

SILICA FIBER COMPOSITIONS AND METHODS OF USE

Related Applications

5 This application claims the benefit of and priority to U.S. Patent Application
Serial No. 16/131,531, filed September 14, 2018, U.S. Patent Application Serial No.
15/934,599, filed March 23, 2018, U.S. Provisional Patent Application No. 62/710,305,
filed February 16, 2018, and U.S. Provisional Patent Application No. 62/643,946, filed
March 16, 2018, the entire disclosure of each of which is hereby incorporated herein by
10 reference.

Technical Field

 In various embodiments, the present invention relates to the fabrication and use of
silica fibers.

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Background

 Wound healing involves a well-coordinated series of biological processes that
include both tissue destruction and tissue regeneration. For example, during normal
wound healing, neutrophils and monocytes are recruited to the wound during an early
20 inflammatory phase. The neutrophils phagocytize debris and micro-organisms;
monocytes and other cells release enzymes in the surrounding matrix to digest damaged
tissue. Fibrin is broken down as part of this process, and the degradation products attract
fibroblasts and epithelial cells to the site of the wound. Macrophages recruited to the
wound (as well as other cells) secrete extracellular enzymes that act on all components of
25 the extracellular matrix and are responsible for removal of devitalized tissue.
Macrophages also secrete a variety of cytokines and growth factors that can stimulate
keratinocytes, fibroblasts and angiogenesis, which promotes the transition to the
proliferative phase of healing. The proliferation phase is characterized by angiogenesis,
collagen deposition, granulation tissue formation, wound contraction and
30 epithelialization. Proliferation involves replacement of dermal tissues as well as
contraction of the wound.

While destruction of collagen is important during the early phases of wound healing, its deposition and remodeling is critical for later stages. During wound healing, the wound bed fills in from the bottom up with collagen and must be maintained in an optimal environment (appropriate moisture balance and temperature) before the epithelial cells will begin to proliferate and migrate across the wound's surface to close the wound. The collagen structures provide the cells with the needed biological environment for development, organogenesis, cell growth, and wound repair.

Chronic wounds are wounds that have not progressed through this normal, orderly sequence of repair. Further, chronic wounds may eventually pass through the repair process without restoring sustained anatomical and functional tissue. Chronic wounds can result when the body has failed to correct for the causes of the wound, and/or where there is not a conducive environment for healing. For example, newly deposited collagen can be enzymatically destroyed by an uncontrolled inflammatory response, making it difficult for dermal cells to populate the wound and proliferate.

The present invention provides compositions and methods for promoting wound healing, including for acute and chronic wounds, and wounds that result from physical, biological, or genetic causes that interfere with normal wound healing physiology.

Summary

The present invention in various aspects and embodiments provides methods for making silica fiber mats useful for treatment of animal wounds and tissue, as well as for other applications in industry. The methods comprise preparing a sol with a silicon alkoxide reagent, such as tetraethyl ortho silicate (TEOS), alcohol solvent, and an acid catalyst, and transitioning the sol for at least 2 days (and, in some embodiments, no more than 7 days) under conditions where humidity and temperature are controlled. The sol-gel is electrospun to create a silica fiber mat with superior texture and properties.

In some embodiments, the composition is a lightweight structure composed of silica fiber (e.g., silicon dioxide nanofiber). By ripening (or "transitioning") the sol under controlled environmental conditions, and/or monitoring the properties of the sol during the ripening/transitioning process, the relatively short window to successfully electrospin

the sol-gel can be identified to prepare a superior composition for wound care and other applications.

5 In various aspects, the present invention provides compositions and methods for improving integrity of injured tissue in a subject, including for accelerating or improving healing of acute or chronic wounds. The compositions comprise a silica fiber matrix, which is applied to injured tissue to support tissue regeneration and healing. In some embodiments, the silica fiber matrix is a permanent (and, in various embodiments, non-biodegradable) scaffold that is not removed from the wound (unlike a conventional wound dressing), but becomes integrated with the regenerated tissue.

10 In accordance with embodiments of the invention, the silica fiber composition, when applied to wounded tissue, acts as a scaffold (e.g., a non-biodegradable scaffold) that supports tissue healing, regeneration, and/or integrity. The composition acts as a collagen biomimetic at the site of tissue injury, providing an environment conducive for regeneration and growth of, for example, dermal cells.

15 In various embodiments, the controlled environment for transitioning the sol may involve controlled conditions in terms of humidity, temperature, and optionally barometric pressure. For example, the humidity may be controlled within the range of about 30% to about 90% or from about 40% to about 80%. The temperature may be controlled within the range of from about 50° F to about 90° F. By controlling the environmental conditions during transitioning, the gel can be electrospun during the time when spinning is optimal, which can occur in a very small window of only several minutes if the ripening process is accelerated by direct heat. When transitioning the sol at a constant humidity in the range of about 50% to 70% and a temperature of about 60 to 80° F, the sol will transition (gelatinize) in a few days, and the window for successful electrospinning can be expanded to at least several hours, and in some embodiments several days. The sol may therefore be transitioned in an enclosure which may include an exhaust fan and one or more environmental monitors or sensors, such as a temperature reading device and/or a humidity reading device. Further, gases produced or released by the sol during the transitioning process and/or relative weight of the sol can be monitored to determine the suitable or optimal time for electrospinning.

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If the sol-gel is prepared to allow for optimal electrospinning, as described herein, it is possible to electrospin fiber mats having a thickness of at least about 1/8 inch, or at least about 1/4 inch, or at least about 1/3 inch, or at least about 1/2 inch, which are easier to handle for application of fibers to a wound. Indeed, formation of fiber mats of
5 thicknesses in accordance with embodiments of the present invention enables the separation, if necessary or desired, of one or more layers of entangled fibers from a single mat for applications such as wound care.

