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(54) Title: ANTIMICROBIAL ELASTOMER COMPOSITION AND METHOD FOR MAKING

(57) Abstract: A method for making an elastomeric material containing an antimicrobial composition such as a dispersion of silver oxide that is suitable for implantation within the body. The elastomer made in accordance with this method extends the amount of work-time available for processing the elastomer into an article as compared with the work-time available when using prior art compounding methods.

TITLE: ANTIMICROBIAL ELASTOMER COMPOSITION AND METHOD FOR MAKING

INVENTOR: JESSE NELSON

SPECIFICATION

BACKGROUND OF THE INVENTION

1. Field of the Invention

The present invention relates to a method for making an antimicrobial elastomeric material containing an antimicrobial composition such as a dispersion of silver oxide that is suitable for implantation within the body

2. Description of the Prior Art

Medical devices, particularly implantable elastomeric prostheses which are used in environments where micro-organisms are actively growing, can become covered with a biofilm comprising a colonized layer of microorganisms such that the function of the prosthesis is impaired. After growth of the biofilm microbial layer, filaments can grow and descend into the body or wall of the prosthesis and detrimentally affect its physical properties until the device no longer functions. The fouled device must be cleaned or discarded.

Whenever a prosthesis is in contact with moisture in a warm, nutrient rich environment, the surfaces of the prosthesis may support microbial growth which may include, *inter alia,* bacteria. The microbial growth can interfere with the functioning of the prosthesis, requiring removal of the prosthesis for disposal or cleaning. The microbial growth is a persistent problem in the management and care

of patients who have had their larynx removed and utilize a voice prosthesis since the prosthesis is exposed to a non-sterile, humid, warm, nutrient rich environment.

Various methods for preventing microbial growth on an indwelling device have been proposed. One approach for reducing bacterial infection encountered with the use of medical devices inserted into body cavities has been to apply an antimicrobial coating to the surface of the medical device. For example, U.S. Pat. No. 4,592,920 to Murtfeldt; U.S. Pat. No. 4,603,152 to Laurin et al and U.S. Pat. No. 4,677,143 to Laurin et al. each teach applying a coating containing an antimicrobial agent such as silver oxide to the outer surfaces of medical devices such as catheters, enteral feeding tubes, endotracheal tubes and other hollow tubular devices. The '920 patent to Murtfeldt is primarily concerned with providing a surface coating of an antimicrobial metal compound on a medical device such as a catheter, but also discloses that the metal compound can be "imbedded" within the entire catheter. However, the Murtfeldt patent teaches that the imbedded construction is less desirable since the antimicrobial metal compound imbedded within the side wall of the catheter has less likelihood of encountering migrating microbes and, by inference, is less effective than a surface coating.

Seder et al., in pending U.S. Patent application serial number 09/833,961, the content of which is incorporated herein by reference thereto, teach that antimicrobial agents can be compounded (i.e., embedded) into those portions of a prosthesis that are not in contact with tissue. The antimicrobial portions remain free of microbial growth for an extended period which contributes to longer use of the prosthesis *in vivo*. For example, the valve in most voice prostheses is not in contact with tissue. It is only in intermittent contact with body fluids. The same is true of

the inside surface of the tubular prosthesis and/or the facial and inside surfaces of rings or cartridges that are present to reinforce the soft body of a prosthesis. By adding an amount of microbial agent effective to resist growth onto (or into) the valve, ring or cartridge, it is found that microbial growth is delayed for a significant period without any evidence of irritation or toxicity to the tissue. Seder et al. further teach that the antimicrobial agent-bearing elastomer can be compounded by dispersion of the antimicrobial agent into the raw elastomer material. For example, silicone elastomer can contain at least 10 percent of an antimicrobial agent such as silver, or silver compounds such as silver oxide. Other suitable antimicrobial compounds such as, for example, gold, platinum, copper, zinc metal powder or oxides and salts thereof, can be used in the non-tissue contacting portions of the prosthesis. A more complete discussion of prior art methods for incorporating antimicrobial agents into, or upon, a prosthesis is also presented in Seder et al.

