(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
20 October 2011 (20.10.2011)

PCT

(10) International Publication Number
WO 2011/130246 A2

(51) International Patent Classification:
A61K 33/14 (2006.01) *A61K 47/30* (2006.01)
A61K 9/46 (2006.01) *A61P 17/02* (2006.01)
A61K 9/70 (2006.01) *A61P 17/00* (2006.01)
A61K 47/34 (2006.01)

(21) International Application Number:
PCT/US2011/032086

(22) International Filing Date:
12 April 2011 (12.04.2011)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/323,663 13 April 2010 (13.04.2010) US

(71) Applicant *(for all designated States except US)*: **KCI LICENSING, INC.** [US/US]; P.O. Box 659508, San Antonio, TX 78265 (US).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: **HONG, Kz** [US/US]; Kci Licensing, Inc., P.O. Box 659508, San Antonio, TX 78265 (US). **INGRAM, Shannon, C.** [US/US]; C/o Kci Licensing, Inc., P.o. Box 659508, San Antonio, TX 78265 (US). **ZIMMNITSKY, Dmitry** [BY/US]; C/o Kci Licensing, Inc., P.O. Box 659508, San Antonio, TX 78265 (US). **LONG, Justin** [US/US]; C/o Kci Licensing, Inc., P.O. Box 659508, San Antonio, TX 78265 (US). **KAZALA, Richard, M.** [US/US]; C/o Kci Licensing, Inc., P.O. Box 659508, San Antonio, TX 78265 (US). **RAMIREZ, Hugo** [US/US]; C/o Kci Licensing, Inc., P.O. Box 659508, San Antonio, TX 78265 (US).

(74) Agent: **ROBINSON, Eagle, H.**; Fulbright & Jaworski L.L.P., 600 Congress Ave., Suite 2400, Austin, TX 78701 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— *without international search report and to be republished upon receipt of that report (Rule 48.2(g))*

WO 2011/130246 A2

(54) **Title**: COMPOSITIONS WITH REACTIVE INGREDIENTS, AND WOUND DRESSINGS, APPARATUSES, AND METHODS

(57) **Abstract**: Wound dressings and wound inserts comprising substantially dry reactive agents, methods of forming wound inserts comprising dry reactive agents, and wound- treatment methods.

DESCRIPTION

COMPOSITIONS WITH REACTIVE INGREDIENTS, AND WOUND DRESSINGS, APPARATUSES, AND METHODS

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority to U.S. Provisional Patent Application No. 61/323,663, filed April 13, 2010, which is incorporated herein in its entirety.

BACKGROUND

1. Field of the Invention

[0002] The present invention relates generally to healing of wounds and wound-treatment therapies. More particularly, but not by way of limitation, the present invention relates to fluid-instillation and negative-pressure wound therapies, comprising a foam (and/or other porous material) wound insert containing reactive agents.

2. Background Information

[0003] Clinical studies and practice have shown that providing a reduced pressure in proximity to a tissue site augments and accelerates the growth of new tissue at the tissue site. The applications of this phenomenon are numerous, but application of reduced pressure has been particularly successful in treating wounds. This treatment (frequently referred to in the medical community as "negative pressure wound therapy," "reduced pressure therapy," or "vacuum therapy") provides a number of benefits, including faster healing and increased formulation of granulation tissue. Typically, reduced pressure is applied to tissue through a wound insert (e.g., a porous pad or other manifold device). The wound insert typically contains cells or pores that are capable of distributing reduced pressure to the tissue and channeling fluids that are drawn from the tissue. The wound insert can be incorporated into a wound dressing having other components that facilitate treatment, such as, for example, a drape (e.g., adhesive surgical drape). Instillation of fluids (e.g., irrigation fluids and/or medicaments) may be used in conjunction with negative pressure wound therapy to promote healing and/or improve efficacy. One example of a system for delivering active solutions to a wound is disclosed in U.S. Patent No. 6,398,767.

SUMMARY

[0004] The present disclosure includes embodiments of wound inserts, wound dressings, methods of forming wound inserts, and wound-treatment methods.

[0005] Some embodiments of the present wound inserts are for use between a wound of a patient and a drape coupled to skin around the wound such that the drape covers the wound and forms a space between the drape and the wound. Some embodiments of the present wound inserts comprise: an open-celled foam (e.g., configured to be disposed between a wound of a patient and a drape coupled to skin adjacent the wound, e.g., such that the drape forms a space between the wound and the drape); and a reactive agent disposed within the foam, and configured to be inert in the absence of an activating fluid and to exhibit antimicrobial properties when released by an activating fluid.

[0006] In some embodiments, the reactive agent is configured to react with water (and/or aqueous solution) to release hypochlorite ion and/or form hypochlorous acid, depending on pH. In some embodiments, the reactive agent comprises a hypochlorite salt. In some embodiments, the reactive agent comprises a substance defined by M(OCl)n, where n=1 if M is K^+, Li^+, or Na^+, and where n=2 if M is Ca^{2+} or Mg^{2+}. In some embodiments, the reactive agent comprises at least one of: an N-chloro taurine; an N,N-dichloro taurine; an N-halogenated amino acid; an N,N-dihalogenated amino acid; or a combination of any two or more of these. Some embodiments comprise (alternatively or additionally) an agent comprising a growth factor; a protein; a peptide; or a combination thereof.

[0007] In some embodiments, the wound insert comprises a suspension agent including at least one of: a polyvinylpyrrolidone, a polyethylene oxide, a polyvinyl acetate (PVA), a polyvinyl alcohol (PVOH), an ethylene vinyl alcohol (EVOH) copolymer, an ethylene styrene copolymer, polycaprolactone (PCL), polysorbate, or a combination of any two or more of these. In some embodiments, the suspension agent couples the reactive agent to the foam. In some embodiments, the suspension agent encapsulates the reactive agent. In some embodiments, the suspension agent is configured to dissolve in the presence of a solvent. In some embodiments, the suspension agent is water soluble. In some embodiments, the wound insert is configured to release a hypochlorite ion in the presence of a volume of activating liquid such that after release the volume of activating liquid will have a concentration of hypochlorite ion between 0.7 and 20 millimolar. In some embodiments, the wound insert is configured to release a hypochlorite ion in the presence of each of three or more sequential volumes of activating liquid such that after release each sequential volume of activating liquid will have a concentration of hypochlorite ion between 0.7 and 20 millimolar.

[0008] In some embodiments, the reactive agent is dispersed throughout at least a portion of the foam. In some embodiments, the foam comprises silicone polymer. In some embodiments, the foam comprises a fluoropolymer. In some embodiments, the fluoropolymer comprises at least one of: polytetrafluoroethylene (PTFE), polyvinylidene fluoride (PVDF), perfluoroalkoxy (PFA) polymer, fluoroethylkene (FEP), or a combination of any two or more of these. In some embodiments, the foam comprises at least one of a polyolefin or polyolefin copolymer. In some embodiments, the polyolefin includes at least one of: polyethylene (PE), polypropylene (PP), polybutylene (PB), ethylene-vinyl acetate (EVA), copolymers of any of these or a combination of any two of these.

[0009] Some embodiments further comprise: a second open-celled foam that is not coupled to the reactive agent; where the first open-celled foam is configured to be inert in the present of the reactive agent, and forms a first layer of the wound insert; and where the second open-celled foam forms a second layer of the wound insert, and is coupled to the first open-celled foam.

[0010] Some embodiments of the present wound inserts comprise: an open-celled foam configured to be disposed between a wound of a patient and a drape coupled to skin adjacent the wound (e.g., such that the drape forms a space between the wound and the drape), the foam having an upper side and lower side configured to face the wound; a plurality of particles of a first metal dispersed within the foam; and a second metal coupled to the lower side of the foam, and configured such that a fluid can be introduced to generate microcurrents between the first metal and the second metal. In some embodiments, the first metal is dispersed in the foam such that if a fluid passes through the foam at least some portion of the first metal will exit the foam.

[0011] Some embodiments further comprise: a permeable layer coupled to the lower side of the foam; where the second metal is coupled to the permeable layer. In some embodiments, the wound insert is configured such that if a fluid is passed through the foam from the upper side through the lower side, at least some portion of the first metal will exit the foam through the lower side and pass through the permeable layer. In some embodiments, the wound insert is configured such that if the wound insert is disposed such that the permeable layer is in contact with a wound and a fluid is passed through the foam from the upper side to the lower side, at least some portion of the first metal will exit the foam through the permeable layer and microcurrents will be generated between the first metal and the second metal coupled to the permeable layer. In some embodiments, the first metal comprises silver. In some embodiments, the second metal comprises zinc.

[0012] In some embodiments, the present wound inserts are in combination with a drape configured to be coupled to skin adjacent a wound of a patient. In some embodiments, the present wound inserts are in combination with a fluid delivery pad configured to be coupled to the drape and a fluid source such that the fluid source is actuatable to deliver a fluid to a wound through the wound dressing. In some embodiments, the present wound inserts are in combination with a fluid source configured to be coupled to the wound dressing such that the fluid source is actuatable to deliver a fluid to the wound dressing. In some embodiments, the present wound inserts are in combination with a vacuum source configured to be coupled to the wound dressing such that the vacuum source is actuatable to apply negative pressure to the wound dressing.

[0013] Some embodiments of the present wound dressings comprise: one or more of any of the present wound inserts; and a drape configured to be coupled to skin adjacent a wound of a patient (e.g., such that the drape covers the wound insert and forms a space between the wound and the drape). Some embodiments further comprise: a fluid delivery pad configured to be coupled to the drape and a fluid source such that the fluid source is actuatable to deliver a fluid to a wound through the wound dressing.

[0014] Some embodiments of the present wound-treatment apparatuses comprise: a wound dressing with a drape and one or more of any of the present wound inserts; and a fluid source configured to be coupled to the wound dressing such that the fluid source is actuatable to deliver a fluid to the wound dressing. Some embodiments further comprise: a vacuum source configured to be coupled to the wound dressing such that the vacuum source is actuatable to apply negative pressure to the wound dressing.

[0015] Some embodiments of the present methods comprise: adding (e.g., dry) hypochlorite salt particles to a solution such that the solution and hypochlorite salt form a slurry, the solution comprising a polymer and a liquid that is a solvent of the polymer but not a solvent of the hypochlorite salt; and substantially removing the liquid from the slurry such that at least a portion of the hypochlorite salt particles are at least partially encapsulated by the polymer. In some embodiments, the hypochlorite salt is defined by M(OCl)n, where n=1 if M is K^+, Li^+, or Na^+, and where n=2 if M is Ca^{2+} or Mg^{2+}. In some embodiments, the hypochlorite salt is defined by $Ca(OCl)_2$. In some embodiments, the polymer is biocompatible and optionally biodegradable. In some embodiments, the polymer is not water soluble. In some embodiments, the polymer comprises polycaprolactone (PCL). In some embodiments, the solvent is non-aqueous. In some embodiments, the solvent comprises at least one of Dichloromethane (DCM or methylene chloride), Tetrahydrofuran (THF), or

Cyclohexane. Some embodiments further comprise: disposing, prior to substantially removing the liquid, a foam in the slurry such that hypochlorite salt particles and polymer are dispersed within the foam. Some embodiments further comprise: reducing, prior to adding the hypochlorite salt particles into the solution, the size of the hypochlorite salt particles such that a majority of the hypochlorite salt particles have a size at or below a target size. In some embodiments, the target size is 180 microns.

[0016] Some embodiments of the present methods of forming a wound insert comprise: applying negative pressure to an open-celled foam to draw particles into the foam such that the particles become dispersed throughout at least a portion of the foam. In some embodiments, the foam has a first side and a second side opposite the first side, and the method further comprises: disposing the foam between a filter configured and a particle reservoir such that the filter is adjacent the first side of the foam and the reservoir is adjacent the second side, the filter configured to substantially prevent passage of the particles through the filter; and where applying negative pressure comprises applying negative pressure to the filter such that the particles are drawn from the reservoir into the foam.

[0017] In some embodiments, the particles comprise a reactive agent. In some embodiments, the reactive agent is configured to react with water (and or aqueous solution) to release hypochlorite ion and/or form hypochlorous acid, depending on pH. In some embodiments, the reactive agent comprises hypochlorite. In some embodiments, the reactive agent comprises a substance defined by M(OCl)n, where n=1 if M is K^+, Li^+, or Na^+, and where n=2 if M is Ca^{2+} or Mg^{2+}. In some embodiments, the reactive agent comprises at least one of: an N-chloro taurine; an N,N-dichloro taurine; an N-halogenated amino acid; an N,N-dihalogenated amino acid; or a combination of any two or more of these. Some embodiments comprise (alternatively or additionally) an agent comprising a growth factor; a protein; a peptide; or a combination thereof. In some embodiments, the particles comprise a metal. In some embodiments, the particles comprise silver.

[0018] In some embodiments, the particles comprise a suspension agent including at least one of: a polyvinylpyrrolidone, a polyethylene oxide, a polyvinyl acetate (PVA), a polyvinyl alcohol (PVOH), an ethylene vinyl alcohol (EVOH) copolymer, an ethylene styrene copolymer, polycaprolactone (PCL), polysorbate, or a combination of any two or more of these. In some embodiments, the suspension agent is configured to bind the reactive agent to the foam. In some embodiments, the suspension agent encapsulates the reactive agent. In some embodiments, the suspension agent is configured to dissolve in the presence of a solvent. In some embodiments, the suspension agent is water soluble.

[0019] In some embodiments, the foam comprises silicone polymer. In some embodiments, the foam comprises a fluoropolymer. In some embodiments, the fluoropolymer comprises at least one of: polytetrafluoroethylene (PTFE), polyvinylidene fluoride (PVDF), perfluoroalkoxy (PFA) polymer, fluoroethylkene (FEP), or a combination of any two or more of these. In some embodiments, the foam comprises at least one of a polyolefin or polyolefin copolymer. In some embodiments, the polyolefin includes at least one of: polyethylene (PE), polypropylene (PP), polybutylene (PB), ethylene-vinyl acetate (EVA), copolymers of any of these, or a combination of any two of these.

[0020] Some embodiments of the present wound-treatment methods comprise: delivering a fluid to a wound through a wound dressing comprising: a drape coupled to skin adjacent a wound of a patient (e.g., such that the drape covers the wound and forms a space between the drape and the wound); an open-celled foam wound insert disposed between the drape and the wound (e.g., in the space); and a reactive agent dispersed throughout at least a portion of the wound inserts such that upon delivery of the fluid to the wound insert the fluid causes at least a portion of the reactive agent to pass from the wound insert to the wound. In some embodiments, delivering a fluid comprises activating a fluid source that is coupled to the wound dressing to deliver the fluid to the wound through the wound dressing. Some embodiments further comprise: applying negative pressure to the wound through the wound dressing. In some embodiments, applying negative pressure comprises activating a vacuum source that is coupled to the wound dressing to apply the vacuum to the wound through the wound dressing.

[0021] Some embodiments of the present wound-treatment methods comprise: delivering a fluid to a wound through a wound dressing comprising: a drape coupled to skin adjacent a wound of a patient (e.g., such that the drape covers the wound and forms a space between the drape and the wound); an open-celled foam wound insert disposed between the drape and the wound (e.g., in the space); and a plurality of particles of a first metal dispersed within the foam; a second metal coupled to the lower side of the foam, and configured such that upon delivery of the fluid microcurrents are generated between the first metal and the second metal. In some embodiments, the first metal is dispersed in the foam such that when the fluid is delivered it passes through the foam and at least some portion of the first metal exits the foam.

[0022] In some embodiments, the wound dressing further comprises: a permeable layer coupled to a lower side of the wound insert; and where the second metal is coupled to the permeable layer. In some embodiments, the wound dressing is configured such that upon

delivery of the fluid to the wound dressing the fluid passes through the wound insert from an upper side through the lower side, and at least some portion of the first metal exits the foam through the lower side and passes through the permeable layer. In some embodiments, the wound insert is disposed such that the permeable layer is in contact with the wound such that upon delivery of the fluid to the wound dressing the fluid passes through the foam from the upper side to the lower side, at least some portion of the first metal exits the foam through the permeable layer and microcurrents are generated between the first metal and the second metal coupled to the permeable layer. In some embodiments, the first metal comprises silver. In some embodiments, the second metal comprises zinc.

[0023] Some embodiments of the present wound inserts comprise: an open-celled and/or hydrophilic foam configured to be disposed between a wound of a patient and a drape coupled to skin adjacent the wound (e.g., such that the drape forms a space between the wound and the drape); and a liquid solution comprising an antimicrobial agent, the liquid solution disposed within the foam. In some embodiments, the foam comprises a PVOH foam. In some embodiments, the antimicrobial agent comprises polyhexanide. Some embodiments comprise a container enclosing the foam and configured to prevent evaporation of the liquid solution. In some embodiments, the container comprises a foil pouch. In some embodiments, the container comprises a plastic pouch.

[0024] Some of the present embodiments include an open-celled foam wound insert comprising a reactive agent disposed within the wound insert, and configured to be inert in the absence of an activating fluid and to exhibit antimicrobial properties in the presence of an activating fluid, for use in a wound treatment method comprising the step of delivering a fluid to a wound through a wound dressing comprising: a drape coupled to skin adjacent a wound of a patient such that the drape covers the wound and forms a space between the drape and the wound; the insert disposed in the space; and where the wound insert is configured such that when the fluid is delivered to the wound insert, at least a portion of the reactive agent passes from the wound insert to the wound. Such embodiments may optionally include any features described herein in relation to other embodiments, such as, for example, the features described in relation to methods of treatment.

[0025] Some of the present embodiments include a reactive agent configured to be inert in the absence of an activating fluid and to exhibit antimicrobial properties in the presence of an activating fluid, for use in a wound treatment method comprising the step of delivering a fluid to a wound through a wound dressing comprising: a drape coupled to skin adjacent a wound of a patient such that the drape covers the wound and forms a space

between the drape and the wound; the insert disposed in the space; and the reactive agent disposed within the wound insert, and configured to be inert in the absence of an activating fluid and to exhibit antimicrobial properties in the presence of an activating fluid; where the wound insert is configured such that when the fluid is delivered to the wound insert, at least a portion of the reactive agent passes from the wound insert to the wound. Such embodiments may optionally include any features described herein in relation to other embodiments, such as, for example, those features described in relation to methods of treatment.

