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Vivien et al.

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[54] **COLLAGEN BASED THREADS**

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[52] **U.S. Cl.**..... **128/335.5;** 117/139.5 F; 117/141; 161/176; 161/226

[51] **Int. Cl.**..... **A611 17/00**

[58] **Field of Search** ..... 128/335, 335.5; 161/175, 161/176, 226; 117/141, 139.5 F; 57/153; 106/155, 161

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[57] **ABSTRACT**

A new type of thread comprising collagen or catgut, remaining supple in dry condition is described.

The thread is treated with water and with one or more products capable of maintaining moisture on the surface of the thread and/or in the thread. The thread can be rendered smooth in the same bath or by treatment in a further bath with a lubricating product, such as a silicone. The treatment products proper are fatty compounds or derivatives of fatty compounds, such as glycerine, polyoxyalkylenes such as polyethylene glycol, or glycol derivatives. The treated threads are useful in surgery.

4 Claims, No Drawings

COLLAGEN BASED THREADS

BACKGROUND OF THE INVENTION

The invention relates to the field of collagen based threads which are mainly used in surgery. An object of the invention is a process for the treatment of such threads in order to make them durably supple. The invention also relates to threads obtained by the said process and to applications thereof, notably in the field of surgery.

The thread known as catgut, which is at present used in surgery, is a resorbable ligature of animal origin. It is normally prepared from mammifer collagen. In the present description, the expression "catgut" designates a collagen based thread of any type and origin.

PRIOR ART

In the known art, the cords of collagen are immersed in an alcohol, sterilized and supplied to users, such as surgeons, in tubes or packets. The alcohol is generally ethanol or isopropanol. The function of this alcohol is to permit sterilization and preservation of the ligature. Alcohol, with the small percentage of water it contains, also confers a certain suppleness on the ligature as long as it remains in contact with it. This suppleness disappears rapidly when the alcohol and the small amount of water evaporate, notably during use of the thread in an operating room with a high ambient temperature. The catgut then becomes stiff, which makes it difficult to use. Furthermore, both its diameter and its resistance decrease and the knots no longer hold in a satisfactory manner.

Another drawback of the prior art is that catgut, delivered with an alcohol, must be conditioned in suitable packages which should be both impervious to alcohol and microbes and easy to open. These requirements are contradictory, which makes it necessary to resort to compromise solutions in the conception of conditioning which do not always give complete satisfaction in practice.

THE PRESENT INVENTION

The aim of the invention is to avoid the inherent drawbacks in the prior art by doing away with the necessity of conditioning catgut in the presence of a volatile alcohol. A first object of the invention is therefore a collagen thread or catgut which can be supplied and used as such in a lasting manner, after having been subjected to a treatment to render it supple prior to sterilization.

Another object of the invention is a collagen based thread for use in surgery which retains its suppleness under the normal conditions of temperature and hygroscopy obtaining during preservation and use. The treated thread according to the invention can be sterilized and preserved without liquid, then employed by the user in the state in which it is sold.

Another object of the invention is to provide a process for treating threads comprising collagen, notably the catgut used in surgery, in order to make it durably supple prior to and during use.

The invention therefore provides a collagen thread permanently containing an amount of residual water at least equal to 10 percent by weight based on the thread and at least one treatment agent capable of maintaining the thread moisture by preventing evaporation of the water contained therein, the said agent being present in an amount of at least 15 percent by weight based on the dry thread and having a molecular weight no greater than about 400.

The treatment agents capable of retaining moisture in the collagen thread can be present on the surface of the thread and/or in the mass of the thread. They prevent evaporation of the water contained in the thread, generally owing to their hygroscopicity. The association of water-treatment agent renders the therad supple. In certain cases, the surface state of the thread can be still further improved by the presence of a lubricating product which is well tolerated by the human or animal organism. It is also obvious that the treatment agents, which are organic substances, should be well tolerated by the tissues of human or animal body.