A problem with prior art methods of dispersing an antimicrobial agent such as Ag_2O into an elastomer prior to forming a prosthetic article therefrom is the short work-time available for forming the elastomer into a prosthesis, or a portion thereof, after compounding; sometimes the work-time being as short as a minute or two. It is, therefore, desirable to provide a method for incorporating an antimicrobial agent such as, for example, silver oxide, into an elastomer such as silicone that provides a longer work-time for fabricating an article therefrom.

SUMMARY OF THE INVENTION

The present invention is directed to an antimicrobial elastomer composition and a method for making the composition that substantially obviates one or more of the limitations of the related art. To achieve these and other advantages and in

accordance with the purpose of the invention, as embodied and broadly described herein, the method of making the antimicrobial elastomer of the present invention includes the steps of: (a) presenting a two-part, addition-curable silicone elastomeric dispersion consisting of Part A and Part B; (b) mixing part A with part B to form a liquid, moldable silicone elastomer; (c) dispersing additional inhibitor into the silicone elastomer wherein the inhibitor is any agent that affects the cure time of the liquid elastomer; and (d) compounding an antimicrobial agent into the liquid silicone elastomer. The resulting liquid silicone may be molded to form an article over an extended period of time (i.e., "work-time"). In a second embodiment of the method of the present invention, the mixing of Part A and Part B may be delayed by adding additional inhibitor to one or both parts of the silicone, followed by the addition of the antimicrobial agent to one or both parts of the silicone prior to the step of mixing Part A and Part B.

The features of the invention believed to be novel are set forth with particularity in the appended claims. However the invention itself, both as to organization and method of operation, together with further objects and advantages thereof may be best understood by reference to the following description.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

A first preferred method for making an antimicrobial elastomeric composition in accordance with the present invention comprises the steps of: (a) presenting Part A and Part B of a silicone elastomer wherein when Part A and Part B are mixed together in the presence of an initiator, a curable, injection moldable silicone elastomer is formed; (b) mixing part A with part B to form a liquid, moldable silicone elastomer; (c) dispersing additional inhibitor into the silicone elastomer wherein the

inhibitor is any agent that affects the cure time of the liquid elastomer; and (d) compounding an antimicrobial agent into the liquid silicone elastomer.

A second preferrend method for making an antimicrobial elastomeric composition in accordance with the present invention comprises the steps of: (a) presenting Part A and Part B of a silicone elastomer wherein when Part A and Part B are mixed together in the presence of an initiator, a curable, injection moldable silicone elastomer is formed; (b) adding additional inhibitor to Part A or Part B; (c) dispersing particles of an antimicrobial agent in Part A or Part B; and (d) mixing Part A with Part B.

In yet a third preferred method for making an antimicrobial elastomeric composition in accordance with the present invention, the method comprises the steps of (a) presenting Part A and Part B of a silicone elastomer; again wherein when Part A and Part B are mixed together in the presence of an initiator, a curable, injection moldable silicone elastomer is formed; (b) adding additional inhibitor to both Part A and Part B; (c) dispersing particles of an antimicrobial agent in Part A or Part B; and (d) mixing Part A with Part B.

In all of the methods for making an antimicrobial silicone elastomer having an extended work-time in accordance with the present invention, the preferred antimicrobial agent is silver oxide. It is clear to artisans that in order to form an elastomeric article by injection molding, the moldable elastomer comprising the article must be in a physical form operable for conforming to the contour of a mold into which it is injected. The term "work-time", as used herein, means the length of time after Part A and Part B of a 2-part elastomer composition are admixed that the elastomer composition remains injection moldable at or near room temperature. Part A and Part B

are preferably platinum cured and provide a silicone elastomer having a durometer between 40 and 70, and most preferably about 60, when cured.

