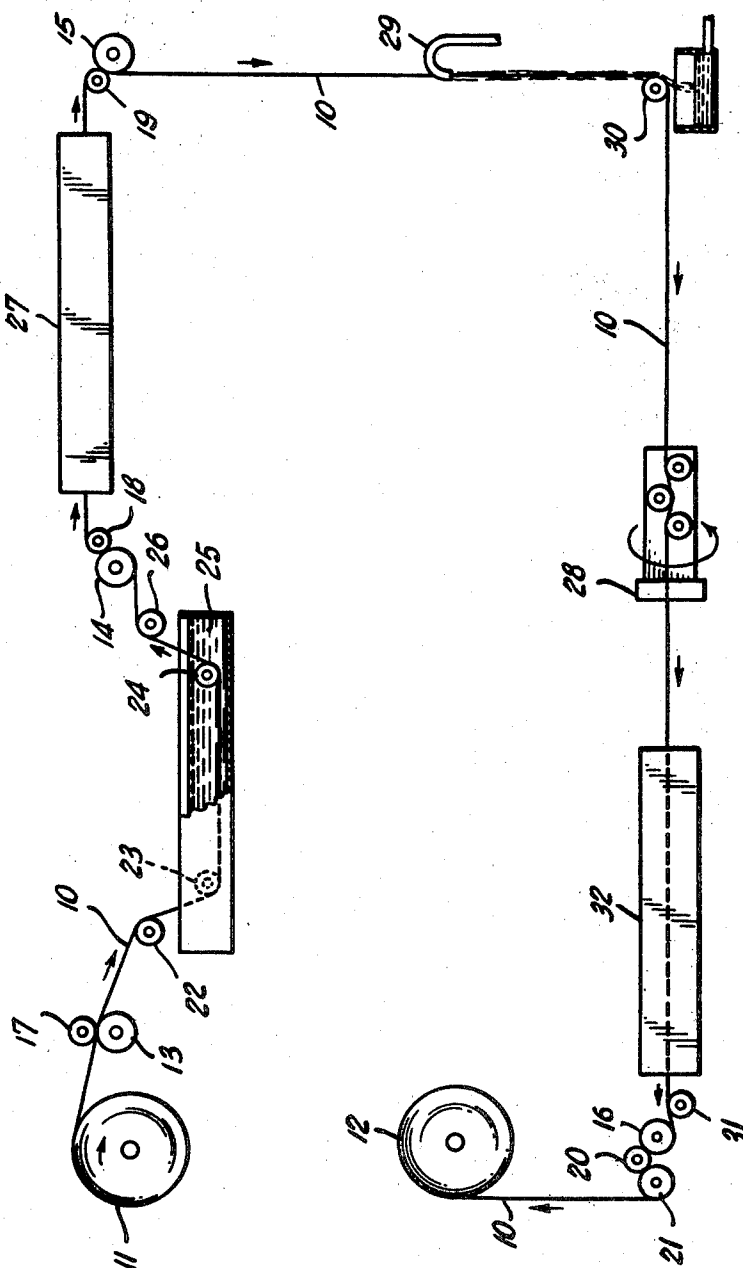


June 15, 1965

E. J. GRISET, JR
SIMULTANEOUS ALDEHYDE, CHROME AND AROMATIC ALCOHOL
OR QUINONE TANNAGE OF SPUN COLLAGEN FIBER
Filed May 29, 1963

3,189,401



INVENTOR.
ERNEST J. GRISET JR.
BY

Lynn, Mann & Jangorath
ATTORNEYS

1

3,189,401

SIMULTANEOUS ALDEHYDE, CHROME AND AROMATIC ALCOHOL OR QUINONE TANNAGE OF SPUN COLLAGEN FIBER

Ernest J. Griset, Jr., Bound Brook, N.J., assignor to Ethicon, Inc., Somerville, N.J., a corporation of New Jersey

Filed May 29, 1963, Ser. No. 284,255

12 Claims. (Cl. 8—94.11)

The present invention relates to the treatment of collagen and the product so obtained with particular emphasis on the method of chemically treating substantially pure collagen filaments and strands for surgical uses such as suturing and ligating.

