PROCESS FOR CLEANING POLYGLYCOLIC ACID FILAMENTS
USEFUL AS ABSORBABLE SURGICAL SUTURES
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PROCESS FOR CLEANING POLYGLYCOLIC ACID FILAMENTS USEFUL AS ABSORBABLE SURGICAL SUTURES

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10 Claims

ABSTRACT OF THE DISCLOSURE

Polyglycolic acid filaments containing surface soil are effectively cleaned by contacting them with ultrasonically agitated solutions, said solutions comprising a solvent and from 1% to 10% by weight of a biologically innocuous surfactant.

BACKGROUND OF THE INVENTION

U.S. Patent 3,297,033 (incorporated herein by reference) discloses that polyglycolic acid can be used to prepare acceptable absorbable sutures for use in humans and animals thereby affording a long sought after substitute for the "catgut" sutures heretofore used for this purpose. Polyglycolic acid is typically spun into a multifilament which is separated into bundles of appropriate dimensions for use as sleeves and cores in standardized braiding procedures. The strands and cores are then braided to form a suture braid of the desired diameter.

Both prior to the braiding step and, in particular, during the braiding step, the filaments are subjected to processing conditions which may, on occasion, cause surface soiling of the filaments. This surface soiling is reflected by the change in color of the filaments from an unblanished pearl color (the natural color of polyglycolic acid) to a substantially uniform grayish color. Such coloration indicates that the filaments are contaminated with oily or greasy substances to which the filaments can be exposed during their processing. This discoloration and contamination of the suture is intolerable in a product which must not only meet the stringent aesthetic standards of the medical profession but which is also destined for implantation in the living tissue of the body. Obviously to meet such requirements clean filaments are essential. The term "clean" when used with respect to the polyglycolic acid braids means braids which have a uniform pearl color, and which are substantially free from oily, greasy substances, and other similar foreign matter.

The cleaning of a medical product such as a suture raises many problems not found in the more typical industrial cleaning applications. For example, the cleaning procedure must produce no adverse effect on either the package or in-vivo tensile strength of the suture. Such effects might be expected if excessive temperatures or residence times in cleaning baths are used or if the cleaning agent in some way interacts with the suture. Moreover, there is the possibility of cleaning agent remaining on the suture from the cleaning operation which may be toxic or irritating to living tissue when the suture is implanted herein. Furthermore, since the product is absorbable, it must be thoroughly cleaned. Therefore, when the suture is a braid with numerous interstitial voids, penetration of the cleaning agent into these voids must be assured to guarantee removal of soil from all of the filament surfaces.

The above problems can be conveniently overcome by employing the cleaning process of this invention.

SUMMARY OF THE INVENTION

This invention relates to a process for cleaning filaments of polyglycolic acid which are useful as absorbable surgical sutures. In accordance with said process, polyglycolic acid filaments of acceptable cleanliness are prepared by contacting polyglycolic acid filaments having surface soil- ing with an ultrasonically agitated solution comprising:

(a) a liquid selected from the group consisting of water and organic solvents having an affinity to dissolve, emul- sify, or entrain the oily, greasy contaminant on the surfaces of the poliglycerolic acid filament; and

(b) a surfactant which is biologically innocuous towards living tissue, the amount of said surfactant in the solution ranging from about 1% to about 10% by weight; and

at temperatures ranging from 20°C to 100°C for at least about 10 seconds whereby said surface soilings is dis- solved, emulsified, or entrained in said solution and there- by removed from contact with the filament when the solu- tion is removed from contact with the filament.

A surfactant is "biologically innocuous" towards living tissue when it is substantially non-toxic and non-inflam- matory towards the tissue so as to safely permit its usage within the body.

The surface soilings may be contacted with the solution one or more times although ordinarily a single contact is sufficient to adequately clean the filament.

It has been found that ultrasonic agitation of the above described solution is essential for achieving adequate cleaning of the braid. Mechanical agitation and other conventional methods of agitation have proved unsuccessful. Whereas filaments can be adequately cleaned in a few seconds using ultrasonic agitation of the bath, the same filaments can sit for hours in the same bath without ultrasonic agitation with little, if any, detectable cleaning of the filament taking place.

It has been further found that if feasible residence times in the cleaning bath are to be obtained, it is essential that the bath contain a surfactant. Whereas filaments can be adequately cleaned in an ultrasonically agitated solution containing a surfactant in a very short time, the same filament when placed in an ultrasonically agitated bath not containing surfactant can remain dirty even after several hours in the bath.