Such treatment agents can be selected singly or in combination from fatty compounds and the derivatives thereof, higher alcohols having a low level of volatility at ambient temperature, fatty acids, esters and ethers of fatty acids and polyalcohols and fatty alcohols, fatty derivatives in the monomer or polymer form such as glycerine, glycols and derivatives thereof, and polyoxalkylenes such as polyoxyethylene glycol.

In combination with the above mentioned treatment agents, various compounds such as lipoids, silicones and other similar products can also be present in the thread.

As examples of lubricating products essentially present on the surface of the thread may be mentioned fatty compounds and derivatives of the fatty compounds themselves already mentioned as treatment agents, and, essentially silicones and derivatives thereof.

The amount of water contained in the thread is at least equal to 10 percent by weight based on the thread, and generally in the range of 10 percent to 50 percent, for example about 27 percent by weight. The values corresponding to variations in the diameter of the thread, which has the form of a swollen thread. The increased diameter of the thread based on the dry state can range from 5 percent to 50 percent, in the order of 20 percent for instance.

The amount of the treatment agent obviously varies with the nature thereof. Generally, substantially equal amounts of water and the treatment agent are used during treatment, but the amount of the agent remaining in the thread and/or on the surface of the thread can be smaller than the amount of residual water. One skilled in the art can easily determine the optimum proportions of water and the particular treatment agent by carrying out preliminary trials.

The amount of lubricating agent, such as silicone, which may be present on the surface of the thread is notably smaller than that of the treatment agent. For example, the silicone films on the periphery of the thread can represent about 0.05 percent by weight of the thread.

It will be noted that the combination water-treatment agent is indispensable to obtain the results of the invention. Indeed, a treatment agent of a hygroscopic nature, such as glycerine, is incapable of penetrating the collagen thread by itself. Furthermore, water used alone swells the thread but cannot remain therein in a lasting manner as it evaporates a short while after being applied. According to the invention, the association of water-treatment agent permits at the same time the penetration of water into the thread, with swelling of the latter, and the retention of moisture in the thread.

The combination of means proposed by the invention is therefore crucial.

The molecular weight of the treatment agent mixed with water provides a direct influence on the swelling of the thread; the higher the molecular weight the less the swelling, and swelling is not permanent if the molecular weight of the treatment agent is higher than 400.

To obtain supple thread, according to the invention, it is possible to simply soak the thread in at least one bath consisting of a solution of distilled water and the treatment agent. The treatment can also be carried out in a single bath comprising distilled water and at least one agent capable of maintaining moisture in the thread and/or on the surface thereof. The treatment agents can be used in solution, in emulsion or in suspension in the bath of distilled water or in a third solvent.

The temperature at which the thread is impregnated by the treatment bath can vary between 10° and 50°C, but it is possible to diverge from this range without drawbacks arising, so long as the bath remains liquid. For obvious practical reasons, it is preferable to carry out impregnation of the thread at a temperature close to ambient temperature.

The duration of treatment can vary from one second to several days according to the nature of the treatment agent. Generally speaking, durations of 10 minutes to 8 hours are suitable. Duration of treatment obviously depends on factors such as temperature, diameter of the treated thread and the degree of desired suppleness. For a given temperature, and the diameter of the thread being equal, the longer the treatment the greater the degree of suppleness.

Use of a treatment bath maintained at a higher pressure than normal atmoshperic pressure does not lie outside the scope of the invention. Pressurized treatment can facilitate the desired improvement in suppleness of the thread and decrease the time of treatment.

It is suitable to maintain the pH of the treatment bath within certain limits to obtain a thread with a substantially neutral pH at the end of the treatment. Generally, the pH is included in the range of 5 to 9. The subsequent sterilization operation somewhat modifies the pH, resulting in an increase in the pH values. It is therefore suitable to compensate for this variation by previously introducing a weak acid, such as acetic acid or citric acid, into the treatment bath.

