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PREPARATION OF POLYGLYCOLIC ACID IN FINELY DIVIDED FORM

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U.S. Cl. 260—535 P 9 Claims

ABSTRACT OF THE DISCLOSURE

This invention relates to a process for producing finely divided polyglycolic acid comprising dissolving said polyglycolic acid in an inert solvent and then adding a non-solvent for the polyglycolic acid to the solution thereby producing polyglycolic acid particles in finely divided form.

CROSS REFERENCES TO RELATED APPLICATIONS

Reference is made to the U.S. patent application Ser. No. 770,792, filed Oct. 25, 1968 which is directed to a synthetic biodergradable medical dusting powder, now abandoned. This patent application is incorporated herein by reference. In said patent application a disclosure is made of the use of a finely divided polyglycolic acid powdery material as a biodegradable medical dusting powder for use by surgeons on the conventional surgical rubber gloves. Reference is made to the U.S. patent application Ser. No. 117,998, filed Feb. 23, 1971 which is a continuation-in-part of the forementioned abandoned patent application.

BACKGROUND OF THE INVENTION

This invention relates to a process for preparing a finely divided synthetic biodegradable medical dusting powder suitable for a wide variety of medical usages and in particular, for the use as a surgical glove powder. Polyglycolic acid is a very hard, tough material and it is with extreme difficulty that it is reduced in size to a powdery material in finely divided form without so much degradation as to render it unusable as a dusting powder for use with surgical gloves. By way of background it should be pointed out that various dusting powders have been used for years with a prime use meaning to facilitate insertion of the hands of operating room personnel into rubber or latex gloves worn during surgery. A usable glove powder should at least meet the following requirements:

(1) It should be non-toxic to living tissue.

(2) It should be biodegradable, i.e. absorbed by living tissue. This is most important since, during a surgical procedure, powder may fall from the surgeon's gloved hand into an exposed body cavity or it may be carried from other areas of the operating room into the exposed body cavity by air currents.

(3) The powder should have no adverse effect within the body such as the creation of lesions (i.e. adhesions, granulomas, or such).

(4) The glove powder must be capable of sterilization by conventional hospital techniques such as gaseous ethylene oxide sterilization.

(5) The powder must possess sufficient lubricity to permit rapid insertion of hand into the glove and must be of sufficiently fine particle size to permit such lubricity.

(6) It must be inexpensive and readily available.

(7) It must be non-irritating to skin.

Talc was among the earliest surgical glove powders used by the medical profession. However, since the report by Antopol (Lycopodiumgranuloma Ach. Path. 16, pg. 326 (1933)) that talc caused granulomas in the body, the use of talc as a glove powder was rapidly abandoned. Talc was replaced by starch glove powders since starch was known to be biodegradable and was not believed to cause granulomas or other aggravating conditions within the body. Currently, a widely used commercial surgical glove powder is specially treated homogeneous anylose which contains about 2% magnesium oxide to prevent clumping of the powder.

However, starch glove powders have a number of disadvantages. They offer high resistance to flow and they tend to gelatinize or agglutinate in the presence of hot water thereby creating problems when they are sterilized in a steam autoclave. Ordinarily, the starch must be treated in some way to minimize these properties. For example, as shown in U.S. Pat. 2,626,257, the starch may be treated with an agent, such as epichlorohydrin, which partially etherifies the starch in order to make the powder free flowing after steam sterilization.

Starch is also an excellent nutrient medium for virtually all vegetative bacteria such as various pathogenic microorganisms and is objectionable for that reason.

According to Lee and Lehman (Surgery, Gynecology, and Obstetrics 84, pgs. 689–695 (1947)), starch, unlike talc, was completely absorbed within the peritoneal cavity without causing adhesions. This conclusion was challenged by Sneierson and Woo (Annals of Surgery 132, pgs. 1045–1050 (1955)) who reported two cases of large granulomas occurring in surgical wounds as a result of starch powder contamination. McAdams (Surgery 39, pgs. 329–336 (1936)) reported three cases of intraperitoneal granulomas caused by starch glove powder. The Saxens (Acta Pathology Microbiology Scand. 64, pgs. 55–70 (1965)) postulated that the magnesium oxide which acts as an anti-clumping material was causing the lesions. Myllarniemi and Frilander (Journal of the International College of Surgeons 44, No. 6681, pgs. 677–681 (1965)) concluded that the harmful effects of starch glove powders containing magnesium oxide might be due to a combined effect of two irritating constituents. Other publications which indicate the serious concern of the medical profession over granulomas traced to starch glove powders are those of Lehman and Wilder (Journal of Abdominal Surgery 4, No. 3, pgs. 77–80 (1962)), Webb and Regan (Archives of Surgery 84, No. 3, pgs. 282–285 (1962)), and Walczak and Collura (American Journal of Surgery 103, No. 5, pgs. 611–612 (1962)).

