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PLASTIC COLLAGEN SUTURES

3,435,825

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Fig. 1.

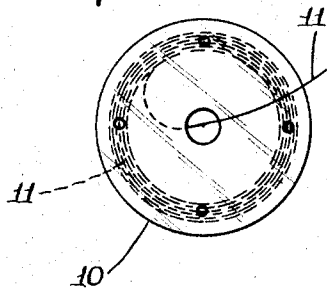


Fig. 2.



Fig. 3.

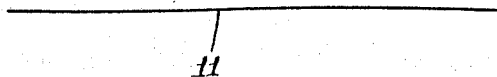
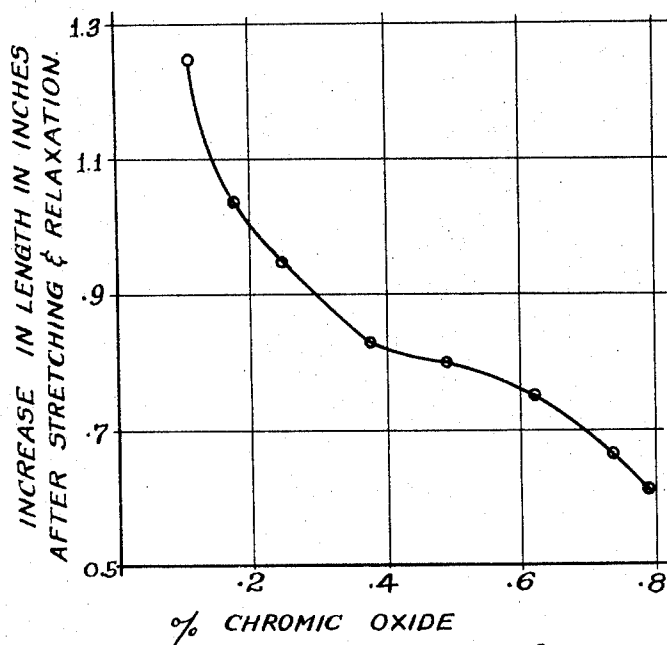


Fig. 4.



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1

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PLASTIC COLLAGEN SUTURES

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10 Claims

ABSTRACT OF THE DISCLOSURE

A novel chromicized suture strand and method of making same is disclosed. This suture strand is made by treating raw natural unreconstituted collagen with a dichromate salt and a phenolic derivative, such as pyrogalllic acid, so that the reaction product has a chrome content equivalent to that in chromic oxide in the range of 0.1% to 0.3% of the dry weight of the suture.

This application is concerned with plastic collagen sutures, specifically with chrome tanned sutures having the usual strength and body absorption properties characteristic of chromicized sutures but unlike such sutures having sufficient plasticity to permit easy removal of set bends therefrom by the usual stretching procedure employed by surgeons.

It is a characteristic of collagen sutures, tanned to increase strength and body absorption time, to assume a permanent set when stored in the form of coils or in turns upon a reel in a confined package. Numerous softening agents including water and various plasticizers have been applied to such tanned collagen sutures in attempts to eliminate this tendency or at least to permit the easy removal of set bends when the surgeon stretches the suture. However, all such softening agents or plasticizers when used in sufficient amounts to be completely effective have seriously weakened collagen sutures so that tanned sutures as sold prior to this invention have been only partially plasticized. If one observes such tanned collagen sutures after stretching in the manner employed by surgeons, the suture begins to retract as soon as the stretching force is removed and soon assumes an elongated form of the configuration it had when stored in the confinement of the suture tube or package.

It is an object of this invention to provide tanned collagen sutures comparable in body absorption time and strength characteristics to usual chromicized sutures but which, when stretched from a coil-like configuration in the usual manner employed by surgeons, exhibit a very much reduced tendency to return to the original coiled form.

FIGURE 1 illustrates a coiled suture in a typical suture package.

FIGURE 2 illustrates a portion from a coil as in FIGURE 1 of the usual chromed collagen suture after a 60-inch length has been stretched with a 3-pound pull and allowed to relax for 5 minutes.