For the sake of clarity, the terms used herein are defined as follows:

The term "tendon collagen fibril" as used herein means a thread-like collagen structure derived from beef tendon that is round in cross section. These fibrils in the completely dehydrated state measure about 500 to 2000 Angstroms in diameter.

The term "swollen tendon collagen fibril" as used herein means a collagen fibril derived from beef tendon that has been swollen in acid solution. The diameters of swollen collagen fibrils range from less than 5000 Angstroms to about 90,000 Angstroms.

The term "monofilament" as used herein means a single thread of oriented collagen fibril as extruded through a single orifice in a spinnerette.

The term "multifilament" as used herein means a group of individual separate filaments extruded through a spinnerette.

The term "strand" as used herein means a group of filaments that have been united to form a unitary structure.

The protein collagen has exceptional tensile strength and is essentially non-antigenic, which properties have resulted in the wide use of substantially pure collagen strands in surgery. It is well known that collagen sutures which have been implanted in the human body are slowly attacked by proteolytic enzymes with a resulting decrease in tensile strength and ultimate absorption. It is also known that the rate of absorption can be controlled by treating the collagen strand with chemical reagents such as chromium salts. Thus, chromium treated sutures have been prepared from sheep intestines which retain one-half of their original tensile strength from 7 to 10 days after implantation.

A particular problem exists, however, in the case of extruded collagen strands. It has been noted that collagen strands obtained by extruding a dispersion of collagen fibrils into a coagulating bath are characterized by a rapid in vivo digestion. Thus, a collagen suture prepared under conditions that involve swelling collagen fibrils in acid solution, extruding the swollen collagen fibrils to form a filament and subsequently dehydrating the swollen collagen fibrils is more rapidly attacked by proteolytic enzymes than sutures prepared from sheep intestines.

While chromium has been used to increase the initial wet tensile strength of a collagen strand, it has only a minor effect on the rate of tensile strength loss of the collagen at the concentrations employed in the present invention. Correspondingly, it is known that formaldehyde alone will increase the initial wet strength of collagen; but, if formaldehyde alone is used in the amount required for adequate in vivo properties, the strand is embrittled and the knot strength is lowered. A solution of polyhydric phenol and/or quinone, if used alone, provides a collagen strand which has inadequate initial wet strength and which has an excessively rapid rate of in vivo tensile strength

2

loss. However, when the said solution is followed by a second solution containing formaldehyde, the said rate is decreased. The use of a combination of polyhydric phenol and/or quinone solution and formaldehyde solution, however, will not afford a suture having requisite initial wet strength nor a satisfactory rate of in vivo tensile strength loss.

Improvements over such earlier developments have been described in application Serial No. 85,302 (now ETH 201) of John Kurilla and application Serial No. 85,289 (now ETH 202) of Richard L. Kronenthal. As described in application Serial No. 85,302, two distinct solutions are required to provide the desired strength, in vivo characteristics and uniformity of product. Initially, a bonded collagen multifilament is treated with a solution of a polyhydric phenol, and then with a second solution containing an aldehyde and a chromium salt. Alternatively, the collagen can be treated with the solution containing an aldehyde and a chromium salt, thence with the polyhydric phenol solution. A related disclosure is made in application Serial No. 85,289, wherein a quinone is used in place of the polyhydric phenol.

Thus, it has been considered necessary to use two separate solutions to obtain collagen sutures of such desired properties.

Surprisingly, it has now been found that two consecutive treating steps are not required to produce collagen sutures of at least comparable quality. It has been found that a continuously extruded collagen strand can be treated with a solution containing an aldehyde, a chromium salt and a polyhydric phenol and/or a quinone.

It is an object of the present invention, therefore, to chemically modify collagen and thereby increase its resistance to enzymatic degradation.

It is another object of the invention to provide a chemically treated collagen suture having a suitable wet tensile strength.

Still another object of the invention is to produce an extruded chemically treated absorbable collagen suture that will retain sufficient tensile strength under the conditions of use to accomplish its purpose and be absorbed in the body after the wound has healed when the suture is no longer necessary.

A further object is to provide an extruded chemically treated collagen suture of controlled absorption character when used in a body.

A particular object is to provide a method for controlling in vivo tensile strength loss rates of chemically-modified collagen when used in a body.

