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(54) Title: THE PREPARING METHOD AND THE USE OF ANTISEPTIC MEDICAL DRESSING.

(54) 发明名称: 抗菌医用敷料的制造方法及其用途

(57) Abstract: The present invention discloses a preparing method of antispetic medical dressing which include, basificating chitosan fibre to form alkali chitosan fibre, etherificating the alkali chitosan fibre with chlroacetic acid to form carboxymethyl chitosan fibre, then opening, netting, needling the resultant carboxymethyl chitosan fibre to form a dressing. Optionally, the antiseptic carboxymethyl chitosan medical dressing can be made by producing chitosan non-woven cloth with non-woven technique, followed by carboxymethyl reaction with the dressing, cutting, packaging, sterilization. The present invention also discloses the use of antiseptic medical dressing prepared by method mentioned above. The present invention can be applied on surgery wound, burn, scald and other chronic wounds etc, by covering wound it can prevent water in body fluid from losing, providing a active humid condition for wound healing, keeping wound from hydrops, putrescence, isolating bacteria infection, and having the effects which can diminish inflammation, stanch, ease pain, and accelerating the wound healing.

(57) 摘要:

本发明公开了抗菌医用敷料的制造方法，包括采用壳聚糖纤维经碱化生成碱壳聚糖纤维再与氯乙酸进行醚化反应，制成羧甲基壳聚糖纤维，再经开松、成网、针刺制成敷料。或者先把壳聚糖纤维经无纺布加工处理制成壳聚糖无纺布，再对此敷料进行羧甲基化反应，并裁切、包装、消毒，得到羧甲基壳聚糖抗菌医用敷料。本发明还公开了用上述方法制备的抗菌医用敷料的用途。本发明适用于外科创伤、烧伤、烫伤及其他慢性伤口等，覆盖创面可防止体液中的水分损失，为伤口愈合提供一个积极的湿润环境，并保持创面不积液，无浸蚀，隔绝细菌感染，并可起到消炎、止血、镇痛，促进组织愈合的作用。

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The Preparation Method of an Anti-microbial Wound Dressing and the Use Thereof

Field of the Invention

The present invention relates to a method for the preparation of a wound dressing, in particular to a method for the preparation of an anti-microbial wound dressing, and also to the use of said anti-microbial wound dressing.

Background Art

For a long time, wound dressing for surgery is sterile wadding and cotton-based gauze, the use of which suffers from certain limitations. Cotton gauze doesn't possess any anti-microbial characteristics. Although applied as sterile, cotton gauzes can be infected by microbes in the course of using. These traditional dressings tend to adhere to wound and even be integrated into new-born flesh, causing pain and new wound to patient during dressing change. The remaining fragments of these traditional dressings on the wound bed after dressing change are able to affect the healing of wound. Other dressings made of synthetic materials also have same drawbacks as discussed above.

When treating chronic wounds, a wound dressing is desirable to absorb a high volume of exudate and at the same time promote the healing of the wound. The currently widely used alginate fiber dressing doesn't have enough absorption ability to treat wound exuding high volume of exudate.

When treating burn patient, in order to control water evaporation and germ intrusion, typical therapy is covering the wound with dressing after excising dead tissue. Skin from pig and human is proved to be effective burn wound dressing. However, such skin bears the drawback of high cost and rejection to heterogeneous skin.

WO94/16746 discloses a wound dressing comprising carboxymethyl cellulose which is capable of absorbing 15 times its own weight of saline. Such cellulose can be applied during surgery and treating chronic wound. WO99/02093 discloses a wound dressing made of carboxymethyl cellulose and the production method thereof. However, the above two inventions facilitate wound healing only by providing a moist environment. Therefore, it is very meaningful to create an antiphlogistic, hemostatic biological wound dressing for surgery and burn therapy. Such dressing is not adhesive to wound and is absorbable to human tissue, thus could relieve pain of patient.

