United States Patent [19]

Mast

[11] 3,920,580

[45] Nov. 18, 1975

[54] **LIQUID CONTROL SOLUTION**

[75] Inventor: **Raymond L. Mast**, Elkhart, Ind.

[73] Assignee: **Miles Laboratories, Inc.**, Elkhart, Ind.

[22] Filed: **July 12, 1973**

[21] Appl. No.: **378,687**

[52] **U.S. Cl.** ..... **252/408;** 23/230 B; 23/230 M; 23/253 TP; 195/103.5 C; 424/2; 424/78; 424/80; 424/101

[51] **Int. Cl.**[2] **C09K 3/00;** G01N 31/00

[58] **Field of Search** ..... 252/408; 23/230 B, 230 M, 23/253 TP; 195/103.5 C; 424/2, 101, 80, 78

[56] **References Cited**

UNITED STATES PATENTS

3,050,373	8/1962	Collins	252/408
3,104,209	9/1963	Scott	252/408
3,546,131	12/1970	Stern et al.	252/408
3,558,522	1/1971	Louderback et al.	23/230 B
3,598,704	8/1971	Dahlqvist	23/230 B
3,630,958	12/1971	Free et al.	252/408
3,753,863	8/1973	Speck	195/103.5 C
3,753,925	8/1973	Louderback et al.	252/408
3,814,668	6/1974	Blake et al.	195/103.5 C

FOREIGN PATENTS OR APPLICATIONS

867,192	5/1961	United Kingdom	252/408
880,526	10/1961	United Kingdom	252/408

Primary Examiner—Benjamin R. Padgett
Assistant Examiner—T. S. Gron

[57] **ABSTRACT**

A stable liquid control solution useful with dry reagent strips which strips are for determining whether or not glucose is present in blood or serum. The control solution comprising water, an antidiffusing agent and glucose. The antidiffusing agent may be selected from materials such as polyvinylpyrrolidone, polyvinyl alcohol, polyethylene glycol, dextran and bovine serum albumin. The control solution may also include adjuvants such as preservatives, common salts, dyes, colored latex particles, etc.

7 Claims, No Drawings

LIQUID CONTROL SOLUTION

BACKGROUND OF THE INVENTION

This invention relates to a stable liquid control solution for use in establishing the validity of dry reagent strips which strips are for determining whether or not glucose is present in blood or serum. More specifically, this invention relates to a stable control solution including a predetermined amount of glucose which solution emulates whole blood or blood serum when applied to a reagent strip for glucose.

It is recognized that reagent strips are widely used for detecting specific materials in solutions. Such strips have become popular because of the accuracy and convenience thereof and the rapid production of results thereby. It is also known that data generated by these strips are highly reproducible if the strips have been properly prepared, stored and handled. An example of such a reagent strip for determining glucose in blood is sold under the trademark DEXTROSTIX by Ames Company Division, Miles Laboratories, Inc.

Recently machines have been available that read such strips. Some of these machines are even capable of giving quantitative amounts of the unknown material in the solution being tested. With such accuracy, it is important that the reagent strips function properly. Further, although these machines yield accurate determinations with properly prepared, stored and handled strips, they cannot readily detect faulty strips as can a human counterpart. One such machine is the Ames Reflectance Meter available from Ames Company Division, Miles Laboratories, Inc.

To insure the proper reactivity and to establish the validity of such test devices, it has been desirable to have available a control solution. Although the ideal control would be a whole blood solution for which these test devices are primarily designed, this material is unsuitable because of its instability when stored, glycolysis of glucose in the whole blood, the inherent variability of blood from one individual to another and the critical storage conditions required for this material. Accordingly, whole blood has not been found suitable for use as a control for this test.

It has also been suggested that a simple aqueous solution of glucose be employed as a control solution. In practice, however, such solutions have not produced results consistent with the amount of glucose therein. Also, a noticeable lack of reproducibility has been observed when such solutions are used with dry reagent strips.

