink to the full yellow of methyl red, as indicated by comparing it with that of a solution prepared by adding 0.1 ml. of *N*/10 sodium hydroxide to 10 ml. of the acid solution of methyl red.

NOTE: Ampoules which have once passed the test on whole ampoules, may fail to do so after being stored. Whenever possible the test is carried out not more than fourteen days before the ampoules are to be used. If a batch of ampoules, which has passed the test but has been stored, does not subsequently pass the test, a sample of them may be resubmitted to the test after each ampoule has been washed internally with a 5 per cent v/v aqueous solution of glacial acetic acid followed by three washings with water. If the sample then passes the test each ampoule of the batch is similarly washed before being used.

British Pharmacopœia Method (Crushed Glass).—(a) Testing the apparatus to be used. A test solution consisting of 100 ml. of water, 0.4 ml. *N*/100 hydrochloric acid and 0.4 ml. of strong solution of methyl red is boiled, and, while boiling, transferred to a conical flask of resistant glass of 250 ml. capacity. The flask is fitted with a reflux condenser, or with a suitable condensing apparatus, made of resistant glass. The flask is quickly placed in a bath of boiling water, so that the contained solution is below the level of the water in the bath. Boiling is continued for one hour. At the end of this time the color of the solution is observed. If any change of color has taken place, the flask and the condenser are unsuitable for use in the test.

(b) Test of the glass. The glass is crushed and sieved, the particles which pass through a No. 25 sieve but fail to pass through a No. 36 sieve being used for the test. Five grams of the sieved glass are washed free from dust in a small conical flask by repeatedly washing with alcohol (95 per cent), and are dried at 100° C. The sieved glass is placed with 100 ml. of a fresh portion of the test solution into the conical flask, and the test is repeated, but the boiling is continued for half an hour instead of an hour. The glass passes the test, if at the end of this time the color of the test solution has not changed from pink to the full yellow color of methyl red, as indicated by comparing it with that of a solution prepared by adding 0.1 ml. of *N*/10 sodium hydroxide to 10 ml. of the test solution.

Strong Solution of Methyl Red: Dissolve 0.04 gram of methyl red in 50 ml. of alcohol (95 per cent), add 1.5 ml. of *N*/20 sodium hydroxide, or a quantity sufficient to ensure that the color of the solution corresponds to about p_H 5.2 and dilute to 100 ml. with water.

Acid Solution of Methyl Red: Mix 20 ml. of strong solution of methyl red with 8.3 ml. of *N*/50 hydrochloric acid and a sufficient quantity of water to produce 1000 ml.

Comments: We sifted the glass through No. 20 and No. 40 sieves as No. 25 and No. 36 sieves were not available. This may have made some difference in the results we obtained, for the alkalinity yielded by crushed glass increases according to its fineness of particles.

German Pharmacopœia Method.—Five grams of coarsely crushed glass is placed in a Jena glass flask, previously rinsed with hot distilled water, with 100 cc. of water to which has been added 0.3 cc. of *N*/100 hydrochloric acid and 1 drop of methyl red solution. The flask is then heated for one-half hour in a boiling water-bath. At the end of the heating period the color of the solution is observed. The glass passes the test if the color of the solution has not become completely yellow.

Comment: This method is listed here, though we did not work with it. The method states no degree of fineness to which the glass shall be reduced and this is an omission of a most important detail. (See comment above.) Furthermore, the test is very similar to that of the British Pharmacopœia for crushed glass as given above.

Titration Method, Lilly.—Break sample in a perfectly clean mortar and grind to a 40 to 60 powder. First put through a 40-sieve, discarding all coarse material. The portion passing the 40-sieve is next put in a 60-sieve. All that passes this sieve is also discarded. All that will pass the 40-sieve and will not pass the 60-sieve is suitable for use.