Another particular object is to provide a method in which a single tanning solution can be used to chemically modify collagen, thereby making possible sutures of controlled absorption in a body.

Other objects will be apparent from the following description.

The foregoing objects are realized by a method of treating a bonded collagen multifilament with a solution containing at least one of each of the following components:

- (a) an aldehyde,
- (b) a chromium salts, and
- (c) a polyhydric phenol and/or a quinone.

Component (a), as indicated above, is an aldehyde. Mono- and di-aldehydes can be used herein. Typical of such components are: formaldehyde, acetaldehyde, furfural, glyoxal, succindialdehyde, malonic dialdehyde, glutaraldehyde, etc. Particularly preferred is formaldehyde.

Component (b) is a basic trivalent chromium salt. Typical salts useful herein are chromium (III) sulfate and chromium (III) chloride. The sulfate is preferred.

A polyhydric phenol and/or a quinone, (c), are present in the tanning solutions of this invention. Typical of such compounds are: pyrogallol; resorcinol; hydroquinone; 2,2',4,4'-tetrahydroxy benzophenone; 1,2-naphthoquinone; 1,2-naphthoquinone-4-sulfonic acid sodium salt; 1,4-naphthoquinone; p-toluquinone; 1,2-anthraquinone; etc. Mixtures of these compounds can be used. Polyhydric phenols and quinones that are most effective in the tanning process of the present invention are those which have an unsubstituted position adjacent to the oxygen function.

The invention will appear more clearly from the following detailed description when taken in connection with the accompanying drawing, which shows by way of example, a preferred embodiment of the inventive idea. Referring now to the drawing,

The starting material for the process of the present invention is a bonded collagen multifilament which will be referred to hereafter as collagen tape. This material is ribbon-like in form and is made up of from about 20 to about 500 individual collagen monofilaments. Collagen tape may be prepared by extruding a dispersion of substantially pure swollen tendon collagen fibrils through a multi-orifice spinnerette into an alkaline acetone dehydrating bath. The multifilaments, as they emerge from the spin bath, are very loosely united and are approximately circular in cross-section; however, the filaments are drawn from the spin bath by a rotating godet and the tension on the still wet filaments as they pass over the godet surface bonds the individual filaments together to form a ribbon-like strand. When the bonded multifilament is dried, the ribbon-like shape is retained. It will be understood from the foregoing that the individual filaments are bonded together by cohesive forces to form the collagen tape.

The mechanical handling of the collagen tape as it passes through the tanning solution and is dried and rounded to form a strand of circular cross-section, is illustrated in the figure. The machine employed has been designed for the continuous treatment of collagen tape containing about 195 filaments and shaping the tanned multifilament to form a rounded strand about 14.5 mils in diameter, but it will be understood that strands of smaller or larger diameter may be produced by varying the number of individual filaments in the collagen tape and such modifications are well within the scope of this invention.

Collagen tape 10 is transferred from the supply reel 11 to the take-up spool 12 by the driven godets 13, 14, 15, 16 and 21. The idler rollers 17, 18, 19, and 20 frictionally grip the moving tape or strand and permit stretching thereof.

The collagen tape passes from the driven godet 13 over the guide pulley 22 and around the idler pulleys 23 and 24 immersed in the tanning bath 25. The tanned tape is then guided out of the tanning bath by the idler pulley 26 and is stretched about 5% between the godets 13 and 14.

From the godet 14 the tape passes through a drying chamber 27 where it is heated to about 110° F.-130° F. and stretched another 2%. The tanned and dried strand is then shaped by contact with a false twister 28. This device automatically imparts a so-called false twist to the strand, a false twist being a twist whose directions on one side of a point of contact is reversed on the opposite side, thus cancelling the twist. The twisting cycle is most effective when the collagen tape is in the wet state, and this may be controlled by dripping water on the tape from the jet 29. When the twist backs up to the pulley 30 as the wet tape emerges from it, a gradual tapering effect on the strand takes place, and the tape is rounded out. The circular shape of the strand remains after the twist is cancelled. The false twister is operated in the range of 150 to 600 r.p.m., and the strand is stretched about 6% between the godets 15 and 16. An idler pulley

31 guides the rounded strand from the false twister through the drying chamber 32 where excess moisture is removed from the strand.