In some embodiments, the fiber composition is applied to the tissue or wound as a thin layer of fibers, e.g., just enough to cover the wound, followed by repeated
10 application as necessary. In some embodiments, the fiber composition is processed into a fine powder or dust, which is applied to the tissue. In some embodiments, the powder or dust is mixed with a topical composition, such as a lotion, ointment, paste, cream, foam, or gel. In these embodiments, the topical composition may comprise one or more pharmaceutical or antimicrobial agents, such as an antibiotic, an antiseptic, an anti-
15 inflammatory agent, or immunosuppressant.

Application of the composition during the healing process can provide for accelerated healing, of both acute and chronic wounds, and can prevent or reduce tissue scarring. When the topical composition is applied to the skin that has a blemish like acne, cracks in skin, loss of integrity due to age or environmental insult (sun, wind, or cold,
20 etc.), the scaffolding is left behind in the small wound for cells to grow into. This speeds up the healing process and helps to reduce scarring.

In some embodiments, the wound is a first or second degree burn, scrape, or cut, or a minor wound that does not go deeper than the base lamina. In some embodiments, the wound includes damage including or past the base lamina. In some embodiments, the
25 wound is a third degree burn, diabetic ulcer, chronic pressure sore, or gangrenous wound. In some embodiments, fibers are applied once to four times daily to cover the wound. Fibers are generally reapplied when fibers are no longer visible in the wound. An additional wound cover can be employed where necessary, as long as air and oxygen are not restricted from the wound.

30 In some embodiments, the subject has a genetic blistering disease, such as epidermolysis bullosa (EB). In people born with EB, the two skin layers lack the protein

anchors that hold them together, resulting in extremely fragile skin, where even minor mechanical friction like rubbing or pressure will separate the layers of the skin and form blisters and painful sores. In these embodiments, the composition will become integrated with the base lamina, and help anchor the skin. Thus, over time, the skin exhibits

5 improved integrity as sores and blisters are continually treated. Further, the reduction in pain can be important for these patients to perform daily activities, such as bathing or traveling.

In an aspect, embodiments of the invention feature a method for improving integrity of injured tissue in a subject. The method includes, consists essentially of, or

10 consists of applying a silica fiber composition to the injured tissue. The silica fiber composition, or at least a substantial amount thereof, may remain in place (i.e., not be removed) from the tissue during and after the healing of the tissue. (As utilized herein, “a substantial amount” of the composition means 70%-100%, 80%-100%, 90%-100%, or even 95%-100% of the composition.)

15 Embodiments of the invention may include one or more of the following in any of a variety of combinations. The silica fiber composition may be a permanent scaffold that supports tissue healing, regeneration, and/or integrity. The silica fiber composition may be non-biodegradable. The composition may act as a collagen replacement, and/or cell scaffold for wound healing. The composition may be prepared by electrospinning a sol-

20 gel. The sol-gel may be prepared with tetraethyl orthosilicate (TEOS). The sol-gel may contain 70% to 90% TEOS by weight, 8% to 25% ethanol by weight, an acid catalyst, and the balance water. The sol-gel may contain 70% to 90% TEOS by weight, 8% to 25% ethanol by weight, 1% to 10% water by weight, and the acid catalyst. The sol-gel may contain 75% to 85% by weight TEOS, 12% to 20% by weight ethanol, and about 2%

25 to 5% by weight water. The sol-gel may contain about 80% by weight TEOS, about 17% by weight ethanol, and about 3% by weight water. The acid catalyst may include, consist essentially of, or consist of HCl. The sol-gel may contain less than about 0.1% of the acid catalyst by weight. The sol-gel may contain from 0.02% to 0.08% of the acid catalyst by weight. The sol-gel may contain less than about 1%, less than about 0.8%,

30 less than about 0.5%, less than about 0.3%, or less than about 0.2% of the acid catalyst by

weight. The sol-gel may contain at least about 0.005%, at least about 0.01%, or at least 0.02% of the acid catalyst by weight.

The sol-gel may be allowed to transition for at least 2 days under conditions where humidity is within the range of about 40% to about 80%, and the temperature is within the range of 50° F to 90° F. The sol-gel may be allowed to transition for at least 3 days, at least 4 days, at least 5 days, at least 6 days, or at least 7 days. The sol-gel may be allowed to transition for 2 days to 7 days. The sol-gel may be electrospun when the weight is at from 20% to 40% of the starting weight before ripening (transitioning). The sol-gel may be electrospun when the production of ethylene vapor is 10% to 20% relative to the peak production of ethylene vapors during ripening (transitioning). The sol-gel may be electrospun when the production of ethylene vapor therefrom is 10% to 40% relative to the sol-gel before ripening (transitioning). Fibers of the silica fiber composition may have a variable diameter of from about 50 nm to about 5 μ m. The fibers may have a variable diameter of from about 200 nm to about 1000 nm.

The composition may include, consist essentially of, or consist of SiO₂. The composition may be electrospun with a thickness of from about 1/8 inch to about 1/4 inch. The composition may be electrospun with a thickness of greater than about 1/8 inch, or greater than about 1/4 inch. The fiber composition may be applied to the tissue as a thin layer (e.g., a layer having a thickness less than about 1 inch, less than about 1/2 inch, less than about 1/4 inch, or less than about 1/8 inch; the thickness may be greater than about 1/32 inch or greater than about 1/16 inch). The fiber composition may be processed into a powder or dust or a plurality of fibrous fragments, and the powder or dust or fragments may be applied to the tissue. The powder or dust or fragments may be mixed or suspended in a topical composition. The topical composition may be a lotion, ointment, paste, cream, foam, or gel. The topical composition may include one or more pharmaceutical and/or antimicrobial agents. The topical composition may include an antibiotic and/or an antiseptic. The topical composition may include an anti-inflammatory agent and/or an immunosuppressant. During and/or after healing of the injured tissue, at least some of (or even all of) the silica fiber composition may not be removed from the tissue. The silica fiber composition may be reapplied one or more times to the injured tissue once the silica fiber composition is no longer visible (e.g., to

the naked eye) on the injured tissue. The injured tissue may not be covered with any other wound dressing. At least a portion of the injured tissue may be covered by an additional wound dressing (e.g., over the composition).