Ten-gram sample is weighed into a 250-cc. clean Pyrex (or other insoluble glass) flask, 20 cc. $N/20$ hydrochloric acid added and the mixture allowed to stand 24 hours. It is then titrated with $N/10$ sodium hydroxide using phenolphthalein indicator. Alkalinity calculated as per cent potassium hydroxide.

Comments: This method was presented to us by Eli Lilly & Co. The following modification of the method was also tried out: To the powdered glass in the flask add 25 cc. of $N/50$ hydrochloric acid; back titrate with $N/50$ sodium hydroxide using phenol red indicator; report as the number of cc. of $N/50$ hydrochloric acid consumed.

Titration Method, Kimble.—If necessary the sample glass is washed with distilled water and then dried. Break up the glass in a steel mortar and screen out using U. S. Standard screens No. 40 and No. 60. Spread out the No. 40–60 grains on a clean sheet of white paper and remove any iron derived from the mortar by repeated use of a magnet.

Place a 10-Gm. sample in a 125-cc. Pyrex (or other insoluble glass) flask, add 40 cc. of freshly boiled distilled water and cap the flask loosely with a small beaker or tin foil. A blank should be prepared in the same manner excluding the crushed glass. Place the flasks in an autoclave and heat for 30 minutes at a pressure of 15 pounds. After the heating, remove the flasks from the autoclave, cool rapidly in cold water and when cool titrate with $N/50$ hydrochloric acid, using phenol red indicator. Report number of cc. of $N/50$ hydrochloric acid used.

Hydrogen-Ion Concentration Method Using the Quinhydrone Electrode.—Clean ampuls are filled with freshly boiled distilled water, of which the p_H has been determined with a potentiometer using a quinhydrone electrode. The ampuls are then sealed, and autoclaved for 30 minutes at 15 pounds pressure. When cooled to 25° C. the ampuls are opened and the p_H of the solute from the ampul is determined with the same apparatus. The difference between the two values is due to the alkalinity yielded by the ampul.

Hydrogen-Ion Concentration, Colorimetric Method.—Clean ampuls are filled with freshly boiled distilled water of which the p_H has been determined colorimetrically according to the directions for colorimetric p_H determinations in the U. S. P. XI. They are then sealed and autoclaved for 30 minutes at 15 pounds pressure. When cool, the ampuls are opened and the p_H of the solution contained in them is determined by the same method. The amount of difference in p_H , between the water placed in the ampuls and the solution removed from them determines the amount of free alkalinity of the glass.

Bromthymol Blue Method.—The U. S. P. XI colorimetric Solution of Bromthymol Blue was diluted with freshly boiled distilled water to make a concentration of 8 mg. of dye per liter. Although this concentration is less than that of phenolphthalein in the N. F. VI solution, it is the same as that of methyl red in the B. P. test and falls within the limits of the U. S. P. XI for the dilution of the indicator in colorimetric p_H determinations.

Clean ampuls are filled with this solution and sealed. One is kept for comparison and the rest are autoclaved for 30 minutes at 15 pounds pressure. When cool, the color is observed and compared with that of the unheated ampul.

RESULTS OF OUR TESTS.

A sufficient number of empty glass ampuls were prepared in the laboratory or were supplied by certain manufacturers so that 13 different kinds were available, and representing the several kinds of glass that have been used for ampuls.

Several methods of colorimetric testing (though but four methods are reported here); three titration methods and two hydrogen-ion concentration methods were conducted on the 13 lots of ampuls so far as the supply of each was sufficient. The work is being continued with these and other methods of estimating alkalinity. Also tests to determine the conductivity of water after being heated in ampuls are under way.

Some of the results are presented in Tables I and II.

DISCUSSION OF THE METHODS USED.

Cleansing the Ampuls before Testing.—In several of the methods described, the ampul (or glass) is to be cleansed before the test is conducted.