In tanning bath 25, all of the components (a), (b) and (c) are present. The concentration of formaldehyde in the bath 25 can be varied to compensate for the time collagen is in contact with the bath. The tensile strength of the finished collagen suture decreases when the concentration of formaldehyde in bath 25 exceeds 0.32 percent; and the in vivo absorption of the suture is quite rapid if the formaldehyde concentration is less than about 0.05 percent.

Relative to the amount of chromium in tanning bath 25, if the treated collagen strand (size 2/0) contains less than about 0.5 percent of chromium calculated as the corresponding oxide, low wet tensile strength results. Strands containing more than about 1.5 percent of chromic oxide have poor dry knot strength. Therefore, the concentration of chromium in the tanning bath (25) can be adjusted within limits so that the collagen, in passing through the bath 25, will absorb about 1 percent by weight of chromium as chromic oxide. Generally, the concentration of chromium in the bath will range from about 0.1 to about 2 percent by weight (as Cr_2O_3).

Correspondingly, the concentration of pyrogallol (c) in tanning bath 25 is from about 0.2 percent to about 2 percent. The concentration of component (c) in the bath is so regulated that the collagen strand will absorb from about 0.2 to about 2 percent by weight thereof.

Other materials which can be used in the single tanning bath 25 include sodium hydrosulfite or like reducing agents. A strong reducing agent such as formaldehyde sodium sulfoxylate (marketed as Formopan), about 0.1%, can be used in the bath to prevent oxidation of the polyhydroxy compound therein. A small amount, about 0.5 percent by weight, of a chelating agent such as the disodium salt of ethylene diamine tetraacetic acid, can be used to associate with any undesirable contaminating metals present in the bath.

The pH of the tanning bath (25) should be between about 2 and about 4.5. If the pH is below about 2, the collagen will pick up too much water and is likely to break. If the pH of the bath is about 4.5, the chromium salt present in the bath tends to precipitate. It is desirable, therefore, to adjust the pH of bath 25 within the above-mentioned limits. Excellent results have been obtained when the pH of the tanning bath 25 is between about 2.8 and about 3.5.

It has been observed that atmospheric humidity, a variable during the spinning of a strand, plays an important part in the stretch and the final tensile strength of the strand. The humidity is preferably controlled by encasing the spinning operation within the smallest practical enclosure into which the air of controlled humidity may be introduced. Superior uniform strands may be obtained when the relative humidity is maintained at about 40%.

The continuous processing of collagen tape to obtain a unitary strand of outstanding properties is illustrated by the following examples. By way of contrast, a number of additional examples are provided which demonstrate that tanning of collagen with individual reagents such as a chromium salt, formaldehyde, polyhydric phenol and quinone, results in products having characteristics unsatisfactory for a surgical suture. Still other examples are offered by way of contrast of the presently claimed invention and the multiple treatments of the aforementioned applications Serial Nos. 85,302 and 85,289. Throughout the specification, all quantities are expressed in parts by weight unless otherwise indicated.

EXAMPLE 1

A tanning composition is prepared by the following procedure.

A chrome stock solution is prepared by adding 672

parts of $\text{Cr}_2(\text{SO}_4)_3 \cdot 15\text{H}_2\text{O}$ to 250 parts of water heated to 60°C . with stirring. An additional 100 to 200 parts of water can be added if needed to dissolve all of the chromic sulfate. Two hundred and four parts by volume of a 5 normal solution of sodium hydroxide are added slowly and with stirring from a separatory funnel to the chromic sulfate solution. Sufficient water is then added to bring the total volume up to 2000 parts. This stock solution analyzes 8.8 percent Cr_2O_3 .

A tanning composition is prepared by dissolving 8 parts of pyrogallol in 3500 parts of water, adding 12 parts by volume of 37 percent aqueous formaldehyde, then adding 57.5 parts by volume of the said 8.8 percent chrome stock solution, and finally adding water to a total volume of 4000 parts of desired composition. The pH of the composition is adjusted to 3.2 by the addition of 5 normal sodium hydroxide solution.

The final analysis of this tanning solution is:

Chromium ----- 0.9% Cr_2O_3 .
Pyrogallol ----- 0.2%.
Formaldehyde ----- 0.1%.