FIGURE 3 illustrates a portion from a coil as in FIGURE 1 of a collagen suture of this invention after a 60-inch length has been stretched with a 3-pound pull and allowed to relax for 5 minutes.

FIGURE 4 illustrates graphically the difference in elongation of coiled tanned collagen sutures of various chrome content, previously stored in 10% water and 90% ethanol, after such stretching.

The objects of this invention are obtained by treatment of raw collagen strands with a combination of two compounds in solution preferably in succession and preferably in a given order. Satisfactory results may be obtained, however, by treatment with the two compounds

2

combined and reacted into a single treating solution or by treatment with the compounds successively in the reverse of the preferred order.

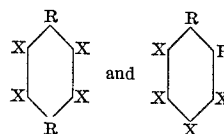
In the preferred method of treatment, the raw collagen strand is first treated by immersion in a solution of a dichromate. Sodium dichromate is the preferred dichromate but potassium dichromate, calcium dichromate, ammonium dichromate or any other dichromate soluble to the extent of .01% in water at room temperature is suitable, it being necessary only that the dichromate ion be in sufficient concentration in the water. A pH of 5 to 6½ is preferred. In tanning collagen strands according to this method, the ratio of volume of solution to the weight of the strand has little effect provided there is sufficient dichromate and reducing agent in solution. With concentrations of 0.1% sodium dichromate and 0.2% pyrogalllic acid, volume-weight ratios between 30-1 and 200-1 give very little difference in the final chrome content of the suture or the degree of plasticity produced when the time of immersion is maintained constant between 1 to 2 hours. With extremely dilute solutions of .01% or less, a longer period of immersion is necessary, being roughly inversely proportional to the concentration of dichromate ions in the solution. With a solution of .0025% dichromate, a 12-hour bath followed by a 2-hour bath in .034% pyrogalllic acid gave a chrome content equivalent to that of an amount of chromic oxide .174% of the dry chromed suture weight.

After the proper period of immersion in the dichromate bath, the solution is drained and replaced with a second bath of a solution of the phenol derivative defined below preferably having at least a mole to mole relationship with the dichromate in an equal volume bath. The preferred ratio of concentrations of the dichromate and phenol derivative solutions is

$$\frac{.04}{.034}$$

when the first bath is a solution of sodium dichromate and the second of equal volume is a solution of pyrogalllic acid.

The phenol derivative is one or more of those selected from the group consisting of compounds corresponding to the formulae



where R is a hydroxyl or an amino group and X is any radical chosen from the group consisting of hydrogen, hydroxyl, amino, an alkyl of less than 5 carbon atoms, carboxyl, nitro and carbalkoxyl radicals.

After immersion for from 1 to 3 hours with 2 hours preferred in the phenol derivative bath in the preferred molar relationship, the collagen strand will have been properly tanned and will be found to have a chrome content equivalent to that of chromic oxide in the range of .1 to .3% of the dry chromed suture. The method of measuring the chrome content of the tanned collagen strand in terms of chromic oxide is as follows:

Ash .8 gram of dried chromed collagen strand at 500° C. When cooled, boil the ash in an Erlenmeyer flask with 10 cc. of perchloric acid for 10 minutes after the liquid turns orange. Cool and dilute to about 200 cc. with distilled water. Boil for 20 minutes, then cool to 65° F. Add 15-20 cc. of concentrated hydrochloric acid and 10 cc. of potassium iodide solution made by dissolving 100 grams in 500 cc. of water. Titrate with standardized sodium thiosulphate solution until the solution is pale yellow. Add

a few drops of starch indicator and titrate to the disappearance of any blue coloration. Calculate

$$\text{Percent Chromic Oxide} = \frac{\text{cc. of Na}_2\text{S}_2\text{O}_3 \times \text{Factor} \times 100}{\text{Wt. of sample}}$$

Factor is that obtained by multiplying the normality of $\text{Na}_2\text{S}_2\text{O}_3$ by .0253.

The preferred chrome content of the tanned collagen strands of this invention is equivalent to that in an amount of chromic oxide in the range of .15% $\pm$.05% of the weight of such strand. This is in distinct contrast with the chrome content of chrome tanned collagen strands prior to this invention, the chrome content of which was normally equivalent to that of chromic oxide in amounts about .5% and frequently in amounts as much as 2% of the dry weight of the tanned collagen strand.

