STERILIZED DISTILLED WATER.*

BY HENRY KRAEMER.

Distilled water is the most important substance in any laboratory. Too much attention cannot be given to its preparation and testing its quality. The distilled waters on the market should not be used unless they are tested chemically and bacteriologically. We have all seen distilled water which had a greater pollution than river water. The bottles holding distilled water usually show a growth of algae on the bottom and sides. Frequently it is nothing more than spring water or well water. It usually contains carbon dioxide, ammonia and other gases and not unfrequently organic matter in suspension. It is extremely hazardous to use any distilled water except that which has been personally prepared in one's own laboratory.

In pharmacy, sterilized distilled water is a most important solvent and vehicle and when needed must be absolutely pure and free from traces of either organic or inorganic matter and absolutely sterile. It can only be prepared under one's own supervision and every precaution should be taken to be sure that it is absolutely pure. Both distilled water and sterilized distilled water are very easily prepared and may be made in such quantities to supply the ordinary needs of the pharmacist. There is unfortunately a great amount of confusion that regards the preparation, preservation and specifications of distilled water.

Distilled water is prepared on chemical and bacteriological principles. It is because pharmacists generally are not well prepared in the fundaments of these sciences that the preparation and dispensing of distilled water is attended with so much misgiving that very few of them could be relied upon to make up solutions for intravenous or intramuscular injection. The subject, however, is so simple that the pharmacist with his training and skill should be able not only to make both distilled water and sterilized distilled water but also be prepared to meet any emergency which comes up in connection with their use.

METHOD OF PREPARATION.

First a word should be said with regard to the preparation of distilled water It should be made in apparatus consisting entirely of glass. The use of metallic condensers is to be condemned. Furthermore, the flask should be of such a size that the glass tubing from it to the condenser should be such that it may be connected with a rubber fitting. This insures the condensed liquid from meeting with any contamination or having in it any of the dissolved substances of the cork. We prefer to use in our work a 3- or 4-liter flask, the distillate from this being sufficient for most general purposes.

In the preparation of distilled water the U. S. Pharmacopœia permits the use of any kind of water, presumably tap water and this is distilled. The first 100 cc. of distillate, or about 10%, is rejected. Then 750 cc. are to be accepted and the residue rejected. Water prepared under these conditions may be considered distilled water but it has been shown that distilled water as a by-product from the condensed steam in artificial ice factories will answer the requirements of the U. S. Pharmacopœia. Water prepared under U. S. P. conditions deteriorates rapidly

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and it probably should not be included as a Pharmacopœial article. In fact for most purposes any sterilized potable water would be less objectionable, more economical and more readily obtained.

In following the Pharmacopœia one neither knows what he is doing or what the final product is going to be when it is used. One is in the dark as to what he is doing and the operation should be considerably modified. Distilled water should be dropped and sterilized distilled water only retained. It takes only a little more time to prepare the sterilized distilled water and as it may be readily tested from time to time one can ascertain its chemical as well as bacteriological purity. Ordinary distilled water as commonly prepared and used is far from pure and sooner or later breeds microörganisms which cannot be removed and are sure to produce a great deal of trouble. They may be gotten rid of by autoclaving, but the toxins are present and even the organisms and their spores are in suspension.

ACID SHOULD BE ADDED.

Distilled water cannot be prepared alone by merely distilling water. To the water to be distilled either sulphuric acid or a chromic acid mixture should be added. Sulphuric acid alone is sufficient and a 1% solution in the original water is required. For every 1000 cc. of water to be distilled, 10 cc. of sulphuric acid are added. We prefer to let the acid act for a short time, usually allowing it to act on the organic matter over night. Then the water is distilled using a glass condenser as above indicated and instead of arbitrarily rejecting 100 cc. and collecting 750 cc. of the distillate, it is advisable to test the distillate by Nesslerizing and then accepting only such portions of the distillate as are free from ammonia. The testing with Nessler's reagent must be performed anyway and it might as well be performed at the logical place, which is the beginning of the operation.

The U. S. Pharmacopœia gives no specification as to how long distilled water may be kept and yet it is directed to be used as such in the preparation of syrups and in other cases upon recently boiling it. It makes a great deal of difference in the outcome of the use of distilled water in the making of any preparation as to how recently it has been distilled and how it has been kept. There is no necessity for this uncertainty and as there must be a need for its use in those preparations where it is required, it might be just as well to prepare it right at the outset, seeing that it is absolutely pure and preserving it under conditions where it can be used economically as well as with safety.

HARD GLASS VESSELS.

In the preparation of sterilized distilled water the U. S. Pharmacopœia directs that the recently distilled water shall be collected in flasks of hard glass and sterilized by boiling the contents for thirty minutes. As this is only a partial sterilization, it stands to reason that the water should be used within a reasonable period of time. This is why the Pharmacopœia directs that sterilized distilled water of this kind should be used within 48 hours of its preparation. Practically the making of sterilized distilled water under these conditions is a positive waste in time and materials and it is very doubtful if it is practicable to use an absolutely pure sterilized distilled water prepared under these conditions. It may however be prepared by adopting two precautions and we have prepared it absolutely pure

and kept it for three years so that it was just as sterile and pure as the day it was made.