This tanning composition is used in bath 25 of the figure shown. A collagen tape approximately 4 mils thick and 60 mils wide containing 192 individual filaments is treated as described above in connection with the figure. The length of tape immersed at any one time in bath 25 is 60 inches, and the rate of travel through the bath is 40 inches per minute. The finished rounded collagen strand analyzes 1 percent Cr_2O_3 .

EXAMPLES 2-11

Sutures are prepared exactly as described in Example 1, above, except that the composition of the tanning bath 25 is varied as indicated in Table I following. The pH of each bath was 3.2.

In the table, the in vivo tensile strength and other physical properties are given in pounds.

Table I

Example No.	Bath composition	Strand analysis	Physical properties				In vivo	
			Diameter	Dry straight	Dry knot	Wet knot	3 days	20 days
2-----	0.6% pyrogallol; 0.1% CH_2O ; 0.7% Cr_2O_3 .	1.89% Cr_2O_3 ; 1.16% pyrogallol; Trace CH_2O .	15.0	10.7	4.83	4.31	5.77	3.97
3-----	0.4% pyrogallol; 0.2% CH_2O ; 0.6% Cr_2O_3 .	1.56% Cr_2O_3 ; 0.61% pyrogallol; 0.047% CH_2O .	15.4	9.43	5.05	4.14	6.09	2.25
4-----	0.2% pyrogallol; 0.1% CH_2O ; 0.8% Cr_2O_3 .	1.17% Cr_2O_3 ; 0.32% pyrogallol; 0.037% CH_2O .	14.6	11.1	5.62	3.93	3.02	0
5-----	0.6% resorcinol; 0.1% CH_2O ; 0.7% Cr_2O_3 .	0.92% Cr_2O_3 ; 0.29% resorcinol; 0.15% CH_2O .	15.0	11.3	4.8	3.7	-----	-----
6-----	0.4% resorcinol; 0.2% CH_2O ; 0.6% Cr_2O_3 .	0.94% Cr_2O_3 ; 0.47% resorcinol; 0.15% CH_2O .	15.1	10.6	4.7	4.1	-----	-----
7-----	0.2% resorcinol; 0.1% CH_2O ; 0.8% Cr_2O_3 .	1.28% Cr_2O_3 ; 0.2% resorcinol; 0.13% CH_2O .	15.1	11.5	4.8	4.2	-----	-----
8-----	0.6% pyrogallol; 0.4% glyoxal; 0.8% Cr_2O_3 .	-----	15.2	10.9	4.4	3.7	-----	-----
9-----	0.8% 1,2-naphthoquinone-4-sulfonic acid sodium salt; 0.1% CH_2O ; 0.8% Cr_2O_3 .	-----	15.3	11.0	4.8	3.8	-----	-----
10-----	0.4% benzoquinone; 0.2% CH_2O ; 0.6% Cr_2O_3 .	-----	15.3	9.4	4.3	3.5	-----	-----
11-----	0.4% hydroquinone; 0.2% CH_2O ; 0.6% Cr_2O_3 .	-----	15.3	9.5	4.3	3.5	-----	-----

EXAMPLE 12

Extruded collagen multifilament was tanned in a basic chromium sulfate bath containing 1.25 percent Cr_2O_3 . No formaldehyde or polyhydric phenol was used in the tanning process. Properties of the product are set forth in Tables II and III.

EXAMPLE 13

Extruded collagen multifilament was tanned in a bath containing 0.15 percent formaldehyde. No chromium or polyhydric phenol was used in the tanning process. Tables II and III reveal properties of the product so obtained.

EXAMPLE 14

Extruded collagen multifilament was tanned in a bath containing 0.5 percent quinone. No chromium or formaldehyde was used in the tanning process. Properties of the product are shown in Tables II and III.