Despite the aforementioned disadvantages associated with starch glove powders, they are still used by the medical profession due to the unavaliability of an improved substitute. It becomes apparent that a dusting powder which does not suffer these disadvantages of starch powders would be a welcome addition to the arsenal of the medical profession. It is an object of this invention to provide such a dusting powder. It is a further object to provide such a dusting powder which has all of the aforementioned desirable properties of a medical dusting powder.

FIELD OF THE INVENTION

This invention is in the field of the process for producing finely divided polyglycolic acid comprising dissolving said polyglycolic acid in an inert solvent by heating the solvent containing the polyglycolic acid and cool-

ing the solution to room temperature and adding a non-solvent to the polyglycolic acid solution in order to precipitate the polyglycolic acid in finely divided form. The finely divided powdery material is filtered from the supernatant liquid, washed, dried and ground up in order to break up any agglomerates which may be present.

DESCRIPTION OF THE PRIOR ART

The known prior art is represented by the U.S. Pats. 2,676,945 and 2,668,162 as well as the U.S. Pat. 3,297,-033. These references are each incorporated herein by reference.

SUMMARY OF THE INVENTION

This invention relates to a process for producing finely divided polyglycolic acid comprising dissolving said polyglycolic acid in an inert solvent by heating the solvent containing the polyglycolic acid, cooling the solution to room temperature, adding a non-solvent for the polyglycolic acid to the solution, filtering the solid finely divided particles of polyglycolic acid from the supernatant liquid, washing the polyglycolic acid particles with a non-solvent, drying and grinding the polyglycolic acid to break up the agglomerates.

Polyglycolic acid can be prepared according to the process of any of the above cited references and may then be dissolved in an inert solvent by heating the solvent to a temperature not in excess of its boiling temperature. Polyglycolic acid is insoluble in a substantial number of liquids which are normally solvents for other materials but there are a few solvents in which polyglycolic acid can be dissolved such as dimethyl sulfoxide, hexafluoroacetone sesquihydrate, dimethyl formamide, hexafluoroisopropyl alcohol. The preferred solvent for the polyglycolic acid is dimethyl sulfoxide. The amount of the polyglycolic acid dissolved in the selected solvent is not critical and may be varied from a few parts to the amount required to saturate the solution at the temperature selected for dissolving the polyglycolic acid therein. Certain solvents, such as the fluorinated solvents will dissolve the polyglycolic acid without heating but others may require heating to make the slurry.

A non-solvent is selected for addition to the polyglycolic acid solution in order to cause the polyglycolic acid to precipitate from the solution in finely divided form. Among the non-solvents which may be used in the practice in the process of the present invention is water, lower aliphatic monohydric alcohols such as methanol, ethanol, propanol, isopropanol, and the like. The non-solvent is added to the solution of the polyglycolic aci dafter it has been cooled down to about room temperature by use of an ice bath in order to get a slurry of the finely dispersed polyglycolic acid. It would be preferred to stir the cooling solution as to distribute the polyglycolic acid uniformly throughout the slurry. There is then added to the slurry the non-solvent and the precipitated polyglycolic acid is filtered under vacuum from the slurry. It is then desired to wash the filtered material with a suitable non-solvent and to vacuum dry the material at a slightly elevated temperature. The thus dried and washed material is placed in a suitable attritor such as a micro-pulverizer and ground for a few moments in order to break up any agglomerates that may be present. The non-solvent should be at least partially soluble in the solvent and preferably miscible with the solvent.

In order that the concept of the present invention may be more completely understood the following examples are set forth in which all parts are parts by weight unless otherwise indicated:

Example 1

Into a suitable mixing vessel containing 2000 parts of dimethyl sulfoxide there is added 40 parts of a polyglycolic acid such as that prepared by one of the references set forth hereinabove. The dispersion is heated to 150° C. in order to dissolve the polyglycolic acid. Thereupon the solution is cooled to room temperature by use of an ice bath to get a slurry of finely dispersed polyglycolic acid. There is then added 400 parts of the slurry to a Waring Blendor. There is then added quickly 400 parts of water with constant stirring for about one-half of a minute. The slurry is then filtered under vacuum and washed with isopropanol and vacuum dried overnight at 60° C. The thus washed and dried material is placed in a micropulverizer and ground for about 30 seconds in order to break up the agglomerates. The resulting powdery material had less than 1% that was of the size of about 30 microns and had less than 15% that was within the range of about 10 to 15 microns and had more than 80% that was in the range of 1.5 to about 8 microns.