Polyacetylglucosamine, also known as chitosan, is an amylose widely existing in nature. It is a major composition of fungal cell wall and carapace of shrimps, crabs and insects. It has an unique property of being absorbed by human tissue after hydrolysis by lysozyme. This material is non-toxic, odorless and compatible with human tissue and does not cause any immune response. It also has antibiotic, antiphlogistic, hemostatic and antalgic capability. It facilitates wound healing as well.

Carboxymethyl chitosan is a category of Chitosan derivatives after the carboxylmethylation of chitosan. Among numerous Chitosan derivatives, carboxymethyl chitosan is very important and widely used in food conservatives, cosmetics and pharmaceuticals. In *Studies on Carboxymethyl Chitosan's Structure and Anti-microbial Capabilities*, L Chen *et al.* Journal of Wuhan University, April, 2000, the production method of carboxymethyl chitosan and its excellent antimicrobial property is discussed. Chinese invention patent application No. 92106598.7, 03153650.6, 20040015093.1 *etc.* also disclose the application of carboxymethyl chitosan in different fields.

Chinese invention patent (Publication No.CN1298972A) disclosed a chitosan fiber non-woven fabric and the production method thereof. Although the chitosan non-woven fabric dressing obtained is widely applied in medical field, it has unsatisfying exudate absorbency. Further more, the dressing thereof is not able to lock exudate and has a poor moisture retaining property, thus making the surface of wound quite dry and shrink into dark brown scar.

US 20050058694 disclosed a dressing containing chitosan fiber. In this invention, chitosan fiber is soaked in a solvent that does not dissolve chitosan fiber. After reacting with organic acid which is added to the solvent, the fiber swells to gel after absorbing liquid. The mechanism of the invention is that chitosan reacts with organic acid and forms a high-molecular salt. It is not a compound with covalent bonding. Although the high-molecular salt can become gel after absorbing fluid, the non-covalent bonding is not as strong as covalent bonding, therefore it may not be stable.

In addition, Chinese invention patent (Publication No.CN1431229) disclosed a method for producing carboxymethyl chitosan, which is a direct carboxylmethylation of raw chitosan material (powder or particle form). The carboxylmethylated product is still in powder state or particle state. Owing to the limitations of the production process, said method is unable to be applied upon chitosan fiber or non-woven fabric made of chitosan fiber. It is known for a skilled person in the art that, the specific surface area of chitosan fiber is much larger than that of raw chitosan material, and chitosan is quite absorptive, thus if such process as described in the above patent is directly applied to chitosan fiber or non-woven fabric made of chitosan fiber, chitosan fiber can not maintain the original

fiber form, leading to decreased yield of carboxymethyl chitosan fiber. In addition, if such process as described in the above patent is applied on chitosan fiber, the modified chitosan fiber obtained will dissolve when absorbing exudate, thus not able to obtain wound dressing that has excellent wet strength and promotes wound healing after absorping exudate. The resulting carboxymethyl chitosan product can only be used as moisturizer, but can not be further converted into medical fabrics.

Disclosure of the Invention

The first technical problem that the present invention solves is to provide a method of preparation of an anti-microbial wound dressing. Said dressing can be applied in surgical wound, burn, and other chronic wound. Said dressing, when covering wound, is able to prevent water in body fluids from losing, provide a favorable moist environment for wound healing and maintain a fluid-free, maceration-free, germ-free wound surface. Said dressing is antiphlogistic, hemostatic and antalgic and promote wound healing.

Another technical problem that the present invention overcomes is the drawback in directly applying the existing chitosan carboxymethylation technique on chitosan fiber. According to the present invention, chitosan fiber is modified directly without altering the original form of chitosan fiber to obtain the carboxymethyl chitosan fiber or non-woven fabric with desirable properties.