It thus becomes apparent that ultrasonic agitation with- out addition of a surfactant to the bath is unsatisfactory. Similarly, addition of a surfactant to the bath without ultrasonic agitation is also unsatisfactory. It is only when ultrasonic agitation is applied to a bath which contains a surfactant that adequate cleaning is achieved. In such cases cleaning is achieved with bath residence times as short as 10 seconds. When filament is being processed on a continuous basis, it is, of course, desirable that residence times in a cleaning bath be as short as possible in order that the filament cleaning step not become a "bottleneck" in the overall process.
Brief Description of the Drawing

The figure is a schematic flowsheet depicting an embodiment of the process of this invention.

Description of the Preferred Embodiments

Process

A polyglycolic acid braid 10 is prepared by conventional methods and wound on creel 11. Braid 10 contained some surface soiling due to prior processing and had a grayish color. Braid 10 is then passed through the solvent-surfactant cleaning bath 12 contained in tank 13 by Godets 14 and 15, being taken up by winder 16. Tank 13 is equipped with appropriate ultrasonic transducers which are connected to ultrasonic generator 13B to ultrasonic agitation of bath fluid 12. Clean braid 17 emerges from bath 12. Winder 16 containing clean braid 17 is then dried in oven 18 to remove bath liquid remaining on the braid.

Bath 12 is continuously recirculated by pump 19 through filter 20 which removes suspended matter in bath 12. Bath overflow 21 is sent to bath still 22 where it is distilled to produce an overhead vapor stream 23 of substantially pure solvent and a bottoms stream 24 consisting of the soil removed from the braid surface as well as some of the surfactant from bath 12. Vapor stream 23 is passed through condenser 25. Condensate 26 is collected in storage tank 27. Make-up surfactant 28, preferably already solubilized in a small amount of solvent, is then fed to tank 27 in an appropriate amount where it is intimately mixed with condensate 26 to form stream 29 which is recirculated by pump 30 to bath 12.

In another embodiment of the inventive process, the process is as heretofore described except that the cleaned braid 17 emerges from bath 12 and passes into a second tank which contains a surfactant-free solvent of the types described hereinbelow which solvent is preferably the same solvent and is used in bath 12. The purpose of this second bath is to rinse away residual surfactant picked up by braid 17 in bath 12. Ordinarily, one rinse bath will suffice although more than one may be used particularly if the surfactant concentration of bath 12 is high. After braid 17 leaves the rinse baths it is dried in oven 18 to remove solvent.

It is preferable that the amount of surfactant or solvent on the finished suture braid be sufficiently low so as to be non-toxic and non-inflammatory to tissue.

Bath Solvents

Among the illustrative organic solvents which can be employed in the process of this invention are:

1. The aromatics such as benzene, toluene, and xylene
2. Cyclic aliphatics such as cyclopentane, cyclohexane, cycloheptane, and cyclooctane
3. Aliphatics such as hexane, heptane, and butane
4. Chlorinated aliphatics such as dichloromethane, chloroform, carbon tetrachloride, 1,1-dichloroethane, 1,1,1-trichloroethane, and 1,2-dichloroethylene
5. Ketonic solvents such as acetone, methylisobutylketone, and cyclohexanone
6. Kerosene
7. Terpine; and
8. Stoddard solvent

Other solvents having a high affinity for grease and oil are, of course, also operable in the process of this invention. Xylene is a preferred solvent.

Water although not having an affinity for grease and oil by itself, is very suitable when mixed with a surfactant. Due to the low cost and high availability of water, it also represents a preferred solvent.

Surfactants of the anionic, nonionic, and cationic variety are suitable for use in the process of this invention. Due to the difficulty of totally removing surfactant from the cleaned filament, it is essential that the surfactant selected be non-toxic and non-inflammatory towards living tissue and in general be biologically innocuous. Illustrative surfactants are the nonionic Spans (Atlas Industries) such as sorbitan monolauroate, sorbitan monooleate, sorbitan monostearate, sorbitan tristearate, sorbitan monolaurate, sorbitan trilaurate; the nonionic Tweenes (Atlas Industries) such as polyoxyethylene sorbitan monooleate, polyoxyethylene sorbitan monostearate, polyoxyethylene sorbitan monooleate, polyoxyethylene sorbitan monooleate, and sorbitan tristearate, sorbitan monooleate, sorbitan tritallowste; and the anionic surfactants such as sodium bis(hydroxyethyl)ammonium cyanide (American Cyanamid).