The method may prevent or reduce scarring of the injured tissue. The subject
5 may be a mammal. The injured tissue may be skin. The subject may be a veterinary patient, e.g., a dog, cat, or horse. The subject may be a human patient. The composition may be applied to a skin lesion, ulcer, wound, burn, cut, scrape, or blister. The composition may be applied to a diabetic ulcer. The subject may have a genetic blistering disease. The subject may have epidermolysis bullosa. The subject may have a
10 burn, e.g., a second-degree or third-degree burn. The composition may be applied to a pressure sore or pressure ulcer. The injured tissue may be gangrenous and/or may be an amputation wound. The injured tissue may be a cancer lesion. The injured tissue may include, consist essentially of, or consist of a skin burn, cut, or scrape, and the composition may be applied in one or more layers (e.g., a plurality of layers) in an
15 amount sufficient to cover the injured tissue. The composition may not be removed from the injured tissue, and the composition may be reapplied once no longer visible at the injured tissue. The composition may be reapplied after bathing of the subject.

In another aspect, embodiments of the invention feature a silica fiber mat composition that includes, consists essentially of, or consists of silica fibers prepared by
20 electrospinning a sol-gel prepared with tetraethyl orthosilicate (TEOS), an alcohol solvent, and acid catalyst; the sol-gel having been allowed to transition for at least 2 days under conditions where humidity is within the range of about 40% to about 80%, and the temperature is within the range of 50° F to 90° F.

Embodiments of the invention may include one or more of the following in any of
25 a variety of combinations. The sol-gel may be allowed to transition for at least 3 days, at least 4 days, at least 5 days, at least 6 days, or at least 7 days. The sol-gel may be allowed to transition for 2 days to 7 days. The sol-gel may be electrospun when the weight is at from 20% to 40% of the starting weight before ripening (transitioning). The sol-gel may be electrospun when the production of ethylene vapor is 10% to 20% relative
30 to the peak production of ethylene vapors during ripening (transitioning). The sol-gel may be electrospun when the production of ethylene vapor therefrom is 10% to 40%

relative to the sol-gel before ripening (transitioning). Fibers of the silica fiber composition may have a variable diameter of from about 50 nm to about 5 μ m. The fibers may have a variable diameter of from about 200 nm to about 1000 nm. The composition may include, consist essentially of, or consist of SiO₂. The composition may be electrospun with a thickness of from about 1/8 inch to about 1/4 inch. The composition may be electrospun with a thickness of greater than about 1/8 inch, or greater than about 1/4 inch. The sol-gel may be prepared with 70% to 90% TEOS by weight, 8% to 25% ethanol by weight, an acid catalyst, and the balance water. The sol-gel may be prepared with 70% to 90% TEOS by weight, 8% to 25% ethanol by weight, 1% to 10% water by weight, and the acid catalyst. The sol-gel may be prepared with 75% to 85% by weight TEOS, 12% to 20% by weight ethanol, and about 2% to 5% by weight water. The sol-gel may be prepared with about 80% by weight TEOS, about 17% by weight ethanol, and about 3% by weight water. The acid catalyst may include, consist essentially of, or consist of HCl. The sol-gel may be prepared with less than about 0.1% of the acid catalyst by weight. The sol-gel may be prepared with from 0.02% to 0.08% of the acid catalyst by weight. The sol-gel may be prepared with less than about 1%, less than about 0.8%, less than about 0.5%, less than about 0.3%, or less than about 0.2% of the acid catalyst by weight. The sol-gel may be prepared with at least about 0.005%, at least about 0.01%, or at least 0.02% of the acid catalyst by weight.

The composition may further include (e.g., be mixed with) a topical carrier. The topical carrier may be a lotion, ointment, paste, cream, foam, or gel. The topical carrier may include one or more pharmaceutical and/or antimicrobial agents. The topical carrier may include an antibiotic and/or antiseptic. The topical carrier may include an anti-inflammatory agent and/or immunosuppressant.

In yet another aspect, embodiments of the invention feature a fiber composition that includes, consists essentially of, or consists of (i) a silica fiber powder or dust or plurality of fibrous fragments, and (ii) a topical carrier.

Embodiments of the invention may include one or more of the following in any of a variety of combinations. The topical carrier may be a lotion, ointment, paste, cream, foam, or gel. The topical carrier may include one or more pharmaceutical and/or

antimicrobial agents. The topical carrier may include an antibiotic and/or antiseptic. The topical carrier may include an anti-inflammatory agent and/or immunosuppressant.

In another aspect, embodiments of the invention feature a method for making a silica fiber composition. A sol is prepared. The sol includes, consists essentially of, or consists of tetraethyl orthosilicate (TEOS), ethanol, water, and an acid catalyst. The sol may include, consist essentially of, or consist of 70% to 90% TEOS by weight, 8% to 25% ethanol by weight, the acid catalyst, and the balance water. For example, the sol may include, consist essentially of, or consist of 70% to 90% TEOS by weight, 8% to 25% ethanol by weight, 1% to 10% water by weight, and the acid catalyst. The sol is transitioned to a sol-gel for at least 2 days. The sol may be transitioned under conditions where humidity is within the range of 40% to 80%, and the temperature is within the range of 50 to 90° F. The sol-gel is electrospun into a silica fiber mat.

Embodiments of the invention may include one or more of the following in any of a variety of combinations. The sol may be transitioned for 2 to 7 days. During preparation and/or transitioning, the sol may not be exposed to heat over 150° F, over 100° F, over 90° F, or over 80° F. The sol may contain 75% to 85% by weight TEOS, 12% to 20% by weight ethanol, and about 2% to 5% by weight water. The sol may contain about 80% by weight TEOS, about 17% by weight ethanol, and about 3% by weight water. The acid catalyst may include, consist essentially of, or consist of HCl. The sol may contain less than about 0.1% of the acid catalyst by weight. The sol may contain from 0.02% to 0.08% of the acid catalyst by weight. The sol may contain less than about 1%, less than about 0.8%, less than about 0.5%, less than about 0.3%, or less than about 0.2% of the acid catalyst by weight. The sol may contain at least about 0.005%, at least about 0.01%, or at least 0.02% of the acid catalyst by weight.