In a first aspect, the invention provides a method for the preparation of an anti-microbial wound dressing, comprising preparing carboxymethyl chitosan non-woven fabric from chitosan fiber which is then made into wound dressing by cutting, packaging and sterilizing, wherein the steps of preparing carboxymethyl chitosan non-woven fabric from chitosan fiber comprising:

contacting chitosan fiber with 40~50% NaOH solution with bath ratio being 1:20~60 for 0.5~6 hours at room temperature to obtain alkalized chitosan fiber, washing said alkalized product with absolute ethanol;

contacting said product with chloroacetic acid in isopropanol with the concentration of chloroacetic acid being 20~40%, reaction temperature being 35~75°C, reaction time being 1~8 hours;

removing the remaining solution after the reaction, and then washing with absolute ethanol to obtain carboxymethyl chitosan fiber after air dry;

preparing non-woven fabric by fiber chopping, opening, web formation and needling.

In a second aspect, the invention provides a method for the preparation of an anti-microbial wound dressing, comprising preparing carboxymethyl chitosan non-woven

fabric from chitosan fiber which is then made into wound dressing by cutting, packaging and sterilizing, wherein the steps of preparing carboxymethyl chitosan non-woven fabric from chitosan fiber is as follows:

preparing non-woven fabric from chitosan fiber by fiber chopping, opening, web formation and needling,

contacting said non-woven fabric with 40~50% NaOH solution with bath ratio being 1:20~60 for 0.5~6 hours at room temperature to obtain alkalized product, washing said alkalized product with absolute ethanol;

contacting said product with chloroacetic acid in isopropanol with the concentration of chloroacetic acid being 20~40%, reaction temperature being 35~75°C, and reaction time being 1~8 hours;

removing the remaining solution after the reaction, and then washing with absolute ethanol and air dry to obtain carboxymethyl chitosan non-woven fabric.

In a third aspect, the invention provides use of the anti-microbial wound dressing according to the first or second aspect for producing surgical wound, burn, and other chronic wound dressing.

In a fourth aspect, the invention provides use of the anti-microbial wound dressing according to first or second aspect for producing antiphlogistic and hemostatic wound wadding.

In a fifth aspect, the invention provides use of the anti-microbial wound dressing according to first or second aspect for producing antiphlogistic drainage sliver.

In a sixth aspect, the invention provides use of the anti-microbial wound dressing according to first or second aspect for producing surgical dressing as an inner layer of the composite dressing.

In a seventh aspect, the invention provides an anti-microbial wound dressing produced in accordance with the method of the first aspect.

In an eighth aspect, the invention provides an anti-microbial wound dressing produced in accordance with the method of the second aspect.

In order to solve the above technical problems, according to the present invention, there is provided a two-step method to produce carboxymethyl chitosan dressing, which comprises:

Contact chitosan fiber with 40~50% NaOH solution with bath ratio being 1:20~60 for 0.5~6 hours at room temperature to obtain alkalized chitosan fiber, wash said alkalized product with absolute ethanol;

Contact said product with chloroacetic acid in isopropanol. The concentration of chloroacetic acid is 20~40%. Reaction temperature is 35~75°C. Reaction time is 1~8

hours. After the reaction, remove the remaining solution and then wash with absolute ethanol. Carboxymethyl chitosan fiber is thus obtained after air drying.

Convert the air dried carboxymethyl chitosan fiber into non-woven fabric of 30~200g/m^2 after fiber opening, web formation and needling. Convert said non-woven fabric into anti-microbial carboxymethyl chitosan dressing by cutting, packaging and sterilizing.

Preferably, un-modified chitosan fiber is added after air dry but before fiber opening. The weight ratio of chitosan fiber to carboxymethyl chitosan fiber is 1:9 to 9:1. After mixing, strength of the non-woven wound dressing is improved.

More preferably, different additives are added into the wound dressing according to the present invention by different methods to change or improve the therapeutic property of the dressing. For example, nano-silver is added in the process of manufacturing said chitosan fiber to improve the anti-microbial property of the dressing. The production method is as follows:

In preparing chitosan fiber, add 0.1%~1% by weight of nano-silver particles into spinning solution.