It has been discovered, however, that the proportion of chrome equivalent to that of chromic oxide above .3% of the dry tanned suture weight does not contribute appreciably to its strength and may delay the rate of absorption in the body undesirably. Such excess above the equivalent amount of chrome in chromic oxide above .3% of the dry tanned gut does have a very adverse effect on the plasticity of the tanned strand. At .3% chromic oxide or below, equivalent chrome permits removal of configurations by stretching to the point where they are not particularly obvious or objectionable with the .3% equivalent chrome suture being barely satisfactory. With chrome contents above this equivalent, the set configurations become increasingly more difficult to remove and constitute a most objectionable feature as can be easily observed.

Examples of the two-bath method with the first bath constituting the dichromate solution are as follows:

TABLE I

1st bath	Concentration, percent	Period (hr.)	2nd bath	Concentration, percent	Period (hr.)	Chrome equiv. to chromic oxide, percent
Sodium dichromate.....	.1	1	Pyrogallie acid.....	.2	2	.31
Potassium dichromate.....	.1	1	do.....	.2	2	.24
Ammonium dichromate.....	.1	1	do.....	.2	2	.24
Calcium dichromate.....	.1	1	do.....	.2	2	.24
Sodium dichromate.....	.1	1	Quinone.....	.2	2	.13
Do.....	.1	1	2-6 dimethoxy-phenol...	.2	2	.17
Do.....	.1	1	Elon.....	.2	2	.21
Do.....	.1	1	Orthophenylenediamine	.2	2	.23
Do.....	.1	1	Orthoprotocatechuic acid.	.2	2	.14
Do.....	.1	1	Orthoveratric acid.....	.2	2	.17
Do.....	.1	1	Amino phenol.....	.2	2	.16
Do.....	.1	1	Chestnut extract.....	.2	2	.21
Do.....	.1	1/4	Pyrogallie acid.....	.2	2	.03
Do.....	.1	1/2	do.....	.2	2	.21
Do.....	.1	1	do.....	.2	1/4	.29
Do.....	.025	2	do.....	.2	2	.13
Do.....	.025	1	do.....	.2	2	.1
Do.....	.02	4	do.....	.2	2	.3
Do.....	.01	4	do.....	.2	2	.1
Do.....	.1	1	do.....	.1	4	.4
Do.....	.05	1	do.....	.3	1	.17
Do.....	.05	1	do.....	.1	4	.16
Do.....	.05	1	do.....	.2	2	.13
Do.....	.05	1	Catechol.....	.2	2	.11
Do.....	.05	1	Hydroquinone.....	.2	2	.14

The accompanying graph FIGURE 4 illustrates average increase in length in inches 1 minute after momentarily stretching with a 3-pound pull, 60-inch pieces of collagen suture of various chrome content stored in the form of circular coils of 1 1/2 inches in diameter for a minimum period of 1 week in tubing fluid of 10% water and 90% ethanol.

When the one-bath method of chromicization is utilized in accordance with the invention, the phenol derivative concentration is preferably in excess of the molar rela-

tionship with the dichromate concentration. Where the bath volume in cc. to the collagen weight in grams is in the range of 200 to 1, a phenol derivative concentration of .2% is preferred. With dichromate concentrations in the range of .05% to .2%, a two-hour bath produces chromicized collagen sutures with chrome contents equivalent to that of chromic oxide in the range of .17 to .2% of the dry chromicized suture. One may reduce the chrome content by reducing the bath period or one may reduce the chrome content by retaining the two-hour bath period and reducing the dichromate concentration below .05% and down to about .03% to obtain sutures with chrome contents equivalent to chromic oxide in amounts as low as .1% of the dry weight of the chromicized suture.