[0026] Any embodiment of any of the present systems and/or methods can consist of or consist essentially of – rather than comprise/include/contain/have – any of the described steps, elements, and/or features. Thus, in any of the claims, the term "consisting of" or "consisting essentially of" can be substituted for any of the open-ended linking verbs recited above, in order to change the scope of a given claim from what it would otherwise be using the open-ended linking verb.

[0027] Details associated with the embodiments described above and others are presented below.

BRIEF DESCRIPTION OF THE DRAWINGS

[0028] The following drawings illustrate by way of example and not limitation. For the sake of brevity and clarity, every feature of a given structure is not always labeled in every figure in which that structure appears. Identical reference numbers do not necessarily indicate an identical structure. Rather, the same reference number may be used to indicate a similar feature or a feature with similar functionality, as may non-identical reference numbers.

[0029] **FIG. 1** depicts a side view of one of the present wound dressings having one of the present wound inserts and coupled to a wound site and to a wound treatment apparatus.

[0030] **FIG. 2** depicts an enlarged side view of the wound insert of **FIG. 1**.

[0031] **FIG. 3A** depicts a schematic block diagram of one embodiment of a wound treatment apparatus that can comprise and/or be coupled to and/or be used with the present wound dressings and/or wound inserts.

[0032] **FIG. 3B** depicts an enlarged cross-sectional view of one of the present wound dressings coupled to a wound.

[0033] **FIG. 4** depicts a photograph of a silicone foam suitable for some embodiments of the present wound inserts.

[0034] **FIG. 5** depicts a photograph of a silicone foam deposited with $Ca(OCl)_2$ salt.

[0035] **FIGS. 6A-6C** illustrate certain characteristics of various components of the present wound inserts.

[0036] **FIG. 7** depicts release profiles of silicone foam deposited with NaOCl salt.

[0037] **FIG. 8** depicts a release profile of silicone foam deposited with PEO/NaOCl.

[0038] **FIG. 9** depicts a release profile of silicone foam deposited with PCL/$Ca(OCl)_2$.

[0039] **FIG. 10** depicts a release profile of foam deposited with Luvitec® K90/NaOCl.

[0040] **FIGS. 11** depicts a release profile of foam deposited with PSES/NaOCl.

[0041] **FIGS. 12A** and **12B** depict charts of stability data for hypochlorous acid solutions in various foams.

[0042] **FIGS. 13A-13E** depict photographs illustrating tests performed on various foams to determine stability of the foams in contact with hypochlorous acid solution.

[0043] **FIG. 14** depicts a chart of hypochlorite concentration (at various times) over multiple cycles of instilling saline solution through one of the present wound inserts at two different hold times for each cycle.

[0044] **FIG. 15** depicts a flowchart of one of the present methods.

[0045] **FIG. 16** depicts a housing suitable for use in certain embodiments of the present methods.

[0046] **FIG. 17** depicts a chart of hypochlorite concentration for two different concentrations of calcium hypochlorite in a wound insert over multiple sequential cycles.

[0047] **FIG. 18** depicts an alternate embodiment of one of the present wound inserts.

[0048] **FIG. 19** depicts a cross-sectional side view of an apparatus for making some embodiments of the present wound inserts.

[0049] **FIG. 20** depicts an exploded perspective view of another embodiment of the present wound inserts.

DESCRIPTION OF ILLUSTRATIVE EMBODIMENTS

[0050] The term "coupled" is defined as connected, although not necessarily directly, and not necessarily mechanically; two items that are "coupled" may be integral with each other. The terms "a" and "an" are defined as one or more unless this disclosure explicitly requires otherwise. The terms "substantially," "approximately," and "about" are defined as largely but not necessarily wholly what is specified, as understood by a person of ordinary skill in the art.

[0051] The terms "comprise" (and any form of comprise, such as "comprises" and "comprising"), "have" (and any form of have, such as "has" and "having"), "include" (and any form of include, such as "includes" and "including") and "contain" (and any form of contain, such as "contains" and "containing") are open-ended linking verbs. As a result, a wound-treatment method that "comprises," "has," "includes" or "contains" one or more steps possesses those one or more steps, but is not limited to possessing only those one or more steps. Likewise, a wound dressing that "comprises," "has," "includes" or "contains" one or more elements possesses those one or more elements, but is not limited to possessing only those elements. For example, in a wound dressing that comprises one of the present wound inserts and a drape, the wound dressing includes the specified elements but is not limited to having only those elements. For example, such a wound dressing could also include a connection pad configured to be coupled to a negative pressure wound therapy (NPWT) apparatus (e.g., including a vacuum source and/or a fluid source).

[0052] Further, a device or structure that is configured in a certain way is configured in at least that way, but it may also be possible for it to be configured in other ways than those specifically described.

[0053] Referring now to the drawings, and more particularly to **FIG. 1**, shown therein is an embodiment of one of the present wound treatment system **10**. In the embodiment shown, apparatus **10** comprises a wound-treatment apparatus **14**, and a wound dressing **18**. In the embodiment shown, apparatus **14** is coupled to wound dressing **18** by a conduit **22**. As shown, dressing **18** is configured to be coupled to (and is shown coupled to) a wound **26** of a patient **30**. More particularly, in the embodiment shown, dressing **18** comprises a wound insert **34** and a drape **38**. As shown, wound insert **34** is configured to be positioned (and is shown positioned) on wound **26** (e.g., on or adjacent to wound surface **42**), and drape **38** is configured to be coupled to (and is shown coupled to) skin **46** of the patient adjacent to wound **26** such that drape **38** covers wound insert **34** and wound **26** (e.g., such that drape **38** forms a space **50** between drape **38** and wound **26** (e.g., wound surface **42**)).

[0054] Apparatus **14** can comprise, for example, a vacuum source configured to be actuatable (and/or actuated) to apply negative pressure (e.g., via conduit **22**) to wound dressing **18**, a fluid source configured to be actuatable (and/or actuated) to deliver (e.g., via conduit **22**) a fluid (e.g., and instillation fluid such as a medicinal fluid, antibacterial fluid, irrigation fluid, and or the like) to wound dressing **18**. System **10** can be implemented and/or actuated and/or coupled to patient **30** in any of various configurations and/or methods described in this disclosure. Additionally, various wound therapy systems and components

are commercially available through and/or from KCI USA, Inc. of San Antonio, Texas, U.S.A.

[0055] Conduit **22** can comprise a single lumen conduit (e.g., switched between a vacuum source and/or a fluid source and apparatus **14**), or can comprise multiple single-lumen conduits or a multi-lumen conduit such that, for example, fluid can be delivered and/or negative pressure can be applied to wound dressing **18** individually and/or simultaneously. Additionally, conduit **22** can comprise, for example, a first lumen for the application of negative pressure and/or fluid delivery, and at least one additional lumen for coupling to pressure sensor(s) to sense pressure or negative pressure between drape 38 and surface 42. In some embodiments, conduit **22** can comprise multiple lumens (e.g., as in a single conduit with a central lumen for application of negative pressure and/or fluid delivery, and one or more peripheral lumens disposed adjacent or around the central lumen such that the peripheral lumens can be coupled to a pressure sensor to sense a pressure or negative pressure between drape **38** and surface **42** (e.g. in space **50**). The lumens may be arranged with a central lumen and other lumens disposed radially around the central lumen, or in other suitable arrangements. The lumens may also be provided in separate conduits. In the embodiment shown, system **10** further comprises a wound dressing connection pad **54** configured to be coupled (and is shown coupled) to conduit **22**. One example of a suitable connection pad **54** is the "V.A.C. T.R.A.C.® Pad," commercially available from KCI. One example of a suitable drape **38** includes the "V.A.C.® Drape" commercially available from KCI. Another example of a connection pad 54 is disclosed in U.S. Pat. App. No. 11/702,822, incorporated above.

[0056] Referring now to **FIG. 2**, a side view of a wound insert **34** is shown. Wound insert **34** has an upper side **100**, a lower side **104**, lateral sides **108**, **112** and interior volume **116**. Although one side is shown of wound insert **34**, it will be understood by those of ordinary skill in the art to wound insert **34** includes a three-dimensional, rectangular volume (shown with rectangular faces) having a depth extending perpendicular to the side shown. In other embodiments, wound insert **34** can have a suitable shape, such as, for example, a round cylindrical shape, a fanciful shape, or may be trimmed to fit an irregular shape of a wound (e.g., **26** and/or wound surface **42**). Wound insert **34** may comprise a foam, such as, for example, an open-celled (and/or reticulated) foam.

[0057] Embodiments of the present wound treatment methods may be better understood with reference to **FIG. 3**, which depicts a schematic block diagram of one embodiment of system **10**. In the embodiment shown, wound dressing **18** is coupled to apparatus **14**, and apparatus **14** comprises a vacuum source **200** (e.g., a vacuum pump and/or

the like) coupled to a canister **204** (e.g., configured to receive exudate and/or the like from wound dressing **18**) by way of a conduit **208**. In the embodiment shown, apparatus **14** further comprises: a pressure sensor **212** having a first pressure transducer **216** coupled to conduit **208** by way of conduit **220** and/or tee-fitting **224**, and a second pressure transducer **228** coupled to canister **204** and/or wound dressing **18** by way of conduit **232**. In this way pressure sensor **212** can sense and/or detect the negative pressure in wound dressing **18** and/or any of the various conduits coupled wound dressing **18**, pressure sensor **212**, and/or vacuum source **200**.

[0058] In the embodiment shown, apparatus **14** further comprises a pressure release valve **236** coupled to conduit **232**. Further, in the embodiment shown, canister **204** and vacuum source **200** are coupled to wound dressing **18** by way of conduit **240**. In the embodiment shown canister **204** can comprise a filter **244** at or near an outlet of canister **204** to prevent liquid or solid particles from entering conduit **208**. Filter **244** can comprise, for example, a bacterial filter that is hydrophobic and/or lipophilic such that aqueous and/or oily liquids will bead on the surface of the filter. Apparatus **14** is typically configured such that during operation vacuum source **200** will provide sufficient airflow through filter **244** that the pressure drop across filter **244** is not substantial (e.g., such that the pressure drop will not substantially interfere with the application of negative pressure to wound dressing **18** from vacuum source **200**).

[0059] In the embodiment shown, apparatus **14** further comprises a fluid source **248** coupled to wound dressing **18** by way of a conduit **252** that is coupled to conduit **240** such as, for example, by way of a tee- or other suitable fitting **256**. In some embodiments, tee fitting **256** can comprise a switch valve and with like such that communication can be selectively permitted between wound dressing **18** and vacuum source **200**, or between wound dressing **18** and fluid source **248**. In some embodiments apparatus **14** comprises only one of vacuum source **200** and fluid source **248**. In embodiments of apparatus **14** that comprise only fluid source **248**, canister **204** and/or pressure sensor **212** can also be omitted. Various embodiments, such as the one shown, conduit **232** and/or conduit **240** and/or conduit **252** can be combined and/or comprised in a single multi-lumen conduit, such as is described above with reference to **FIG. 1**. In various embodiments, such as the one shown in **FIG. 3A**, apparatus **14** can be configured such that as soon as the liquid in the canister reaches a level where filter **244** is occluded, a much-increased negative (or subatmospheric) pressure occurs in conduit **208** and is detected by transducer **216**. Transducer **216** can be connected to circuitry that interprets such a pressure change as a filled canister and signals this by means of

a message on an LCD and/or buzzer that canister **204** requires emptying and/or replacement, and/or that automatically shuts off or disables vacuum source **200.**

[0060] Apparatus **14** can also be configured to apply intermittent negative (or subatmospheric) pressure to the wound site, and/or such that pressure relief valve **236** enables pressure at the wound site to be brought to atmospheric pressure rapidly. Thus, if apparatus **14** is programmed, for example, to relieve pressure at ten-minute intervals, at these intervals pressure relief valve **236** can open for a specified period, allow the pressure to equalize at the wound site (to allow pressure at the wound site to equalize with atmospheric pressure), and then close to restore the negative pressure (allow the pump to restore negative pressure at the wound site). It will be appreciated that when constant negative pressure is being applied to the wound site, valve **236** remains closed to prevent leakage to or from the atmosphere. In this state, it is possible to maintain negative pressure at the wound site without running and/or operating pump **200** continuously, but only from time to time or periodically, to maintain a desired level of negative pressure (i.e. a desired pressure below atmospheric pressure), which is detected by transducer **216**. This saves power and enables the appliance to operate for long periods on its battery power supply.

[0061] **FIG. 3B** depicts an enlarged cross-sectional view of one of the present wound dressings **18** coupled to wound **26**. In **FIG. 3B**, wound **26** is illustrated as an infected wound having a plurality of microorganisms **28** (e.g., bacteria) or biofilm infecting wound surface **42** and/or a depth of tissue beneath wound surface **42**. More particularly, and as described above for **FIG. 1**, wound dressing **18** comprises wound insert **34** disposed adjacent or on wound **26** (e.g., wound surface **42**), and drape **38** coupled to skin **46** adjacent wound **26** such that drape **38** covers wound insert **34** and wound **26** and forms a space **50** between wound surface **42** and drape **38**. In the embodiment shown, a first connection pad **54a** is coupled to drape **38** and configured to be coupled to a fluid source (e.g., **248**) by a fluid conduit (e.g., **252**) such that the fluid source can be activated to deliver a fluid (e.g., saline) to wound **26** (e.g., wound surface **42**) through wound dressing **18**; and a second connection pad **54b** is coupled to drape **38** and configured to be coupled to a vacuum source (e.g., **200**) by a conduit (e.g., **240**) such that the vacuum source can be activated to apply negative pressure to wound **26** (e.g., wound surface **42**) through wound dressing **18**. Wound insert **34** comprises an open-celled foam that is configured to be (and is shown) disposed between wound **26** and drape **38**. Additionally, in the embodiment shown, wound insert **34** comprises a reactive agent deposited on or in (e.g., dispersed throughout at least a portion of) wound insert **34** such that upon delivery of a fluid

to wound insert **34** the fluid reacts with and/or causes at least a portion of the reactive agent to pass from wound insert **34** to wound **26**.

[0062] Some embodiments of the present methods can also be understood with reference to **FIGS. 3A** and **3B**. For example, some embodiments of the present wound-treatment methods comprise delivering a fluid to a wound (e.g., **26**) through a wound dressing (e.g., **18**) comprising a wound insert comprising a reactive agent deposited on or in the wound dressing such that the fluid reacts with and/or causes at least a portion of the reactive agent to pass from the wound insert to the wound. In some embodiments, delivering a fluid comprises activating a fluid source (e.g., **248**) that is coupled to the wound dressing to deliver the fluid to the wound through the wound dressing. Some embodiments further comprise applying negative pressure (e.g., after and/or simultaneously with delivering a fluid) to the wound through the wound dressing. In some embodiments, applying negative pressure comprises activating a vacuum source (e.g., **200**) that is coupled to the wound dressing to apply the negative pressure to the wound through the wound dressing. Arrows in **FIG. 3B** indicate the flow of fluid (and reactive agent and/or a product of the reactive agent and the fluid) to and from wound surface **42** (e.g., through wound insert **34**) such that the reactive agent (and/or a product of the reactive agent and the fluid) can kill microorganisms **28** to reduce and/or eliminate infection of wound **26**.

[0063] Hypochlorous acid (HOCl) and hypochlorite ion (ClO-, which is also commonly referred to, generally understood to be synonymous with, and may be referred to interchangeably in this disclosure as, OCl-) are examples of effective antimicrobial agents for biocidal action. For example, HOCl is typically capable of killing a broad spectrum of microbes (e.g., fungus, bacteria, viruses, fungus, yeast, and the like); often in a relatively short period of time (e.g., is capable of killing greater than 99% of microbes within a period of less than 10 seconds). Such antimicrobial agents can be generated or formed by a combination of the present reactive agents and fluid (e.g., water and/or aqeous solution, such as, for example, saline solution) and may be more effective and/or more versatile than antibiotics and other commonly used antimicrobial agents used in wound treatment in the past. For example, antibiotics may be bacteria-specific such that testing may be required to determine a suitable antibiotic to use for a specific wound or infection; and/or such that antibiotics may have only limited effectiveness for individual wounds and/or infections (e.g., where testing is not performed and/or where a wound is infected with a plurality of different bacteria). Such testing may take as long as several days to determine an appropriate antibiotic, delaying treatment or selection of an effective antibiotic. Additionally, bacteria may develop resistance

to antibiotics, such that antibiotics may have reduced effectiveness after an amount of time. Further, antibiotics are typically administered intravenously (systemically) such that antibiotics may kill beneficial bacteria (e.g., in a patient's digestive system) and/or may cause organ damage (e.g., to a patient's liver).

[0064] Experiments were performed for some of the present reactive agents (and/or resulting solutions) to investigate their antibacterial properties. In a first experiment, an even monolayer of Methicillin-resistant Staphylococcus aureus (MRSA) bacteria was spread across the surface of each of several petri dishes, and either a 30 μg control dose of Vancomycin, or an 8 mm x 5 mm piece of sponge was placed on each petri dish. The pieces of sponge included: a piece of polyurethane foam coated with a silver (Ag), a piece of dry silicone foam, a piece of silicone foam impregnated with a Polyhexanide solution, a piece of silicone foam deposited with $Ca(ClO)_2$ salt, and a piece of silicone foam deposited with NaClO salt. After placement of the pieces of foam, saline was dropped onto the foams deposited with $Ca(ClO)_2$ and NaClO salts, respectively, Each petri dish was incubated for eighteen (18) hours at 37°C, and the clear area in which the bacteria had been killed (inhibition zone) was measured. The foam with NaClO resulted in an inhibition zone of approximately 1600 mm^2, and the foam with $Ca(ClO)_2$ resulted in an inhibition zone of approximately 800 mm^2. The next-closest was the one 30 μg control dose of Vancomycin, which resulted in an inhibition zone of 200 mm^2. In a second, similar experiment, the monolayer of bacteria was E. Coli instead of MRSA, and the remainder of the second experiment was substantially the same as the first. The results of the second experiment were also similar. The foam with NaClO resulted in an inhibition zone of approximately 1050 mm^2, and the foam with $Ca(ClO)_2$ resulted in an inhibition zone of approximately 800 mm^2. The next-closest was the polyurethane foam with silver, which resulted in an inhibition zone of approximately 100 mm^2. From these preliminary experiments, the inventors believe the present reactive agents and the resulting solutions to have effective antimicrobial properties. The reactive agents (and/or antimocrobial products of the reactive agents) of the present embodiments can be configured to have a broad-spectrum killing power that will kill a variety of microbes (e.g., fungus, bacteria, viruses, fungus, yeast, etc.). Additionally, the present reactive agents (and/or antimocrobial products of the reactive agents) can be delivered locally (preventing systemic damage or other side effects to organs and the like).