Table II

Example No.	Denier	Diameter	Tensile strength (grams/denier)		
			Dry straight	Dry knot	Wet knot
12 (only Cr)-----	1,390	-----	2.6	1.5	1.2
13 (only HCHO)-----	1,440	-----	2.41	1.39	0.98
14 (only quinone)-----	-----	-----	3.4	1.4	1.0
Catgut-----	1,210	14.0	3.60	2.40	1.20

Table III

IN VIVO ABSORPTION IN POUNDS

Example	Days Implanted						
	0	1	3	5	7	10	15
12 (only Cr)-----	4.6	1.6	-----	-----	-----	-----	-----
13 (only HCHO)-----	4.0	1.6	-----	-----	-----	-----	-----
14 (only quinone)-----	2.2	2.2	-----	-----	-----	-----	-----
Catgut-----	8.2	5.3	4.6	3.9	3.3	2.5	1.4

EXAMPLE 15

Another series of experiments was carried out to determine the separate effects of chromium sulfate, pyrogallol, and formaldehyde upon an extruded collagen tape. In experiments 15 through 20, pyrogallol or quinone was applied from one bath and distilled water adjusted to pH 3.5 was applied from a second bath. In experiments 21 through 23, distilled water at pH 8.3 was placed in the first bath and formaldehyde at pH .35 in the second bath. In experiments 24 through 26, distilled water at pH 8.3 was placed in the first bath and chromium sulfate at pH

3.5 in the second bath. In all thirteen experiments shown below, the strand was wet out with an aqueous solution of 0.3 percent formaldehyde (pH 8.5). The following results were obtained.

Compound	pH	Levels of treatment bath	Experiment No.
1. Pyrogallol-----	8.3	1, 3 and 5%-----	1, 2, 3.
2. Quinone-----	8.3	1, 2 and 5%-----	4, 5, 6.
3. Formaldehyde-----	3.5	0.3, 0.6 and 1.5%--	7, 8, 9.
4. Chromium sulfate-----	3.5	1.0, 3.0 and 5.0%--	10, 11, 12.
5. Combination run*-----	3.5	-----	13.

* See footnote at bottom of following table.

TENSILE STRENGTH

Exam- ple No.	Tanning Treatment	Denier	Dry straight	Dry knot	Wet knot
15.....	1% pyrogallol, pH 8.3.....	1,170	12.0	4.6	2.1
16.....	3% pyrogallol, pH 8.3.....	1,120	12.8	4.9	2.3
17.....	5% pyrogallol, pH 8.3.....	1,150	12.5	4.6	2.2
18.....	1% quinone, pH 8.3.....	1,130	10.3	5.0	2.0
19.....	3% quinone, pH 8.3.....	1,140	9.7	5.1	2.0
20.....	5% quinone, pH 8.3.....	1,160	10.9	4.7	2.1
21.....	0.3% HCHO, pH 3.5.....	1,100	9.8	4.5	2.8
22.....	0.6% HCHO, pH 3.5.....	1,120	10.1	4.2	2.9
23.....	1.5% HCHO, pH 3.5.....	1,130	8.2	4.1	2.6
24.....	1.0% Cr ₂ (SO ₄) ₃	1,320	9.4	5.6	2.9
25.....	3.0% Cr ₂ (SO ₄) ₃	1,270	10.3	5.3	4.2
26.....	5.0% Cr ₂ (SO ₄) ₃	1,300	12.4	5.9	4.6
27.....	Combination run*.....	1,300	13.1	6.4	4.3

*First bath=1.0% pyrogallol, pH 8.3
Second bath=1.0% Cr₂(SO₄)₃+0.3% HCHO, pH 3.5

IN VIVO TENSILE STRENGTH

Example No.	Days						
	1	3	5	7	10	15	20
15.....	2.08	1.74	1.54	1.66	1.14	0.8	0.3
16.....	1.90	1.80	2.2	1.89	1.93	0.8	0.3
17.....	1.70	2.57	2.1	2.19	1.07	2.9	0.4
18.....	1.06	1.44	1.4	1.01	2.7	-----	-----
19.....	2.16	3.44	2.6	1.78	1.21	2.3	0.6
20.....	4.07	-----	1.7	1.06	1.02	0.7	-----
21.....	2.86	1.31	1.69	2.12	1.25	-----	-----
22.....	4.59	2.55	3.09	2.21	3.20	0.7	-----
23.....	3.84	3.91	3.10	2.49	2.16	0.6	-----
24.....	2.81	-----	2.04	1.13	1.18	-----	-----
25.....	3.93	2.99	3.10	1.97	-----	-----	-----
26.....	4.40	2.42	2.56	1.85	1.67	-----	-----
27.....	6.66	5.24	5.35	4.65	-----	-----	-----