The N. F. method directs any suitable method of cleansing but suggests the use of distilled water containing 0.1% of hydrochloric acid, boiling for five minutes and thoroughly rinsing once with distilled water. The B. P. method suggests the cleansing of ampuls that do not pass the test, by washing with 5% aqueous solution of acetic acid, followed by three washings with water. The B. P. method for crushed glass requires that the properly sifted glass be washed with alcohol to remove dust. The Kimble titration method suggests the washing of the glass with distilled water before it is crushed.

Our work indicates that there usually is an alkaline film on the surface of ampul glass. It has been noted repeatedly that ampuls have responded to the bromthymol blue test when they were filled with the reagent before being rinsed and before the application of heat. When this film had been rinsed off, only ampuls of alkaline glass responded to the test when heated.

The effect of high temperatures, such as are used when ampuls are drawn from tubing or are sealed, is but slight either upon the film or the alkalinity of the glass itself. This effect, if any, would decrease alkalinity rather than increase it, for alkali is somewhat volatile at these high temperatures.

The use of acid for cleansing is not necessary according to our work. Strong acid, particularly, is to be avoided as it not only removes the film but some of the alkalinity of the glass itself; thus an ampul so treated would appear, according to the test, to be of less alkaline glass than it really is.

Dilute acids apparently are no more efficient than water, as the film is water soluble. When acids are used careful washing is required to insure their complete removal and much additional time is consumed, especially so when the dilute acid is heated in the ampul.

Three rinsings with distilled water followed by a rinsing with the reagent solution to be used is fully adequate to cleanse the ampul for the test.

TABLE I. SHOWING RESULTS OF COLOR TESTS.

Glass.	N. F. VI.	B. P. for Ampuls.	B. P. for Crushed Ampuls.	Bromthymol Blue.
No. 1	-	+	+	Blue
No. 2	-	+	+	Blue
No. 3	+	+	+	Blue
No. 4	-	+		Green
No. 5				
No. 6	-	+	+	Green
No. 7	-	-		-
No. 8	-	-		Blue
No. 9	-	-	-	-
No. 10	-	-		-
No. 11	-	-		-
No. 12	-	-	-	-
No. 13	-	-		-

TABLE II. SHOWING RESULTS OF TITRATION TESTS.

Kimble Method.	Lilly Method.	Lilly Method Modified.	p _H Colorimetrically.	p _H by Quinhydrone Electrode.
6.80 cc.	0.0224%	2.30 cc.	Above 8	6.50
5.60 cc.	0.0196%	2.15 cc.	Above 8	6.95
8.00 cc.	0.0252%		Above 8	7.20
8.20 cc.				6.25
5.80 cc.	0.0224%	2.00 cc.		
2.00 cc.	0.0112%			5.90
0.30 cc.				
0.30 cc.				6.40
0.30 cc.	0.0056%	0.15 cc.	6.6	5.80
	0.0112%			
0.50 cc.				
0.40 cc.			6.6	5.80

- No change, glass passed the test. p_H of water colorimetrically 6.4.

+ Change in color, glass failed the test. p_H of water by quinhydrone electrode 5.4.

Glass.	Glass.
No. 1 Ampuls made from bacteriological culture tubes.	No. 7 Kimble ampuls, 2 cc.
No. 2 Ampuls made from ordinary soft glass test-tubes.	No. 8 Kimble ampuls, 5 cc.
No. 3 Ampuls made from Kimble flint glass tubing.	No. 9 Kimble ampuls, retempered, 10 cc.
No. 4 Ampuls for powders.	No. 10 Jena ampuls for powders, small size.
No. 5 Syringe barrels.	No. 11 Jena ampuls, 5 cc.
No. 6 Non-sol ampuls, 50 cc.	No. 12 Jena ampuls, 25 cc.
	No. 13 Violax ampuls, 5 cc.

Heating the Water or Test Solution in the Ampul.—In the N. F. method the sealed ampuls containing the test solution are to be heated in live steam or in boiling water for six hours. In the B. P. method they are to be heated in the autoclave for 30 minutes at 15 pounds pressure.