Although the amount of inhibitor incorporated into Part B of a 2-part silicone elastomer by the manufacturer is generally maintained as a trade secret by the manufacturer, it is believed to be on the order of .02% w/w as supplied. The term "inhibitor", as used herein, refers to any substance that, when added to a silicone elastomer comprising a mixture of Part A and Part B, increases or extends the work-time (i.e., the time required for the elastomer to cure). An example of a suitable inhibitor is 2-methyl-3-butyn-2-ol. The amount of additional inhibitor to be added to Part A and/or Part B, either prior to or after mixing, is related to the amount of work-time altering additive such as silver oxide added to the elastomer. The amount of additional inhibitor added to the silicone elastomer in accordance with the method of the present invention is in the range of .05-.40 % w/w, and preferably in the range .05-.1 % w/w. A preferred mole ratio of additional inhibitor to silver oxide in the silicone elastomer is about 1:40.

Examples:

Example 1:

Present 50 grams silicone part A; then

Add 50 grams of silicone part B to part A; then

Add 0.08 ml of inhibitor to the part A/part B mixture to provide a silicone elastomer; then

Disperse additional inhibitor throughout the part A/part B silicone elastomer; then

Add 7.5 grams silver oxide to the inhibitor/silicone elastomer mixture; then

Disperse silver oxide throughout the inhibitor/silicone elastomer mixture.

The work-time of the antimicrobial silicone elastomer thus formed is on the order of several hours to two days

Example 2:

Present 50 grams of silicone part B; then

Add 0.12 ml of additional inhibitor to silicone part B; then

Disperse the additional inhibitor throughout part B; then

Add 11.1 grams silver oxide to the inhibitor/part B mixture; then

Disperse the silver oxide throughout inhibitor/part B mixture; then

Add 50 grams silicone part A to inhibitor/silver oxide/part B mixture; then

Disperse silicone part A throughout previous mixture.

Elastomers made in accordance with either Example 1 or Example 2 provide a viscous, injection-moldable antimicrobial composition having a work-time of several hours to two days. For example, an addition cure silicone such as those known as gum-stock silicones could be used in lieu of an injection moldable silicone elastomer, maintaining generally the same chemical makeup and curing mechanism, but providing a different presentation for working with and molding the material.While particular embodiments of the present invention have been illustrated and described, it would be obvious to those skilled in the art that various other changes and modifications can be made without

departing from the spirit and scope of the invention. For example, a further method for making an antimicrobial elastomeric composition may comprise the steps of: (a) presenting Part A and Part B of a silicone elastomer wherein when Part A and Part B are mixed together in the presence of an initiator, a curable, injection moldable silicone elastomer is formed; (b) adding additional inhibitor to Part A or Part B; (c) dispersing particles of an antimicrobial agent in Part A and Part B; and (d) mixing Part A with Part B. It is therefore intended to cover in the appended claims all such changes and modifications that are within the scope of this invention.

What I claim is:

CLAIMS

1. A method for making an antimicrobial elastomeric composition comprising the steps of:

(a) presenting Part A and Part B of a silicone elastomer wherein when Part A and Part B are mixed together in the presence of an initiator, a curable, injection-moldable silicone elastomer is formed;

(b) mixing part A with part B to form a injection-moldable silicone elastomer;

(c) dispersing additional inhibitor into the silicone elastomer wherein the inhibitor is any agent that increases the cure time of the silicone elastomer; and

(d) compounding an antimicrobial agent into the silicone elastomer.

2. The method for making an antimicrobial elastomeric composition in accordance with claim 1 wherein said antimicrobial agent is silver oxide.

3. The method for making an antimicrobial elastomeric composition in accordance with claim 1 wherein said inhibitor is 2-methyl-3-butyn-2-ol.

4. A method for making an antimicrobial elastomeric composition comprising the steps of:

(a) presenting Part A and Part B of a silicone elastomer wherein when Part A and Part B are mixed together in the presence of an initiator, a curable, injection-moldable silicone elastomer is formed;

(b) adding additional inhibitor to either Part A or Part B;

(c) dispersing particles of an antimicrobial agent in either Part A or Part B; and

(d) mixing Part A with Part B.