[0065] However, due to the reactivity of HOCl or OCl- with oxidizable organic substances, its utility in wound care applications has previously been limited. For example, some prior art methods of generating hypochlorous acid have required electrolysis of

saltwater or the like (e.g., with expensive equipment at a patient's bedside). By way of another example, commercially available chemicals (e.g., bleach) have a hypochlorous acid concentration of 5% or greater, which is too high to permit medical uses (e.g., will cause cytoxicity). Additionally, at suitable medical concentrations (e.g., 2-20 mM hypochlorous acid solutions), approximately 99% or more of the solution is water, such that shipping is more expensive and/or more difficult than necessary. Further, storage of hypochlorous acid solutions is difficult, as reactions with containers typically degrade or reduce the concentration of the solution. However, the present wound inserts can be deposited with reactive agents (have reactive agents deposited in the foam of the wound inserts) such that upon application of a fluid such as saline or water, OCl (and/or ClO^-) is released (e.g., to form hypochlorous acid) and delivered to a wound for biocidal action.

[0066] In the present embodiments, the foam and reactive agents can be selected such that the foam will not be degraded by the reactive agents (and/or products of the reactive agents and the fluid). The inventors of the present disclosure were surprised to discover the stability of the present silicone foams because testing with silicone tubes resulted in degradation of the hypochlorous acid and/or hypochlorite ion. However, the present silicone foams were compatible with the hypochlorous acid solutions (e.g., 0.1% hypochlorous acid solution), as discussed in this disclosure. For example, **FIG. 4** depicts a photograph of a silicone foam **300** suitable for some embodiments of the present wound inserts, and **FIG. 5** depicts a photograph of silicone foam **300** deposited with particles **304** of $Ca(OCl)_2$ salt. Foam **300** shown in **FIG. 5** is an open-celled foam that is inert and stable in the presence of the $Ca(OCl)_2$ salt particles **304** such that foam **300** can be pre-deposited with the reactive agent, and shipped and/or stored without degradation of the reactive agent and/or without degradation of the foam; and such that foam **300** provides distribution channels or manifolds to permit dispersion of generally non-reactive fluids such as saline through foam **300** to dissolve and/or release the reactive agent (e.g., NaOCl salt, $Ca(OCl)_2$ salt, etc.) and deliver the reactive agent, and/or a reaction product of the reactive agent and fluid, to the wound. For example, in **FIG. 5**, the $Ca(OCl)_2$ salt particles are shown encapsulated in a suspension agent comprising polycaprolactone (PCL). In some embodiments, the reactive agent and/or the suspension agent are in dry and/or particle form. In other embodiments, the reactive agent and/or the suspension agent can be in a gel and/or droplet form. Examples of suitable silicone foams are available from Rogers Corporation, in Rogers, Connecticut, U.S.A. (certain product lines recently acquired from MTI Global, Inc., in Mississauga, Ontario, CANADA; and/or

MTI Specialty Silicones, in Richmond, Virginia, U.S.A.), including for example, foams marketed as MagniFoam MF1-6535, MagniFoam MF1-8055, and/or MagniFoam MF1-9575.

[0067] Embodiments of the present wound inserts can comprise any of a variety of suitable reactive agents (e.g., dry and/or anhydrous reactive agents). For example, in some embodiments, the reactive agent comprises a hypochlorite salt (e.g., a dry and/or anhydrous hypochlorite salt), and/or is configured to react with water to form release hypochlorite ion (e.g., a salt or the like, that when dissolved by a fluid, can react or combine with the fluid to release hypochlorite ion and may also form hypochlorous acid, such as, for example, depending on pH). As used in this disclosure, "dry" refers to the absence of free water molecules in the salt used for the reactive agent (e.g., H_2O molecules may be present in certain salt crystalline structures, but such H_2O molecules are not free). In some embodiments, the hypochlorite salt used to make the present wound inserts may have a free water content of less than 2% by weight or less than 2 %w/v. In some embodiments, the reactive agent comprises a substance defined by M(OCl)n, where n=1 if M is K^+ (potassium), Na^+ (sodium), or LI^+ (lithium); and where n=2 if M is Ca^{2+} (calcium) or Mg^{2+} (magnesium). In some embodiments, the reactive agent comprises at least one of: an N-chloro taurine; an N,N-dichloro taurine; an N-halogenated amino acid; an N,N-dihalogenated amino acid; and/or a combination of any two or more of these. Some embodiments comprise (alternatively or additionally) an agent comprising a growth factor; a protein; a peptide; or a combination thereof.

[0068] In some embodiments, the reactive agent can be deposited onto and/or into the open-cell foam with a chemically compatible polymer suspension or binding agent, such as, for example, to encapsulate the reactive agent for controlled release, improve physical stability of the reactive agent in the foam, and/or bind or adhere the reactive agent to the foam. For example, in some embodiments, the wound insert comprises a suspension agent that includes at least one of: a polyvinylpyrrolidone, a polyethylene oxide (PEO), a polyvinyl acetate (PVA), a polyvinyl alcohol (PVOH), an ethylene vinyl alcohol (EVOH) copolymer, an ethylene styrene copolymer, polycaprolactone (PCL), polysorbate, and/or a combination of any two or more of these. In some embodiments, the suspension agent is configured to dissolve in the presence of a solvent. For example, the suspension agent can be water soluble. In some embodiments, the reactive agent is dispersed throughout at least a portion (up to all) of the foam (e.g., a volume of the foam). In some embodiments, the reactive agent is coupled to a side of the foam (e.g., a bottom side adjacent to the wound when the wound insert is disposed on the wound).

[0069] Embodiments of the present wound inserts can comprise any suitable foam that is inert, chemically stable, and/or resistant to degradation in the presence of the reactive agent (and/or a product of the reactive agent). For example, in some embodiments, the foam comprises a fluoropolymer (e.g., a fluoropolymer comprising at least one of: polytetrafluoroethylene (PTFE), polyvinylidene fluoride (PVDF), perfluoroalkoxy (PFA) polymer, fluorinated ethylene-propylene copolymer (FEP), and/or a combination of any two or more of these). In some embodiments, the foam comprises a polyolefin and/or a polyolefin copolymer, such as, for example, polyethylene vinyl acetate copolymer (EVA), polyethylene vinylalcohol copolymer (EVOH), polyethylene-propylene copolymer, polyethylene-hexene copolymer (e.g., an olefin comprising at least one of: ethylene, propylene, butene, pentene, hexene, heptene, or a combination of any of these).

[0070] The present wound inserts (e.g., comprising a foam deposited with a reactive agent) provides a relatively easy delivery system for delivering or instilling highly effective (but often generally unstable) antimicrobial agents to the wound site at controlled rates for effective infection prevention and/or control to expedite wound healing. The present wound inserts (pre-deposited with reactive agents) can eliminate the need for complex and/or expensive on-site solution generation (e.g., electrolysis solutions such as are offered by PuriCore), and/or can eliminate the need for shipping or storing pre-mixed aqueous antimicrobial solutions (which generally contain more than 99% water); and/or enables the use of antimicrobial solutions (which may generally be chemically unstable) with negative pressure wound therapy (NPWT), such as, for example, by mixing such solutions at the wound.

[0071] Referring now to **FIGS. 6-13**, several experiments were performed on various materials to develop data indicative of which materials would be suitable for foams, reactive agents, and suspension agents of the present wound inserts, and/or suitable for fluids for releasing and/or delivering reactive agents to a wound. Hypochlorite typically has a characteristic absorption wavelength at about 292 nm in the ultraviolet (UV) spectrum. As illustrated in certain of **FIGS. 6-13**, absorbance at 292 nm was used to quantify the presence of hypochlorite OCl-. To capture the total active chlorine, pH of a solution generally should be adjusted to 8 or higher to convert all hypochlorous acid into hypochlorite.

[0072] **FIG. 6A** depicts a chart of ultraviolet (UV) spectra of aqueous solutions of calcium hypochlorite $Ca(OCl)_2$ at various concentrations between 0 and 5 milliMolar (mM—0.001 moles per liter). More particularly, curve **354** corresponds to a solution having 0.56 mg of $Ca(OCl)_2$ per mL; curve **358** corresponds to a solution having 0.16 mg of $Ca(OCl)_2$ per

mL; curve **362** corresponds to a solution having 0.032 mg of $Ca(OCl)_2$ per mL; and curve **366** corresponds to a solution having 0.0064 mg of $Ca(OCl)_2$ per mL. As illustrated, as the concentration of calcium hypochlorite in the solutions decrease, the absorption at 292nm (generally corresponding to the concentration of hypochlorite OCl-) decreased.

[0073] **FIG. 6B** depicts a chart illustrating the correlation of hypochlorite concentration from the UV absorbance of **FIG. 6A** with corresponding concentrations obtained by Iodine titration. **FIG. 6C** depicts a chart of OCl^- concentration in solutions with certain of the present suspension agents, including a control of only Ca(OCl)2 in solution (of methylene chloride), $Ca(OCl)_2$ in PCL-1 solution having 0.5 g of PCL per 100 mL of methylene chloride; $Ca(OCl)_2$ in PCL-2 solution having 1.0 g of PCL per 100 mL of methylene chloride; and $Ca(OCl)_2$ in solution with TWEEN 80 (also known as polysorbate 80) having 0.1 g of TWEEN 80 per 10 g of methylene chloride. As indicated, the suspension agents did not substantially react with or otherwise consume or degrade the OCl^-. For each solution, approximately 13 mg of $Ca(OCl)_2$ was added to each methylene chloride solution and the solution was placed in the dark for a period of about one hour. Then 5 mL of distilled water was added to each solution, and each was shaken to mix its respective ingredients. The PLC-1 and PLC-2 solutions were allowed to sit for approximately five minutes to permit the contents to settle and separate into a PLC layer and an aqueous layer. The TWEEN 80 solution was allowed to sit for approximately two hours to permit the contents to settle and separate into a TWEEN 80 layer and an aqueous layer. After settling, for each solution, one milliliter of the aqueous layer was removed and mixed with 10 mL of 0.1 N NaOH (e.g., to increase the pH to ensure all hypochlorous acid is converted to hypochlorite for complete capture of active chlorine), and evaluated with UV-Vis spectroscopy to determine the concentration of OCl (e.g., to determine whether the OCl- had degraded or been consumed by the polymer). The test results verify that PCL and TWEEN 80 are compatible with $Ca(OCl)_2$ such that PCL or TWEEN 80 can be used as a suspension agent the $Ca(OCl)_2$ salt (e.g., to encapsulate or suspend the $Ca(OCl)_2$ salt).

[0074] Further details of certain examples of reactive agents and suspension agents are listed in **Table 1**. The Luvitec® K materials (e.g. Luvitec® K30, Luvitec® K90, etc.) are polyvinylpyrrolidones commercially available as powder or solution from BASF Corporation, Florham Park, New Jersey, U.S.A. Luvitec® VA64M is a vinylpyrrolidone/vinylacetate copolymer available from BASF Corporation, Florham Park, New Jersey, U.S.A. Chemlock® 607 is manufactured by LORD Corporation and is available from numerous distributors through the U.S.A. KBE-903 refers to 3-trimethoxysilylpropan-1-amine (CAS

No. 86158-92-1; chemical formula $C_6H_{17}NO_3Si$). CF1-141 is a silicone (silane) primer available from numerous distributors throughout the U.S.A. P5200 Adhesion Promoter comprises: octamethyltrisiloxane, 1-Methoxyisopropyl orthosilicate, Tetrapropyl orthosilicate, and Tetrabutyl titanate, and is available from DOW Corning Corporation, Midland, Michigan, U.S.A. 1205 Prime Coat comprises: Propylene glycol methyl ether; Toluene; Butyl glycol acetate; Bisphenol A, p-tert-butylphenol, (chloromethyl)oxirane polymer; and 2-Methoxypropanol; and is available from DOW Corning Corporation, Midland, Michigan, U.S.A. 1200 RTV Prime Coat Clear comprises: Light aliphatic petroleum solvent naphtha; Xylene; Tetrapropyl orthosilicate; Tetrabutyl titanate; Tetra (2-methoxyethoxy) silane; Ethylene glycol methyl ether; and Ethylbenzene; and is available from DOW Corning Corporation, Midland, Michigan, U.S.A.

TABLE 1: Examples of Suspension Agents, Properties, Applications, and Suppliers

Binder	Material Properties	Application	Supplier
Poly(vinylalcohol)	Mw 124,000-186,00	polymer	Aldrich
Polyvinylpyrrolidone	Mw 10,000	polymer, gel	Aldrich
Poly(ethylene oxide)	Mw ~8,000,000	polymer	Aldrich
Poly(vinyl alchohol-co-ethylene)	44 mol % ethylene	polymer	Aldrich
KBE-903	3-Aminopropyltriethoxysilane	primer	ShinEtsu
Luvitec K30	30% solution	polymer, gel	BASF
Luvitec K90	20% solution, Brookfield viscosity 10,000-40,000 mPa s	polymer, gel	BASF
Luvitec VA64W	Vinylpyrolidon Vinylacetate copolymer	polymer, gel	BASF
1200 Clear RTV Prime Coat	Contains: naptha, tetrapropyl othosilicate, tetrabutyl titinate, ethylene glycol methyl ether, tetra(2-methoxyethoxy)silane, ethyl benzene	primer	DowCorning
1205 Prime Coat	propylene glycol methyl ether, toluene, butylglycol acetate, bisphenol A, p-tert-butylphenol, (chloromethyl)oxirane polymer, 2-methoxypropanol	primer	DowCorning
P5200 Adhesion Promoter	octamethyltrisilioxane, tetrabutyl titanate, 1-methoxyisopropylorthosilicate, tetrapropylorthasilicate, n-butyl alcohol	primer	DowCorning
CF1-141 Silicon Primer	Contains: IPA	primer	NuSil
Chemlok 607	Contains: MeOH, EtOH	primer	Lord
Chitosan Low Mw	Brookfield viscosity 20,000 cps	polymer	Aldrich
Chitosan Medium Mw	Brookfield viscosity 200,000 cps	polymer	Aldrich
Poly(styrene-ran-ethylene) sufonate	5% polymer solution in 1-propanol: styrene, 76 wt. %; sulfonated styrene units, 32-38%; vinyl silane crosslinking agent, <0.5%	gel	Aldrich
Polycaprolactone (PCL)	Mx 14,000; 45,000; or 80,000	pellets	Aldrich

[0075] **FIG. 7** depicts release profiles of silicone foam (rectangular pieces of silicone foam (measuring 4 inches x 3 inches x 1.25 inches) deposited with NaOCl salt. Curve **340** shows the molar increase in concentration of NaOCl in 500 milliliters (mL) of saline solution

corresponding to the accumulated release of NaOCl salt from a saturated silicone foam over a period of 60 minutes; and curve **342** shows the corresponding rate of release of NaOCl from the foam over the same 60-minute period. Additionally, curve **344** shows the molar increase in concentration of NaOCl in 500 mL of saline solution corresponding to the accumulated release of NaOCl salt from an unsaturated silicone foam over a period of 60 minutes, and curve **346** shows the corresponding rate of release of NaOCl in the unsaturated foam over the same 60-minute period.

[0076] **FIG. 8** depicts a release profile of silicone foam (rectangular piece of silicone foam measuring 4 inches x 3 inches x 1.25 inches) deposited with PEO/NaOCl (particles of a reactive agent comprising NaOCl, encapsulated in a suspension agent comprising polyethylene oxide (PEO)). More particularly, curve **350** shows the molar increase in concentration of NaOCl in 500 mL of saline solution, as measured by titration; and curve **354** shows the molar increase in concentration of NaOCl in 500 mL of saline solution corresponding to the release of NaOCl from the foam, as measured by UV-visible (UV-Vis) spectroscopy; both over a period of 60 minutes, as shown.

[0077] **FIG. 9** depicts a release profile of PCL/$Ca(OCl)_2$ ($Ca(OCl)_2$ encapsulated in PCL). More particularly, 7.2 g of the PCL-1 solution described above with reference to FIG. 6C was placed in the bottom of a 500 mL glass beaker and allowed to dry overnight. Approximately 0.63 g of PCL/ $Ca(OCl)_2$ remained once the fluid evaporated. Approximately 300 mL of saline solution at pH=4 was added to the beaker, and mechanically stirred to disperse the PCL/ $Ca(OCl)_2$ in the saline. 1 mL aliquots were than removed from the beaker (at various time intervals between 1 and 1380 minutes), diluted with 10 mL of 0.1 NaOH (e.g., to increase the pH to ensure all hypochlorous acid is converted to hypochlorite for complete measurement by UV-Vis spectroscopy), and evaluated with UV-Vis spectroscopy to determine the molar concentration of hypochlorite ClO-, and the results plotted (**FIG. 9**) to approximate the release profile of $Ca(OCl)_2$ from the PCL suspension agent.

[0078] **FIG. 10** depicts a release profile, of a silicone foam deposited with Luvitec® K90/NaOCl (particles of a reactive agent comprising NaOCl encapsulated in a suspension agent comprising Luvitec® K90) released in two liters (L) of saline solution. More particularly, **FIG. 10** depicts the release profile of the silicone foam (rectangular piece of silicone foam measuring 4 inches x 3 inches x 1.25 inches) deposited with Luvitec K90/NaOCl (a reactive agent comprising NaOCl encapsulated in a suspension agent comprising Luvitec® K90). More particularly, curve **370** shows the accumulated molar increase in concentration of NaOCl in 500 mL of saline solution, as measured by titration; and

curve **374** shows the accumulated molar increase in concentration of NaOCl in 500 mL of saline solution corresponding to the release of NaOCl from the foam, as measured by UV-visible (UV-Vis) spectroscopy; both over a period of 60 minutes, as shown.

