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2,970,945

DIAGNOSTIC COMPOSITION

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No Drawing. Filed Oct. 3, 1958, Ser. No. 765,065

8 Claims. (Cl. 167—84.5)

This invention relates to diagnostic compositions for the detection of gonococci, and is particularly concerned with such compositions in tablet form affording accurate and convenient means for preparing a solution of oxydase reagent for use in detecting colonies of *Neisseria gonorrhoeae* in accordance with the well known oxydase test.

In the oxydase test, the presence of gonococci is determined by incubating genital tract exudate on a Petri plate containing blood agar or some other suitable medium at 37° C. in the presence of increased carbon dioxide tension. At the end of 36 to 48 hours, a freshly prepared solution of p-aminodimethylaniline monohydrochloride is added to the plate and gonococcal colonies quickly assume a characteristic pink color which changes to maroon and finally to black. While the test is fairly simple to perform and provides accurate results when conducted with ordinary care, its popularity has been confined essentially to clinics and other institutional practices where numbers of tests are performed daily, and fresh solutions of the p-aminodimethylaniline monohydrochloride are routinely prepared daily. The test has been readily adaptable to private practice where, because the aqueous solution of p-aminodimethylaniline monohydrochloride is unstable, it is necessary to prepare a fresh solution at the time each test is to be made, requiring the expenditure of valuable time by the physician or his technician.

It is an object of the invention to provide a diagnostic composition in tablet form which may be carried conveniently in the physician's bag, and which will not deteriorate over long periods of time under ordinary conditions of temperature and humidity, but which may be quickly converted to a solution for use in the oxydase test for gonorrhea simply by dropping a tablet into a measured quantity of water.

Other objects will be apparent from the description of the invention which follows.

A diagnostic composition in accordance with the invention comprises an oxydase reagent, such as p-aminodimethylaniline monohydrochloride or tetramethyl-p-phenylenediamine, and an effervescent couple, the ingredients being intimately mixed in finely divided form, and preferably compressed into tablets of convenient size for use in preparing predetermined quantities of the oxydase solution. The oxydase reagent is the active agent for the test, while the effervescent couple hastens disintegration of the tablet and dissolution of the oxydase reagent when the tablet is dissolved in water. A further function of the effervescent couple is that it provides components which tend to buffer the solution, thereby promoting the reaction of the oxydase reagent with the oxydase-positive colony.

The effervescent couple may be formed from any of a number of solid acids and/or acid-reacting salts in combination with any of the alkali metal carbonates and/or bicarbonates. As the acid component we prefer to use citric acid because it is highly efficient, stable and

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readily available at low cost. However, other acids or acid reacting substances such as tartaric acid, alkali metal acid citrates, such as potassium acid citrate, or alkali metal acid sulfates, such as sodium or potassium acid sulfate, may be used instead for this purpose, if desired.

As the carbonate component of the effervescent couple, we prefer to use sodium bicarbonate, but other water-soluble salts of carbonic acid, including the alkali metal normal carbonates, sesquicarbonates and bicarbonates, e.g., sodium carbonate, sodium sesquicarbonate, or potassium bicarbonate may be used instead with satisfactory results.

Example I

The following ingredients:

5 grams of p-aminodimethylaniline monohydrochloride
41 grams of citric acid
54 grams of sodium bicarbonate

are mixed until a homogeneous mixture of all of the ingredients has been achieved. The mixture is then preferably pressed into tablets of convenient size, e.g., 1000 mg., so that each tablet contains about 50 mg. of p-aminodimethylaniline monohydrochloride.

In the above example, the acid and carbonate components of the effervescent couple are in substantially stoichiometric proportions. This is the preferred condition, although a slight excess of either the acid or carbonate, to give a pH between 6 and 8, is permissible.

When one of the present diagnostic compositions, as represented by the formulation of Example I, is dropped into 10 ml. of water, it effervesces vigorously during solution due to the reaction between the citric acid and the sodium bicarbonate. The p-aminodimethylaniline monohydrochloride is thus quickly dissolved and is uniformly distributed throughout the solution, which utilizes the buffering activity of the effervescent couple. After effervescence ceases, the solution may be added directly to the petri plate where any colonies of gonococci will be detected by the procedure described above.

The proportion of the effervescent couple with respect to the oxydase reagent is not closely critical and may be considerably varied. We prefer to prepare our compositions so that the proportion of the effervescent couple is between about 85% and about 98% of the total weight of the composition. Smaller proportions of the effervescent couple correspondingly delay solubility of the composition, and larger proportions do not afford any significant advantage in increasing the solubility rate.

Instead of p-aminodimethylaniline monohydrochloride, tetramethyl-p-phenylenediamine may be used as the oxydase reagent, as shown in the following example.

Example II

5 grams tetramethyl-p-phenylenediamine
41 grams citric acid
54 grams sodium bicarbonate

The above ingredients, finely divided, are intimately mixed and preferably pressed into 1000 mg. tablets following the procedure described in Example I.

The p-aminodimethylaniline monohydrochloride is preferred over the tetramethyl-p-phenylenediamine as the oxydase reagent since it is much less expensive and gives tablets of better stability.

What we claim is:

1. As a diagnostic composition, an intimate admixture of dry ingredients consisting essentially of an effervescent couple and a member of the group consisting of p-aminodimethylaniline monohydrochloride and tetramethyl-p-phenylenediamine.

2. A composition in accordance with claim 1 wherein the effervescent couple consists of a water-soluble salt of

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carbonic acid and a member of the group consisting of solid acids and acid-reacting salts.

3. A composition in accordance with claim 2 wherein the components of said effervescent couple are present in substantially stoichiometric quantities.

4. A composition in accordance with claim 3 wherein the proportion of the effervescent couple is between about 85% and about 98% of the total weight of said composition.

5. As a diagnostic composition, an intimate admixture of dry ingredients in tablet form consisting essentially of p-aminodimethylaniline monohydrochloride and an effervescent couple.

6. A diagnostic composition comprising an intimate admixture, in tablet form, of a minor proportion of p-aminodimethylaniline monohydrochloride and a major proportion of an effervescent couple consisting essentially of citric acid and sodium bicarbonate.

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7. An aqueous solution of the composition claimed in claim 6.

8. A diagnostic composition comprising an intimate admixture, in tablet form, of a minor proportion of tetramethyl-p-phenylenediamine and a major proportion of an effervescent couple consisting essentially of citric acid and sodium bicarbonate.

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