Example 2

A slurry of the polyglycolic acid is prepared in dimethyl sulfoxide as in Example 1 but the slurry is centrifuged and the solvent is decanted and replaced with a non-solvent namely benzene. The mixture of the benzene and the polyglycolic acid is then centrifuged and the procedure is repeated 5 times. Finally additional benzene is added and mix is freeze dried and when dry the powdery material is ground briefly in the micropulverizer as in the first example in order to break up the agglomerates. A comparable finely divided powdery polyglycolic acid material is produced.

Example 3

Example 1 is repeated in all essential details except that in the place of the dimethyl sulfoxide there is substituted an equivalent amount of hexafluoroisopropanol and because of the solubility characteristics of said solvent no heating is necessary or used.

Example 4

Example 3 is repeated in all essential details except that in the place of the hexafluoroisopropanol there is substituted an equivalent amount of hexafluoroacetone sesquihydrate and again because of the fluorinated characteristic of the solvent no heating is necessary.

High molecular weight polyglycolic acid is so strong and tough that it cannot be readily pulverized to the particle sizes shown in Example 1 by ordinary grinding techniques. This polyglycolic acid powdery material when used in form as a surgeons dusting powder for his surgical gloves if introduced into the body will be completely dissolved causing no adverse affect whether used as a lubricant filler, hemostat or wound treatment. The U.S. Pat. 3,297,033 teaches the polyglycolic acid is absorbable in living tissue.

We claim:

1. A process for producing finely divided polyglycolic acid comprising dissolving said polyglycolic acid in an inert solvent selected from the group consisting of dimethyl sulfoxide, hexafluoroacetone sesquihydrate, dimethyl formamide, and hexafluoroisopropyl alcohol, adding a non-solvent for the polyglycolic acid to the solution thereby precipitating said polyglycolic acid in finely divided form, filtering the solid finely divided particles of polyglycolic acid from the supernatant liquid, washing the polyglycolic acid particles with a non-solvent, drying and deagglomerating by mechanical attrition of the polyglycolic acid.

2. The process according to claim **1** in which the solvent is dimethyl sulfoxide.

3. The process according to claim **1** in which the solvent is hexafluoroacetone sesquihydrate.

4. The process according to claim **1** in which the solvent is hexafluoroisopropanol.

5. The process according to claim **1** in which the non-solvent is water.

6. The process according to claim **1** in which the non-solvent is isopropanol.

7. The process according to claim 1 in which the non-solvent is ethanol.

8. A process for producing finely divided polyglycolic acid comprising dissolving said polyglycolic acid in an inert solvent selected from the group consisting of dimethyl sulfoxide, hexafluoroacetone sesquihydrate, dimethyl formamide, and hexafluoroisopropyl alcohol by heating the solvent containing the polyglycolic acid, cooling the solution to room temperature, centrifuging the solution, decanting the solvent, replacing the solvent with a non-solvent, freeze drying the mix and grinding the resulting dry material to break up agglomerates.

9. The process according to claim 8 in which the solvent is dimethyl sulfoxide and the non-solvent is benzene.

References Cited

Vogel Practical Organic Chemistry, 3rd ed., p. 125.

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U.S. Cl. X.R.

260—484 A

UNITED STATES PATENT OFFICE
CERTIFICATE OF CORRECTION

Patent No. 3,781,349 Dated December 25, 1973

Inventor(s) Wallace Burton Ramsey and Darwin Fiske DeLapp

It is certified that error appears in the above-identified patent and that said Letters Patent are hereby corrected as shown below:

1. Column 1 line 33. Delete the punction " . " after the word application, insert the following: --now U.S. Patent 3,728,739 issued April 24, 1973.--.

2. Column 2 line 10. Delete the word "anylose" and in its place substitute the following: --amylose--.

3. Column 3 line 50. Delete the words "aci dafter" and substitute in their place the following: --acid after--.

4. Column 7 line 47. Delete the word "surgeons" and substitute in its place the following: --surgeon's--.

Signed and sealed this 24th day of September 1974.

(SEAL)
Attest:

McCOY M. GIBSON JR.
Attesting Officer

C. MARSHALL DANN
Commissioner of Patents

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