SUMMARY OF THE INVENTION

This invention is embodied in a stable liquid control solution including a predetermined amount of glucose for use with dry reagent glucose indicating strips. The solution comprises water, an antidiffusing agent, and a predetermined quantity of glucose.

Accordingly, it is an object of this invention to provide a stable control solution for confirming the validity of a dip-and-read dry reagent strip of the type for determining an unknown glucose concentration in a solution.

Another object of this invention is to provide a control solution for evaluating the technique of a user of such a strip.

A further object of this invention is to provide a control solution that is stable for an extended period of time at normal room temperatures which solution emulates the behavior of whole blood or serum when used with a dry reagent strip.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

It has unexpectedly been found that a control solution suitable for use with dry reagent glucose indicating strips with a high degree of reproducibility in test results may be formed by including in an aqueous solution of glucose an antidiffusing agent. With the incorporation of such an agent in this solution, results are obtained with reagent strips which are substantially identical to or proportional to the results observed when whole blood or serum having similar quantities of glucose is evaluated. Although the mechanism of action of this antidiffusing agent is not fully understood, it is believed that it modifies the viscosity and the osmotic pressure of the control solution so as to avoid the adverse effects previously mentioned for an aqueous glucose solution. Such materials are readily soluble in water and have a medium or high molecular weight. Examples of such antidiffusing agents, which may be used singly or in combination, include polyvinylpyrrolidone, polyvinyl alcohol, polyethylene glycol, dextran and bovine serum albumin. Beneficially, the control solution includes between about 3 and 35% of antidiffusing agent and preferably between about 20 and 30% thereof.

The D-glucose included in the control solution is preferably a high grade glucose such that an accurate weight percent thereof in the control solution may be determined. It is understood in this application that D-glucose and dextrose are considered equivalent materials and may be substituted one for the other without altering the novel control solution of this invention. Although the amount of glucose in the solution is not considered critical, within the solubility limit of the solution, it is preferable to include between about 1–1000 mg % (mg/100 ml solution) therein.

It has been found advantageous, although not essential, to include in this control solution common salts such as, for example, alkali metal salts of halogens, a phosphate or a sulfate. Preferred salts include sodium chloride, potassium chloride, potassium phosphate and the like. It is believed that such salts further adjust the osmotic pressure of this control solution so that it more closely emulates whole blood or serum. Satisfactory control solutions are obtainable with between about 0 and 25% salt therein, and preferably between about 1 and 4% salt is included in the solution.

It is benefical to include in the novel control solution of this invention a preservative so as to avoid microbial growth therein. Such preservative may be selected from the numerous materials which are known to have this property. Representative compositions for this function include benzoic acid, sodium benzoate, dichlorophene, hexachlorophene, quaternary ammonium compounds, sorbic acid, phosphoric acid and esters of p-hydroxybenzoic acid. The preservative may be included in an amount corresponding to accepted levels, such as, between about 0.01 and 0.3%.

Further adjuvants may be added to the solution to obtain a particular color or physical appearance. A red blood color may be obtained by incorporating therewith a red, water insoluble lake dye. Other water insoluble or water soluble dyes producing desired colors may be included therein. Further, a blood appearance

may be enhanced by the addition of inert colored latex particles thereto.

The novel liquid control solution of this invention and the preparation thereof will be further described in the following examples which set forth specific embodiments of this invention which are only representative thereof and do not limit the scope or use of this invention in any way.

EXAMPLE 1

A stable liquid control solution was prepared by dissolving in 88 ml. of water at a temperature of about 100°C. 0.2 gm. benzoic acid, 30 gm. of polyvinylpyrrolidone and 45 mg. of anhydrousdextrose. Upon dissolution of these ingredients in the warm water, water was added to bring the solution to a volume of 100 ml. This procedure was further used to prepare four more solutions having glucose concentration of 90, 130, 175 and 250 mg. %. Upon cooling, these solutions had a clear appearance and were free of precipitants.