[0079] **FIG. 11** depicts a release profile of a silicone foam deposited with the PSES/NaOCl (a reactive agent comprising NaOCl encapsulated in a suspension agent comprising PSES) in two liters (L) of saline. Details for the PSES are provided above in **Table 1**. More particularly, **FIG. 11** depicts the release profile from a rectangular piece of silicone foam (measuring 4 inches x 3 inches x 1.25 inches) deposited with the PSES/NaOCl. More particularly, curve **390** shows the molar increase in concentration of NaOCl in 500 mL of saline solution, as measured by titration; and curve **394** shows the molar increase in concentration of NaOCl in 500 mL of saline solution corresponding to the release of NaOCl from the foam, as measured by UV-visible (UV-Vis) spectroscopy; both over a period of 60 minutes, as shown.

[0080] **FIGS. 12A-12B** depict charts of stability data for various foams soaked in hypochlorous acid solution. **FIG. 12A** illustrates HOCl concentration over time relative to initial HOCl concentration in a solution (initially 10mM HOCl solution) passed through silicone foam (curve **396**) and passed through polyurethane foam (curve **398**) using a wound treatment system such as a VAC Instill device available from KCI. As shown, the polyurethane foam reacted with the HOCl to reduce the HOCl concentration in the solution, while the silicone foam was relatively stable such that the HOCl concentration remained relatively constant over the 12-minute test period. For **FIG. 12B**, various foams were soaked in 0.1% hypochlorous acid (HOCl) solutions for 12 minutes. Curves **400-410** show concentration of HOCl (e.g., fluctuations in concentration due to reaction with the foam) for several foams, such that the greater the reduction in concentration, the less stable the foam. Curve **400** shows the concentration over time for a polyurethane foam; curve **402** shows the concentration over time for MF1-6535, a silicone foam; curve **404** shows the concentration over time for MF1-8055, a silicone foam; curve **406** shows the concentration over time for MF1-9575, a silicone foam; and curve **408** shows the concentration over time for Virgin HOCl in a glass bottle for control (baseline and comparison) purposes. As shown, the polyurethane foam degraded in the hypochlorous acid solution, while the silicone foams were relatively stable.

[0081] **FIGS. 13A-13E** depict photographs illustrating tests performed on various foams to determine stability or physical integrity of the foams in hypochlorous acid solution. **FIG. 13A** depicts an experimental apparatus **450** used to evaluate stability or physical

integrity of each of the foams evaluated for **FIG. 11** through a number of cycles over a period of five days. Apparatus **450** is similar to the wound dressing **18** shown in **FIGS. 1** and **3B**, in that apparatus **450** includes a foam wound insert **454** covered by a drape **38**, and in communication with a fluid source via connection pad 54a, and in communication with a vacuum source via connection pad **54b**. An apparatus **450** was configured for the PU foam, and each of the silicone foams referenced above for **FIG. 12B**. The fluid source and vacuum sources were each sequentially activated repeatedly over a five-day period for each of the foams to deliver and remove a 0.1% hypochlorous acid solution to each of the foams. As shown in **FIGS. 13B-13D**, the silicone foams remained stable for the exposure. As shown in **FIG. 13E**, polyurethane foam collapsed and disintegrated as a result of oxidation.

[0082] **FIG. 14** depicts a chart of hypochlorite concentration at various times over multiple cycles of saline solution through one of the present wound inserts. For the chart shown, a suspension (or binding) agent, PCL (Mw 80,000), was mixed with Dichloromethane (DCM or methylene chloride) to form a 10 %w/v PCL/DCM solution. $Ca(OCl)_2$ was then mixed into the PCL/DCM solution to form a slurry ($Ca(OCl)_2$ is generally not soluble in DCM). An oval-shaped piece of silicone foam having a volume of 12.05 cubic inches (in^3) was then placed in the PCL/DCM/$Ca(OCl)_2$ slurry and the foam alternately compressed and relaxed to draw the slurry into the foam, which resulted in a dispersion or loading of 0.63 grams of Calcium hypochlorite salt in the foam. Once the foam was substantially saturated, the foam was allowed to dry such that the DCM substantially evaporated from the foam to leave PCL-suspended (and/or PCL-encapsulated) $Ca(OCl)_2$ dispersed and deposited in the foam. The wound insert was then placed in an experimental apparatus **450** (FIG. 13A), and the experimental apparatus 450 was coupled to a VAC-Instill device commercially available from KCI for delivery/removal of fluids to/from the wound insert in the experimental apparatus. Normal saline solution (0.9% NaCl) was then delivered to the wound insert and the wound insert allowed to soak in the saline solution (e.g., to allow the saline solution to dissolve a portion of the $Ca(OCl)_2$ reactive agent to release hypochlorite ion in experimental apparatus **450**. Each cycle included: activating a pump for 40 seconds to deliver the saline solution to the wound insert, allowing the wound insert to soak in the saline solution for 14 minutes, measuring the concentration of hypochlorite in the experimental apparatus 450 at various periods during the 14-minute soak period, and activating a vacuum source for 5 minutes to draw at least a portion the fluid out of the wound insert. This sequence was repeated 5 times (5 cycles). The hypochlorite concentrations for each cycle are shown in FIG. 14, with the hypochlorite concentration at 6 minutes into the soak period shown by the left

bar, and the hypochlorite concentration at 12 minutes into the soak period shown by the right bar. As is shown, the hypochlorite concentration increases with soaking time, but decreases over multiple cycles. The suspension (or binding) agent (e.g., PCL) can be configured to permit the controlled release of an effective (e.g., antimocrobially effective) dose of the reactive agent, while still permitting substantially all of the reactive agent to be flushed from the wound insert over multiple cycles, thus reducing potential for long-term tissue damage that may otherwise result from the sustained or un-dissipating presence of reactive agents.

[0083] **FIG. 15** depicts a flowchart conceptually illustrating an embodiment **500** of the present methods of manufacturing the wound insert tested to obtain the data of **FIG. 14**. In the embodiment, shown, the method comprises a step **504** of adding dry hypochlorite salt particles to a solution containing dissolved binding and/or encapsulating agent (e.g., polymer) such that the solution and hypochlorite salt form a slurry. Calcium hypochlorite (and other hypochlorite) salts are commercially available from a variety of sources. For example, Calcium hypochlorite is available from Sigma-Aldrich, PPG Industries, and Arch Chemicals, Inc. Such Calcium hypochlorite salts are also available with a range of available Chlorine contents (e.g., 34% - 76%). In some embodiments, the hypochlorite salt has an available Chlorine content of 50% or more (e.g., at least 60%, at least 70%, or more). Other examples of hypochlorite salts are defined by M(OCl)n, where n=1 if M is K^+, Li^+, or Na^+, and where n=2 if M is Mg^{2+}.

[0084] In some embodiments, the solution comprises a polymer (binding agent and/or encapsulating agent) and a liquid that is a solvent of the polymer but not a solvent of the hypochlorite salt. For example, in the embodiment shown, the polymer is PCL. In other embodiments, the polymer can be another suitable biocompatible (e.g., biodegradable) polymer that is not water-soluble. For example, in the embodiment shown, the liquid is non-aqueous and comprises Dichloromethane (DCM or methylene chloride). In other embodiments, the liquid comprises a different non-aqueous solvent of the polymer (e.g., Tetrahydrofuran (THF) or Cyclohexane for PCL). The concentration of polymer in the liquid can be, for example, between 5 %w/v and 10 %w/v. For example, a concentration of 7 %w/v (which may in some embodiments be between 6% and 8%) has worked well for certain experiments described below. In the embodiment shown, method **500** further comprises a step **508** of substantially removing the liquid from the slurry such that at least a portion of the hypochlorite salt particles are at least partially encapsulated by the polymer. For example, removing the liquid may be performed by drying (e.g., in vacuum and/or at ambient pressure). In the embodiment shown, all references to "solvent" are to DCM, which is also noted as a

"Non-solvent" at step **504** because DCM is not a solvent for Ca(OCl)2 (e.g., Calcium Hypochlorite is generally not soluble in DCM).

[0085] In some embodiments, method **500** comprises a step **512** of forming the solution by combining the liquid and the polymer (to dissolve the polymer in the liquid). In some embodiments, method **500** comprises a step **516** of reducing, prior to adding the hypochlorite salt particles into the solution, the size of the hypochlorite salt particles such that a majority of the hypochlorite salt particles have a size at or below a target size. For example, for certain silicone foams discussed in this disclosure, the pore size is such that a target size of 180 microns permits adequate dispersion of the salt particles through the foam. For example, in some embodiments of commercially available $Ca(OCl)_2$, the average particle or aggregate size is approximately 1 millimeter (MM), and average particle size is reduced by disposing hypochlorite particles (e.g., pellets) into a slurry with Dichloromethane (DCM or methylene chloride) and shearing with a high-shear mixer (e.g., at 7000 rpm for 5 minutes, 7000 rpm for 7 minutes, 10000 rpm for 7 minutes, and/or other speeds or durations) to break larger particles into smaller particles. Particle size (e.g., the target size for a group of particles) may be adjusted for various applications of the present embodiments. For example, in a wound insert with hypochlorite salt at least partially encapsulated by PCL, larger salt particles will generally dissolve more slowly than smaller salt particles., and vice versa. In the embodiment shown, the solvent (DCM) is removed from the salt (or the salt is removed from the solvent) after reducing the particle size (e.g., may be filtered, evaporated, and/or otherwise recovered prior to introducing the hypochlorite salt particles into the solution).

[0086] In some embodiments, method **500** comprises a step **520** of disposing a foam wound insert in the slurry such that hypochlorite sale particles and polymer are dispersed within the wound insert, prior to step **508** of substantially removing the liquid. For example, the foam may be compressed and released one or more times in the presence of the slurry such that expansion of the foam will draw the slurry into the pores of the foam. The foam may be any suitable open-celled foam that is stable (will not degrade) in the presence of hypochlorite ion or hypochlorous acid (e.g., at least at concentrations present in the discussed embodiments). Examples of suitable foams include Silicone foams having a density in the range of 25-150 kg/m^3 (e.g., MagniFoam 6535, MagniFoam 8055, and MagniFoam 9575, manufactured by Rogers Corporation), Polyvinyl alcohol (PVOH), and the like.

[0087] In some embodiments, step **520** may be accomplished with the apparatus **524** of **FIG. 16**. Apparatus **524** includes a body **528** defining a chamber **532** sized to receive a piece of foam to be used for a wound insert. The polymer/solvent/salt slurry and the foam can

be disposed in chamber **532**, and the foam compressed and permitted to expand to draw the slurry into the pores of the foam (e.g., can be sequentially compressed and allowed to expand multiple times). In some embodiments, the foam is compressed in the chamber with a plunger (not shown) having openings therethrough (and/or corresponding in shape to the chamber). Chamber **532** can be sized to correspond to a single wound insert, can be sized to correspond to a larger piece of foam from which multiple wound inserts can be cut after being infused with the slurry. Other embodiments may include multiple cavities each corresponding to a single wound insert. For example, the data shown in **FIG. 14** was obtained with a mold having cavity dimensions of l=4.5 inches x w=3.5 inches x h=2 inches. Although not shown in **FIG. 16** for simplicity, the inside corners of cavity **532** were also filleted (rounded) on radiuses of 0.5 inches. For other sizes of individual wound inserts, the cavity may be provided with any suitable dimensions (e.g., l=3.5 inches x w=3.5 inches x h=2 inches).

[0088] In some embodiments, the slurry is dispersed into the foam such that once the solvent is removed and the foam dried, the hypochlorite salt concentration in the foam is between 0.03 and 0.2 grams per cubic inch (g/in^3). For example, to generate the data of **FIGS. 14** and **17**, a 4-inch x 3-inch x 1.25-inch oval-shaped piece of foam was used having a volume of 12.05 cubic inches (in^3), and between 0.5 and 2.0 grams of Calcium hypochlorite salt were infused into the foam for various iterations. The concentration of hypochlorite per cubic inch of foam can be increased or decreased to vary the release profile of hypochlorite ion from the foam, and may vary for different foams and/or polymers (binding/encapsulating agents).

[0089] Referring now to **FIG. 17**, the experiments described above for **FIG. 14** were also performed with additional foams, one foam in which 1 gram of Calcium hypochlorite salt was infused (D100, shown as left column for each cycle), and one foam in which 2 grams of Calcium hypochlorite salt was dispersed (D200, shown as right column for each cycle). As shown in **FIG. 17**, a single foam wound insert released enough hypochlorite ion to cause the liquid to have a concentration of hypochlorite ion in each of twelve sequential cycles between 0.5 and 18 mM. As discussed additionally below, the minimum concentration is significant because testing identified concentrations of hypochlorite-ion as low as 0.5-0.7 mM to have effective antibacterial and antimicrobial properties. Additional testing was performed to measure the zone of inhibition (ZOI) and Log Reduction of microbes for various samples of released aqueous solutions having various concentrations of hypochlorite ion, as listed in Tables 2 and 3. Table 2 lists ZOI and Log reduction data for a single cycle measured at hold

times (exposure duration) of 30 seconds and 5 minutes of bacterial exposure to solution. Table 3 lists ZOI and Log reduction data for multiple cycles (each cycle including introduction of hypochlorite solution, and removal of solution prior to beginning next cycle). In the ZOI experimentation, foam discs having a diameter of 8 millimeters (mm) and a height of 5 mm were each saturated with hypochlorite-ion solution as indicated. Table 3 also lists the initial microbe count in log form (10^X, where X is listed in Table 2), log reduction in microbe count, and ZOI in mm. For the data of Table 3, the initial concentration (1x) of hypochlorite ion in solution was 5.7 mM of hypochlorite ion, which corresponds to 0.041 %w/v of $Ca(OCl)^2$. In the Log reduction experimentation, the microbes were exposed to the respective concentration of solution for 30 seconds per cycle. It was observed that five (5) cycle sat even the lowest concentration (0.7 mM) killed substantially all microbes present. The bold entries in Table 3 are indicative of substantially all microbes being killed. In the biofilm eradication cycles listed in Table 6 below, probes were cultured with microbes and incubated to permit formation of a biofilm on the probe. The probe was then exposed to solutions having various concentrations of Calcium hypochlorite solution for multiple cycles, with each cycle including exposure of the probe to solution for a duration of 5 minutes.

TABLE 2: ZOI and Log Reduction Data for OCl^- Solutions

HOCl/OCl- mM	ΔLog - MRSA		ΔLog - C. alb.		ZOI, D in mm	
	30 sec.	5 min.	30 sec.	5 min.	MRSA	C. alb.
15.7	>6.93	>7.13	3.50	>7.18	13.0	44.3
10.7	>6.93	>7.13	7.18	>7.18	13.0	45.7
4.0	5.52	>7.13	3.94	>7.18	0.0	34.3
3.1	3.55	>7.13	3.08	>7.18	0.0	22.0
1.9	2.93	4.09	2.94	3.77	0.0	24.3
0.8	2.96	2.99	2.87	>7.18	0.0	15.0
Microbe Count	7.93	8.13	8.18	8.18	---	---

TABLE 3: ZOI and Log Reduction Data for OCl^- Solutions

Sample Dilution	Pseudomonas aeruginosa ATCC 27853			Staphylococcus aureus ATCC 10832			Staphylococcus aureus USA 400 (MRSA)		
	1 Cycle	3 Cycles	5 Cycles	1 Cycle	3 Cycles	5 Cycles	1 Cycle	3 Cycles	5 Cycles
1x	-0.16	**5.87**	**5.83**	**3.21**	**2.82**	**2.66**	**4.15**	**3.63**	**3.91**
2x	-0.98	**5.87**	**5.83**	**3.21**	**2.82**	**2.66**	**4.15**	**3.63**	**3.91**
4x	-0.48	3.92	**5.83**	**3.21**	**2.82**	**2.66**	**4.15**	**3.63**	**3.91**
8x	-1.11	1.26	5.39	**3.21**	**2.82**	**2.66**	**4.15**	**3.63**	**3.91**

[0090] As illustrated by the data in Table 2 and Table 3, the minimum inhibitory concentration (MIC), minimum bactericidal concentration (MBC), and minimum biofilm eradication concentration (MBEC) of hypochlorite ion in solution (e.g., the solution formed by the release of hypochlorite ion when aqueous solution is added to the impregnated foam) for each of Pseudomonas aeruginosa ATCC 27853, Staphylococcus aureus ATCC 10832, and Staphylococcus aureus USA 400 (MRSA), at each of 1 3, and 5 cycles, are listed in Tables 4, 5, and 6. 0.0051 %w/v Ca(OCl)2 in water corresponds to 0.7 mM hypochlorite ion in water

TABLE 4: Minimum Inhibitory Concentration (MIC) (%w/v)

Bacteria	1 Cycle	3 Cycles	5 Cycles
Pseudomonas aeruginosa ATCC 27853	< 0.005%	< 0.005%	< 0.005%
Staphylococcus aureus ATCC 10832	< 0.005%	< 0.005%	< 0.005%
Staphylococcus aureus USA 400 (MRSA)	< 0.005%	< 0.005%	< 0.005%

TABLE 5: Minimum Bactericidal Concentration (MBC) (%w/v)

Bacteria	1 Cycle	3 Cycles	5 Cycles
Pseudomonas aeruginosa ATCC 27853	< 0.005%	< 0.005%	< 0.005%
Staphylococcus aureus ATCC 10832	< 0.005%	< 0.005%	< 0.005%
Staphylococcus aureus USA 400 (MRSA)	< 0.005%	< 0.005%	< 0.005%

TABLE 6: Minimum Biofilm Eradication Concentration (MBEC) (%w/v)

Bacteria	1 Cycle	3 Cycles	5 Cycles
Pseudomonas aeruginosa ATCC 27853	> 0.041%	0.021%	0.041%
Staphylococcus aureus ATCC 10832	< 0.005%	< 0.005%	< 0.005%
Staphylococcus aureus USA 400 (MRSA)	< 0.005%	< 0.005%	< 0.005%

[0091] In alternate embodiments (not shown), the polymer (PCL)/salt ($Ca(OCl)_2$) slurry can be formed into or added to alternate delivery structures (e.g., instead of dispersion in foam). For example, the liquid (e.g., Dicloromethane) can be partially removed, and the slurry can be extruded or otherwise formed (e.g., cast) into sheets or fibers with encapsulated

hypochlorite salt that can be reacted with water to release hypochlorite ion and/or hypochlorous acid. Such sheets can be sized to be used for wound dressings, and used as wound dressings (e.g., in the systems and methods similar to those described above). Such fibers can be woven into mats or sheets that can be used as wound dressings (e.g., in the systems and methods similar to those described above). In other embodiments, the slurry can be deposited on substrates other than foams. For example, the slurry can be sprayed or "printed" (e.g., using known spraying or printing devices) onto wound dressings or other medical devices (e.g., onto a side of drape 38 that is configured to face a wound).