The sol may not contain an organic polymer. The composition may include, consist essentially of, or consist of SiO₂. The sol may be allowed to transition for 2 to 4 days, e.g., about 3 days. The humidity may be about 50% to about 70%. The temperature may be about 60° F to about 80° F. The conditions may include an exhaust system (e.g., one or more fans) exhausting gases from the sol. The sol-gel may be electrospun when the weight is at from about 20% to about 40% of the starting weight of the sol. The sol-gel may be electrospun when the production of ethylene vapor is about

10% to about 20% relative to the peak production of ethylene vapors from the sol. The mat may have a thickness of at least about 1/8 inch, or at least about 1/4 inch. The mat may have a thickness of less than about 6 inches, less than about 5 inches, less than about 4 inches, less than about 3 inches, less than about 2 inches, or less than about 1 inch.

5 At least a portion of the silica fiber mat may be combined with a liquid or gelatinous composition. The liquid or gelatinous composition may include, consist essentially of, or consist of a paint, an epoxy, a urethane, and/or an adhesive. The at least a portion of the silica fiber mat may be processed into a plurality of fragments or a powder for combination with the liquid or gelatinous composition, whereby a modified
10 composition is formed. The modified composition may be applied as a coating to a solid object and/or a fabric. The modified composition may be molded into a solid object.

 In yet another aspect, embodiments of the invention feature a method for making and using a silica fiber composition. A sol is prepared. The sol includes, consists essentially of, or consists of tetraethyl orthosilicate (TEOS), ethanol, water, and an acid
15 catalyst. The sol may include, consist essentially of, or consist of 70% to 90% TEOS by weight, 8% to 25% ethanol by weight, 1% to 10% water by weight, and the acid catalyst. The sol is transitioned to a sol-gel for 2 to 7 days. The sol may be transitioned under conditions where humidity is within the range of 40% to 80%, and the temperature is within the range of 50 to 90° F. The sol-gel is electrospun into a silica fiber mat. At least
20 a portion of the silica fiber mat is applied to injured tissue of a subject, the subject being a human or veterinary patient.

 Embodiments of the invention may include one or more of the following in any of a variety of combinations. At least some of, or even substantially all of, the at least a portion of the silica fiber mat may not be removed from the issue during and/or after
25 healing of the injured tissue. At least a portion of the silica fiber mat may be processed into a powder or dust (e.g., a plurality of powder particles and/or fibrous fragments). The powder or dust may be mixed or suspended with a topical composition. The topical composition may be a lotion, ointment, paste, cream, foam, or gel. The topical composition may include one or more pharmaceutical and/or antimicrobial agents. The
30 topical composition may include an antibiotic, an antiseptic, an anti-inflammatory agent, and/or an immunosuppressant.

In another aspect, embodiments of the invention feature a method for making and using a silica fiber composition. A sol is prepared. The sol includes, consists essentially of, or consists of tetraethyl orthosilicate (TEOS), ethanol, water, and an acid catalyst. The sol may include, consist essentially of, or consist of 70% to 90% TEOS by weight, 5 8% to 25% ethanol by weight, 1% to 10% water by weight, and the acid catalyst. The sol is transitioned to a sol-gel for 2 to 7 days. The sol may be transitioned under conditions where humidity is within the range of 40% to 80%, and the temperature is within the range of 50 to 90° F. The sol-gel is electrospun into a silica fiber mat. At least a portion of the silica fiber mat may be combined with a liquid or gelatinous composition.

10 Embodiments of the invention may include one or more of the following in any of a variety of combinations. The liquid or gelatinous composition may include, consist essentially of, or consist of a paint, an epoxy, a urethane, and/or an adhesive. The at least a portion of the silica fiber mat may be processed into a plurality of fragments or a powder for combination with the liquid or gelatinous composition, whereby a modified 15 composition is formed. The modified composition may be applied as a coating to a solid object and/or a fabric. The modified composition may be molded into a solid object.

These and other objects, along with advantages and features of the present invention herein disclosed, will become more apparent through reference to the following description, the accompanying drawings, and the claims. Furthermore, it is to be 20 understood that the features of the various embodiments described herein are not mutually exclusive and may exist in various combinations and permutations. As used herein, the terms “approximately,” “about,” and “substantially” mean $\pm 10\%$, and in some embodiments, $\pm 5\%$. The term “consists essentially of” means excluding other materials that contribute to function, unless otherwise defined herein. Nonetheless, such other 25 materials may be present, collectively or individually, in trace amounts.

Other applications of the fiber composition in industry are described herein. Other aspects and embodiments are described in the following detailed description.

Brief Description of the Drawings

30 In the drawings, like reference characters generally refer to the same parts throughout the different views. Also, the drawings are not necessarily to scale, emphasis

instead generally being placed upon illustrating the principles of the invention. In the following description, various embodiments of the present invention are described with reference to the following drawings, in which:

FIGS. 1A-1D are scanning electron microscopy (SEM) images of fibers spun in accordance with this disclosure. Images in FIGS. 1A-1D are at, respectively, 50, 100, 200, and 500 micron scale. As shown, the fibers are flexible, smooth, dense, and continuous (not fractured).

FIGS. 2A-2D are SEM images of fibers that were electrospun at a non-optimal time (before the sol-gel was fully ripened). Images in FIGS. 2A-2D are at, respectively, 50, 100, 200, and 500 micron scale. As shown, the fibers appear rigid, with many fractures visible, and with formation of clumps.

FIG. 3 shows an SEM image (20 micron scale is shown) of fibers spun at a non-optimal time. The fibers are rigid, with fractures clearly evident.

FIG. 4 shows a fiber mat spun with a thickness of about 1/4 inch in accordance with the disclosure. The mat has a soft, flexible texture.