EXAMPLE 28

Extruded collagen tape was tanned in a bath containing chromium sulfate and formaldehyde. The bath contained chromium sulfate equivalent to 10 grams of Cr₂O₃ per liter, and 0.32% of formaldehyde. Properties of the tanned tape are given below:

Denier	130
Dry straight	8.5
Dry knot	5.5
Wet knot	4.3
In vivo:	
0 days	6.8
1 day	3.8
5 days	3.0
7 days	1.7

Results given above in Examples 1 through 28 and data given in the tables in connection therewith reveal that:

(1) Chromium alone does not provide a collagen suture having satisfactory in vivo tensile strength properties; (Examples 12 and 24 through 26)

(2) Pyrogallol alone does not provide such a suture having satisfactory tensile strength; (Examples 15 through 17)

(3) Quinone alone fails on the same basis as pyrogallol; (Examples 18 through 20)

(4) Formaldehyde alone does not provide a collagen suture having adequate tensile strength properties; (Examples 21 through 23)

(5) Chromium and formaldehyde together in a solution does not provide a suture having satisfactory in vivo tensile strength properties; (Example 28)

(6) A pyrogallol solution followed by a solution of formaldehyde and chromium provides a collagen suture of an excellent combination of properties, i.e., desired tensile strength, in vivo digestion time and uniformity of product; (Example 27)

(7) A single solution containing pyrogallol, formaldehyde and chromium provides a product having char-

acteristics corresponding to those of the product described in (6) above; (Examples 2 through 4)

(8) A single solution containing a quinone, formaldehyde and chromium provides a product having characteristics corresponding to those of the product described in (6) above; (Examples 9 and 10).

EXAMPLE 29

Sutures prepared according to the method of the present invention contain polyhydric phenols and/or quinone reduction products that are chemically combined with the collagen. A quantitative determination of the amount of polyhydric phenol or quinone that is present in the finished suture can be made by the following method.

A 10-milligram sample of a polyhydric phenol and/or quinone tanned suture is placed in a test tube and 1 milliliter of sodium borohydride solution is added. The solution of sodium borohydride is prepared by dissolving 0.60 gram of sodium borohydride in 20 milliliters of distilled water and adding one pellet of sodium hydroxide. This solution is prepared fresh for each group of samples. The test tube containing the suture to be analyzed and borohydride solution is heated over a Bunsen flame until the suture is dissolved. The contents of the test tube are then neutralized with concentrated sulfuric acid and the test tube is heated to decompose any excess sodium borohydride solution. The reaction mixture so obtained is cooled and diluted to 3 milliliters with distilled water.

One milliliter of a vanillin reagent, prepared by dissolving 7.5 grams of vanillin in 50 milliliters of ethyl alcohol, is added and the mixture is diluted with 79% sulfuric acid to 23 milliliters. After 20 minutes, the absorbance at 520 mμ is compared with a reagent blank using a Beckman D.U. spectrophotometer and four standards containing 0.01, 0.02, 0.03 and 0.04 milliliter of a standard solution of the polyhydric phenol or quinone subject of the analysis, such as a pyrogallol solution, prepared by dissolving 0.130 gram of pyrogallol in 4 N sulfuric acid to a total volume of 100 milliliters.

The absorbance values are plotted against the volume of standard and the percent polyhydric phenol or quinone in the same is calculated according to the formula

$$\frac{K \times A \times 100}{\text{Sample weight (mg.)}}$$

in which A is the absorbance obtained from the curve and K, for the 0.04 milliliter standard, is 0.052 milligram pyrogallol divided by A from the curve.