In preparing sterilized distilled water we collect the distillate which has been tested as previously stated in flint bottles holding from 100 to 500 cc. These are then plugged with cotton and wrapped with parchment paper and autoclaved at 10 to 15 pounds pressure for 20 to 30 minutes. Of course the bottles which are used as containers have been carefully tested and have been sterilized with dry heat. The idea of collecting it in small bottles is that when small quantities are to be used the contents of the entire bottle may be employed so that practically only what one needs is used. The stock can be kept in absolutely sterile condition and that it is holding its own may be shown by the appearance as well as by testing it. From time to time we withdraw from 1 to 5 cc. of the water planting it in a test-tube containing a nutrient broth which must remain sterile in the test from 24 to 72 hours of incubation.

In summarizing our work it may be given in the following method of procedure.

Aqua Distillata Sterilisata.

(Sterilized Distilled Water.)

Water (any potable water)	1000 cc.
Sulphuric Acid	10 cc.

Add the sulphuric acid to the water in a suitable flask and allow it to stand at least 30 minutes. Connect with flask with a glass condenser and distil the water. Collect the first portion of the distillate in Nesslerizing tubes and test with 2 cc. of Nessler's reagent. Then collect a 50-cc. portion and again test for ammonia. When any one of these portions develops no color after standing 5 minutes, the distillate may be considered free from ammonia and is now collected as distilled water. The distillate is collected in flint glass bottles which have been previously cleansed and sterilized as described under Sterilization on page 616 of the U. S. Pharmacopœia IX. The bottles should hold from 100 to 500 cc. depending upon the quantities ordinarily used for any one operation. The bottles are stoppered with cotton, which is covered with parchment paper. When the distillation is completed and there have been collected about 750 cc. of distillate the bottles are placed in an autoclave and heated from 20 to 30 minutes at a pressure from 10 to 15 pounds. Distilled water so prepared should be examined from time to time and tested for bacteriological purity by adding 1 cc. of the water to a nutrient broth which is then incubated from 24 to 72 hours. The broth should show no cloudiness or growth of microörganisms.

The preparation of the nutrient broth is made according to the method of the American Public Health Association as follows:

1. Add 3 grams of beef extract and 5 grams of peptone to 1000 cc. of distilled water.
2. Heat slowly on steam-bath to at least 65° C.
3. Make up lost weight and adjust the reaction to a faint pink with phenol red, or if the phenolphthalein titration is used, and the reaction is not already between +0.5 and +1, adjust to +1.
4. Cool to 25° C. and filter through paper until clear.
5. Distribute in test-tubes, 10 cc. to each tube.

6. Sterilize in the autoclave at 15 pounds (120° C.) for 15 minutes after the pressure reaches 15 pounds.

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In briefly discussing the foregoing paper, Ivor Griffith and William Gray expressed the thought that in the process of distillation acid might be carried over. The former stated that in the laboratory under his supervision the distilled water is sealed as promptly as possible. It was suggested that the method of preparing distilled water might be a subject for another paper next year.

TINCTURE OF FERRIC CITRO-CHLORIDE.*

BY ADLEY B. NICHOLS.

In preparing Tincture of Ferric Citro-Chloride according to the N. F. IV, the writer has always noticed the difficulty of bringing the sodium citrate into solution and the heavy separation of saline matter, as the product was allowed to stand. It seemed to him that this excessive separation was uncalled for and needless, but the fact always remained that the N. F. III formula was not quite satisfactory, for the amount of sodium citrate had been increased from 425 Gm. to 500 Gm. per 1000 cc. of tincture.

A number of samples of the tincture had been prepared from various samples of sodium citrate on hand, and it was noted that there was a marked difference in the amount of salt which separated out in the different lots. Additional samples of sodium citrate were ordered from as many different firms as possible and tinctures prepared from each of these. The separation of salt again varied and in some cases it was quite difficult to dissolve the sodium citrate, even with aid of considerable heat.

In checking up the samples of sodium citrate, it was noted that several were labeled U. S. P. VIII, while others were U. S. P. IX, and the samples of tincture showed that there was the least precipitation in the tinctures prepared from the U. S. P. VIII salts. Upon referring to the two books, it was discovered that the salt official in the U. S. P. VIII had contained five and one-half molecules of water, while that in the U. S. P. IX contains only two molecules.

This discovery settled the trouble at once, for while the U. S. P. IX had recognized a different form of sodium citrate because of its better stability, the N. F. had missed this subsequent change in strength. Where the N. F. had raised the quantity of sodium citrate from 425 Gm. to 500 Gm. to insure a better Tincture of Ferric Citro-Chloride, they had apparently based their quantities on a U. S. P. VIII salt, while the salt which became official in the new revision was considerably stronger. The N. F. III tincture had actually contained 307 grams of anhydrous sodium citrate and the amount intended for the N. F. IV formula was 361 grams, while that actually present with the new salt amounted to 439 grams.

Two tinctures were prepared with the U. S. P. VIII salt, one using the original N. F. III formula, and the other the formula in the N. F. IV, and two tinctures

* Section on Practical Pharmacy and Dispensing, A. Ph. A., Asheville meeting, 1923.