Alternatively, the two-step method to produce carboxymethyl chitosan dressing can also be:

Chitosan fiber is made into non-woven fabric of 30~200g/m^2 after fiber opening, web formation and needling;

Contact said non-woven fabric with 40~50% NaOH solution with bath ratio being 1:20~60 for 0.5~6 hours at room temperature to obtain alkalized product, wash said alkalized product with absolute ethanol;

Contact said product with chloroacetic acid in isopropanol. The concentration of chloroacetic acid is 20~40%. Reaction temperature is 35~75°C. Reaction time is 1~8 hours. After the reaction, remove the remaining solution and then wash with absolute ethanol and air dry;

Carboxymethyl chitosan fabric is then made into carboxymethyl chitosan non-woven dressing by cutting, packaging and sterilizing.

Said dressing swells in water to become elastic gel material which is capable of absorbing about 30 times its own weight of water, which is much higher than other wound dressing.

Carboxymethyl chitosan fiber according to the present invention has a monofilament denier of 0.5~5dtex, a strength of 0.8~2.2cN/dtex.

The therapeutic property of the wound dressing according to the present invention can also be improved by introducing nano-silver in the process of manufacturing

carboxymethyl chitosan fiber or carboxymethyl chitosan non-woven fabric to improve the anti-microbial property of the dressing. The production method is as follows:

Contact said carboxymethyl chitosan fiber or carboxymethyl chitosan non-woven fabric obtained with silver nitrate in ethanol solvent to exchange sodium ion with silver ion. The concentration of silver nitrate solution is 0.5~10%. Reaction temperature is 20~30°C. Reaction time is 0.5~2 hours. After the reaction, remove the remaining solution and then wash with absolute ethanol and air dry.

The hydrophilicity of the wound dressing according to the present invention can be improved by plasma treatment.

The mechanism of plasma treatment in improving hydrophilic property of the wound dressing is opening the chemical bond on the surface of wound dressing to facilitate grafting hydrophilic group onto it. Plasma treatment is performed to greatly increase the hydrophilicity when inert gases or hydrophilic material are used as carrier. Plasma is used as an energy source to initiate polymerization. After a short period of irradiation from several seconds to several minutes at appropriate temperature, polymerization reaction is initiated in gas phase. Chain extention and termination is carried out in liquid and solid phase. The reaction initiated by low temperature plasma can significantly improve the property of medical biomaterials characterized in that (1) it is only effective on the surface of material upto to a depth of several dozens of nanometers and will not affect the property of basal materials; (2) it is capable of treating surfaces of different shapes; (3) it is highly germicidal and considered to be a satisfying surface treatment technique in the field of medical biomaterial.

In the plasma treatment of said wound dressing obtained under atmospheric pressure, the power of plasma discharge is 20W~100W, discharge time is 10 seconds~30 minutes. Suspend said dressing in certain hydrophilic solution for 5 seconds ~ 60 minutes.

In the plasma treatment of said wound dressing obtained at low temperature, the non-woven dressing prepared is juxtaposed in a plasma reactor which is connected to capacitive coupling.

In the hydrophilic grafting or polymerization of said dressing, modifying gas ventilated into vacuum reactor, modification pressure is 20~80Pa, modification time is 1~30 minutes;

Grafting polymerization is performed after modification, background vacuum is 2~8Pa, during glow discharge, the pressure of grafting polymerization is 10~60Pa, discharge time is 2~60 minutes and discharge power is 30~80W.

The dressing after plasma treatment swells in water to become elastic gel material which is capable of absorbing more than 30 times its own weight of water, which is higher than untreated wound dressing.

The practicality of wound dressings is significantly increased after plasma treatment as discussed above. The hydrophilicity of dressings is thus improved. Said dressing can be applied to stop bleeding in surgical wounds, be left inside the body and absorbed afterwards. Said dressing can be applied in surgical wound, burn, and other chronic wound. Said dressing, when covering wound, is able to prevent water in body fluids from losing, provide a favorable moist environment for wound healing and maintain a fluid-free, maceration-free, germ-free wound surface. Said dressing is antiphlogistic, hemostatic and antalgic and facilitates wound healing.