5. The method for making an antimicrobial elastomeric composition in accordance with claim 4 wherein said inhibitor is 2-methyl-3-butyn-2-ol.

6. The method for making an antimicrobial elastomeric composition in accordance with claim 4 wherein said antimicrobial agent is silver oxide.

7. A method for making an antimicrobial elastomeric composition comprising the steps of:

(a) presenting Part A and Part B of a silicone elastomer wherein when Part A and Part B are mixed together in the presence of an initiator, a curable, injection-moldable silicone elastomer is formed;

(b) adding additional inhibitor to both Part A and Part B;

(c) dispersing particles of an antimicrobial agent in Part A or Part B; and

(d) mixing Part A with Part B.

8. The method for making an antimicrobial elastomeric composition in accordance with claim 7 wherein said inhibitor is 2-methyl-3-butyn-2-ol.

9. The method for making an antimicrobial elastomeric composition in accordance with claim 7 wherein said antimicrobial agent is silver oxide.

10. A method for making an antimicrobial elastomeric composition comprising the steps of:

(a) presenting Part A and Part B of a silicone elastomer wherein when Part A and Part B are mixed together in the presence of an initiator, a curable, injection-moldable silicone elastomer is formed;

(b) adding additional inhibitor to either Part A or Part B;

(c) dispersing particles of an antimicrobial agent in Part A and Part B; and (d) mixing Part A with Part B.

11. The method for making an antimicrobial elastomeric composition in accordance with claim 10 wherein said antimicrobial agent is silver oxide.

12. The method for making an antimicrobial elastomeric composition in accordance with claim 10 wherein said inhibitor is 2-methyl-3-butyn-2-ol.

13. The method for making an antimicrobial elastomeric composition in accordance with claim 1 wherein said microbial agent is 5-50% w/w silver oxide and said additional inhibitor is 2-methyl-3-butyn-2-ol and wherein the mole ratio of additional inhibitor to silver oxide when Part A and Part B are mixed is about 1:40.

14. The method for making an antimicrobial elastomeric composition in accordance with claim 4 wherein said microbial agent is 5-50% w/w silver oxide and said additional inhibitor is 2-methyl-3-butyn-2-ol and wherein the mole ratio of additional inhibitor to silver oxide when Part A and Part B are mixed is about 1:40.

15. The method for making an antimicrobial elastomeric composition in accordance with claim 7 wherein said microbial agent is 5-50% w/w silver oxide and said additional inhibitor is 2-methyl-3-butyn-2-ol and wherein the mole ratio of additional inhibitor to silver oxide when Part A and Part B are mixed is about 1:40.

16. The method for making an antimicrobial elastomeric composition in accordance with claim 10 wherein said microbial agent is 5-50% w/w silver oxide and said additional inhibitor is 2-methyl-3-butyn-2-ol and wherein the mole ratio of additional inhibitor to silver oxide when Part A and Part B are mixed is about 1:40.

17. A method for making an antimicrobial elastomer composition in accordance with any of the above claims wherein said silicone elastomer is an addition cure elastomer.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US05/26723

A. CLASSIFICATION OF SUBJECT MATTER
IPC(7) : A61K 31/28, 9/52, 9/58
US CL : 424/404, 457, 486, 618
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 424/404, 457, 486, 618

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 6,361,526 B1 (REISDORF et al.) 26 March 2002 (26.03.2002), Abstract, column 3, lines 39-44, column 4, lines 27-47, claims 1-3.	1-17
Y	US 6,013,711 A (LEWIS) 11 January 2000 (11.01.2000), column 3, lines 8-67, column 4, lines 1-2, column 6, lines 10-42, claims 7 and 10.	1-17
Y	US 3,445,420 A (KOOKOOTSEDES et al.) 20 May 1969 (20.05.1969), Abstract, column 3, lines 38-40, column 5, inhibitor(b), column 6, lines 24-45.	1, 3-5, 7, 8, 10, 21-17

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

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Continuation of B. FIELDS SEARCHED Item 3:
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