

UNITED STATES PATENT OFFICE.

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REAGENT.

No Drawing.

Application filed May 7, 1923. Serial No. 637,368.

To all whom it may concern:

Be it known that we, GERRIT JOHN VAN ZOEREN and EDWARD JOHN DE PREE, citizens of the United States, and both residents of Holland, in the county of Ottawa and State of Michigan, whose post-office addresses both are Holland, Michigan, have invented an Improvement in Reagents, of which the following description is a specification.

Our invention aims to provide an improved reagent which may be used to test solutions and mixtures for the presence of glucose. The invention aims further to provide a new reagent, in convenient form for carrying about, which may be readily dissolved in water to form a solution useful for the same purposes as Fehling's solution.

In a medical examination of a living person, one of the most usual steps is the testing of the urine to determine whether the subject has certain organic diseases, such as Bright's disease or diabetes. The urine of a diabetic patient is distinguished from normal urine by the presence of an appreciable quantity of sugar in the form of glucose. The reagent almost universally used to test for the presence of glucose in urine (or in any other solution or mixture) is which is known as Fehling's solution, which usually consists of an aqueous solution of copper sulphate, potassium sodium tartrate and sodium hydroxide.

Because of the inconvenience of transporting Fehling's solution, as well as its instability it is now the common practice to market separate packages of compressed tablets respectively of crystalline copper sulphate and potassium sodium tartrate, said tablets being of such size that when one tablet from each package is dissolved in sodium hydroxide solution of a certain strength, a standard Fehling's solution will be formed. It has been found impracticable to make up either a powder or single tablets containing the right proportions of copper sulphate, potassium sodium tartrate and sodium hydroxide because such a powder or tablet will invariably decompose after a time, due to various causes, such as the ionization of the sodium hydroxide, and the reactions which would take place under such circumstances owing to the hygroscopicity of sodium hydroxide and due to its chemical activity. These changes are such

that after a very short time Fehling's solution cannot be prepared from such a tablet, even though kept in the dark and out of contact with moisture. Accordingly, some manufacturing chemists at the present time sell pocket cases containing three bottles, in one of which are tablets of copper sulphate; in a second, tablets of potassium sodium tartrate; and in a third, lumps of sodium hydroxide. To make Fehling's solution from these, the physician or other user dissolves a lump of sodium hydroxide in a certain quantity of water, according to directions, and adds one tablet from each of the other bottles to a measured portion of this caustic solution, dissolving with the aid of heat.

There is general complaint made by those who have worked with one of these pocket kits, because the sodium hydroxide (lye) lumps burn the fingers, and because of the nuisance of handling and dissolving three different substances. The technic is too involved for the layman and for the busy practitioner. Furthermore, the sodium hydroxide lumps are so extremely hygroscopic that unless maintained in an air-tight vessel they will take up water from the air and gradually deliquesce and lose their physical identity, thereby making the preparation of a reliable Fehling's solution difficult or impossible.

Another disadvantage of these pocket kits is that the sodium hydroxide because of its hygroscopicity cannot be compressed into tablets of the proper size but must be made up as lumps which are several times larger than necessary, the object being to reduce the proportion of exposed surface to the total volume of the lump. The smaller the lump, the greater is the surface exposed, proportionately, and the more rapid is the absorption of moisture from the air. Now, when one of these large lumps is dissolved in water, there is sufficient caustic solution for a considerable number of tests. Assuming that the physician makes only one test at a call, he must either carry the remaining caustic solution with him or throw it away, necessitating the making up of a fresh solution for the next test. The transportation of the surplus caustic solution and the frequent preparation of new quantities of it are two of the annoyances which our invention eliminates.

According to our invention, we provide a novel composition of matter, which may be in a dry form for use as a reagent in testing for glucose, and which we believe has none of the objectionable features of the compositions for making Fehling's solution found on the market. Our new reagent may be sold as a powder or in tablet form, and in either case, to make a solution reacting exactly like but more dependably than Fehling's solution it is only necessary to dissolve the reagent in the proper quantity of water.

Our invention may be illustrated by the following composition:

0.111 parts by weight of copper sulphate, anhydrous or substantially so;

0.7025 parts by weight of potassium tartrate, anhydrous;

0.150 parts by weight of dry lithium hydroxide.