The wound dressing according to the present invention is applicable in the field of surgical and burn treatment. Said wound dressing can be made into dressing for surgical wound, burn as well as chronic wound.

The wound dressing according to the present invention can be made into antiphlogistic and hemostatic wound wadding and drainage sliver which can be applied on surgical wounds to stop bleeding, be left inside human body and be absorbed afterwards.

The wound dressing according to the present invention can be used as an inner layer of composite dressings. When transparent or opaque film with adhesive on one side is used as an outer layer, said dressing can be made into island dressing for surgical wound.

Compared to prior arts, the present invention possesses the following advantages: the anti-microbial wound dressing according to the present invention can be applied in surgical wound, burn, and other chronic wound. Said dressing, when covering wound, is able to prevent water in body fluids from losing, provide a favorable moist environment of wound healing and maintain a fluid-free, maceration-free, germ-free wound surface. Said dressing is antiphlogistic, hemostatic and antalgic and facilitates wound healing.

In addition, the method according to the present invention overcomes the drawback in directly applying the existing chitosan carboxymethylation technique on chitosan fiber. According to the present invention, chitosan fiber is modified directly without altering the original form of chitosan fiber to obtain carboxymethyl chitosan fiber or non-woven fabric with desirable properties.

Embodiments

The present invention is further illustrated by the following examples:

Example 1:

Contact 100g chitosan fiber with 40% NaOH solution with bath ratio being 1:20 for 0.5 hour at room temperature to obtain alkalized chitosan fiber, wash said alkalized product with absolute ethanol; contact said product with chloroacetic acid in isopropanol, the concentration of chloroacetic acid is 20%, reaction temperature is 35°C, reaction time is 1 hour. After the reaction, remove the remaining solution and then wash with absolute ethanol. Carboxymethyl chitosan fiber is obtained after air dry. Said product is made into non-woven fabric of 50g/m^2 after chopping, fiber opening, web formation and needling. Obtain dressing a1 by cutting, packaging and sterilizing said non-woven fabric. Dressing a1 is suitable for wound smaller than 10 cm^2.

Example 2:

Add chitosan fiber to carboxymethyl chitosan fiber which is used to manufacture a1. The weight ratio of chitosan fiber to carboxymethyl chitosan fiber is 9:1. The product is made into non-woven fabric of 100g/m^2 after mixing, chopping, fiber opening, web formation and needling. Obtain dressing a2 by cutting, packaging and sterilizing said non-woven fabric. Dressing a2 is suitable for relatively larger burn wound.

Example 3:

Contact 100g chitosan fiber with 45% NaOH solution with bath ratio being 1:40 for 1 hour at room temperature to obtain alkalized chitosan fiber; wash alkalized product with absolute ethanol; contact said product with chloroacetic acid in isopropanol, the concentration of chloroacetic acid is 30%, reaction temperature is 60°C, reaction time is 3 hours. After the reaction, remove the remaining solution and then wash with absolute ethanol. Obtain carboxymethyl chitosan fiber after air dry. The product is made into non-woven fabric of 50g/m^2 after chopping, fiber opening, web formation and needling. Obtain dressing b1 by cutting, packaging and sterilizing said non-woven fabric. Dressing b1 is suitable for wound smaller than 10 cm^2.

Example 4:

Add chitosan fiber to carboxymethyl chitosan fiber which is used to manufacture b1. The weight ratio of chitosan fiber to carboxymethyl chitosan fiber is 8:2. The product is made into non-woven fabric of 100g/m^2 after chopping, mixing, fiber opening, web formation and needling. Obtain dressing b2 by cutting, packaging and sterilizing said non-woven fabric. Dressing b2 is suitable for relatively larger burn wound.