[0092] **FIG. 18** depicts an alternate embodiment of one of the present wound inserts **34a** that comprises an inert foam layer **600** that is deposited with a reactive agent (e.g., comprising any of the materials and/or components such as a suspension agent, as described above for wound insert **34**); and a second open-celled foam layer **604** that is coupled to the first layer **600**, and is not coupled to (not deposited with) the reactive agent. In accordance with the description above for the wound insert **34**, the first open-celled foam **600** is configured to be inert in the presence of the reactive agent. Additionally, in the embodiment shown, foam **600** forms a first layer of wound insert **34a**, and foam **604** forms a second layer of wound insert **34a**.

[0093] Referring now to **FIG. 19**, a cross-sectional side view of an apparatus **700** is shown for making some embodiments of the present wound inserts (e.g., wound insert **34**). Apparatus **700** comprises a housing **704**, a lower filter **708**, a reservoir region **712**, a foam region **716**, an upper filter **720**, and a vacuum manifold **724**. Filters **708**, **712** are coupled to housing **704**, and are configured to permit air to pass through filters **708**, **712**, and to prevent particles of reactive agent from passing through filters **708**, **712**. Reservoir region **712** is configured to receive and/or be filled with particles (e.g., a predetermined amount or volume of particles or powder) of any of the reactive agents and/or suspension agents discussed in this disclosure. Foam region **716** is configured to receive a piece **618** of any of the foams discussed in this disclosure (e.g., a silicone or other inert foam). Once a reactive agent (and/or suspension agent) is disposed in reservoir region **712**, a foam **718** is disposed in foam region **716**, top filter **720** can be coupled to housing **704** to substantially enclose reservoir region **712** and foam region **716**. Some embodiments of the present methods of forming a wound insert comprise: applying negative pressure (e.g., via vacuum manifold **714**) to an open-celled foam (e.g., **718**) to draw particles (e.g., of a reactive agent) into the foam such that the particles become dispersed throughout at least a portion of the foam.

[0094] In the embodiment shown, foam **718** has a first side (adjacent top filter **720**) and a second side (adjacent reservoir region **712**), and some embodiments of the present methods further comprise: disposing the foam between a filter (e.g., top filter **720**) and a particle reservoir (e.g., reservoir region **712**), where top filter **720** is configured to substantially prevent passage of the particles (of reactive agent and/or suspension agent) through top filter **720**. In such embodiments, applying negative pressure can comprise: applying negative pressure to the filter (top filter **720**) such that the particles (of reactive agent and/or suspension agent) are drawn from the reservoir (reservoir region **712**) into the foam (e.g., **718**) but are prevented from passing through the filter (top filter **720**). In addition to the reactive agents described above, in some embodiments of the present methods of forming a wound insert, the particles comprise a metal (e.g., silver) such that the silver particles are drawn into the foam. These methods of forming the present wound inserts permit loading, dispersion, and/or deposition of reactive agents in foam without soaking the foam in a liquid solution and drying the foam to leave the solid agent in the foam. In contrast to prior methods, the present methods of vacuum loading is more efficient and can directly "charge" the foam with solid particles (e.g., powder). In some embodiments, the present wound inserts are configured to be disposed with the bottom side (side adjacent reservoir region 612) adjacent a wound, such that as fluid is introduced it will direct the particles in an opposite direction from the direction in which they were drawn into the foam.

[0095] In some embodiments of the present wound inserts, rather than dispersing a dry reactive agent in a foam, the foam is packaged in a wet state in which the foam contains a liquid containing a reactive agent. For example, WhiteFoam is a polyvinyl alcohol (PVOH) open-celled foam wound insert, currently available from KCI U.S.A., Inc., which is typically packed when the foam contains water in a moisture-barrier foil pouch to prevent evaporation of the water. In some embodiments, the present wound inserts comprise foam containing a liquid solution comprising antimicrobial agents (e.g., polyhexanide). In some embodiments, the present wound inserts comprise a container enclosing the wound insert and configured to prevent evaporation of the solution from the wound insert.

[0096] Referring now to **FIG. 20,** an exploded perspective view is shown of another embodiment **34b** of the present wound inserts. In the embodiment shown, wound insert **34b** comprises an open-celled foam **750** configured to be disposed between a wound (e.g., **26**) of a patient (e.g., **30**) and a drape (e.g., **38**) coupled to skin (e.g., **46**) of the patient such that the drape forms a space (e.g., **50**) between the wound and the drape. Foam **750** has an upper side **754** and a lower side **758** that is configured to face the wound. In the embodiment shown,

foam **750** comprises a plurality of particles **A** dispersed within foam **750**, and a second metal **B** coupled to (e.g., coated on) lower side **758** of the foam. Additionally, foam **750** is configured such that a fluid can be introduced to generate microcurrents between first metal **A** and second metal **B** (e.g., such that upon introduction of fluid to the foam, microcurrents are generated between metal **A** and metal **B**). Additionally, in the embodiment shown, particles of first metal **A** are dispersed in foam **750** such that if a fluid passes through the foam at least some portion of first metal **A** will exit the foam. In some embodiments, first metal **A** and first metal **B** comprise anode and cathode materials. For example, in some embodiments, metal **A** comprises an anode metal and metal **B** comprises a cathode metal. By way of another example, in some embodiments, metal **A** comprises a cathode metal, and metal **B** comprises an anode metal. In some embodiments, first metal **A** comprises silver. In some embodiments, second metal **B** comprises zinc.

[0097] In the embodiment shown, wound insert **34b** further comprises: a permeable layer (e.g., mesh) **762** coupled to lower side **758** of foam **750**; where second metal **B** is coupled to permeable layer **762**. Additionally, in the embodiment shown, wound insert **34b** is configured such that if a fluid (e.g., water, saline, etc.) is passed through foam **750** from upper side **754** through lower side **758**, at least some portion of first metal **A** will exit foam **750** through lower side **758** and pass through permeable layer **762** (e.g., to pass to a wound surface **42**). For example, wound insert **34b** is configured such that if wound insert **34b** is disposed such that permeable layer **762** is in contact with a wound **26** (e.g., a wound surface **42**) and a fluid is passed through foam **750** from upper side **754** to lower side **758**, at least some portion of first metal **A** will exit the foam through permeable layer **762** and microcurrents will be generated between first metal **A** and second metal **B** coupled to permeable layer **762**.

[0098] Wound insert **34b** can thus be configured and/or used to provide microcurrents to a wound, such as, for example, to stimulate activities of extracellular matrix (ECM), growth factors, cells, and tissues to enhance tissue regeneration and wound healing process. Additionally, such microcurrents can make microorganisms and associated biofilms more susceptible to attack and destruction by a patient's immune system and/or antibiotics or antiseptics. For example, first metal **A** (especially free metal A that travels to a wound surface) and second metal **B** can act as electrodes (e.g., for $\Delta V \sim 1$ volt) to generate microcurrents within the wound bed.

[0099] The various illustrative embodiments of devices, systems, and methods described herein are not intended to be limited to the particular forms disclosed. Rather, they include all modifications and alternatives falling within the scope of the claims. The claims

are not intended to include, and should not be interpreted to include, means-plus- or step-plus-function limitations, unless such a limitation is explicitly recited in a given claim using the phrase(s) "means for" or "step for," respectively.

[00100] It will be understood that the benefits and advantages described above may relate to one embodiment or may relate to several embodiments. It will further be understood that reference to 'an' item refers to one or more of those items, unless otherwise specified. The steps of the methods described herein may be carried out in any suitable order, or simultaneously where appropriate.

[00101] Where appropriate, aspects of any of the examples described above may be combined with aspects of any of the other examples described to form further examples having comparable or different properties and addressing the same or different problems. It will be understood that the above description of embodiments is given by way of example only and that various modifications may be made by those skilled in the art. The above specification, examples and data provide a complete description of the structure and use of exemplary embodiments. Although various embodiments have been described above with a certain degree of particularity, or with reference to one or more individual embodiments, those skilled in the art could make numerous alterations to the disclosed embodiments without departing from the scope of this invention.

CLAIMS

1. A wound insert for use between a wound of a patient and a drape coupled to skin around the wound such that the drape covers the wound and forms a space between the drape and the wound, the wound insert comprising:

an open-celled foam; and

a reactive agent disposed within the foam, and configured to be inert in the absence of an activating fluid and to exhibit antimicrobial properties in the presence of an activating fluid;

where the reactive agent is configured to react with water to release hypochlorite ion and/or form hypochlorous acid.

2. The wound insert of claim 1, where the reactive agent comprises a dry hypochlorite salt defined by M(OCl)n, where n=1 if M is K^+, Li^+, or Na^+, and where n=2 if M is Ca^{2+} or Mg^{2+}.

3. The wound insert of any of claims 1-2, further comprising

a biocompatible suspension agent that binds the reactive agent to the foam, and optionally at least partially encapsulates the reactive agent.

4. The wound insert of claim 3, where the suspension agent comprises polycaprolactone (PCL).

5. The wound insert of claim 3, where the wound insert is configured to release a hypochlorite ion in the presence of a volume of activating liquid such that after release the volume of activating liquid will have a concentration of hypochlorite ion between 0.7 and 20 millimolar.

6. The wound insert of claim 5, where the wound insert is configured to release a hypochlorite ion in the presence of each of three or more sequential volumes of activating liquid such that after release each sequential volume of activating liquid will have a concentration of hypochlorite ion between 0.7 and 20 millimolar.

7. The wound insert of any of claims 1-6, where the foam comprises silicone.

8. The wound insert of any of claims 1-7, further comprising:

a second open-celled foam that is not coupled to the reactive agent;

where the first open-celled foam is configured to be inert in the present of the reactive agent, and forms a first layer of the wound insert; and

where the second open-celled foam forms a second layer of the wound insert, and is coupled to the first open-celled foam.

9. The wound insert of any of claims 1-8, in combination with a drape configured to be coupled to skin adjacent a wound of a patient.

10. The wound insert of claim 9, in combination with a fluid delivery pad configured to be coupled to the drape and a fluid source such that the fluid source is actuatable to deliver a fluid to a wound through the wound dressing.

11. The wound insert of any of claims 9-10, in combination with a fluid source configured to be coupled to the wound dressing such that the fluid source is actuatable to deliver a fluid to the wound dressing.

12. The wound insert of claim 11, in combination with a vacuum source configured to be coupled to the wound dressing such that the vacuum source is actuatable to apply negative pressure to the wound dressing.

13. A method comprising:

adding dry hypochlorite salt particles to a solution such that the solution and hypochlorite salt form a slurry, the solution comprising a polymer and a liquid that is a solvent of the polymer but not a solvent of the hypochlorite salt;

substantially removing the liquid from the slurry such that at least a portion of the hypochlorite salt particles are at least partially encapsulated by the polymer.

14. The method of claim 13, where the hypochlorite salt is defined by M(OCl)n, where n=1 if M is K^+, Li^+, or Na^+, and where n=2 if M is Ca^{2+} or Mg^{2+}.

15. The method of claim 14, where the hypochlorite salt is defined by $Ca(OCl)^2$.

16. The method of claim 13, where the polymer is biocompatible and optionally biodegradable.

17. The method of claim 16, where the polymer is not water soluble.

18. The method of claim 17, where the polymer comprises polycaprolactone (PCL).

19. The method of any of claims 14-18, where the solvent is non-aqueous.

20. The method of claim 19, where the solvent comprises at least one of Dichloromethane (DCM or methylene chloride), Tetrahydrofuran (THF), or Cyclohexane.

21. The method of claim 13, further comprising:

Disposing, prior to substantially removing the liquid, a foam in the slurry such that hypochlorite sale particles and polymer are dispersed within the foam.

22. The method of claim 21, further comprising:

reducing, prior to adding the hypochlorite salt particles into the solution, the size of the hypochlorite salt particles such that a majority of the hypochlorite salt particles have a size at or below a target size.

23. The method of claim 22, where the target size is 180 microns.

24. An open-celled foam wound insert comprising a reactive agent disposed within the wound insert, and configured to be inert in the absence of an activating fluid and to exhibit antimicrobial properties in the presence of an activating fluid, for use in a wound treatment method comprising the step of delivering a fluid to a wound through a wound dressing comprising:

a drape coupled to skin adjacent a wound of a patient such that the drape covers the wound and forms a space between the drape and the wound;

where the wound insert is disposed in the space, and the wound insert is configured such that when the fluid is delivered to the wound insert, at least a portion of the reactive agent passes from the wound insert to the wound.

25. A reactive agent configured to be inert in the absence of an activating fluid and to exhibit antimicrobial properties in the presence of an activating fluid, for use in a wound treatment method comprising the step of delivering a fluid to a wound through a wound dressing comprising:

a drape coupled to skin adjacent a wound of a patient such that the drape covers the wound and forms a space between the drape and the wound;

where the wound insert is disposed in the space;

where the reactive agent is disposed within the wound insert, and configured to be inert in the absence of an activating fluid and to exhibit antimicrobial properties in the presence of an activating fluid; and

where the wound insert is configured such that when the fluid is delivered to the wound insert, at least a portion of the reactive agent passes from the wound insert to the wound.

26. A method of forming a wound insert, comprising:

applying negative pressure to an open-celled foam to draw particles into the foam such that the particles become dispersed throughout at least a portion of the foam.

27. The method of claim 26, where the foam has a first side and a second side opposite the first side, the method further comprising:

disposing the foam between a filter configured and a particle reservoir such that the filter is adjacent the first side of the foam and the reservoir is adjacent the second side, the filter configured to substantially prevent passage of the particles through the filter;

where applying negative pressure comprises applying negative pressure to the filter such that the particles are drawn from the reservoir into the foam but are prevented from passing through the filter.

28. The method of any of claims 26-27, where the particles comprise a reactive agent configured to react with water or aqueous solution to release hypochlorite ion and/or form hypochlorous acid.

29. The method of any 31, where the reactive agent comprises a hypochlorite salt defined by M(OCl)n, where n=1 if M is K^+, Li^+, or Na^+, and where n=2 if M is Ca^{2+} or Mg^{2+}.

30. The method of any of claims 28-29, where the particles comprise a suspension agent configured to bind the reactive agent to the foam.

31. The method of claim 30, where the suspension agent at least partially encapsulates the reactive agent.

32. The method of any of claims 26-31, where the foam comprises silicone.

33. The method of any of claims 26-27, where the particles comprise a metal.

34. The method of claim 33, where the particles comprise silver.

35. A wound-treatment method comprising:
delivering a fluid to a wound through a wound dressing comprising:
a drape coupled to skin adjacent a wound of a patient such that the drape covers the wound and forms a space between the drape and the wound;
an open-celled foam wound insert disposed in the space; and
a reactive agent disposed within the wound insert, and configured to be inert in the absence of an activating fluid and to exhibit antimicrobial properties in the presence of an activating fluid
where the wound insert is configured such that when the fluid is delivered to the wound insert, at least a portion of the reactive agent passes from the wound insert to the wound.

36. The method of claim 35, where delivering a fluid comprises activating a fluid source that is coupled to the wound dressing to deliver the fluid to the wound through the wound dressing.

37. The method of claim 35, further comprising:
applying negative pressure to the wound through the wound dressing.

38. The method of claim 37, where applying negative pressure comprises activating a vacuum source that is coupled to the wound dressing to apply the vacuum to the wound through the wound dressing.

39. A wound-treatment method comprising:
delivering a fluid to a wound through a wound dressing comprising:
a drape coupled to skin adjacent a wound of a patient such that the drape covers the wound and forms a space between the drape and the wound;
an open-celled foam wound insert disposed in the space;
a plurality of particles of a first metal dispersed within the foam; and
a second metal coupled to the lower side of the foam, and configured such that upon delivery of the fluid microcurrents are generated between the first metal and the second metal.

40. The method of claim 39, where the first metal is dispersed in the foam such that when the fluid is delivered it passes through the foam and at least some portion of the first metal exits the foam.

41. The method of claim 40, where the wound dressing further comprises:
a permeable layer coupled to a lower side of the wound insert;
where the second metal is coupled to the permeable layer.

42. The method of claim 41, where the wound dressing is configured such that upon delivery of the fluid to the wound dressing the fluid passes through the wound insert from an upper side through the lower side, and at least some portion of the first metal exits the foam through the lower side and passes through the permeable layer.

43. The method of claim 42, where the wound insert is disposed such that the permeable layer is in contact with the wound such that upon delivery of the fluid to the wound dressing the fluid passes through the foam from the upper side to the lower side, at least some portion of the first metal exits the foam through the permeable layer and microcurrents are generated between the first metal and the second metal coupled to the permeable layer.

44. The wound insert of any of claims 39-43, where the first metal comprises silver.

45. The wound insert of any of claims 39-44, where the second metal comprises zinc.

46. A wound insert comprising:
an open-celled foam configured to be disposed between a wound of a patient and a drape coupled to skin adjacent the wound; and
a liquid solution comprising an antimicrobial agent, the liquid solution disposed within the foam.

47. The wound insert of claim 46, further comprising:
a container enclosing the foam and configured to prevent evaporation of the liquid solution.