FIGS. 5A and 5B compare a silica fiber mat that was electrospun when the sol-gel was transitioned in accordance with this disclosure (FIG. 5A), with a fiber mat that was spun too early, before the sol-gel was optimally ripened (FIG. 5B). The material in FIG. 5A has a soft texture, is very flexible, and can be spun at a thickness that is easily handled for application of fiber layers to a wound. The material in FIG. 5B is brittle, inflexible, and layers of fiber cannot be easily separated for covering the surface area of a wound.

FIG. 6 shows application of a thin section of fiber to a burn wound.

FIG. 7A is picture of a burn before application of fibers. FIG. 7B shows the same wound after 4 days of treatment with the fiber scaffold. FIG. 7C shows the same wound after 8 days of treatment with the fiber scaffold. FIG. 7D shows the same wound after 12 days of treatment with the fiber scaffold.

FIG. 8A is a picture of a dog leg wound with fiber graft. FIG. 8B shows the wound after about 3 months of treatment.

FIG. 9A is a picture of a wound on a horse leg. The wound after treatment with fibers for about 4 days is shown in FIG. 9B. FIG. 9C shows the wound fully healed.

FIG. 10A is a photograph of a child with Epidermolysis Bullosa (EB), with a graft

of the fibers applied to a large open wound on the hand. FIG. 10B shows the same hand after healing.

FIGS. 11A and 11B show application of fibers to a burn wound.

FIGS. 11C and 11D show the wound of FIGS. 11A and 11B eight days after the
5 burn occurred. The wound has been replaced by healthy tissue, upon which hair is evident. No scarring or scar tissue is visible.

Detailed Description

The present invention in various aspects and embodiments provides methods for
10 making silica fiber mats useful for treatment of animal wounds and tissue, as well as other applications in industry. The methods comprise preparing a sol with a silicon alkoxide reagent, such as tetraethyl ortho silicate (TEOS), alcohol solvent, and an acid catalyst, and transitioning the sol for at least 2 days (and, in various embodiments, less than 7 days)
under conditions where humidity and temperature are controlled. The sol-gel is
15 electrospun to create a silica fiber mat with superior texture and properties.

The present invention provides compositions and methods for improving integrity of injured tissue in a subject, including for accelerating or improving healing of acute or chronic wounds. The compositions comprise a silica fiber matrix, which is applied to injured or inflamed tissue to support tissue regeneration, healing, and/or pain reduction.

20 In some embodiments, the composition is a lightweight structure composed of silica fiber (e.g., silicon dioxide nanofiber). The composition is formed from a gelatinous material that is electrospun to form a fiber mat (e.g., a non-woven mat). For example, the composition may be prepared by electrospinning a sol-gel, which can be prepared with a silicon alkoxide reagent, such as tetraethyl ortho silicate (TEOS), alcohol solvent, and an
25 acid catalyst.

Known processes do not yield a silica fiber composition with sufficient flexibility for many applications, including for wound care or health care applications. Instead, these structures are comparatively brittle, rigid, and compact; mats will easily fracture or break; fiber layers are difficult to separate; and generally lack the physical characteristics
30 to mimic collagen deposition in a wound. In various embodiments, to achieve a superior material for tissue repair, it is important to electrospin the sol-gel once it is appropriately

ripened (or “transitioned”), to achieve a composition with the desired physical characteristics. By transitioning the sol under controlled environmental conditions, and/or monitoring the preparation of the sol-gel during the ripening process, the relatively short window to successfully electrospin the sol-gel can be identified. In accordance with
5 embodiments of the invention, the composition is non-rigid and has a soft texture similar to that of cotton.

 In accordance with embodiments of the invention, the silica fiber composition, when applied to wounded tissue, acts as a non-biodegradable scaffold that supports tissue healing, regeneration, and/or integrity. The composition acts as a collagen biomimetic at
10 the site of tissue injury, providing an environment conducive for regeneration and growth of dermal cells. Without wishing to be bound by theory, the composition and methods described herein avoid the problem of temperature dysregulation as well as excess pain and inflammation at the wound site, allowing for the wound environment to normalize. Further, uncontrolled tissue degradation processes can destroy newly deposited collagen,
15 which is needed to support tissue regeneration. The composition of the invention provides a non-biodegradable cell scaffold that is not destroyed by proteases released at the wound site, but provides an optimal environment for population and growth of dermal cells. The fibers will not be removed from the wound, but will become an integral part of the new tissue.

20 The fibers may have a variable diameter, such as in the range of from about 50 nm to 5 μ m. In some embodiments, the fibers are predominately in the range of about 100 nm to about 2 μ m, or predominately in the range of about 200 to about 800 nm. The variable size of the fibers can be a better mimic for natural collagen, compared to, for example, scaffolding intended to have a more uniform structure. The different cell types involved
25 in tissue healing or regeneration require different size diameters of collagen. Without intending to be bound by theory, cells that migrate into the fibers have the ability to direct positioning of the fibers, as needed to support growth, adherence, or proliferation of the particular cell. Further, tissue requires a lot of surface area, which is provided by the fiber material. This is in contrast to many 3D printing and other synthetic scaffolding
30 alternatives that lack substantial surface area. Further still, biodegradable scaffoldings,

which have been conventionally preferred, typically degrade too quickly, before the tissue has the ability to grow and become self-sustainable.

For example, macrophages secrete a variety of cytokines and growth factors such as fibroblast growth factor (FGF), epidermal growth factor (EGF) and transforming
5 growth factor beta that can stimulate keratinocytes, fibroblasts, and other cells required for angiogenesis, collagen deposition, granulation tissue formation, wound contraction and epithelialization. Fibroblasts secrete the collagen framework that allows for dermal regeneration. However, macrophages as well as epithelial cells and fibroblasts also secrete extracellular enzymes (e.g., matrix metalloproteinases, MMPs) at the site of the
10 wound to degrade necrotic tissue and apoptotic cells. MMPs act on all components of the extracellular matrix and are responsible for removal of devitalized tissue, repair of lost or damaged tissue, and remodeling. MMPs are balanced by tissue inhibitors of metalloproteinases (TIMPs), which are released locally by cells to deactivate the MMPs. Uncontrolled activity of MMPs may result in degradation of newly formed tissue
15 (including collagen) or destruction of growth factors, which will interfere with wound healing. By providing the non-biodegradable scaffold, uncontrolled activity of MMPs will not interfere with population and growth of dermal cells.