One may also increase the chrome content above the equivalent of .2% chromic oxide without modifying the single bath by increasing the period thereof so that at about 3 hours the chrome content will have increased to the equivalent of about .3% chromic oxide. Sutures with chrome contents in the range of .2% to .3% equivalent chromic oxide are increasingly less plastic as the chrome content increases in this range, however until at .3% chromic oxide equivalent, the plasticity is barely satisfactory. One-bath chromicization tends to produce sutures with the degree of chromicization increasing from the center of the suture outwardly whereas two-bath chromicization gives a more uniform through and through chromicization. Moreover, the single-bath method tends to be somewhat gummy so that a cleaning problem is involved with regard to the bath tanks.

When the preferred order of treatment is reversed with the two-bath method so that the collagen strand is first treated with the phenolic derivative, the results are very

comparable with the results obtained when the strand is first treated with the dichromate but it takes less dichromate to accomplish the same results. That is, where the period and concentration of each bath is unchanged but the order is reversed, the procedure in which the phenolic derivative bath is first, produces sutures with higher chrome content. For that reason it is preferred to use the dichromate bath first since any error is less significant.

Typical of two-bath methods involving a phenolic derivative first bath are the following:

TABLE II

1st bath	Concentration, percent	Period (hr.)	2nd bath	Concentration, percent	Period (hr.)	Chrome equiv. to chromic oxide, percent
Pyrogallie acid.....	.2	2	Sodium dichromate.....	.05	1	.32
Do.....	.2	2	do.....	.025	1	.21
Do.....	.2	2	do.....	.01	1	.09

5

The particular tubing fluid used in storing collagen sutures of this invention has considerable effect upon the plasticization of the suture. Water is normally considered a good plasticizer for collagen sutures but both ethyl and methyl alcohol in that order are superior plasticizers for such sutures when plasticity is measured by plastic elongation. Thus sutures chromicized in accordance with this invention may be obtained in more plastic condition with higher percentages of ethyl or methyl alcohol combined with lower percentages of water than are usual in tubing fluids. A tubing fluid made up of a solution of 98% ethyl alcohol and 2% water to which is added .3% of ethylene oxide as a sterilizing agent is preferred. The sutures of this invention in the preferred range of chrome content equivalent to that in chromic oxide in the range of .1% to .2% of the dry weight of the suture are more plastic than plain untanned or non-chromicized sutures. Thus in the tubing solution of FIGURE 4 which was 90% ethyl alcohol, 10% water to which was added .3% ethylene oxide, 60-inch plain sutures averaged 1 inch increase in length when stretched for a minute with a 3-pound pull whereas sutures with chrome content equivalent to .1 to .2% of the dry weight of the suture stretched more. As a more dramatic illustration of the superiority of chromicized sutures of this invention over plain sutures in the matter of plasticity an experiment was performed using five 10-foot strands of #1 catgut. The strands were cut in half and half of each strand was left untreated or plain and packaged in 2 cc. of preferred tubing solution. The other half of each strand was treated with a solution of .04% sodium dichromate for one hour after which the solution was drained and replaced by a solution of .034% pyrogallol acid solution for two hours which was also drained. These treated sutures were later determined to have a chrome content equal to that in chromic oxide in the amount of .17% of the dry weight of the suture. These suture halves of the 10-foot original strands were then packaged in 2 cc. of the same tubing fluid as the plain halves. After one week the packages were opened and the sutures were tested for plasticity by stretching the 60-inch lengths for 1 minute with a 3-pound pull and measuring the increase of length after release. The plain suture halves had an increase in length of 1.15 inches whereas the suture halves treated in accordance with this invention had an increase of 2.16 inches. With sutures of greater chrome content, the effect of tubing fluid is less pronounced. A suture having a chrome content equivalent to that of chromic oxide in an amount .3% of the dry weight of the suture was elongated .9 inch under the test conditions when tubed in 90% ethyl alcohol and 10% water to which .3% ethylene oxide was added as in FIGURE 4. When a similar suture was tubed in the preferred solution, its elongation under the same conditions was 1.3 inches.