Example 5:

Contact 100g chitosan fiber with 50% NaOH solution with bath ratio being 1:60 for 6 hours at room temperature to obtain alkalized chitosan fiber; wash said alkalized product with absolute ethanol; contact said product with chloroacetic acid in isopropanol, the concentration of chloroacetic acid is 40%, reaction temperature is 75°C, reaction time is 8

hours. After the reaction, remove the remaining solution and then wash with absolute ethanol. Obtain carboxymethyl chitosan fiber after air dry. The product is made into non-woven fabric of 50g/m^2 after chopping, fiber opening, web formation and needling. Obtain dressing c1 by cutting, packaging and sterilizing said non-woven fabric. Dressing c1 is suitable for wound smaller than 10 cm^2.

Example 6:

Add chitosan fiber to carboxymethyl chitosan fiber which is used to manufacture c1. The weight ratio of chitosan fiber to carboxymethyl chitosan fiber is 1:9. The product is made into non-woven fabric of 100g/m^2 after chopping, mixing, fiber opening, web formation and needling. Obtain dressing c2 by cutting, packaging and sterilizing said non-woven fabric. Dressing c2 is suitable for relatively larger burn wound.

Example 7:

Contact 100g chitosan non-woven fabric with 40% NaOH solution with bath ratio being 1:20 for 0.5 hour at room temperature to obtain alkalized non-woven chitosan fabric, wash alkalized product with absolute ethanol; contact said product with chloroacetic acid in isopropanol, the concentration of chloroacetic acid is 20%, reaction temperature is 35°C, reaction time is 1 hour. After the reaction, remove the remaining solution and then wash with absolute ethanol. Obtain carboxymethyl chitosan non-woven fabric after air dry. Obtain dressing d1 by cutting, packaging and sterilizing said non-woven fabric. Dressing d1 is suitable for wound smaller than 10 cm^2.

Example 8:

Contact 100g chitosan non-woven fabric with 45% NaOH solution with bath ratio being 1:40 for 1 hour at room temperature to obtain alkalized non-woven chitosan fabric, wash alkalized product with absolute ethanol; contact said product with chloroacetic acid in isopropanol, the concentration of chloroacetic acid is 30%, reaction temperature is 60°C, reaction time is 3 hours. After the reaction, remove the remaining solution and then wash with absolute ethanol. Obtain carboxymethyl chitosan non-woven fabric after air dry. Obtain dressing e1 by cutting, packaging and sterilizing said non-woven fabric. Dressing e1 is suitable for wound smaller than 10 cm^2.

Example 9:

Contact 100g chitosan non-woven fabric with 50% NaOH solution with bath ratio being 1:60 for 6 hours at room temperature to obtain alkalized non-woven chitosan fabric, wash said alkalized product with absolute ethanol; contact said product with chloroacetic acid in isopropanol, the concentration of chloroacetic acid is 40%, reaction temperature is 75°C, reaction time is 8 hours. After the reaction, remove the remaining solution and then wash with absolute ethanol. Obtain carboxymethyl chitosan non-woven fabric after air

dry. Obtain dressing f1 by cutting, packaging and sterilizing said non-woven fabric. Dressing f1 is suitable for wound smaller than 10 cm^2.

Example 10:

Juxtapose dressing a1 in a plasma reactor which is connected to capacitive coupling. In the hydrophilic grafting or polymerization of said dressing, oxygen is added into vacuum reactor, grafting polymerization is performed after modification, background vacuum is 2Pa, glow discharge. Modification pressure is 20Pa, modification time is 1 minute; the pressure of grafting polymerization is 10Pa, discharge time is 2 minutes and discharge power is 30W. The product obtained is A1.

Example 11:

Juxtapose dressing a1 in a plasma reactor which is connected to capacitive coupling. In the hydrophilic grafting or polymerization of said dressing, nitrogen or hydrogen is added into vacuum reactor, grafting polymerization is performed after modification, background vacuum is 6Pa, glow discharge. Modification pressure is 40Pa, modification time is 15 minutes; the pressure of grafting polymerization is 30Pa, discharge time is 20 minutes and discharge power is 50W. The product obtained is B1.