48. The wound insert of claim 47, where the container comprises a foil pouch.

49. The wound insert of claim 47, where the container comprises a plastic pouch.

50. A wound insert comprising:

an open-celled foam configured to be disposed between a wound of a patient and a drape coupled to skin adjacent the wound, the foam having an upper side and lower side configured to face the wound;

a plurality of particles of a first metal dispersed within the foam; and

a second metal coupled to the lower side of the foam, and configured such that a fluid can be introduced to generate microcurrents between the first metal and the second metal.

51. The wound insert of claim 50, where the first metal is dispersed in the foam such that if a fluid passes through the foam at least some portion of the first metal will exit the foam.

52. The wound insert of claim 51, further comprising:

a permeable layer coupled to the lower side of the foam;

where the second metal is coupled to the permeable layer.

53. The wound insert of claim 52, where the wound insert is configured such that if a fluid is passed through the foam from the upper side through the lower side, at least some portion of the first metal will exit the foam through the lower side and pass through the permeable layer.

54. The wound insert of claim 53, where the wound insert is configured such that if the wound insert is disposed such that the permeable layer is in contact with a wound and a fluid is passed through the foam from the upper side to the lower side, at least some portion of the first metal will exit the foam through the permeable layer and microcurrents will be generated between the first metal and the second metal coupled to the permeable layer.

55. The wound insert of any of claims 50-54, where the first metal comprises silver.

56. The wound insert of any of claims 50-55, where the second metal comprises zinc.

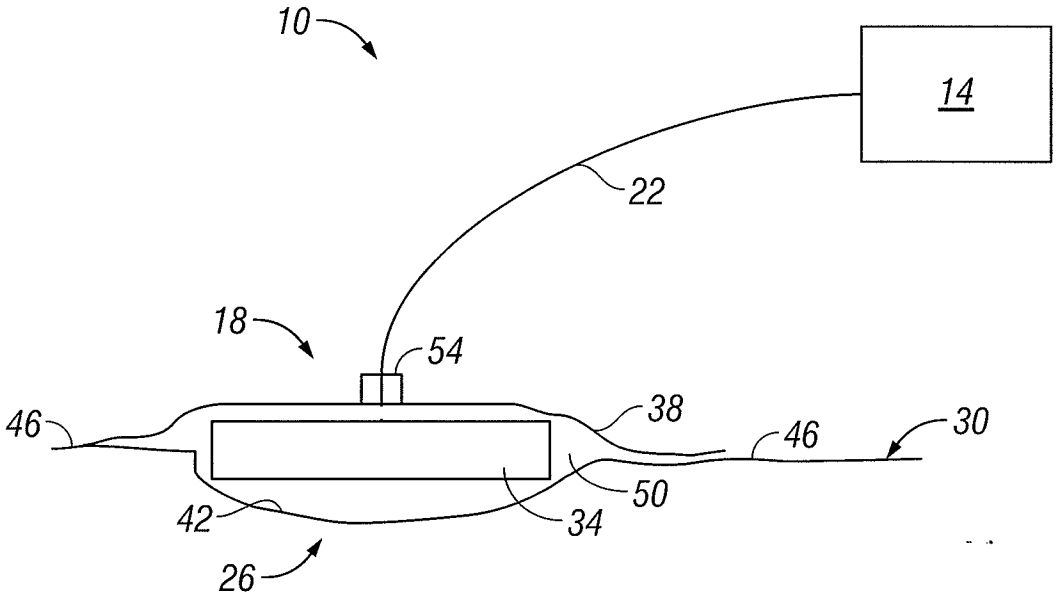


FIG. 1

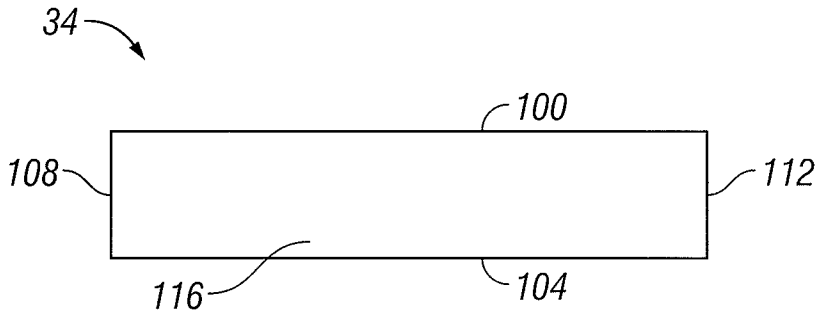


FIG. 2

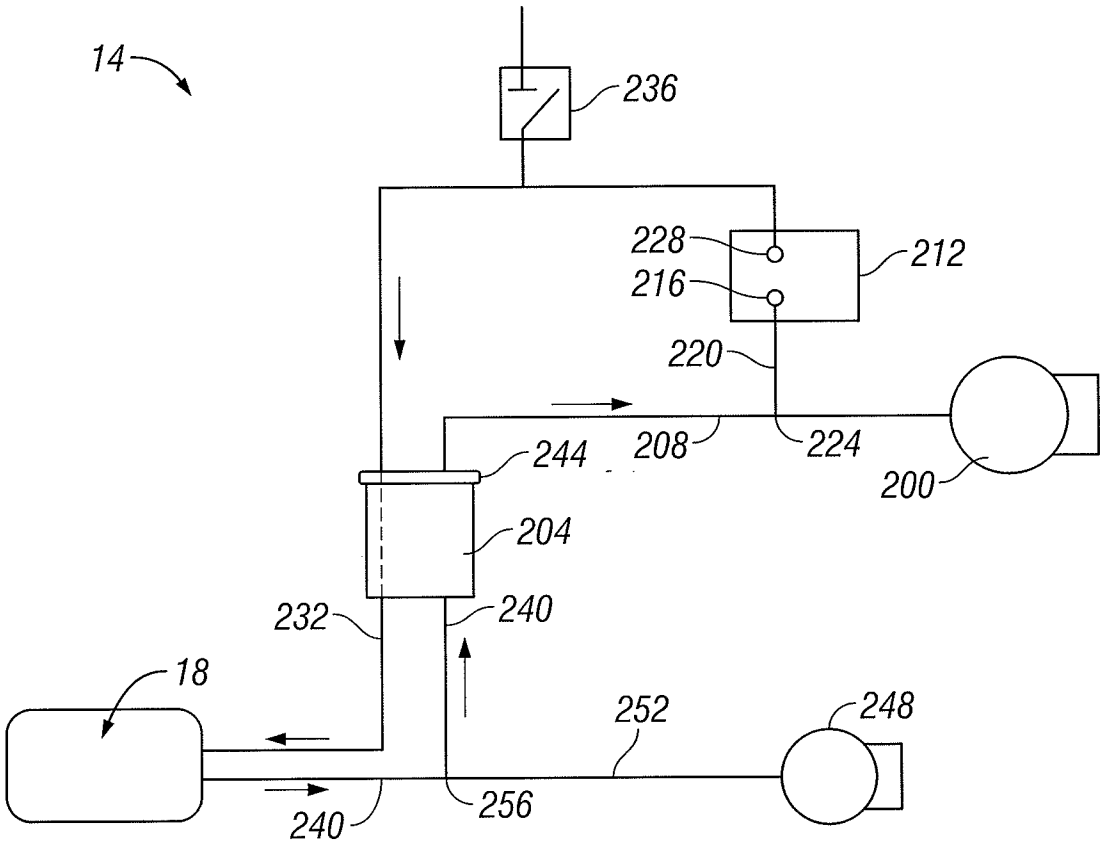

14
236
228
216
212
220
208
224
244
200
204
232
240
18
252
248
240
256

FIG. 3A

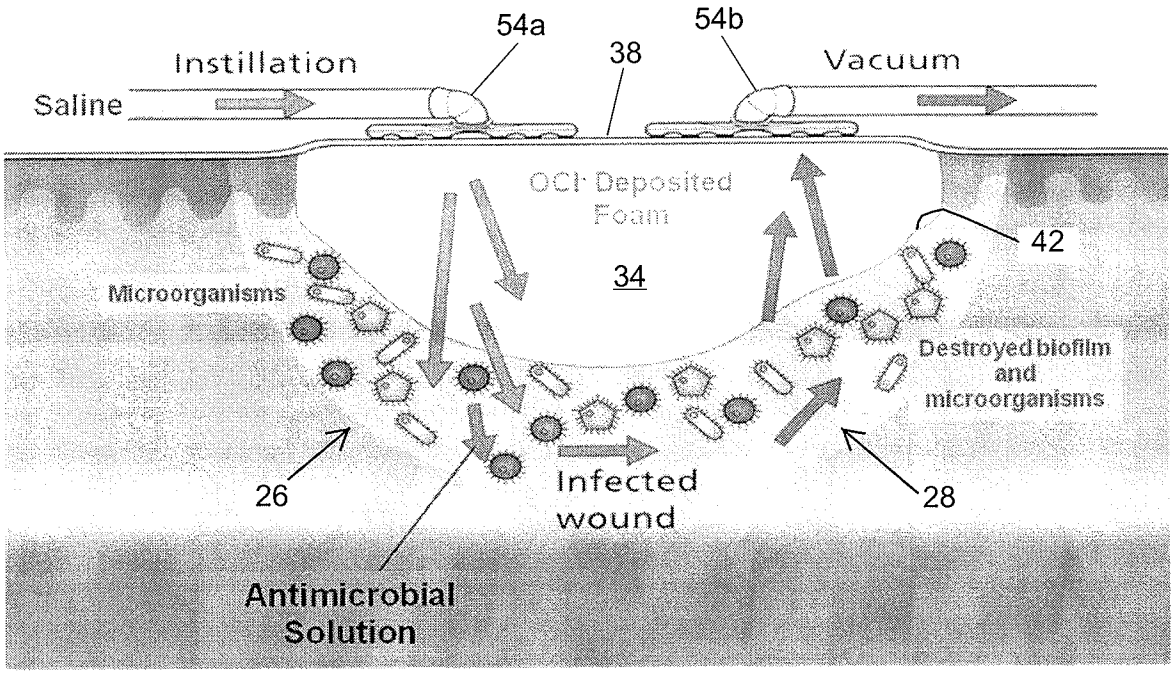


FIG. 3B

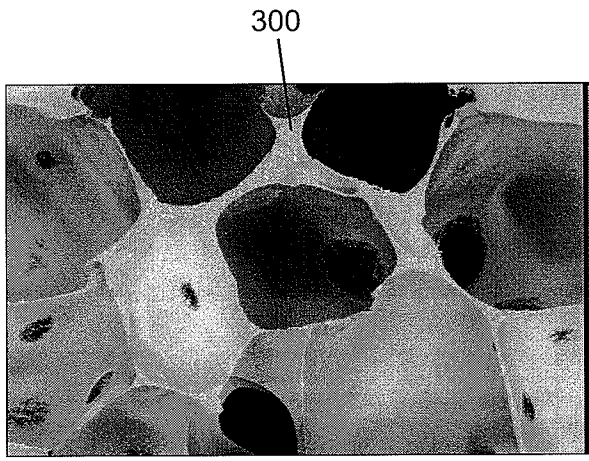


FIG. 4

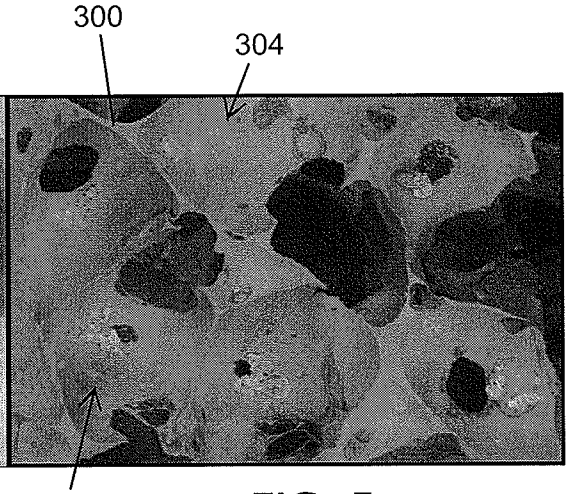


FIG. 5

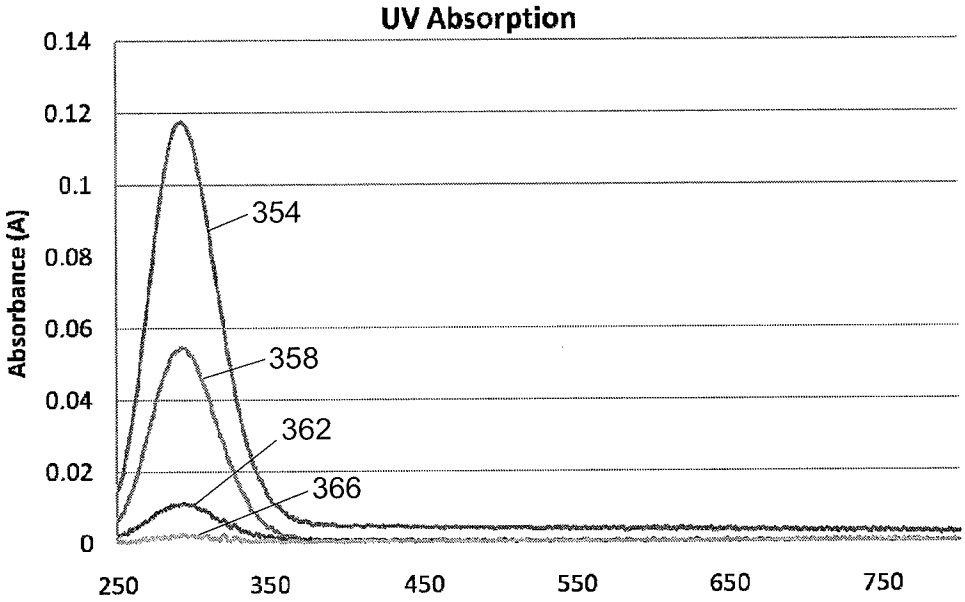

UV Absorption
Absorbance (A)
0.14
0.12
0.1
0.08
0.06
0.04
0.02
0
354
358
362
366
250
350
450
550
650
750

FIG. 6A

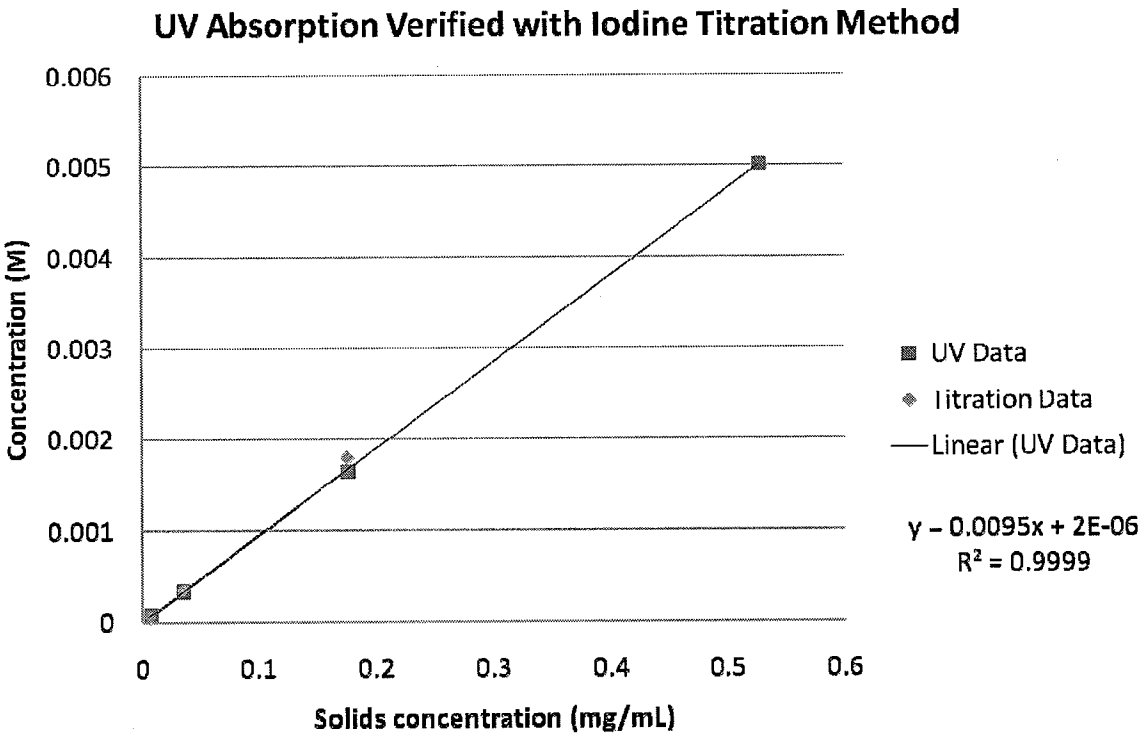

UV Absorption Verified with Iodine Titration Method
Concentration (M)
0.006
0.005
0.004
0.003
0.002
0.001
0
0
0.1
0.2
0.3
0.4
0.5
0.6
Solids concentration (mg/mL)
UV Data
Titration Data
Linear (UV Data)
y = 0.0095x + 2E-06
R² = 0.9999

FIG. 6B

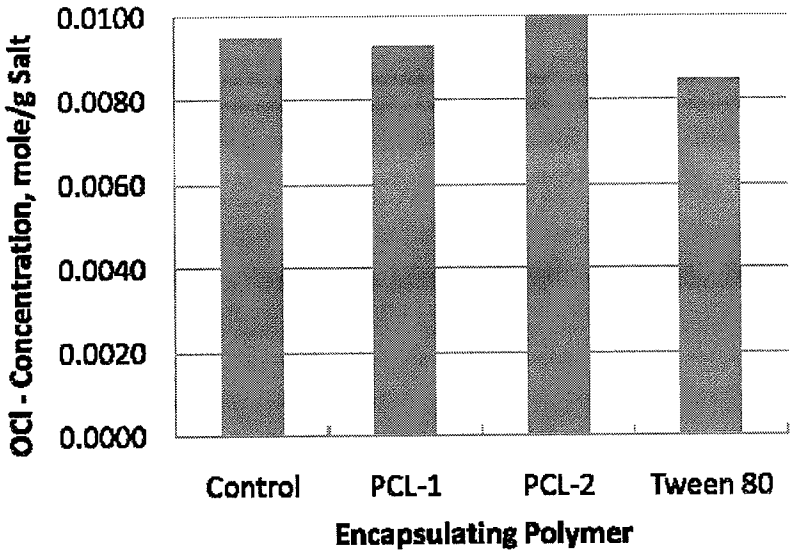

0.0100
0.0080
0.0060
0.0040
0.0020
0.0000
OCl - Concentration, mole/g Salt
Control
PCL-1
PCL-2
Tween 80
Encapsulating Polymer