Our work indicates that the boiling method has very little, if any, advantage over the autoclaving method. Autoclaving has a great advantage in the saving of time. After our first experimental work demonstrated this point—we have used autoclaving exclusively (except in the N. F. method).

The N. F. VI Method.—This method is entirely unsatisfactory. Any glass except the poorer grades of soda-lime glass will pass the test. Furthermore, the test requires much more time than nearly any of the other methods of testing.

Phenolphthalein begins to change color at a p_H of 8. Any ampul glass that will increase the alkalinity of freshly distilled water (with a p_H of about 6.5) to a p_H of 8, is not suitable for containing injectable solutions. Furthermore, the alkaline form of phenolphthalein is not stable; in alkaline medium it changes to a colorless trivalent ion derived from the carbinol form. Therefore, alkaline solutions of phenolphthalein fade on long standing and more rapidly if heat is applied. For instance, when we filled two soft-glass ampuls of one lot, one with the N. F. test solution of phenolphthalein and the other with distilled water and autoclaved them; the one with the test solution remained colorless; the other, opened and receiving 1 or 2 drops of phenolphthalein T. S., immediately became red.

The B. P. Method for Whole Ampuls.—This method gives fairly satisfactory results. The reagent used is an $N/7500$ solution of hydrochloric acid containing methyl red as an indicator. When the acid has been neutralized the indicator changes to a yellow color. The test passes all ampuls that do not develop a full yellow color. The soda-lime glasses will not pass the test but several of the glasses tested gave only an orange color, therefore passing the test. All of the better grades of ampuls failed to change the color at all.

From the results obtained in our work, the test would be more suitable if no change from the acidic red (or pink) of the indicator were permitted.

The volume of the test solution in the ampul in relation to the area of glass exposed to the solution plays an important rôle in the test. Hence the size of ampuls to be tested is limited to a maximum of 25 cc. This is an undesirable limitation.

B. P. Method for Crushed Glass.—This method, while giving satisfactory results and being more selective than the above method, is undesirable on a technical basis. The test solution is so sensitive that there is the possibility of other factors besides the alkalinity of the glass affecting the final results.

Bromthymol Blue Method.—This procedure is the N. F. VI method with bromthymol blue substituted for phenolphthalein and autoclaving in place of boiling. This test gives quite satisfactory results because the p_H range of the indicator is more suitable (6.0 to 7.6) but the change in color to a green or a blue can be read as indicating roughly the degree of alkalinity. The indicator does not seem to be affected by the heating.

Hydrogen-Ion Concentration Method Using the Quinhydrone Electrode.—The results obtained with this method in our work have not been satisfactory. They are variable, cannot be duplicated and do not correspond to those obtained by the colorimetric method. This variability of results as obtained on water by the quinhydrone electrode has been observed by other workers.

Hydrogen-Ion Concentration by the Colorimetric Method.—This method has given entirely satisfactory results. By determining the p_H of the freshly distilled water just before using it in the ampul, and then of the solution after heating in the ampul and cooling, the difference in p_H between the two becomes a fairly constant figure for that lot of ampuls and can be readily duplicated. It is suggested tentatively that the maximum change be limited to 0.5 p_H .

Titration Method, Kimble.—This procedure has given very satisfactory results. It permits a very close differentiation in the alkalinity of ampul glass. It also permits the testing of used ampuls more easily than the other methods do, except the titration method, Lilly. Furthermore glassware may be tested in which ampul solutions are prepared or stored. A disadvantage of this method is the time consumed in grinding and sifting the glass, which requires about 45 minutes for a 10-Gm. sample. Another disadvantage is the relatively large number of ampuls required to obtain a sample. It was found that it was hardly possible to get more than one-third of the glass that would pass through a No. 40-screen but not pass through a No. 60-screen. This means at least 60 Gm. of the glass was required to produce two 10-Gm. samples. Two types of mortars were tried for efficiency, the ordinary cast-iron mortar and the Plattner hardened steel mortar. They both require about the same amount of time to prepare a 10-Gm. sample, but the former produced about 35% of particles of the desired size while the latter produced about 25%. However, the latter was much easier and more pleasant to use.

