It is interesting to compare the yearly survival percentages at the two dosage levels.

	Per Cent Survivals.			
	A Mg./Kg.		B Mg./Kg.	
	Average.	Limits.	Average.	Limits.
First year	89.2	84–100	..	....
Second year	85.8	76–100	65.4	39–86
Third year	86.5	72–100	64.1	27–100
Fourth year	86.7	79–100	80.9	67–92

These figures show that even when neoarsphenamine gives a high percentage of survivals at a dosage level at which deaths occur, the use of still higher doses enables one to demonstrate differences in toxicity in batches which give practically identical results at the lower dose. Thus, the testing at A mg./Kg. during the second, third and fourth years shows that at this dose about 13% of the rats died and the fluctuations were all of about the same order whereas the testing at the higher dose showed a much lower per cent of deaths for the fourth year than for the second and third.

The toxicity tests were carried out in the Biological Laboratories of E. R. Squibb and Sons, at New Brunswick, N. J.

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FREE ALKALI IN GLASS.*

BY L. F. GABEL.

It is obvious that glass bottles and ampuls of high soluble alkali content are unfit for use in finely adjusted pharmaceutical and chemical solutions.

The following experiment demonstrates the possible reactions resulting from glass of high soluble alkali content: A benzoic acid solution in an ordinary glass bottle is heated sufficiently to volatilize traces of benzoic acid in the neck of the bottle. The sealed bottle is permitted to stand several months and upon testing, the traces of volatilized benzoic acid will be converted to the sodium salt.

In the days before the advent of facilities to measure alkali and acids in minute amounts by the potential hydrogen apparatus, the soluble alkali in glass was determined by heating accurately measured amounts of $N/20$ HCl in the glass on test. Titrating the excess of $N/20$ HCl with $N/20$ NaOH (Phenolphthalein T.S.) and calculating the free alkali in the glass from the amount of $N/20$ HCl reacting with the free sodium in the glass.

For the past seven years we have used the following method for determining the amount of free alkali in glass:

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* Scientific Section, A. PH. A., Washington meeting, 1934.

Boil fresh distilled water to one-third the original volume. Allow to cool sufficiently to permit the colorimetric determination of p_H, using Methyl Red p_H indicator. The water, with the carbon dioxide excluded, has a p_H of about 5.6.

Immediately fill the ampuls with the water, seal, immerse in water and place on steam-bath (approximately 80° to 90° C.) for 16 consecutive hours. The contents of the ampuls are then tested with Brom Thymol Blue p_H indicator, or Cresol Red, and the increase of p_H noted. The increase in p_H is used as the basis for comparing different stocks of glass for soluble alkali.

Bottles are tested in like manner with the exception that the bottles remain uncorked during the heat test and are submerged up to the neck in hot water. A layer of liquid petrolatum on the surface of the water-bath prevents evaporation of the bath.

The following data is an example of a test run of ampuls and bottles by the above procedure:

TABLE I.

Glass Sample.	Original p_H of Boiled Distilled Water.	p_H of Water after 16 Hrs. at 80° C.	Average Increase in p_H.	Glass Sample.	Original p_H of Boiled Distilled Water.	p_H of Water after 16 Hrs. at 80° C.	Average Increase in p_H.
27	5.5	6.3–6.3–6.4	0.82	Bottles	5.4	6.5	1.28
Ampuls	5.5	6.5–6.4–6.2	..	Lot No. 1	5.4	6.7	..
Lot "A"	5.5	7.2–7.6–6.6	..		5.4	6.6	..
	5.5	6.5–6.2–6.3	..		5.4	7.0	..
	5.5	6.2–6.1–6.2	..		5.4	6.7	..
	5.5	6.6–6.8–6.5	..		5.4	6.8	..
	5.5	6.1–6.6–6.1	..		5.4	6.5	..
	5.5	6.2–6.0–6.0	..		5.4	6.5	..
	5.5	6.1–6.1–6.2	..		...	...	..
27	5.5	6.6–6.6–6.6	1.26	Bottles	5.4	7.5	2.1
Ampuls	5.5	6.9–6.4–6.4	..	Lot No. 2	5.4	7.4	..
Lot "B"	5.5	6.8–6.9–7.0	..		5.4	7.6	..
	5.5	7.0–7.2–7.0	..		5.4	7.6	..
	5.5	7.0–7.2–6.9	..		5.4	7.6	..
	5.5	6.6–7.0–6.5	..		5.4	7.5	..
	5.5	6.8–6.6–6.0	..		5.4	7.4	..
	5.5	6.7–6.9–6.6	..		5.4	7.4	..
	5.5	7.2–6.7–6.9	..		...	...	..

In the above table, ampuls labeled lot "A" are superior to lot "B" in regard to free alkali content, as the average ampul in lot "A" contained less soluble alkali than in lot "B."