Example 12:

Juxtapose dressing a1 in a plasma reactor which is connected to capacitive coupling. In the hydrophilic grafting or polymerization of said dressing, inert gas is added into vacuum reactor, grafting polymerization is performed after modification, background vacuum is 8Pa, glow discharge. Modification pressure is 80Pa, modification time is 30 minutes; the pressure of grafting polymerization is 60Pa, discharge time is 60 minutes and discharge power is 80W. The product obtained is C1.

Example 13:

Cut the non-woven dressing according to examples 1 to 12 into 10cm*10cm, obtain wound dressing for surgery, burn, and chronic wound after packaging and sterilization.

Example 14:

Cut the non-woven dressing according to examples 1 to 12 into 4cm*20cm, and stick it onto the adhesive side of a 9cm*25cm transparent film with medical adhesive on one side. Stick silicon paper onto the adhesive side. Obtain surgical island dressing after packaging and sterilization.

Example 15:

The non-woven fabric according to examples 1 to 12 can be made into antiphlogistic and hemostatic wound wadding after packaging and sterilization.

Example 16:

Cut the non-woven dressing according to examples 1 to 12 into 4cm*10cm, obtain antiphlogistic drainage sliver after packaging and sterilization.

The present invention is further illustrated by the following experiments:

Experiment 1: Anti-microbial test result 1 of carboxymethyl chitosan dressing (see Table 1)

Test samples are products according to examples 1~9; control sample is normal medical gauze (Shanghai No. 21 fabric factory).

Test method is in accordance with AATCC100—1999, Evaluation of Anti-microbial Property of Fabrics.

Table 1, anti-microbial test result

Group	*E. coli* (ATCC8099)	*P. aeruginosa* (ATCC27653)	Methicillin-resistant *S. aureus*	*E. faecalis* (ATCC51575)
Control	4.73%	27.1%	6.47%	0
a1	>99%	>99%	>99%	>99%
a2	>99%	>99%	>99%	>99%
b1	>99%	>99%	>99%	>99%
b2	>99%	>99%	>99%	>99%
c1	>99%	>99%	>99%	>99%
c2	>99%	>99%	>99%	>99%
d1	>99%	>99%	>99%	>99%
e1	>99%	>99%	>99%	>99%
f1	>99%	>99%	>99%	>99%
Difference	mean >26%			

Note 1. The difference between average bacterial colonies before and after vibration without sample being added is <10%. The test is credible.

2. Test sample is anti-microbial when the difference of anti-microbial rate between test sample and control is >26%.

According to the experiment result, the products according to examples 1~9 all have anti-microbial property.

Experiment 2: Liquid absorption test

Preparation of test samples: Obtain carboxymethyl chitosan non-woven fabric a1 according to Example 1 (test sample). Obtain low temperature plasma treated products A1, B1, C1 (test sample) according to Examples 10-12. Normal medical two-layer gauze

is used as control (Shanghai No. 21 fabric factory). All the above samples are cut into 5cm*5cm.

Preparation of test solution: 8.298g sodium chloride and 0.368g calcium chloride are dissolved in 1000ml deionized water.

Test equipments

Analytical balance with an accuracy of 0.001g; incubator; Petri dish.

Test method

1 Get a sample with weight W1 in gram by balance;

2 Place the sample into a Petri dish, add test solution 40 times the weight of sample;

3 Place the Petri dish into 37°C incubator for 30 minutes;

4 Suspend the sample with forceps and stay in air for 30 seconds;

5 Obtain sample weight W2 in gram by balance;

6 Calculate liquid absorbency according to formula:

$a = (W2 - W1)/W1$, a is liquid absorbency

7 Calculate the arithmetic mean for two test results (see Table 2)

Table 2, liquid absorbency test

Sample	Test 1			Test 2			a mean
	W1	W2	a	W1	W2	a	
a1	0.283	8.695	29.724	0.258	8.632	32.457	31.090
A1	0.247	8.731	34.348	0.265	9.113	33.389	33.868
B1	0.258	9.662	36.450	0.276	9.601	33.786	35.118
C1	0.273	9.459	33.648	0.259	9.591	36.031	34.839
Control	0.155	2.514	15.219	0.158	2.594	15.418	15.318

Result: the liquid absorbency of a1 is 2.03 times that of the control sample, the liquid absorbency of A1 is 1.09 times that of a1 and 2.14 times that of the control sample, the liquid absorbency of B1 is 1.13 times that of a1 and 2.29 times that of the control sample, the liquid absorbency of C1 is 1.12 times that of a1 and 2.27 times that of the control sample. It proves that plasma treatment can increase hydrophilicity of wound dressings.