In addition to agents to adjust pH, treatment baths can contain antioxidants or reducing agents with a view to preventing the formation of rust on the steel needles by means of which the catgut threads are inserted. An example of such an antioxidant is sodium nitrite $NaNO_2$.

It a lubricating product, containing silicone for instance, is to be used, it can be added to the same single treatment bath in the form of an emulsion or, when the thread is treated in several baths, in the form of a solution in an organic solvent.

When the thread, in the form of a skein or loose cell for example, has been soaked in the treatment bath, the residual amount of the bath is removed by conventional means, such as draining or rinsing; the thread is then ready to be sterilized.

The conventional sterilization treatment of catgut consists in exposing the thread to a sterilizing gas, such as ethylene oxide or to the action of beta or gamma radiations. It is, moreover, known that the sterilization of dry catgut with ethylene oxide is always difficult. According to the present invention, on the other hand, the presence of residual water in the thread enhances sterilization in depth through the thin strips of the thread.

In the prior art, it is generally necessary to effect sterilization in the presence of moisture. In the present invention, this additional introduction of moisture is avoided since the thread itself contains a suitable amount of water for sterilization.

The advantages provided by the catgut threads according to the invention are numerous.

For the manufacture of catgut, conditioning is greatly simplified. Indeed, as the catgut has undergone treatment prior to sterilization it can be conditioned as it is, without its being necessary to immerse it in alcohol. It therefore suffices if the used packing is sealed against microorganisms. It therefore becomes possible to use packages made of plastic, treated paper or cardboard, in the form of a rigid container or a thin envelope. Another advantage for the manufacturer is that threads are easily sterilized, the sterilizing gas penetrating deeply into the thread.

The advantages of the new thread are clearly apparent to the user. No manipulations are necessary to remove alcohol from the tubes. The air of the operating room is not tainted by alcohol vapours and the risk of fire does not exist. As the catgut cannot dry as a result of the effects of heat and light owing to the evaporation of the alcohol incorporated to conserve it, it remains permanently supple and pleasant to use for the surgeon. The catgut remains supply in a sterile pack for several years. Owing to its slightly lubricated surface, the thread is easy to use and does not cause traumatisms to the tissues into which it is inserted.

A variant of the catgut thread used in surgery is chromium plated catgut, which is resorbed more slowly and which is much stiffer than normal catgut, and therefore more difficult to use. Chromium plated catgut can also be rendered supple according to the present invention. The duration of treatment in the bath is then 2 to 5 times longer than the duration of treatment of normal catgut.

If the swelling and diameter of chromium plated catgut and ordinary catgut are comparable, their suppleness is substantially identical. Chromium plated catgut (like ordinary catgut) thus becomes easy and pleasant to use.

Comparative measurements carried out with the rigidimeter confirm this fact:

N°4 Dec-catgut thread sterilized and preserved in alcohol, during use 8′ after removal from the tube:

Rigidity in milli Newton/m^2 0.013

N°4 Dec. catgut thread sterilized according to the présent invention, suppled at use:

Rigidity in milli Newton/m^2 0.006

N°4 Dec. chromium plated catgut thread according to the present invention, suppled, at use:

Rigidity in milli Newton/m^2 0.0063

The invention will not be illustrated, while in no way limited, by the following examples:

EXAMPLE 1

A single treatment bath having the following composition is used:

Glycerol	50 parts by weight
Distilled water	50 parts by weight
Acetic acid	0.1 part by weight
$NaNO_2$	0.1 part by weight
Silicone emulsion	2.5 parts by weight

A 45/**100** th diameter catgut thread comprising collagen, formed into a skein, is immersed in the above bath at ambient temperature for 1 ½ hours. After rapid rinsing with ethyl alcohol, or simple draining, the catgut is rolled or swedged on needles, then sterilized by being exposed to ethylene oxide.