The selection of the appropriate surfactant will in turn depend upon which solvent has been selected. Since it is essential to obtain solubility of the surfactant in the solvent, a surfactant which is hydrophilic is preferred when the solvent is one which is lipophilic is preferred when the surfactant is of an organic origin. A particularly useful method of matching surfactant and solvent is through the use of the HLB (hydrophilic-lipophilic balance) system developed by Atlas Industries. This system assigns a surfactant a numerical place on a scale running from 0 to 20. This number is called the HLB value. The lower the HLB value, the more hydrophilic (water-loving) is the material. Those in the HLB range of 0-10 are intermediates. In general, materials of low HLB value tend to be oil-soluble, and those of high HLB tend to be water-soluble. The procedure for procuring the HLB value for a particular surfactant is well-known and does not bear repeating herein.

If water is the solvent of choice, surfactants having a HLB value in excess of ten, and preferably in excess of 14, are suitable since sufficient solubility of the surfactant is achieved to give the desired efficacy. In the case of water, a preferred surfactant is polyoxyethylene sorbitan monooleate containing 20 moles of ethylene oxide. This surfactant has an HLB value of 15 and is sold commercially as Tween-80 by Atlas Industries. This surfactant is preferred not only because it is readily soluble in water but also because it is known to be physiologically innocuous and has already been approved by the Federal Food and Drug Administration for internal consumption in such items as food and candy. It has also been approved for use in intravenous and intramuscular pharmaceutical preparation such as those of tetracycline and chlorotetra-cycline. This surfactant is listed under the name Polyethylene 80 in the Merck Index, 7th ed. (1960) at pg. 833 and in the U.S. Pharmacopoeia XV at pg. 566, said publications incorporated herein by reference.

If an organic solvent is to be used, surfactants having an HLB value less than ten, and preferably less than 5 are preferred. Preferred surfactants in this case are sorbitan monooleate (HLB value of 4.7) and sorbitan monolauroate (HLB value of 4.3), said surfactants sold commercially as Span-60 and Span-80, respectively, by Atlas Industries. These surfactants are preferred not only for their high solubility in organic solvents but because they also are known to be biologically innocuous having properties similar to Tween-80.

The amount of surfactant may vary from about 1% to about 10% based on the total weight of the cleaning bath. An amount of 1% is required for a suitable rate of cleaning. Amounts in excess of 10% do not appreciably increase the rate of cleaning and have the dis-
advantage of making it more difficult to thoroughly remove the surfactant from the filament.

As the surfactant concentration is increased from 1% to 10%, the rate of cleaning is improved; however, the removal of the surfactant becomes a greater problem. Therefore, it is desirable to use as small an amount of surfactant as is compatible with effective cleaning. A preferred amount is about 1 to 2%.

### Ultrasonic agitation

The cleaning solution must be ultrasonically agitated as discussed heretofore. A solution is ultrasonically agitated when high frequency, mechanical vibrations are transmitted into, and substantially uniformly, through the solution. High frequency or ultrasonic vibrations are similar to audible sound, but the frequencies used are generally somewhat above a level that can be heard. Since sound is a compressional wave, the action of this high frequency energy in a liquid may be considered as the rapid generation and violet collapse of minute bubbles. Countless small but intense impacts erode surface soil from the immersed polyglycolic acid filament. This action is called "cavitation." It wears away surface soil.

In a typical ultrasonic cleaning operation, a generating unit provides electrical energy at a desired frequency. This energy is fed to one or more transducers wherein the electrical energy is converted into mechanical energy (vibrations) which are then transmitted into the solution which is ordinarily contained in a tank. A generator will typically produce frequencies ranging from 10 to 120 kilocycles with 10, 25, 40, 90, and 120 kilocycle generators representing a cross section of typical commercially available ultrasonic generators. Higher frequencies produce a great number of small bubbles in the solution. Lower frequencies produce a smaller number of large bubbles and more intense energy. The cleaning efficiency will depend on the solvent media used, the frequency selected and the item to be cleaned. With respect to polyglycolic acid sutures and the cleaning solutions of this invention, frequencies in the range of 25 to 40 kilocycles are preferred.

The power level at which the electrical energy of constant frequency is sent to the transducer will vary depending upon the number of transducer elements used for effective transmission of mechanical energy into the solution. This, of course, depends on the quantity of solution to be ultrasonically agitated. As a rule, as solvent volume increases, the number of transducers required also increases warranting a corresponding increase in power input. For example, a large solvent tank, i.e. 16" x 16" x 16" may require from 18 to 24 transducers for effective cleaning with a power output of about 1000 watts being required. On the other hand, a smaller tank, i.e. 8" x 10" x 10" may only require 6 to 12 transducers for effective cleaning with a power output of only 500 watts being required.