FIG. 6C

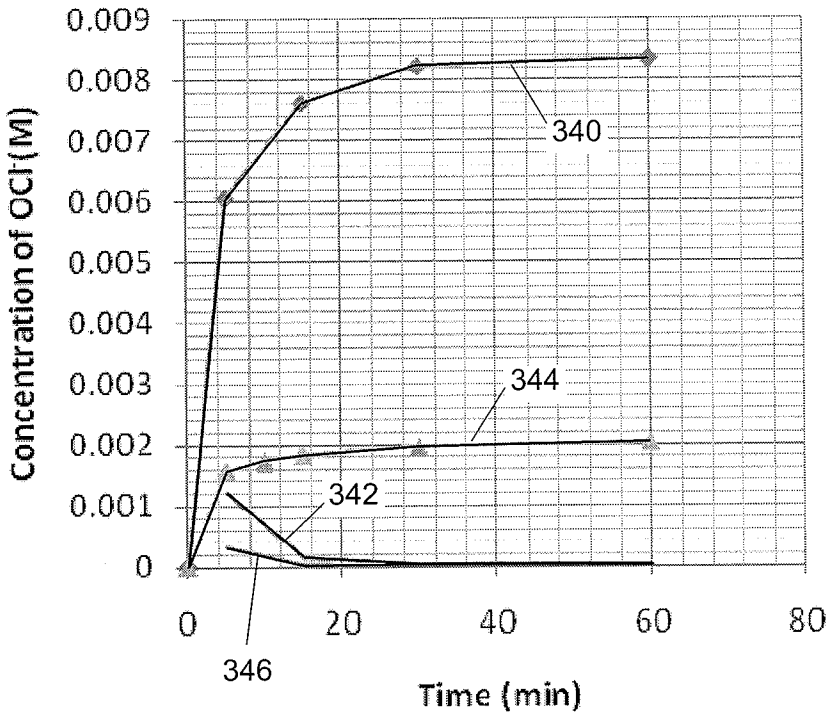

0.009
0.008
0.007
0.006
0.005
0.004
0.003
0.002
0.001
0
Concentration of OCl-(M)
0
20
40
60
80
Time (min)
340
344
342
346

FIG. 7

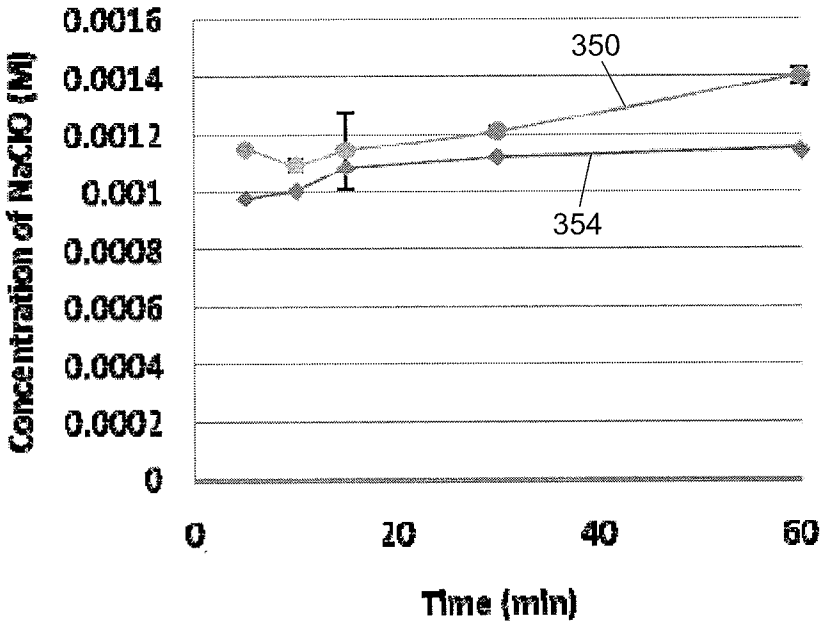

0.0016
0.0014
0.0012
0.001
0.0008
0.0006
0.0004
0.0002
0
Concentration of NaClO (M)
350
354
0
20
40
60
Time (min)

FIG. 8

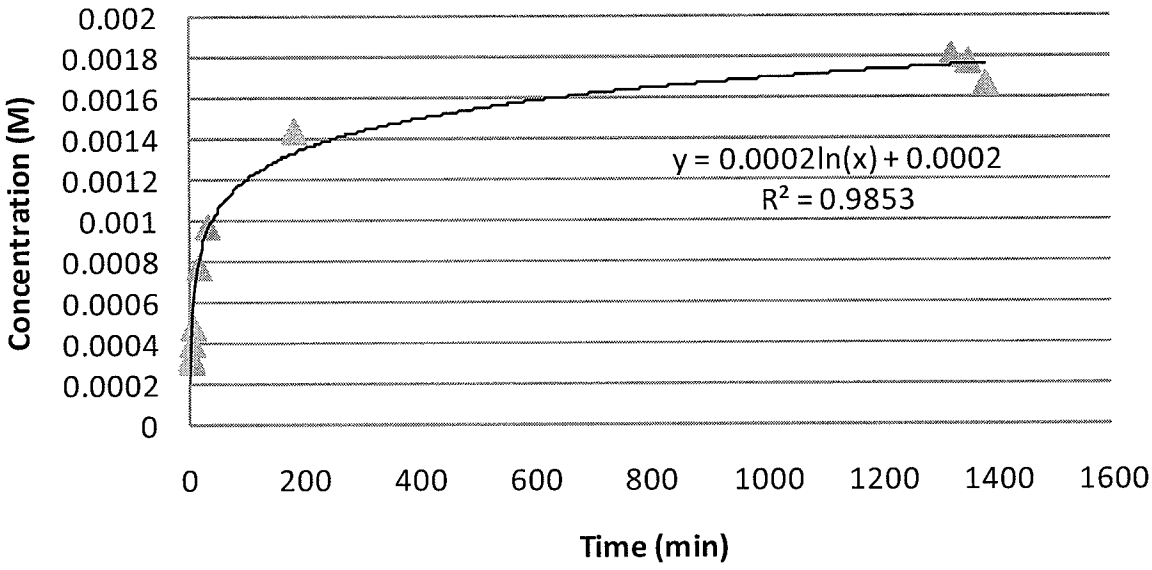

0.002
0.0018
0.0016
0.0014
0.0012
0.001
0.0008
0.0006
0.0004
0.0002
0
Concentration (M)
y = 0.0002ln(x) + 0.0002
R² = 0.9853
0
200
400
600
800
1000
1200
1400
1600
Time (min)

FIG. 9

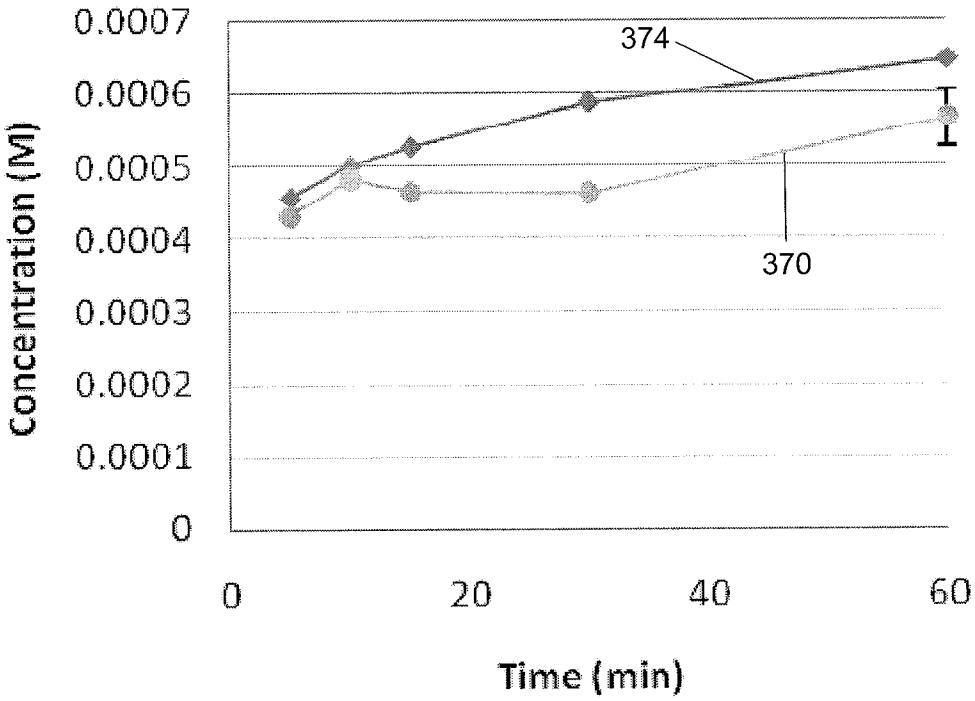

0.0007
0.0006
0.0005
0.0004
0.0003
0.0002
0.0001
0
Concentration (M)
374
370
0
20
40
60
Time (min)

FIG. 10

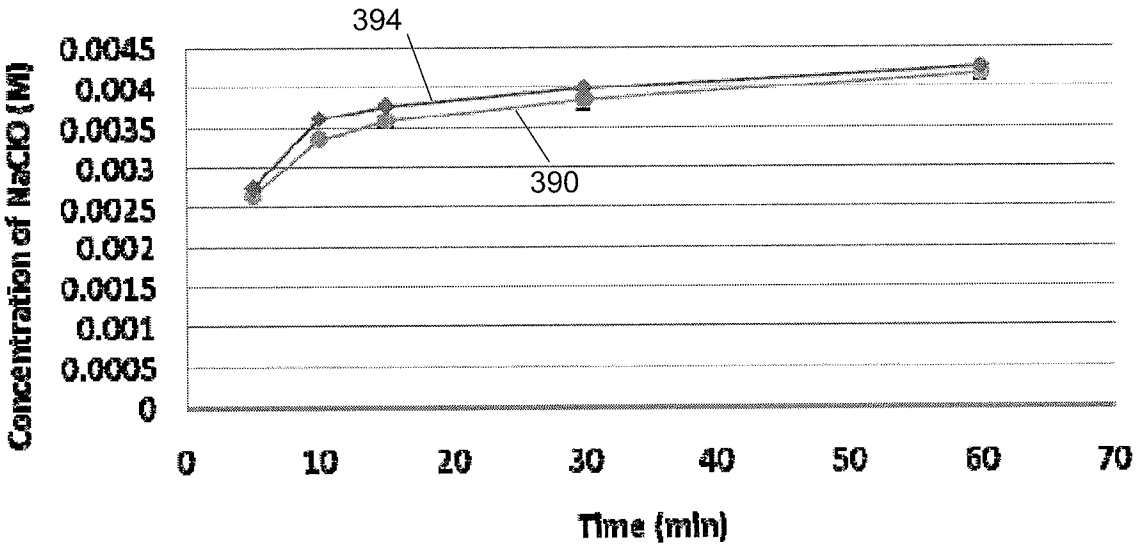

394
390
0.0045
0.004
0.0035
0.003
0.0025
0.002
0.0015
0.001
0.0005
0
Concentration of NaClO (M)
0
10
20
30
40
50
60
70
Time (min)

FIG. 11

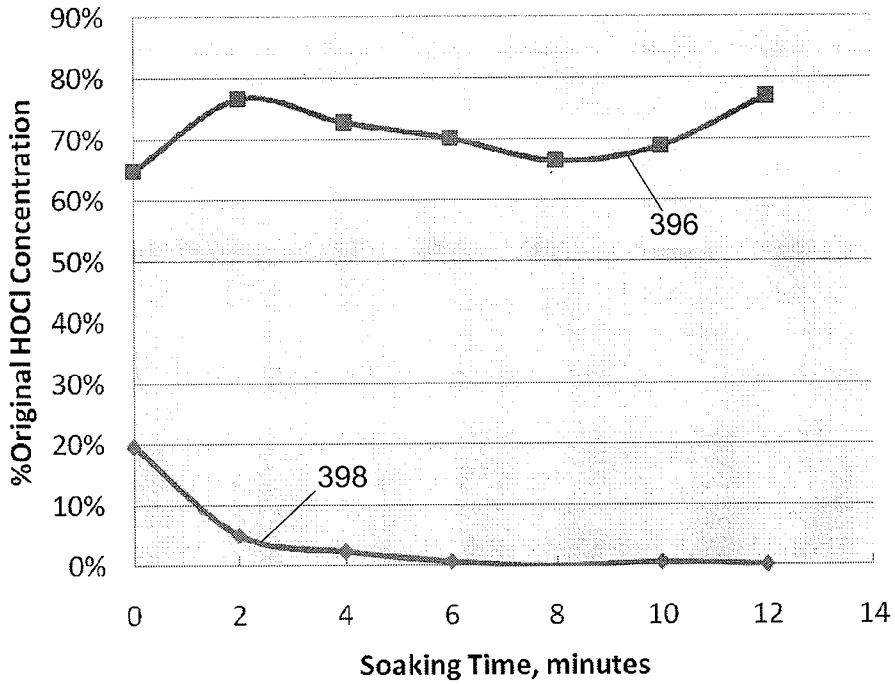


FIG. 12A

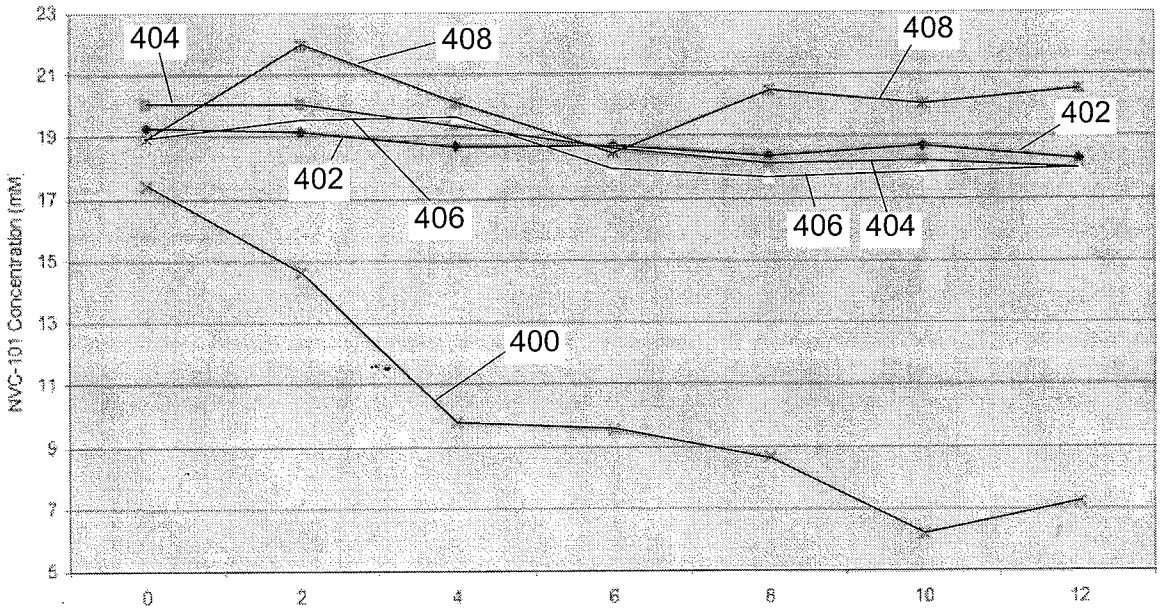
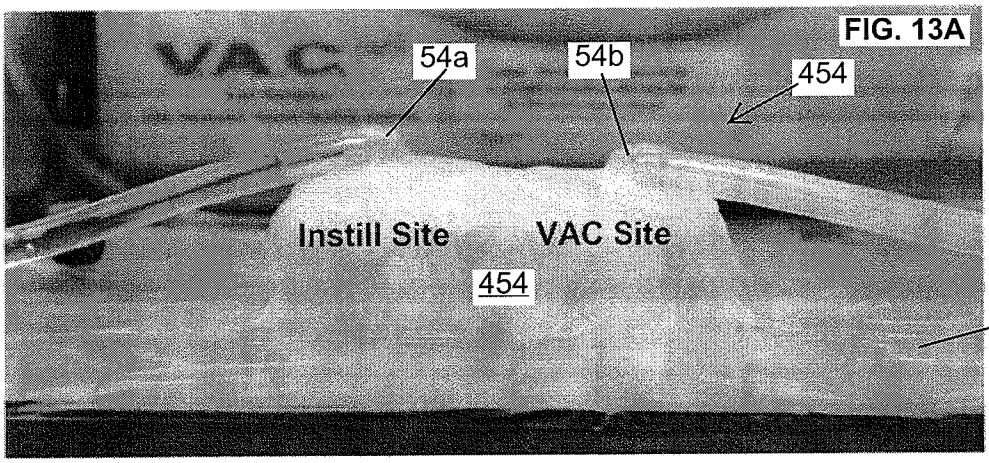
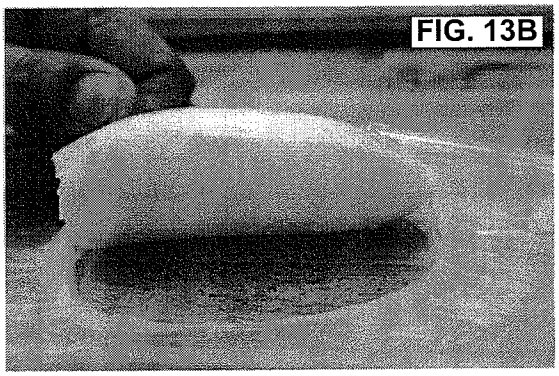
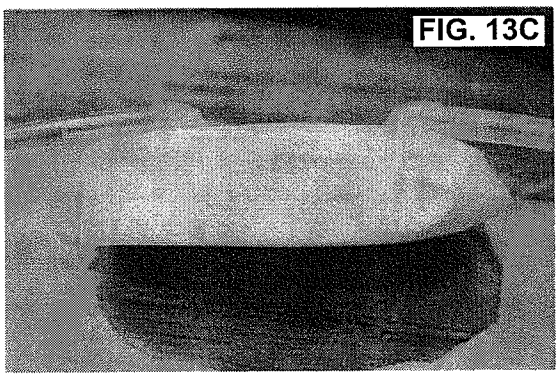


