The Hydrogen Ion Concentration of Solutions of Sodium Citrate Used for Preservation of Fluid Blood*

Edward C. Watts†

Cotter and MacNeal (1) in June, 1938, stated that "solutions of sodium citrate have been used to prevent coagulation of blood for many years, and these solutions have become increasingly important in preserving the fluid blood for transfer from one human being to another." The conclusion of this statement was, no doubt, at least partly inspired by the establishment of "blood banks" in many of the large medical centers of our country. Such a unit was opened for use at University Hospital, Ann Arbor, Michigan, early in 1940. Prior to this time the Hospital Pharmacy had been advised that solutions of sodium citrate would be used in increased quantities and preparation had been made, therefore, to anticipate the demands of the new department.

In their study of ampul solutions of sodium citrate intended for use as anticoagulants, Cotter and MacNeal found the solutions which they examined to be definitely alkaline, with *p*H values ranging from 8.0 to 8.5. They themselves prepared a 2.5% solution of sodium citrate in 0.6% sodium chloride, and found this solution to have a *p*H of 8.7. On the basis of their results they advised the use of citric acid to reduce the *p*H of solutions of sodium citrate intended for use as anticoagulants. Attempts to follow their directions in the laboratory of the Hospital Pharmacy were not satisfactory because the solutions so prepared were too acid. Consequently the amount of citric acid was reduced materially before the following satisfactory formula was obtained:

Sodium citrate U. S. P.	140.0 Gm.
Citric acid U. S. P.	0.5 Gm.
Distilled water, fresh, *q. s. ad.*	4.0 L.

Solutions made in accordance with this formula in pyrex glassware had a *p*H of 7.0 to 7.1. When filtered through paper, bottled in pyrex bottles and sterilized for one-half hour at 240° F. they underwent no change in *p*H value. Hundreds of bottles of this solution had been made and used with complete satisfaction when those in charge of the "blood bank" requested that the *p*H value of the finished citrate solutions be adjusted closer to the *p*H value of blood, namely, 7.3 to 7.4.

With this request came the realization, that inasmuch as the solution as formulated had a *p*H of 7.0 to 7.1 it would, in all probability, be necessary to eliminate the citric acid entirely in order to achieve the desired result. If this were so, there seemed to be some question as to the accuracy of Cotter and MacNeal's determination of the *p*H of solutions of sodium citrate and of the necessity for the use of citric acid. It was decided, therefore, to check back on one of the solutions described in the original article. This, a 2.5% solution of sodium citrate in 0.6% sodium chloride, was described as having a *p*H of 8.7. As prepared in the Hospital Pharmacy in pyrex glassware, the same solution had a *p*H value of 6.8. A second solution of 3.5% sodium citrate in freshly distilled water, made in pyrex ware was found to have a *p*H value of 7.3. This solution, when filtered through paper, bottled in pyrex bottles, sterilized for one-half hour at 240° F. and cooled, was discovered to be of the same *p*H as when first prepared. A third solution made in the same manner as the second, but bottled in a soft glass bottle, and sterilized similarly had a *p*H value of 8.8 after sterilization. This solution was more alkaline than any of the ampuls observed by Cotter and MacNeal, but it was sterilized in a container made of glass which was not intended for ampul medications.

Thinking that the high *p*H values obtained by Cotter and MacNeal may have been due to characteristics of some particular brand of salt, it was decided to study sodium citrate solutions made from the salts of different manufacturers. As only one brand was available in the laboratory, requests were made to three manufacturers of chemicals for *p*H readings on 2.5% and 3.5% solutions of their salt. Results were as follows:

Source	Sample	Solution, %	*p*H
Manufacturer No. 1	1	3	7.95
	2	3	7.55
Manufacturer No. 2	1	2.5	7.61
	2	3.5	7.58
Manufacturer No. 3	1	2.5	7.4
	2	2.5	7.4

The salt used in the Hospital Pharmacy's tests and from which a 3.5% solution with a *p*H of 7.3 was made, was of the same brand as that of manufacturer No. 3.