It is suggested tentatively that a titration value of 0.5 cc. be set as a limit for the alkalinity of a 10-Gm. sample.

Titration Method, Lilly.—Both the original method of Lilly and the modification of it have given very satisfactory results; however, the latter is to be preferred because the difference in values between different kinds of glass is more apparent. The advantages and disadvantages of this method are the same as those of the titration method, Kimble, except that it takes longer, due to the 24-hour standing period.

Used Ampuls.—Tests were run on ampuls of commercial makes and on ampuls made of both hard and soft glass which were filled in this laboratory and then aged. The results of these tests are listed in the following table and indicate that the storage of solutions in the ampuls does not interfere with the test providing the used ampuls have been properly cleansed.

The tests used were the B. P. for whole ampuls and the titration method, Kimble. Both gave good results. However, unless the ampuls are of such size that they can be handled easily in the flame for redrawing and sealing, the titration method is more convenient besides being more desirable for the reasons listed in the comments on the method.

TABLE III.—SHOWING RESULTS OF TESTS ON USED AMPULS.

	Kimble Method.	B. P. Method.
1 Culture tube glass	6.80 cc.*	Orange
1a Culture tube ampuls that have been filled with boiled redistilled water, sterilized for 30 minutes at 15 pounds, aged 22 days, emptied and dried	7.30 cc.*	Changed from red to a slightly pinkish yellow, almost a complete yellow
1b Culture tube ampuls filled with ampul solution of Green Iron and Amm. Cit., sterilized for 30 minutes at 65° C. on three successive days, aged 22 days, emptied and washed	7.00 cc.*	Same results as in No. 1a
2 Lilly's retempered ampuls	0.30 cc.	No change
2a Lilly's retempered ampuls treated as in No. 1a	0.20 cc.	No change
2b Lilly's retempered ampuls treated as in No. 1b	0.20 cc.	No change
3 Ampuls of Sodium Iodide, Lilly and Abbott, emptied, cleansed and dried	0.25 cc.

3a	Ampuls of Sodium Cacodylate, S. & D. and P. D. Co., emptied, cleansed and dried	0.35 cc.
3b	Ampuls of Green Iron and Ammonium Cit., S. & D., emptied, cleansed and dried	0.25 cc.

Kimble Method: Kimble titration method on powdered glass.

B. P. Method: B. P. Methyl red test on whole ampuls.

* 5-Gm. sample was used, but the report is based on 10 Gm. of the powdered glass.

SUMMARY.

1. For the cleansing of ampuls preparatory to testing them for the free alkalinity of the glass, it has been found that several rinsings with distilled water is all that is necessary.

2. Autoclaving the ampuls filled with water or the test solution for 30 minutes at 15 pounds pressure is to be preferred to boiling for six hours.

3. The phenolphthalein test for free alkalinity in ampul glass as found in the National Formulary VI is entirely unsatisfactory and should be replaced by a better method of testing.

4. The Hydrogen-Ion Concentration Colorimetric Method, in which is determined the amount of difference in p_H between that of the freshly boiled distilled water to be used in the ampul and that of the solution removed from the ampul, is quite satisfactory. This difference can be readily duplicated and is fairly constant for the individual ampuls of a lot of ampuls.

It is recommended that a difference of 0.5 p_H be the maximum limit of change.

5. The Kimble Titration Method is satisfactory. It indicates the amount of free alkalinity in glass very closely. The marked disadvantage of the method is that it requires such a large amount of crushed glass, approximately 60 Gm., to run the test in duplicate.

It is recommended that a titration value of 0.5 cc. of $N/50$ hydrochloric acid be set as a limit for the alkalinity of a 10-Gm. sample.

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