The following list of polyhydric phenols and quinones has also been analyzed by this procedure. In this list, the visible wave length at which maximum absorption occurs, follows the name of the compound:

	Mu
2,2',4,4'-tetrahydroxybenzophenone	520
1,2-naphthoquinone	570
1,4-naphthoquinone	575
p-Toluquinone	560
1,2-anthraquinone	545
Resorcinol	510

Accurate and reproducible results are obtained with the foregoing procedure with phenols and with quinones, with the exception of benzoquinone. A separate procedure is followed in determining benzoquinone content of a suture obtained in accordance with this invention. A 500-milligram sample of a benzoquinone-tanned suture is placed in a test tube. Five (5) milliliters of hydrochloric acid solution (2 N) are added to the tube. The tube and its contents are heated over a Bunsen flame until the suture is dissolved. The contents of the tube are cooled, 5 mls. of ethanol are added thereto, and the resulting solution is shaken. The solution is transferred to a 25 ml. volumetric flask and is made up to volume with distilled water. The resulting solution is filtered into a 50

ml. beaker. Ten (10) milliliters of the filtrate are added to a 25 ml. volumetric flask, whereupon 1 ml. of pyrogallol solution (1% in water) and 10 ml. of ethanol are added. Distilled water is then added to the 25 ml. level of the flask. After one hour, the absorbance at 425 μ is compared with a reagent blank using the said spectrophotometer and three standards containing 0.01, 0.02 and 0.03 milliliter of a benzoquinone standard solution. The standards are prepared by dissolving 100 milligrams of benzoquinone in 100 milliliters of distilled water.

The absorbance values are plotted against the volume of the standard and the percent benzoquinone in the sample is calculated according to the formula:

$$\text{Percent benzoquinone} = \frac{\text{Density reading at 425 } \mu \times \text{factor}}{\text{weight of sample (mg.)}}$$

$$\text{Factor} = \frac{\text{milligrams of benzoquinone}}{\text{absorbing unit}} \times \frac{25 \times 100}{10}$$

Sutures prepared by the method of the present invention contain about 0.25% to about 0.92%, and preferably from about 0.30% to about 0.70%, polyhydric phenol and/or quinone as determined by the foregoing analytical method.

It will be understood that the process described above may be utilized in the preservation of other collagenous materials such as leather, the useful life of which is frequently shortened by the attack of micro-organisms and enzymes produced by such micro-organisms.

While the invention has been described in detail according to the preferred method of carrying out the process and yielding the products, it will be obvious to those skilled in the art that changes and modifications can be made without departing from the spirit or scope of the invention, and it is intended in the appended claims to cover such changes and modifications.

I claim:

1. In a method of tanning collagen that has been acid-swollen, extruded and reconstituted; the steps of contacting said collagen with a solution containing an aldehyde, a basic trivalent chromium salt and an aromatic compound selected from the group consisting of monocyclic and dicyclic polyhydric phenols, and monocyclic, dicyclic and tricyclic quinones.

2. The method of claim 1 in which said aldehyde is formaldehyde.

3. The method of claim 1 in which said aldehyde is glyoxal.

4. The method of claim 1 in which the collagen is in the form of a tape.

5. The method of claim 1 in which said aromatic compound is p-benzoquinone.

6. The method of claim 1 in which said aromatic compound is pyrogallol.

7. The method of claim 1 in which said aromatic compound is hydroquinone.

8. The method of claim 1 in which said aromatic compound is resorcinol.

9. The method of claim 1 in which the pH of the solution is between about 2 and about 4.5.

10. In a method of tanning collagen that has been acid-swollen, extruded and reconstituted; the steps of contacting said collagen with a solution containing an aldehyde, a basic trivalent chromium salt and a monocyclic polyhydric phenol.

11. In a method of tanning collagen that has been acid-swollen, extruded and reconstituted; the steps of contacting said collagen with a solution containing an aldehyde, a basic trivalent chromium salt and a dicyclic quinone.

12. The method of claim 11 in which said dicyclic quinone is 1,2-naphthaquinone-4-sulfonic acid sodium salt.

References Cited by the Examiner

UNITED STATES PATENTS

2,240,388 4/41 Calva 8-94
2,418,528 4/47 Robinson 8-94.24 X

FOREIGN PATENTS

508,781 6/39 Great Britain.

OTHER REFERENCES

O'Flaherty et al.: Chemistry and Technology of Leather, vol. 2, A.C.S. Monograph No. 134, pages 254-255 and 465-466, pub. by Reinhold Pub. Co., N.Y.C., 1958.

NORMAN G. TORCHIN, *Primary Examiner.*