The results obtained by this method are purely comparative but are sufficient to base a judgment on the glass in question, as standard stock samples can be tested at the same time and under the exact conditions as the submitted samples.

Methyl Red and Brom Thymol Blue p_H indicators are acid in reaction, and as there is no buffer action in distilled water, the p_H obtained would be influenced by the slight acidity of the indicator.

In the following experiments, neutralized indicators were used to arrive at a more accurate determination of increase in p_H due to the soluble alkali in glass.

You will note that in the case of the neutral indicator, the p_H of the original water was 6.9 and the gain in p_H was 0.5. In the acid indicator the water was 5.6 p_H and the gain in p_H was 0.6.

In order to use the neutralized indicators it would require more work, involving

TABLE II.

Ampuls Same Stock.	Acid Indicator p_H of Original Water.	p_H after Heat Treatment.	Gain in p_H.
No. 1	5.6	6.2	0.6
2	5.6	6.3	0.7
3	5.6	6.2	0.6
	Neutral Indicator.		
No. 4	6.9	7.4	0.5
5	6.9	7.4	0.5
6	6.9	7.5	0.6

the use of buffer solutions, whereas the acid indicators simplify the p_H determinations with the use of the Hellige Comparator.

A series of experiments was made to note the results in regulating the original p_H of water used in the bottles and ampuls on test.

Fresh distilled water of 5.5 p_H was used in one set of 2-oz. flint glass bottles; to another set, water of 6.0 p_H was added; and another, 6.9 p_H; also, 7.2 p_H. We prepared water of p_H 4.5 in one experiment. These varying p_H's were obtained by adding alkali to the water to increase, and acid to decrease the p_H.

Bottles Same Stock.	Original p_H of Water.	p_H After Heat Test.	Gain in p_H.
No. 1	4.5	7.6	
	4.5	7.2	2.9
	4.5	7.4	
No. 2	5.5	8.5	
	5.5	8.5	3.0
	5.5	8.5	
No. 3	6.0	8.9	
	6.0	8.8	2.9
	6.0	9.0	
No. 4	6.9	8.8	
	6.9	8.8	1.9
	6.9	8.8	
No. 5	7.2	9.0	
	7.2	8.9	1.7
	7.2	8.9	

We also ran a series of ampuls in similar manner (with varying p_H).

Ampuls Same Stock.	Original p_H.	p_H After Heat Test.	Gain in p_H.
No. 1	5.4	5.9	
		5.9	0.5
		5.9	
No. 2	6.4	6.7	
		6.9	
		6.7	0.4
		6.8	
No. 3	7.6	8.2	
		8.1	
		8.1	0.6
		8.3	

In the preceding series of tests on ampuls, very slight differences in free alkali were observed. The results would indicate that regardless of the initial p_H, the final results are practically identical. We are dealing, in the case of ampuls, with very slight amounts of alkali.

An analysis of the series of tests on bottles reveals that regardless of the initial p_H, up to 6.0, the gain in p_H is similar. When the original p_H of water is adjusted to 7.0, the increase in p_H upon applying the heat test is but 60% of that obtained with original water at 5.5 p_H.

The length of time of the heat test used in our procedure is too severe, as will be shown by the following observation:

Bottles of the same stock were completely filled with water of known p_H. The sealed bottles were permitted to stand at room temperature for one year. The gain in p_H in one year at room temperature was but 0.5. Ordinary glass bottles increase the p_H of water 3.0 after 16 hours at 80–90° C.

SUMMARY.

This paper was written with the object in mind of drawing attention to the necessity of the establishment of a standard method of determining the free alkali in glass.

In our work we attempted to obtain purely relative results in order to make fair comparisons of glass.

A standardized method should be established only for glass bottles and ampuls that are used for finely adjusted pharmaceutical and chemical solutions.

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A NOTE ON THE U. S. P. MONOGRAPH ON CHRYSAROBIN.*,[1]

BY JOHN H. GARDNER.

For several years past, there has been an investigation in progress in this laboratory on the constituents of the anthracene drugs. In the early part of this work, it was shown that the acetate of chrysophanic acid-9-anthranol can be isolated from demethylated and acetylated chrysarobin (1), indicating that chrysophanic acid-9-anthrone is a constituent of the drug. On repeating this work with several samples of chrysarobin, it was found that the yields were extremely variable, ranging from nearly zero to about fifty per cent of the weight of the drug taken. In attempting to trace the cause of this variation, all of the samples were subjected to the tests for identity given in the U. S. P. monograph on chrysarobin. For comparison, similar tests were made on pure chrysophanic acid and on pure, synthetic chrysophanic acid-9-anthrone. The results of these tests are given in Table I.

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[1] Scientific Section, A. PH. A., Washington meeting, 1934.