No. 1 sutures prepared by the usual chromicizing methods and having an average chrome content equivalent to that in chromic oxide in amount of 1% of the dry suture weight were compared with No. 1 sutures prepared in accordance with this invention and having an average chrome content equivalent to that in chromic oxide in amount of .17% of the dry suture weight as follows:

TABLE III

Chrome equiv. to chromic oxide, percent	Straight pull dry (pounds)	Straight pull wet (pounds)	Knot strength (pounds)
1.-----	20.7	15.2	10.1
.17.-----	19.2	14.8	9.6

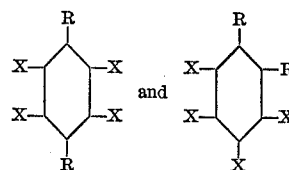
Chrome equiv. to chromic oxide, percent	Straight pull after indicated days in animal tissue (pounds)					
	0 days	7 days	14 days	21 days	28 days	42 days
1.-----	15.2	10.7	6.1	4.2	2.6	1.2
.17.-----	14.8	12.4	8.4	4.0	3.1	1.5

I claim:

1. An absorbable chromicized raw collagen suture

6

comprising the reaction product of a raw natural collagen strand of the size and shape of a suture, a dichromate salt having a solubility in water of at least 0.01% at 70° F. and a phenol derivative selected from the group consisting of compounds corresponding to the formulae



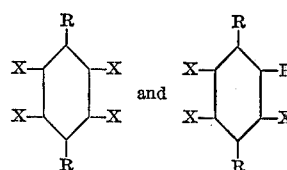
wherein R is a member selected from the group consisting of hydroxyl and amino, and X is a member selected from the group consisting of hydrogen, hydroxyl, amino, nitro, carboxyl, carbalkoxyl and loweralkyl having 1 to 5 carbon atoms, such that said reaction product has a chrome content equivalent to that in chromic oxide weighing in the range of 0.1% to 0.3% of the dry weight of the suture.

2. An absorbable chromicized raw collagen suture according to claim 1 wherein the dichromate salt is a member selected from the group consisting of sodium dichromate, potassium dichromate, calcium dichromate and ammonium dichromate.

3. An absorbable chromicized raw collagen suture according to claim 1 wherein the chrome content of the reaction product is equivalent to that in chromic oxide in the range of 0.1% to 0.2% of the dry weight of the suture.

4. An absorbable chromicized raw collagen suture according to claim 1 wherein the phenol derivative consists of pyrogallol acid.

5. A method of producing an absorbable chromicized raw collagen suture comprising the steps of reacting a strand of raw natural collagen with a dichromate salt having a solubility in water of at least .01% at 70° F. and a phenol derivative selected from the group consisting of compounds corresponding to the formulae



wherein R is a member selected from the group consisting of hydroxyl and amino, and X is a member selected from the group consisting of hydrogen, hydroxyl, amino, nitro, carboxyl, carbalkoxyl and loweralkyl having 1 to 5 carbon atoms, such that the reaction product has a chrome content equivalent to that in chromic oxide weighing in the range of 0.1% to 0.3% of the dry weight of the suture.

6. A method in accordance with claim 5 wherein the raw natural collagen is first treated with the dichromate salt followed by treatment with the phenol derivative.

7. A method in accordance with claim 5 wherein the raw natural collagen is first treated with the phenol derivative followed by treatment with the dichromate salt.

8. A method in accordance with claim 5 wherein the raw natural collagen is treated with a solution of the reaction product of the dichromate salt and the phenol derivative.

9. A method in accordance with claim 5 wherein the dichromate salt is a member selected from the group consisting of sodium dichromate, potassium dichromate, calcium dichromate and ammonium dichromate.

10. A method in accordance with claim 5 wherein the dichromate salt consists of sodium dichromate and the phenol derivative consists of pyrogallol acid.

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DONALD LEVY, *Primary Examiner*.

U.S. Cl. X.R.

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UNITED STATES PATENT OFFICE
CERTIFICATE OF CORRECTION

Patent No. 3,435,825

April 1, 1969

Lawrence A. Thoennes

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

Column 6, line 1, before "a" insert -- applying to --; line 59, "natnural" should read -- natural --.

Signed and sealed this 14th day of April 1970.

(SEAL)

Attest:

Edward M. Fletcher, Jr.

Attesting Officer

WILLIAM E. SCHUYLER, JR.

Commissioner of Patents