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PROCESS OF STABILIZING POLYVINYL PYRROLIDONE-IODINE COMPOSITIONS

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1 Claim. (Cl. 167—70)

This invention relates to a process of stabilizing a dry powdered adduct of iodine and polymeric 1-vinyl-2-pyrrolidone (hereinafter referred to as polyvinyl pyrrolidone) whereby a stable composition is obtained which when dissolved in water will not change its pH and maintain a constant available iodine content.

In the copending application of Herman A. Shelanski, Serial No. 135,519, filed December 28, 1949, now abandoned, there is disclosed a novel composition of polyvinyl pyrrolidone and iodine which has been found to be of substantial value for many applications in which advantage is taken of the bactericidal activity of the iodine but in which the irritating, sensitizing, and toxic properties of the iodine are substantially overcome. As disclosed in this application, this novel iodine-polyvinyl pyrrolidone composition may be prepared by adding a solution of iodine, such as Lugol's solution or tincture of iodine to an aqueous solution of polyvinyl pyrrolidone followed by dessication in a suitable dryer.

To improve on the method of preparing the foregoing novel iodine-polyvinyl pyrrolidone composition, there is disclosed in the copending application of Hans Beller and W. A. Hosmer, Serial No. 282,458, filed April 15, 1952, now U. S. Patent 2,706,701, a process whereby dry elemental iodine is mixed with dry powdered polyvinyl pyrrolidone. The iodine and powdered polymer is mixed until a homogeneous powder is obtained, the mixing being carried out in materials which are not attacked by iodine so as to avoid the introduction of metal ions into the finished composition. This mixing is effected by grinding the iodine and polyvinyl pyrrolidone in a mortar and pestle or more advantageously in a suitable mechanical mixer such as a ball mill. The time of mixing varies only with the efficiency thereof, as the combination of the polyvinyl pyrrolidone with iodine on its surface is rapid, in fact, such combination will occur to some extent on dropping iodine crystals on the dry powdered polymer.

On completion of the mixing there is obtained a compound in a physical state similar to the polymer alone but which contains varying proportions of available iodine (as distinguished from free iodine), iodide ion, and bound iodine. A distinction between these forms may be made on an analytical basis, available iodine being determined directly by dissolving a sample of the product in water and titrating with 0.1-N sodium thiosulfate solution using starch as an indicator. The amount of iodine present as iodide ion is determined by reducing the iodine compound in solution with 1-N sodium acid sulfite, adding enough to make the solution colorless, then adding 0.1-N silver nitrate and enough nitric acid to make the solution acidic and back-titrating with ammonium thiocyanate. The iodide ion is the difference between this figure and the available iodine as determined above. The total iodine may be determined by combustion methods such as that formulated by Hallett in Scott's Standard Method of Chemical Analysis, bound iodine then being determined by subtracting the sum of available iodine

and iodide ion from the total iodine as determined above.

The product thus obtained may have an available iodine content ranging from 8–15% and an iodide ion content from 0.98 to 5.6%. With any given sample of polyvinyl pyrrolidone, the iodine present as available iodine and iodide ion may vary somewhat. On standing, the amount of available iodine slightly decreases while the amount of iodide ion increases. In order to obtain a stable product, Hans Beller et al. referred to above found that a product in which the ratio of available iodine to iodide ion is substantially 2:1 is readily and rapidly obtained by heating the dry blended material in the order of 90–100° C. Further details regarding this process may be obtained by reference to their patent, the contents of which are incorporated herein by reference, especially, the various iodine-polyvinyl pyrrolidone compositions as prepared in accordance with their Examples I to VI inclusive.