FIG. 12B

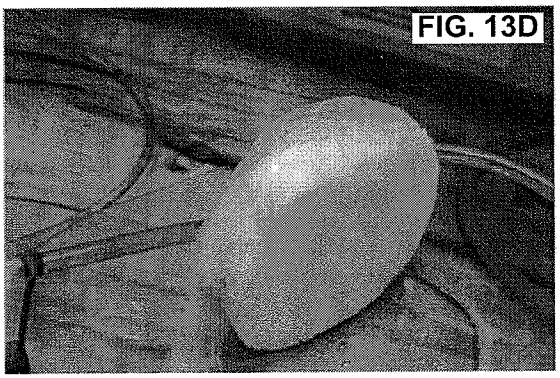




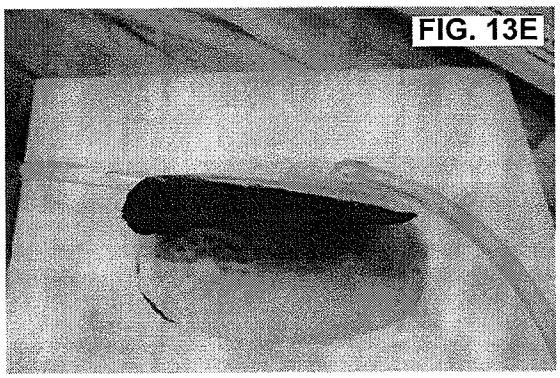
MF1-6535 Post Test



MF1-8055 Post Test



MF1-9535 Post Test



PU Foam Post Test

FIGS. 13A-13E

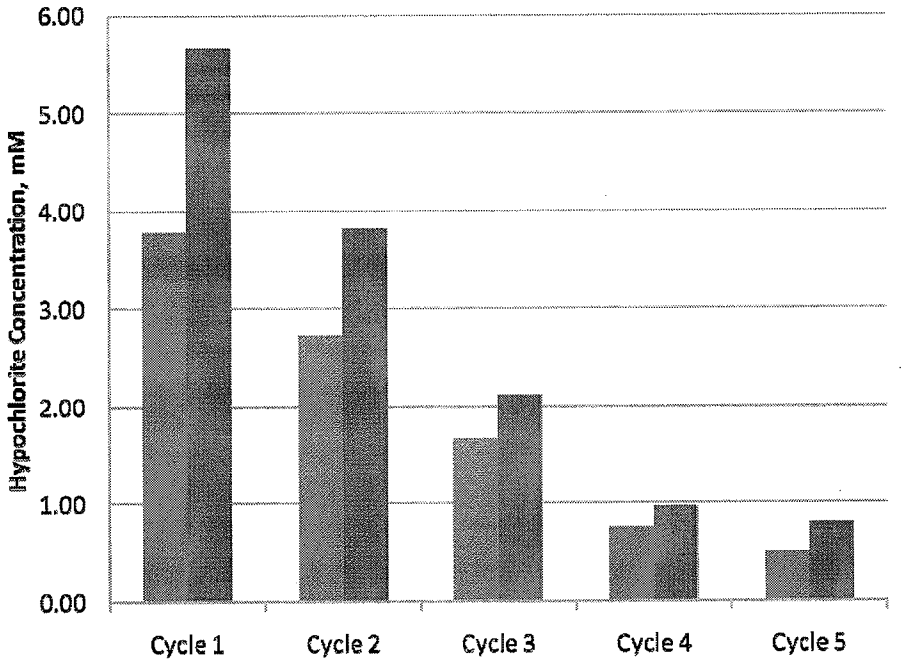

6.00
5.00
4.00
3.00
2.00
1.00
0.00
Hypochlorite Concentration, mM
Cycle 1
Cycle 2
Cycle 3
Cycle 4
Cycle 5

FIG. 14

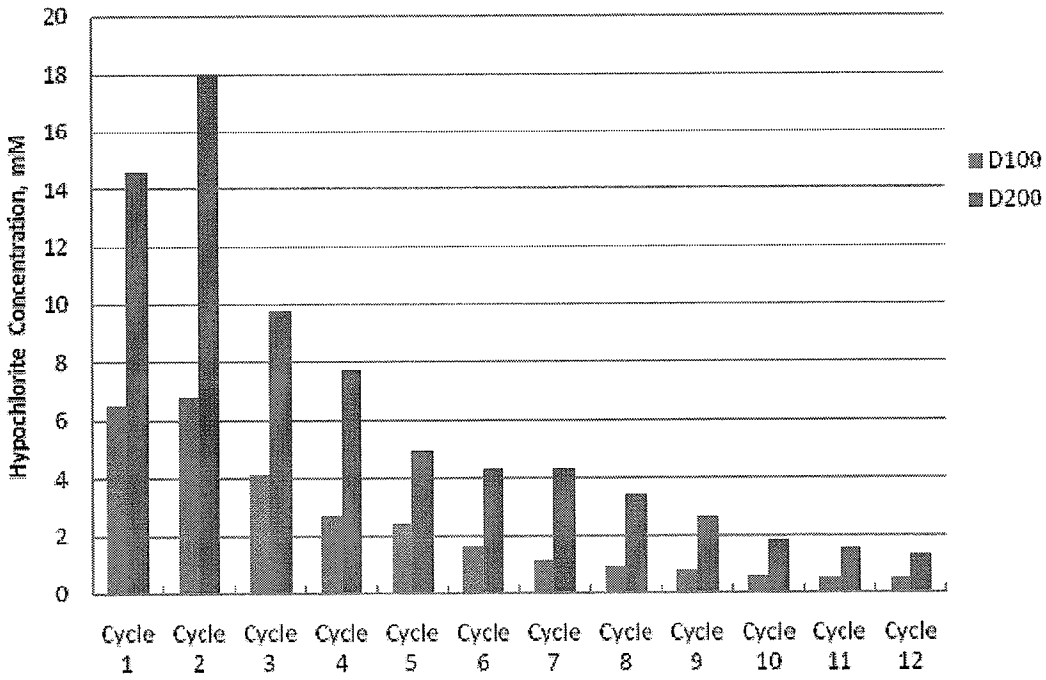

20
18
16
14
12
10
8
6
4
2
0
Hypochlorite Concentration, mM
D100
D200
Cycle 1
Cycle 2
Cycle 3
Cycle 4
Cycle 5
Cycle 6
Cycle 7
Cycle 8
Cycle 9
Cycle 10
Cycle 11
Cycle 12

FIG. 17

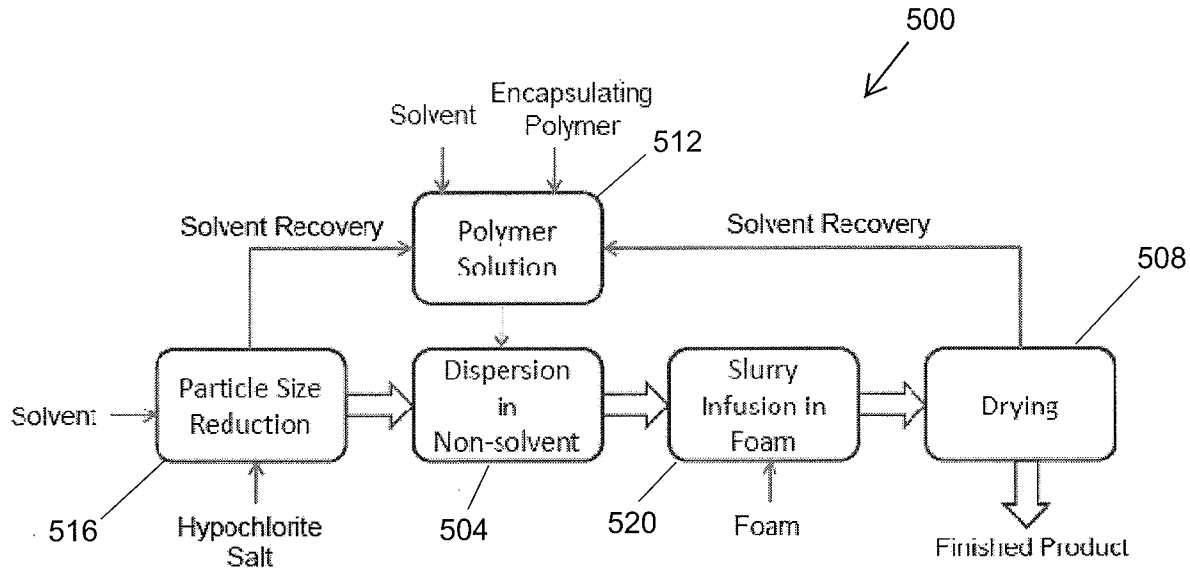

500
Solvent
Encapsulating Polymer
512
Solvent Recovery
Polymer Solution
Solvent Recovery
508
Solvent
Particle Size Reduction
Dispersion in Non-solvent
Slurry Infusion in Foam
Drying
516
Hypochlorite Salt
504
520
Foam
Finished Product

FIG. 15

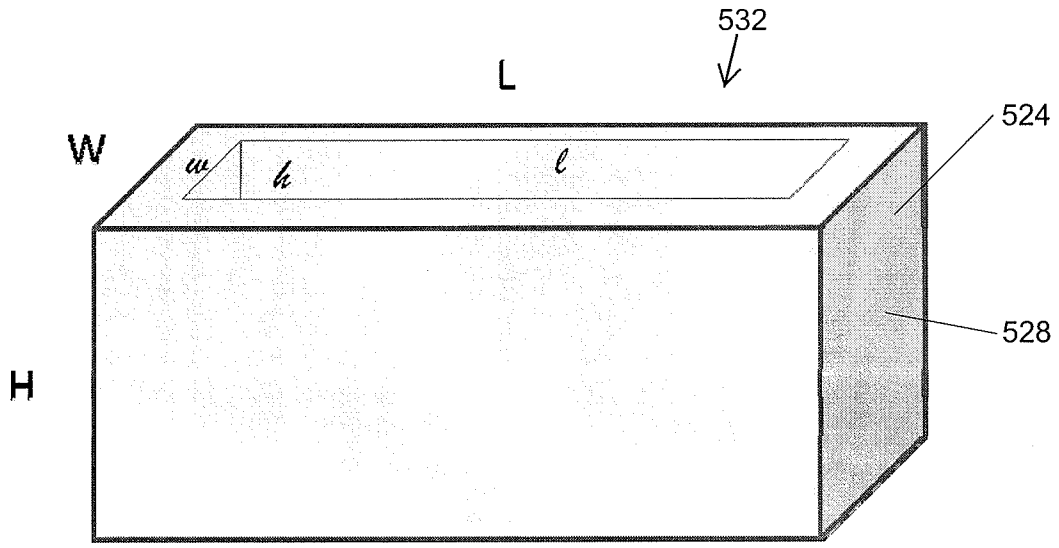

532
L
W
w
h
ℓ
524
528
H

FIG. 16

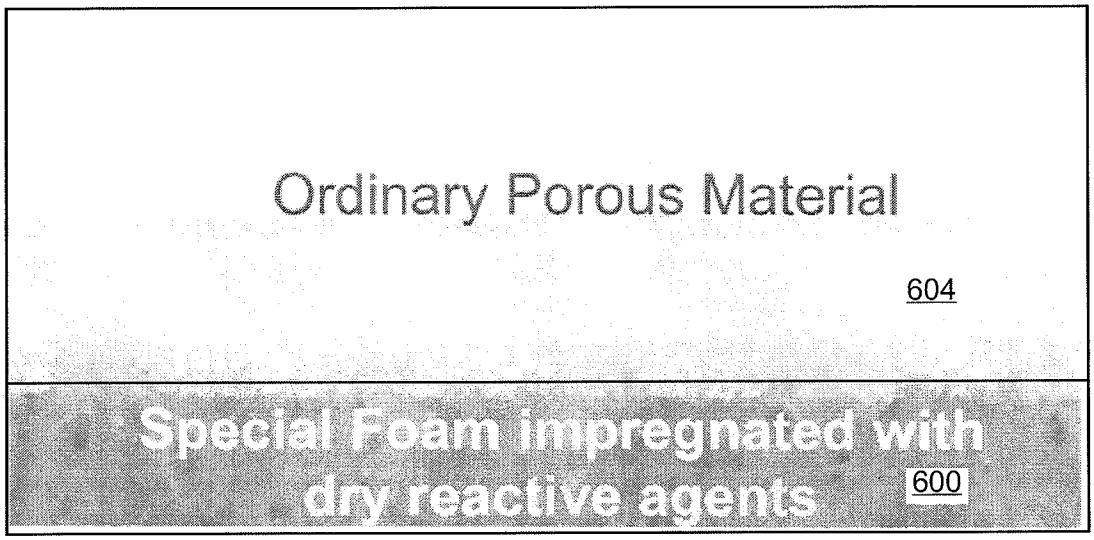

Ordinary Porous Material
604
Special Foam impregnated with dry reactive agents
600

FIG. 18

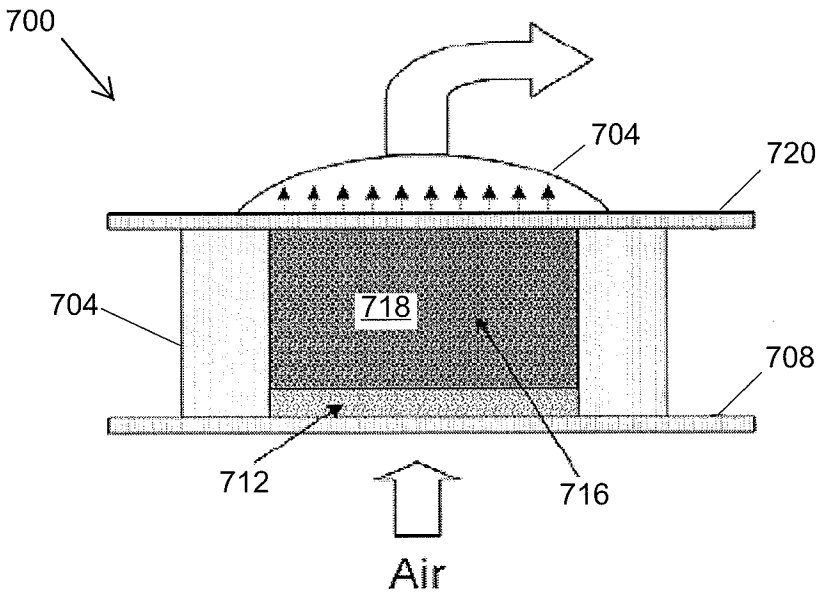

700
704
720
704
718
708
712
716
Air

FIG. 19

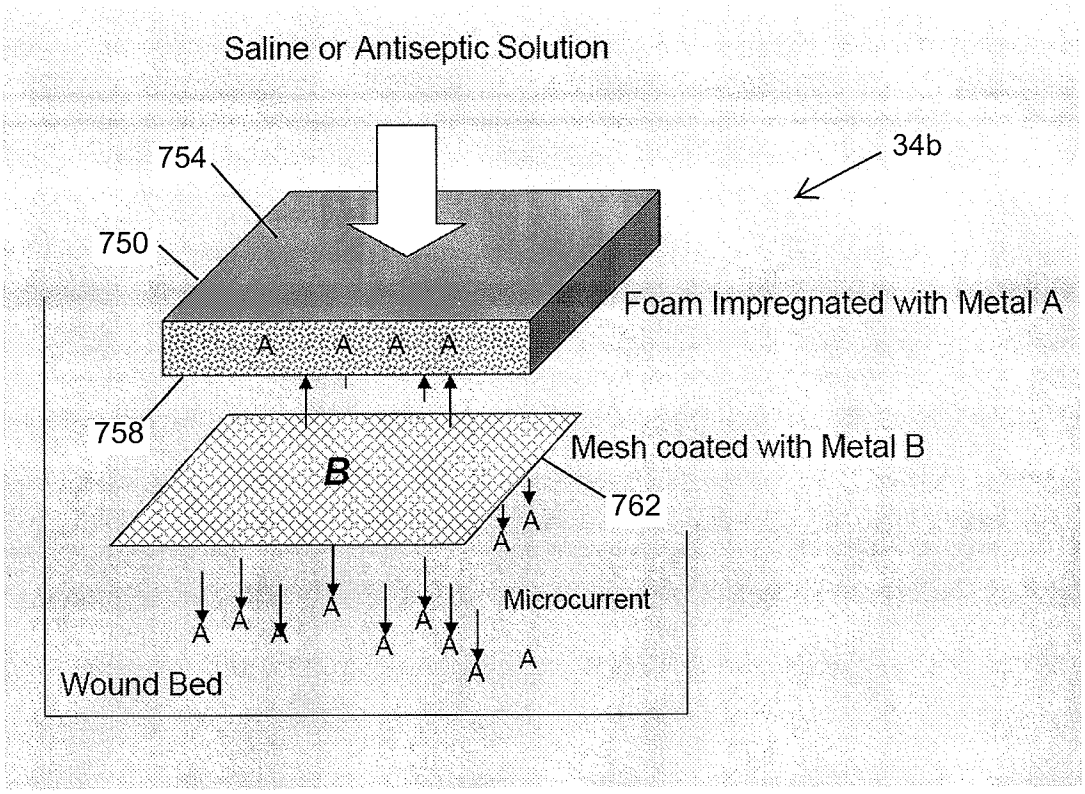

Saline or Antiseptic Solution
754
34b
750
Foam Impregnated with Metal A
A A A A
758
Mesh coated with Metal B
B
762
A
A
Microcurrent
A A A A A A A A
Wound Bed

FIG. 20