In order to compare other figures of the original publication, it was decided to examine ampul solutions of sodium citrate for *p*H values as was done by Cotter and MacNeal. Four well-known pharmaceutical manufacturers generously supplied 50-cc. ampuls of their sodium citrate solutions. In the following table these solutions are described briefly and the results of the examination of these ampuls are noted.

---

* Presented to the Subsection on Hospital Pharmacy, Detroit meeting of the A. PH. A., 1941.

† Chief Pharmacist, St. Luke's Hospital, New York, N. Y.

Source	Nature of Solution	*p*H
A	Simple aqueous, 2.5%	6.6
B	Simple aqueous, 2.5%	7.1
C	Simple aqueous, 2.5%	6.9
D	Aqueous buffered sodium phosphate, 2.5%	7.4

In their paper, Cotter and MacNeal state that each of four ampul solutions of sodium citrate which they observed had a *p*H value of 8.0 or over. As the identity of the manufacturers of the ampuls used by Cotter and MacNeal in their observations is unknown, it is impossible to decide on a definite reason for such divergent results. So far as the ampul solutions examined in the Hospital Pharmacy are concerned, the variations in *p*H values (from 6.6 to 7.4) can, on the basis of the available information, be explained only by assuming that varying grades of glass were used in the manufacture of the empty ampuls.

CONCLUSIONS

1. The *p*H of a 3.5% solution of Sodium Citrate U. S. P. in freshly distilled water is 7.3.

2. This value does not change during the process of sterilization when such solutions are contained in properly prepared pyrex bottles.[1]

3. A simple, aqueous 3.5% solution of Sodium Citrate U. S. P., in freshly distilled water, is satisfactory for use as an anticoagulant, since it is of the proper *p*H and can be prepared, bottled and sterilized without a change of *p*H.[2]

REFERENCES

(1) Cotter, J., and MacNeal, W. J., *Proc. Soc. Exptl. Biol. Med.*, 38 (1938) 757–758.

[1] Such bottles in the proper size are now readily available.

[2] *p*H values determined experimentally by the author are electrometric readings.

Some Notes on Chalk Mixture*

By Louis W. Schleuse† and J. Richard Stockton‡

A chalk mixture was included in the first "Pharmacopœia of the United States," and each revision has retained a mixture of prepared chalk (Table I). Although several changes have been made, the present official product is little different from the original, and both possess two objectionable features: They are fermentable, and the acacia is not a satisfactory suspending agent.

The unstable character of the preparation and the "positively injurious" effect (1) of the sucrose prompted Reynolds (2) in 1870, Kennedy (3) in 1872 and Hommel (1) in 1911 to recommend replacement of the sucrose with glycerin. The Fifth Revision of the "Pharmacopœia" (Convention of 1870) made such a change (Table I), and much later the Tenth Revision (1920) replaced both sucrose and acacia with glycerin (Table I), but neither modification survived the revision in which it appeared.

Jones (4) in 1870 and Rother (5) in 1873 proposed the use of compound chalk powders from which chalk mixture could be prepared when wanted. The Sixth Revision of the "Pharmacopœia" (1880) adopted a method of preparing chalk mixture from compound chalk powder, a practice retained in each subsequent revision except the Tenth (Table I).

Fantus and Snow (6) in 1922 also objected that fermentable carbohydrates (sugar and acacia) were "illogical . . . as ingredients of a medicine employed in fermentative diarrhea." They considered a carbohydrate-free formula containing prepared chalk, saccharin, cinnamon water and water, but found that "when kept exposed to sunlight for quite some time, it developed an offensive odor reminding one somewhat of hydrogen sulfide or of illuminating gas, with progressive diminution and final loss of cinnamon flavor." They observed no decomposition when fennel, anise or peppermint flavors were substituted for cinnamon.

In addition to the ease with which it is fermented, acacia is also objectionable as a suspending agent for prepared chalk. When the official chalk mixture is allowed to stand for a few days, all of the chalk

* From the College of Pharmacy, University of Texas, Austin, Texas.

† Assistant Professor, College of Pharmacy, University of Texas.

‡ Instructor, College of Pharmacy, University of Texas.