With clean eye droppers, a large drop of each solution was applied to separate reagent areas respectively of glucose indicating reagent strips (DEXTROSTIX). After 60 seconds, each drop was washed from the surface of the reagent strip with water and the amount of glucose therein determined by comparing the color of the reagent strip with a color block calibrated therefor. it was observed that the colors of the reagent strips indicated 45, 90, 130, 175 and 250 mgs. glucose per 100 ml. blood respectively corresponding to the amount of glucose incorporated in each control solution.

EXAMPLE 2

The procedure of this example was substantially the same as that of Example 1 except that the following ingredients were combined with the dextrose and the water to form the five dextrose solutions.

Material	Weight
Polyvinylpyrrolidone	13.34 gm.
Bovine Serum albumin, fraction V	3.33 gm.
Sodium Chloride	2.67 gm.
Benzoic Acid	0.2 gm.

These solutions had an appearance substantially the same as the solutions prepared in Example 1 and were observed to develop a proper color change when applied to DEXTROSTIX.

EXAMPLE 3

The procedure of this Example was substantially the same as that of Example 1 except that the following ingredients were combined with the dextrose and the water to form the five dextrose solutions.

Material	Weight
Benzoic Acid	0.2 gm.
Polyvinylpyrrolidone	30. gm.
FD&C Red No. 2, Aluminum Lake	0.175 gm.
FD&C Red No. 40, Aluminum Lake	0.175 gm.

The solutions of this Example had a color appearance substantially the same as whole blood. When applied to DEXTROSTIX according to the procedure of Example 1, correct color changes were observed.

EXAMPLE 4

The procedure of this example was substantially the same as that of Example 1 except that the following ingredients were combined with the dextrose and the water to form the five dextrose solutions.

Material	Weight
Benzoic Acid	0.2 gm.
Polyvinylpyrrolidone	20 gm.
FD&C Red No. 2, Aluminum Lake	0.175 gm.
FD&C Red No. 40, Aluminum Lake	0.175 gm.
Sodium Chloride	2.25 gm.

These solutions had substantially the same appearance and reactivity as the solutions of Example 3.

EXAMPLE 5

The procedure of this example was substantially the same as that of Example 1 except that the following ingredients were combined with the dextrose and the water to form the five dextrose solutions.

Material	Weight
Benzoic Acid	0.2 gm.
Polyethylene glycol (4000–9000 mol. wt.)	25 gm.

These solutions had substantially the same appearance and reactivity as the solutions of Example 1.

EXAMPLE 6

The procedure of this example was substantially the same as that of Example 1 except that the following ingredients were combined with the dextrose and the water to form the five dextrose solutions.

Material	Weight
Benzoic Acid	0.2 gm.
Dextran	25 gm.

These solutions had substantially the same appearance and reactivity as the solutions of Example 1.

Based on accelerated stability evaluations, it has been concluded that the unique liquid control solution of this invention is stable for at least **5** years at about room temperature if properly stored in a closed container. With such stability and reproducible results with reagent strips, a stable liquid control solution is provided which meets the criteria desired for such a control solution but which were previously unobtainable.

What is claimed is:

1. A stable liquid control solution including a predetermined amount of glucose for use in determining the validity of a dry reagent strip capable of indicating amounts of glucose in blood or blood serum which solution emulates whole blood or blood serum used with said strip, the solution comprising water, glucose, a preservative, and between about 3 and 35 percent by weight of an antidiffusing agent selected from the group consisting of polyvinylpyrrolidone, polyvinyl alcohol, polyethylene glycol, dextran and bovine serum albumin.

2. The solution of claim 1 in which said antidiffusing agent is polyvinylpyrrolidone.

3. The solution of claim 1 in which said antidiffusing agent is polyethylene glycol.

4. The solution of claim 1 in which said antidiffusing agent is dextran.

5. The solution of claim 1 in which said preservative is present in an amount between about 0.01 and 0.3 percent by weight.

6. The solution of claim 1 which additionally includes a common salt.

7. The solution according to claim 6 in which said common salt is sodium chloride.

* * * * *