In some embodiments, the sol-gel for preparing the silica fiber composition is prepared by a method that includes preparing a first mixture containing an alcohol solvent,
20 a silicon alkoxide reagent such as tetraethyl ortho silicate (TEOS); preparing a second mixture containing an alcohol solvent, water, and an acid catalyst; fully titrating the second mixture into the first mixture; and processing (ripening) the combined mixture under controlled environmental conditions to form a gel for electrospinning.

In some embodiments, the silicon alkoxide reagent is TEOS. Alternative silicon
25 alkoxide reagents include those with the formula $\text{Si}(\text{OR})_4$, where R is from 1 to 6, and preferably 1, 2, or 3.

In some embodiments, the alcohol solvent is an anhydrous denatured ethanol, or in some embodiments, methanol, propanol, butanol or any other suitable alcohol solvent. The first mixture can be agitated, for example, using a magnetic stirrer or similar agitation
30 means. The second mixture contains an alcohol solvent, water, and an acid catalyst. The alcohol solvent may be an anhydrous denatured alcohol, or may be methanol, propanol,

butanol or any other suitably provided alcohol solvent. Water may be distilled water or deionized water. Enough acid catalyst is added to the mixture to aid in the reaction. This acid catalyst may be hydrochloric acid, or may be sulfuric acid or other suitable acid catalyst. The second mixture may be agitated, for example, with a magnetic stirrer or other
5 agitation means. In some embodiments, the first mixture (or sol) and the second mixture (or sol) are created without the use of direct heat.

In some embodiments, the sol will contain about 70% to about 90% by weight silicon alkoxide (e.g., TEOS), about 5% to about 25% by weight alcohol solvent (e.g., anhydrous ethanol), an acid catalyst (e.g., at least about 0.001% and less than about 0.1%
10 by weight when using HCl) and the balance water.

In some embodiments, the sol contains 70% to 90% tetraethyl orthosilicate (TEOS) by weight, 8% to 25% ethanol by weight, 1% to 10% water by weight, and an acid catalyst. In some embodiments, the sol contains 75% to 85% by weight TEOS, 12% to 20% by weight ethanol, and about 2% to 5% by weight water. An exemplary sol contains about
15 80% by weight TEOS, about 17% by weight ethanol, and about 3% by weight water. In some embodiments, the acid catalyst is HCl. For example, the sol may contain less than about 0.1% HCl by weight. For example, the sol may contain from 0.02% to 0.08% HCl by weight. In various embodiments, the sol does not contain an organic polymer, or other substantial reagents, such that the fiber composition will be substantially pure SiO₂. In
20 various embodiments, the sol does not include inorganic salts (e.g., sodium chloride, lithium chloride, potassium chloride, magnesium chloride, calcium chloride, and/or barium chloride), nor are, in various embodiments, inorganic salts mixed with other components of the sol or into the sol itself. In various embodiments, the fiber composition (and the sol) does not include metals or metal oxides (e.g., TiO₂ or ZrO₂). In
25 various embodiments, the fiber composition consists essentially of SiO₂, i.e., contains only SiO₂ and unintentional impurities, and, in some embodiments, species and/or complexes resulting from the incomplete conversion of the sol to SiO₂ (e.g., water and/or chemical groups such as ethoxy groups, silanol groups, hydroxyl groups, etc.).

According to various embodiments, the first mixture and the second mixture are
30 combined by dripping or titrating the second mixture into the first mixture, preferably with agitation. The combined mixture is then further processed by allowing the sol to ripen in

a controlled environment until a substantial portion of the alcohol solvent has evaporated to create a sol-gel suitable for electrospinning.

In various embodiments, the sol is not exposed to heat over 150° F or heat over 100° F, so as to avoid accelerating the transition.

5 In exemplary embodiments of the invention, the controlled environment may include an enclosure with at least one vent and optionally an exhaust fan to draw gases away from the mixture. The enclosure may involve controlled conditions in terms of humidity, temperature, and optionally barometric pressure. For example, the humidity may be controlled (e.g., via use of conventional humidifiers and/or dehumidifiers) within
10 the range of about 30% to about 90%, such as from about 40% to about 80%, or in some embodiments, from about 50% to about 80%, or from about 50% to about 70% (e.g., about 55%, or about 60%, or about 65%). Some humidity can be helpful to slow evaporation of solvent, and thereby lengthen the window for successful electrospinning. In some
15 embodiments, the temperature is in the range of from about 50° F to about 90° F, such as from about 60° F to about 80° F, or from about 65° F to about 75° F. In some embodiments, barometric pressure is optionally controlled (e.g., using a low pressure vacuum source such as a pump or a fan). By controlling the environmental conditions during ripening, the gel can be electrospun during the time when spinning is optimal, which can occur in a small window of only several minutes if the ripening process is too
20 accelerated, such as with direct heat. When ripening the sol at a constant humidity of about 55% and temperature of about 72° F, the sol will ripen (gelatinize) in a few days, and the window for successful electrospinning can be expanded to at least several hours, and in some embodiments several days. In various embodiments, the ripening process takes at least 2 days, or at least 3 days in some embodiments. However, in various
25 embodiments the ripening does not take more than 10 days, or more than 7 days. In some embodiments, the ripening process takes from 2 to 7 days or from 2 to 5 days or from 2 to 4 days (e.g., about 2, about 3, or about 4 days). In various embodiments, the sol-gel is spinnable well before it transitions into a more solidified, non-flowable mass.

The enclosure space for ripening the sol-gel may include a vent on at least one
30 surface for exhausting gases from within the enclosure, and optionally the vent may include a fan for exhausting gases produced during the ripening process. The enclosure

space may optionally include a heating source for providing a nominal amount of heat within the enclosure space, to maintain a preferred temperature. In some embodiments, a source of humidity (e.g., an open container of water or other aqueous, water-based liquid) is provided within the enclosure environment to adjust the humidity to a desired range or value. The enclosure may further include one or more environmental monitors, such as a temperature reading device (e.g., a thermometer, thermocouple, or other temperature sensor) and/or a humidity reading device (e.g., a hygrometer or other humidity sensor).