Finally, a thread containing 27 percent by weight of water is obtained which represents a swelling, or an increase in diameter, of 20 percent based on the dry thread. This water is associated in the thread with 42 percent glycerol and 0.002 percent silicone.

EXAMPLE 2

The operation is carried out as in example 1, with the same treatment bath, but catgut threads of various diameters and variable durations of treatment are used.

The results are given in table 1.

TABLE 1

Conditions of treatment	Properties of the thread		
	Amount present in the thread in % by weight based on the dry thread		
Diameter:45/100	Water	Glycerol	Silicone
Duration of treatment: 60 min*	22%	34%	0.002
Diameter:60/100 Duration of treatment: 3 hours	28%	41%	0.003

As the duration of treatment in this case was only 60 min., the thread obtained is a little less supple than the thread of example 1 which was treated for 90 min.

EXAMPLE 3

The operation is carried out with the same treatment agents as in example 1, but several successive baths are used, that is to say (A) a bath of distilled water containing glycerol and (B) a silicone bath for finishing the surface state of the thread. The respective compositions of the two baths (A) and (B) are as follows:

(A)		
	Glycerol	50 g
	Distilled water	51 g
	Lactic acid	0.1 g
(B)		
	Silicone oil	1 g
	Pure trichlorethylene	100 g

After treatment of the thread for 1 ½ hours with bath (A) and draining, then for 1′ with bath (B) and draining, the thread is sterilized as in example 1. A supple catgut thread is obtained having similar properties to those of example 1, and which is suitable for use in surgery.

EXAMPLE 4

A catgut thread is treated by soaking in a bath composed of:

Ethylene glycol	50 parts by weight
Distilled water	50 parts by weight

After draining, a durably supple thread is obtained.

In the following examples, other compositions of treatment baths suitable to the requirements of the invention are given.

EXAMPLE 5

Diethylene glycol	70 parts by weight
Distilled water	30 parts by weight
Citric acid	0.1 part by weight

EXAMPLE 6

Trimethylolpropane	50 parts by weight
Distilled water	50 parts by weight
pH adjusted to 6 with HCl	

EXAMPLE 7

Glycolic acid	40 parts by weight
Distilled water	60 parts by weight
pH adjusted to 5.5	

The catguts rendered supple and swollen by the baths defined in examples 3(A) and 4 to 7 can then be treated in a second bath to lubricate their surface, as defined in example 3(B). Examples of the second bath are given hereinbelow.

EXAMPLE 8

Vaseline oil	2g
Xylene	100g

EXAMPLE 9

Castor oil	2g
Chloroform	100g

After application of the baths mentioned in examples 5 to 11, cargut threads having durable suppleness are obtained.

What we claim is:

1. A collagen based suture comprising a collagen surgical thread containing therewithin from about 10 to 50 percent of water based on the weight of the thread and about 10 to 70 percent by weight of at least one hygroscopic agent for retaining the water and selected from the group consisting of glycerols, glycols and polyalkylene oxides, said hygroscopic agent having a low volatility and a molecular weight of up to about 400, and a hydrophobic lubricating agent on the surface and selected from the group consisting of lipoids and silicones, whereby said suture retains its suppleness in dry form.

2. A suture according to claim **1**, wherein the hygroscopic agent is present in about 0.05 percent.

3. A suture according to claim **1**, wherein the hygroscopic lubricating agent is a silicone and is present in about 0.05 percent.

4. A suture according to claim **3** wherein the hygroscopic agent is present in about 0.05 percent.

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UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 3,896,814

DATED : July 29, 1975

INVENTOR(S) : Daniel Vivien & Georg Schwarz

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

Page 1 Item "[76]", line 3, inventor's name incorrect, change "Schwartz" to -- Schwarz --.

Patent Col. 3, line 36, Specification Page 8, line 2, correct spelling of "atmospheric".

Signed and Sealed this

Thirteenth Day of July 1976

[SEAL]

Attest:

RUTH C. MASON
Attesting Officer

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Commissioner of Patents and Trademarks