The power output of a generator is readily adjusted by installing a rheostat in the generator input line. For most operations power outputs of 50-1000 watts are sufficient. However for very large volumes of solvent larger power inputs may be required.

The simplest ultrasonic cleaning system consists of an ultrasonic generator and a transducerized tank. In this case, transducer elements are mounted externally to the bottom or sides of the tank leaving the inside surfaces of the cleaning chamber smooth. Alternatively, immersible type transducers may be mounted directly in the solution in the tank. These transducers may be in the form of hermetically sealed stainless steel cases which contain the active elements mounted to one inner side. Immersible transducers are preferred in larger systems.

### Bath conditions

Bath temperatures can vary from 20° C. to 100° C. Temperature appears to have no significant effect on the cleaning procedure. In a preferred embodiment, the bath is initially at room temperature (20-25° C) until ultrasonic vibration of the bath is initiated when the temperature can gradually rise to as high as 70° C., and typically to 40-60° C.

Bath temperatures in excess of 100° C. must be avoided since higher temperatures, particularly when the solvent is water, can seriously degrade the polyglycolic acid causing appreciable losses in the package and in vivo tensile strength of the resulting sutures. The residence time of the filament in the bath must be at least 10 seconds for suitable cleaning. The filament can be left in the bath for as long as desired. However, in the case where water is the solvent, short residence times are preferred because of the tendency of water to degrade polyglycolic acid after prolonged contact therewith, particularly when such contact is at elevated temperatures.

It is ordinarily preferable to use as short residence times as possible in order to avoid any slow down in the overall suture manufacturing process. Residence times of 10 to 100 seconds are quite suitable with 10 to 20 seconds representing a preferred residence time.

The following examples are provided to further illustrate the invention.

### EXAMPLE 1

A length of braided size 3–0 polyglycolic acid suture was prepared in a conventional manner. The suture was artificially surface soiled to produce a uniformly gray color with occasional darker highlights; the usual color of clean braid is an unblemished pearl or light cream.

The soiled suture length was then drawn through xylene which contained 1% sorbitan monooleate (Span-80, Atlas Industries) dissolved therein. The xylene/Span-80 solution was contained in a 4" x 18" x 5" (about 2 gallons) tank and was ultrasonically agitated using (1) a Branson ultrasonic generator, model 520, 40 kilocycles, having an input of 440 watts at 115 volts, 60 cycle, single phase, and an output of 700 watts on peak pulses and 350 watts average and (2) a Branson Sonogen-Z8 cleaning tank, Model AT-84-8S, 316L stainless steel (16 gauge) containing 8 transducer elements.

The residence time of the suture in the bath was about 10 seconds. The original temperature of the bath was about 23° C.; however, the ultrasonic vibration within the bath raised its temperature to about 60° C. during treatment.

The cleaned suture was then dried in a forced draft oven for 2 hours at 40° C. The color of the suture was unblemished pearl. A comparison of the cleaned and uncleaned braid revealed a striking difference in the color of the two braids thereby showing the efficacy of the cleaning procedure. The cleaned braid was implanted in rabbits using known test procedures. No discernible differences in either in-vivo strength or effect upon living tissue were observed as compared to ordinary braid which did not require cleaning thereby indicating that the cleaning process of this invention produces no adverse effect upon the properties of the suture.

### EXAMPLES 2 TO 17

Following substantially the same procedure as in Example 1 the effect of a variety of process variables upon braid cleaning was investigated. Results are shown below in Table I.
TABLE I