In some embodiments, the sol-gel is electrospun after a ripening process of at least 2 days, or at least 36 hours, or at least 3 days, or at least 4 days, or at least 5 days at the controlled environmental conditions (but in various embodiments, not more than 10 days or not more than 7 days under the controlled environmental conditions). By slowing the ripening process, the ideal time to spin the fibers can be identified. The weight of the sol-gel can be used as an indicator of when the sol-gel is at or near the ideal time to electrospin. Without intending to be bound by theory, it is believed that the viscosity of the sol-gel is a poor determinant for identifying the optimal time for electrospinning. For example, in various embodiments, the sol-gel is from about 10% to about 60% of the original weight of the sol (based on loss of alcohol solvent during transitioning). In some embodiments, the sol-gel is from 15 to 50% of the original weight of the sol, or in the range of about 20 to about 40% of the original weight of the sol.

In some embodiments, the sol-gel is ripened for at least 2 days, or at least 36 hours, or at least 3 days, or at least 4 days, or at least 5 days, and is electrospun when the ethylene vapors produced by the composition are between about 10% and about 40% of the vapors produced by the starting sol, such as in the range of about 10% and about 25%, such as in the range of about 10 to about 20%. Ethylene is a colorless flammable gas with a faint sweet and musky odor (which is clearly evident as solvent evaporation slows). Ethylene is produced by the reaction of ethanol and acid. Ethylene can optionally be monitored in the vapors using a conventional ethylene monitor. In other embodiments, gases produced by the sol during the sol ripening process are monitored to determine the suitable or optimal time for electrospinning. Gas profiles can be monitored using gas chromatography.

The processing of the sol-gel mixture may require stirring or other agitation of the mixtures at various intervals or continuously due to the development of silicone dioxide crystalline material on the top surface of the mixtures. This development of crystalline material on the top surface slows the processing time and it is believed that the crystalline material seals off exposure of the mixture to the gaseous vacuum provided within the enclosure space. In some embodiments, any solid crystalline material is removed from the mixture.

Upon completion of the sol-gel process, the sol-gel is then electrospun using any known technique. The sol or sol-gel may be preserved (e.g., frozen or refrigerated) if needed (and such time generally will not apply to the time for ripening). An exemplary process for electrospinning the sol-gel is described in Choi, Sung-Seen, et al., Silica nanofibers from electrospinning/sol-gel process, *Journal of Materials Science Letters* 22, 2003, 891-893, which is hereby incorporated by reference in its entirety. Exemplary processes for electrospinning are further disclosed in U.S. Patent No. 8,088,965, which is hereby incorporated by reference in its entirety.

In an exemplary electrospinning technique, the sol-gel is placed into one or more syringe pumps that are fluidly coupled to one or more spinnerets. The spinnerets are connected to a high-voltage (e.g., 5 kV to 50 kV) source and are external to and face toward a grounded collector drum. The drum rotates during spinning, typically along an axis of rotation approximately perpendicular to the spinning direction extending from the spinnerets to the drum. As the sol-gel is supplied to the spinnerets from the syringe pumps (or other holding tank), the high voltage between the spinnerets and the drum forms charged liquid jets that are deposited on the drum as small entangled fibers. As the drum rotates and electrospinning continues, a fibrous mat of silica fibers is formed around the circumference of the drum. In various embodiments, the spinnerets and syringe pump(s) may be disposed on a movable platform that is movable parallel to the length of the drum. In this manner, the length along the drum of the resulting fiber mat may be increased without increasing the number of spinnerets. The diameter of the drum may also be increased to increase the areal size of the electrospun mat. The thickness of the mat may be largely dependent upon the amount of sol-gel used for spinning and thus the amount of electrospinning time. For example, the mat may have a thickness of greater

than about 1/8 inch, or greater than about 1/4 inch, or greater than about 1/3 inch, or greater than about 1/2 inch.

Silica fiber mats and compositions produced in accordance with embodiments of the present invention exhibit one or more beneficial properties when compared to fiber compositions spun at non-optimal times (e.g., with inadequate ripening of the sol-gel). For example, fiber mats and compositions in accordance with embodiments of the invention do not burn, char, or visibly degrade upon direct application of heat or open flame. In contrast, various fiber compositions spun at non-optimal times will exhibit charring and/or visible color change when exposed to sufficient heat or open flame. Moreover, fiber mats and compositions in accordance with embodiments of the invention effectively wick moisture (e.g., water or bodily fluids), absorbing such fluid into the fiber mat. In contrast, various fiber compositions spun at non-optimal times will not visibly absorb or wick moisture even when directly applied thereto; such compositions tend to be hydrophobic. Finally, fiber mats and compositions in accordance with embodiments of the invention are fluffy and may be easily shaped to uneven, non-uniform, and/or non-planar (e.g., curved) surfaces or shapes without fracturing or loss of structural integrity; thus, such compositions may be readily applied to or conformed to a variety of different surfaces. In contrast, various fiber compositions spun at non-optimal times tend to be flat, plate-like, brittle, and will at least partially fracture if excessively mechanically shaped or bent.

Fiber layers can be easily separated from the mat for, e.g., application to wounds or to damaged or inflamed tissue. In some embodiments, the composition is electrospun with a thickness of from about 1/8 inch to about 1/2 inch. For example, the composition may be electrospun with a thickness of greater than about 1/8 inch, or greater than about 1/4 inch thick, or about 1/4 thick in some embodiments.

In some embodiments, the fiber composition is applied to the tissue or wound as a thin layer of fibers, e.g., just enough to cover the wound surface. Often, the wound will quickly absorb the fibers. The process is repeated once fibers are no longer visible on the wound. For example, in some embodiments, fibers are reapplied 2 to 5 times per day. In some embodiments, the fiber composition is processed into a fine powder or dust, and the powder or dust is applied to the tissue. For example, a sheet of silica fibers can be rubbed

through one or more screens, and a range of powder sizes obtainable by varying mesh size. In some embodiments, the powder or dust is mixed with a topical composition, such as a lotion, ointment, paste, cream, foam, or gel. In these embodiments, the topical composition may comprise one or more pharmaceutical or antimicrobial agents, such as
5 an antibiotic, an antiseptic, an anti-inflammatory agent, or immunosuppressant.