The iodine-polyvinyl pyrrolidone compositions prepared in accordance with the aforestated application form aqueous solutions which contain iodine having a very high germicidal activity. The iodine-polyvinyl pyrrolidone composition in aqueous solution has a high acid reaction near a pH of 2, which in some instances, such as, for intravenous use or application on sensitive tissue necessitates the adjustment of such solution to near neutrality. Solutions so adjusted by alkaline agents, especially sodium bicarbonate have a tendency to lose their available iodine activity quite rapidly because of the shift of the hydrolysis equation to the right under increasingly alkaline conditions.

$$I_2+H_2O \rightleftharpoons HOI+HI$$

When aqueous solutions of iodine-polyvinyl pyrrolidone compositions are prepared and the pH adjusted to neutrality by the addition of sodium bicarbonate, the available iodine content decreases and the available iodide ion increases upon storage within a few weeks, thus posing a serious problem when shipping such solutions to hospitals and physicians. From the time the actual solution is made at the dispensing plant and the time at which it arrives in the hospital or physician's office, which may require several weeks, the solution loses potency in the available iodine content.

I have discovered that the tendency of the iodine-polyvinyl pyrrolidone composition to lose its available iodine content when prepared in aqueous solution can be very readily overcome by blending 16 to 20 parts by weight of sodium bicarbonate per 100 parts by weight of the iodine-polyvinyl pyrrolidone composition having an available iodine content from 8 to 15% and an available iodide ion content from 0.98 to 5.6% for a period of time ranging from 6 to 36 hours. The resulting product is stable and will readily dissolve in water to form essentially neutral solutions (having a pH range from 6.6 to 6.9). By this procedure, the iodine-polyvinyl pyrrolidone composition is made in a more available and readily useful form for injections and use on mucous tissue.

It is indeed wholly surprising and unexpected that the reaction indicated by the above equation has been found not to occur in the solid state when sodium bicarbonate is blended with the iodine-polyvinyl pyrrolidone composition even though moisture may be present either in the sodium bicarbonate or the iodine polyvinyl pyrrolidone composition, or both. More surprising is the fact that the solid mixture of iodine-polyvinyl pyrrolidone composition and sodium bicarbonate has the same stability as the dry iodine-polyvinyl pyrrolidone composition alone.

The following example will serve to illustrate how the stabilized iodine-polyvinyl pyrrolidone composition may be prepared in accordance with the present invention. It is to be understood, however, that this example is merely

illustrative and is not to be considered limitative of the invention disclosed and claimed herein.

Example I

To 100 parts of iodine-polyvinyl pyrrolidone composition (made by dry-blending 83.2 parts of polyvinyl pyrrolidone having a K value of 30 and 16.8 parts of iodine for 24 hours, followed by 24 hours of heating at 93° C.) there were added 10 parts of anhydrous sodium bicarbonate. The mixture was blended for 24 hours in a rotating glass vessel to insure uniformity. The product was made up as a 1% aqueous solution and had a pH of 6.7 to 6.9. In aging the dry product for six weeks at 100° F. no change in pH was observed, and no change in the available iodine and iodide ion content was noted.

For comparison a 1% aqueous solution of the iodine-polyvinyl pyrrolidone composition utilized above, i. e. prior to blending with sodium bicarbonate (having a pH of 2) and adjusted by the addition of anhydrous sodium bicarbonate to a pH of 6.6 to 6.7, the amount of bicarbonate added was not calculated, but made with vigorous stirring with the pH metered electrodes immersed in the solution. In aging this solution at 100° F. for six weeks, the pH increased from 6.6 to 7.4 and the available iodine content decreased from 11.84 to 11.3%, and the iodide content increased from 3.9 to 4.51%.

By blending sodium bicarbonate with the iodine-polyvinyl pyrrolidone composition, the resulting blend may be packaged as one stable unit and immediately utilized without further compounding. This expedient saves a considerable amount of money in packaging and shipping.

I claim:

The method of forming an aqueous iodine-polyvinyl-pyrrolidone composition which is stable with respect to a change in pH and loss in available iodine content, which comprises blending anhydrous sodium bicarbonate with dry iodine-polyvinyl-pyrrolidone composition until a uniform mixture is obtained, and dissolving the said mixture in water.

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