<table>
<thead>
<tr>
<th>Ex. No.</th>
<th>Solvent</th>
<th>Surfactant</th>
<th>Percent (C.)</th>
<th>Temp. (°C)</th>
<th>Braid residence time (seconds)</th>
<th>Suture site</th>
<th>Color in</th>
<th>Color out</th>
<th>Adequately clotted</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>Xylene</td>
<td>Sorbitan monocaproate</td>
<td>10</td>
<td>28</td>
<td>12</td>
<td>1-2 Gray</td>
<td>Pearl</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>do</td>
<td>Sorbitan monooctanoate</td>
<td>5</td>
<td>55</td>
<td>60</td>
<td>2-6 Gray</td>
<td>do</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>do</td>
<td>Sorbitan trioleate</td>
<td>2</td>
<td>100</td>
<td>20</td>
<td>1-8 Gray</td>
<td>do</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Carbon tetrachloride</td>
<td>Sorbitan monooctanoate</td>
<td>3</td>
<td>55</td>
<td>10</td>
<td>3-8 do</td>
<td>do</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Ethylformarnide</td>
<td>Sorbitan monooctanoate</td>
<td>1</td>
<td>30</td>
<td>120</td>
<td>1-9 do</td>
<td>do</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Tartrazine</td>
<td>Sorbitan monooctanoate</td>
<td>1</td>
<td>40</td>
<td>10</td>
<td>6-6 do</td>
<td>do</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>1,1-trichoethoxyhydrate</td>
<td>Sorbitan monooctanoate</td>
<td>1</td>
<td>40</td>
<td>80</td>
<td>2-6 Gray</td>
<td>do</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>1,1,1-trichoethoxyhydrate</td>
<td>Sorbitan monooctanoate</td>
<td>3</td>
<td>50</td>
<td>100</td>
<td>5-9 do</td>
<td>do</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>Acetone</td>
<td>Sorbitan monooctanoate</td>
<td>1</td>
<td>30</td>
<td>25</td>
<td>6-9 do</td>
<td>do</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>Water</td>
<td>Polyethylene sorbitan monooctanoate 1</td>
<td>1</td>
<td>40</td>
<td>10</td>
<td>1-9 Gray</td>
<td>do</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>do</td>
<td>do</td>
<td>5</td>
<td>25</td>
<td>120</td>
<td>1-9 do</td>
<td>do</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>do</td>
<td>do</td>
<td>10</td>
<td>35</td>
<td>25</td>
<td>1-9 Gray</td>
<td>do</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>do</td>
<td>Polyethylene sorbitan monooctanoate 2</td>
<td>1</td>
<td>50</td>
<td>10</td>
<td>6-6 do</td>
<td>do</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>do</td>
<td>Lecithin sulfate</td>
<td>5</td>
<td>55</td>
<td>10</td>
<td>6-0 Gray</td>
<td>do</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>do</td>
<td>Stearamide propyldimethyl-3-hydroxyethyl</td>
<td>5</td>
<td>100</td>
<td>10</td>
<td>6-0 do</td>
<td>do</td>
<td>Yes</td>
<td></td>
</tr>
</tbody>
</table>

1 With occasional darker highlights.
2 30 moles of ethylene oxide.

We claim:

1. A process for removing surface soil from a filament of polyglycolic acid destined for use as an absorbable surgical suture which comprises contacting said soiled filament at least once with an ultrasonically agitated solution comprising:
   (a) a solvent selected from the group consisting of: water and an organic solvent having an affinity to dissolve, emulsify or entrain oily, greasy substances; and
   (b) a surfactant which is biologically innocuous towards living tissue, the amount of said surfactant in the solution ranging from about 1% to about 10% by weight of the total solution at temperatures ranging from about 20° C. to 100° C. for at least about 10 seconds.

2. The process of claim 1 wherein the solvent is selected from the group consisting of water, aromatics, cyclic aliphatics, aliphatics, chlorinated aliphatics, ketones, terpentine, kerosene, and Stoddard solvent.

3. The process of claim 1 wherein the solvent is water.

4. The process of claim 3 wherein the surfactant is polyoxyethylene sorbitan monooleate containing about 20 moles of ethylene oxide and is present in the amount of about 1%.

5. The process of claim 4 further including the step of contacting said filament with water after it has been contacted with said ultrasonically agitated solution.

6. The process of claim 1 wherein the solvent is xylene.

7. The process of claim 6 wherein the surfactant is sorbitan monooleate.

8. The process of claim 7 wherein the surfactant is present in the amount of about 1%.

9. The process of claim 8 wherein the contact time is about 10 to 20 seconds.

10. The process of claim 9 further including the step of contacting said cleaned filament with xylene.

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MORRIS O. WOLK, Primary Examiner
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U.S. Cl. X.R.

134—15, 17
UNITED STATES PATENT OFFICE
CERTIFICATE OF CORRECTION

Patent No. 3,600,223 Dated August 17, 1971

Inventor(s) Arthur Glick et al.

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

Column 5, line 22, "violet" should read -- violent --.
Table I, Ex. No. 3, "Gray" should read -- Gray1 --; Table I, Ex. No. 4, ".-0" should read -- 3-0 --.

Signed and sealed this 11th day of April 1972.

(SEAL)
Attest:

EDWARD M. FLETCHER, JR.
Attesting Officer

ROBERT GOTTSCHALK
Commissioner of Patents