The three ingredients when in dry power form may be thoroughly mixed together, and the resultant dry powder may be packaged in bulk or in papers, capsules or the like. If it is desired to put up the product in tablet form, crystalline copper sulphate and a crystalline tartrate salt should be used; and in that case the copper sulphate may be compressed separately to form one tablet, while the tartrate and the lithium hydroxide may be mixed together and compressed or put up in separate tablets. To test for glucose, one gram of the improved reagent is dissolved in about five cc. of water, and approximately five parts by volume of the sample to be tested are added to the test solution so formed. Obviously the proportions given above may be varied within wide limits.

The reaction caused by the above described composition in testing for glucose is as follows: Upon dissolving the lithium hydroxide in a solution containing a cupric salt (CuSO_4) there is formed cupric hydroxide solution $\text{Cu}(\text{OH})_2$; and upon adding glucose to cupric hydroxide in the presence of potassium tartrate or equivalent retarding agent, the cupric hydroxide is reduced to cuprous oxide Cu_2O which is a dark red precipitate. The function of the potassium tartrate is to act as a retarder, preventing the precipitation of black cupric oxide (CuO) which would not be a test for glucose. Other salts of tartaric acid may also be used as retarders, such as sodium tartrate and potassium sodium tartrate, the proper amount of each varying slightly from the above proportions, as will be understood. There are other salts which will also act as retarders to prevent the precipitation of black oxide of copper, and we wish to avail ourselves of all such salts in combination with copper sulphate and lithium hydroxide. Our invention is therefore

not to be construed as limited to the use of any particular tartrate or indeed to any particular retarder.

Our experiments indicate that samples of our reagent many months old are equally efficacious in testing for glucose as freshly prepared samples. A primary reason for this is that lithium hydroxide is absolutely non-hygroscopic and very stable and when it is exposed to moist air for long periods of time it remains substantially unchanged. Furthermore, our reagent may be put up in such form as not to require handling with the fingers, and therefore the danger of caustic burns, ever-present when caustic soda is employed, is eliminated. We believe we are the first to discover a water-soluble reagent adapted to make a solution reacting like Fehling's solution, but which is non-decomposing when its various ingredients are brought together in an intimate mixture. The complete absence of hygroscopicity in the reagent makes possible the marketing of a perfectly stable product either in powder or in tablet form. Furthermore, the preferred embodiment of the invention is easily manufactured, is inexpensive, and since it need not be kept from the air, it may be put up in any convenient form of container.

Obviously our invention is not restricted to the particular embodiment thereof herein described.

Having disclosed one illustrative embodiment of our invention, what we claim as new and desire to secure by Letters Patent is:—

1. A dry reagent adapted to be dissolved in water to form a solution for testing for the presence of glucose in solutions, comprising copper sulphate, a crystalline alkali metal tartrate reacting like potassium tartrate, and lithium hydroxide.

2. A reagent for the purpose specified comprising copper sulphate, potassium tartrate, and lithium hydroxide, all in a substantially dry state.

3. A reagent adapted to be dissolved in water to form a solution for testing for the presence of glucose, comprising copper sulphate, a salt of tartaric acid which will act as a retarder, and lithium hydroxide.

4. As a new product, a dry, non-hygroscopic and water-soluble reagent made up of copper sulphate and other ingredients which may be brought together into an intimate physical mixture without causing decomposition of the copper sulphate in the presence of atmospheric air; said reagent, when dissolved in the proper amount of water, forming a solution reacting similarly to Fehling's solution and useful for the same purposes.

5. A reagent adapted when dissolved in water of sufficient quantity to be used for the same purposes as Fehling's solution, comprising copper sulphate, an alkali metal

tartrate which will act as a retarder, and lithium hydroxide.

6. A reagent adapted when dissolved in water of sufficient quantity to be used for the same purposes as Fehling's solution, comprising copper sulphate, potassium tartrate, and lithium hydroxide, substantially in the proportions of 0.111 gm. of copper sulphate, 0.7025 gm. of the tartrate, and 0.150 gm. of lithium hydroxide.

7. A water-soluble reagent to be used for testing for the presence of glucose, comprising copper sulphate, lithium hydroxide, and a salt which will act as a retarder to prevent the precipitation of black cupric oxide and to

permit the precipitation of red cuprous oxide when a solution of the reagent is added to a solution or mixture in which glucose is present.

8. A water-soluble and stable reagent to be used for testing for the presence of glucose, comprising copper sulphate, a salt of tartaric acid which will act as a retarder, and a non-hygroscopic alkali-metal hydroxide in a dry state.

In testimony whereof, we have signed our names to this specification.

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