The claims defining the invention are as follows:

1. A method for the preparation of an anti-microbial wound dressing, comprising preparing carboxymethyl chitosan non-woven fabric from chitosan fiber which is then made into wound dressing by cutting, packaging and sterilizing, wherein the steps of preparing carboxymethyl chitosan non-woven fabric from chitosan fiber comprising:

contacting chitosan fiber with 40~50% NaOH solution with bath ratio being 1:20~60 for 0.5~6 hours at room temperature to obtain alkalized chitosan fiber, washing said alkalized product with absolute ethanol;

contacting said product with chloroacetic acid in isopropanol with the concentration of chloroacetic acid being 20~40%, reaction temperature being 35~75°C, reaction time being 1~8 hours;

removing the remaining solution after the reaction, and then washing with absolute ethanol to obtain carboxymethyl chitosan fiber after air dry;

preparing non-woven fabric by fiber chopping, opening, web formation and needling.

2. The method for the preparation of an anti-microbial wound dressing according to claim 1, wherein upon adding chitosan fiber after air dry but before fiber opening, the weight ratio of chitosan fiber to carboxymethyl chitosan fiber being 1:9 to 9:1.

3. A method for the preparation of an anti-microbial wound dressing, comprising preparing carboxymethyl chitosan non-woven fabric from chitosan fiber which is then made into wound dressing by cutting, packaging and sterilizing, wherein the steps of preparing carboxymethyl chitosan non-woven fabric from chitosan fiber are as follows:

preparing non-woven fabric from chitosan fiber by fiber chopping, opening, web formation and needling,

contacting said non-woven fabric with 40~50% NaOH solution with bath ratio being 1:20~60 for 0.5~6 hours at room temperature to obtain alkalized product, washing said alkalized product with absolute ethanol;

contacting said product with chloroacetic acid in isopropanol with the concentration of chloroacetic acid being 20~40%, reaction temperature being 35~75°C, and reaction time being 1~8 hours;

removing the remaining solution after the reaction, and then washing with absolute ethanol and air dry to obtain carboxymethyl chitosan non-woven fabric.

4. The method for the preparation of an anti-microbial wound dressing according to any one of claims 1-3, comprising:

performing low temperature plasma treatment on said wound dressing product, juxtaposing said wound dressing in a plasma reactor which is connected to capacitive coupling;

hydrophilic grafting or polymerizing said dressing, adding modifying gas into vacuum reactor, background vacuum being 2~8Pa, glowing discharge, modification pressure being 20~80 Pa, modification time being 1~30 minutes;

performing grafting polymerization after modification, background vacuum being 2~8Pa, during glow discharge, the pressure of grafting polymerization being 10~60Pa, discharge time being 2~60 minutes and discharge power being 30~80W.

5. Use of the anti-microbial wound dressing according to any one of claims 1 to 4 for producing surgical wound, burn, and other chronic wound dressing.

6. Use of the anti-microbial wound dressing according to any one of claims 1 to 4 for producing antiphlogistic and hemostatic wound wadding.

7. Use of the anti-microbial wound dressing according to any one of claims 1 to 4 for producing antiphlogistic drainage sliver.

8. Use of the anti-microbial wound dressing according to any one of claims 1 to 4 for producing surgical dressing as an inner layer of the composite dressing.

9. An anti-microbial wound dressing produced in accordance with the method of claim 1.

10. An anti-microbial wound dressing produced in accordance with the method of claim 3.

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