In various embodiments, after completion of the electrospinning process and removal of the mat from the drum, the mat (or a portion thereof) may then be divided into small fibrous fragments that may be incorporated into a topical composition or other composition. The resulting fibrous fragments are each intertwined collections of silica
10 fibers, rather than unitary solid particles. In some embodiments, the electrospun mat may be fractured, cut, ground, milled, or otherwise divided into small fragments that maintain a fibrous structure. In some embodiments, the mat (or one or more portions thereof) is rubbed through one or more screens or sieves, and the mesh size of the screen determines, at least in part, the size of the resulting fibrous fragments produced from the electrospun
15 mat. For example, the mat or mat portions may be rubbed through a succession of two or more screens having decreasing mesh sizes (e.g., screens having mesh numbers of 100, 200, 300, or even 400), in order to produce a collection of fibrous fragments having the desired sizes.

As used herein, the term “fibrous fragments” (or “fibrous-mat fragments,” or
20 simply “fragments”) refers to small dust-like particles, parts, or flakes of a fibrous mat having an average dimension larger (e.g., 5×, 10×, or even 100×) than the width of at least some of the fibers of the mat. In various embodiments, the average size of a fibrous fragment is in the range of approximately 20 μm to approximately 200 μm along the longest axis. Fibrous fragments may thus resemble microscopic-scale versions of the
25 electrospun mat itself, e.g., intertwined collections of silica fibers, and thus typically are porous. Thus, fibrous fragments may be contrasted with other types of micro-scale particles, such as the substantially spherical particles used in colloidal silica, which are each unitary, individual units or grains, rather than small collections of fibers.

Application of the composition during the healing process can provide for
30 accelerated healing, of both acute and chronic wounds, and can prevent or reduce tissue scarring. When the topical composition is applied to the skin that has a blemish like acne,

cracks in skin, small scrapes etc., the scaffolding is left behind in the small wound for cells to grow into. This speeds up the healing process and helps to reduce scarring. In some embodiments, the composition in lotion form is applied to the cracked skin (e.g., on the face or hands) to improve tolerance of the skin to the environment, such as sun, wind, and cold, thereby reducing the impact of age and environment on the appearance and/or function of the skin.

In some embodiments, the subject is a mammal. Subjects include veterinary patients such as a dog, cat, or horse, among others. In some embodiments, the patient is a human patient. The tissue can be of any organ, but in some embodiments comprises skin, muscle, or bone. In some embodiments, the composition is applied to a skin lesion, ulcer, wound, burn, cut, scrape, or blister.

In some embodiments, particularly for chronic or difficult to heal wounds, the fiber scaffold normalizes the wound environment, including temperature dysregulation, may reduce pain and inflammation at the wound site, and/or provides a scaffold for dermal cells to multiply and grow into (e.g., without full, natural deposition of collagen).

In some embodiments, the wound is a burn, scrape, or cut, or a minor wound that does not go deeper than the base lamina. In such embodiments, treatment with the fiber scaffold for 1 to 7 days, e.g., from 3 to 5 days (about 4 days) is sufficient for substantially complete healing. In such embodiments, fibers are applied once to four times daily to cover the wound. Fibers are generally reapplied when fibers are no longer visible in the wound.

In some embodiments, the wound includes damage including or past the base lamina. Such wounds may require treatment for several weeks (e.g., from 2 to 8 weeks), or in some embodiments, several months (e.g., from 1 to 4 months) for very severe wounds. In some embodiments, the wound is a diabetic ulcer, chronic pressure sore, gangrenous wound, or amputation wound. For difficult or hard to treat wounds, such as gangrenous wounds or wounds with substantial necrotic tissue (e.g., necrotizing fasciitis), the fiber compositions may mimic the healing process, and induce gene expression and/or environment conducive to healing. Further, application of the fibers will bypass the need for deposition of natural collagen during the uncontrolled inflammatory state. Further, bacteria at the wound site cannot easily penetrate the fiber to get to the wound. In these

embodiments, fibers are applied once to four times daily to cover the wound. Fibers are generally reapplied when fibers are no longer visible in the wound. A wound cover can be employed where necessary, as long as air and oxygen is not restricted from the wound.

5 In some embodiments, because the fiber material substantially reduces pain from the wound site, the patient may be able to forgo therapy with a pain medication such as an opioid.

In some embodiments, the fibers may be applied to a rash or other manifestation of skin inflammation (e.g., shingles, or an autoimmune rash or lesion, or allergic rash), resulting in reduction in pain and/or inflammation. In some embodiments, the fibers are applied with a gel or cream or other topical composition to mediate adherence of fibers to substantially intact skin.

10 In some embodiments, the subject has a genetic blistering disease, such as epidermolysis bullosa (EB), which is a group of mainly inherited connective tissue diseases that cause blisters in the skin and mucosal membranes. It is a result of a defect in anchoring between the epidermis and dermis, resulting in friction and skin fragility. EB often involves formation of blisters following trivial trauma.

In some embodiments, the subject has EB simplex, which results in blisters at the site of rubbing, and typically affects the hands and feet. In some embodiments, the subject has Junctional epidermolysis bullosa, which affects laminin and collagen.

20 Junctional epidermolysis bullosa also presents with blisters at the site of friction, especially on the hands and feet. Dystrophic epidermolysis bullosa is an inherited variant affecting the skin and other organs, and involves skin that is very fragile. Dystrophic EB is caused by genetic defects (or mutations) within the gene encoding the protein type VII collagen (collagen VII).

25 The human skin consists of two layers: an outermost layer called the epidermis and a layer underneath called the dermis. In individuals with healthy skin, there are protein anchors between these two layers that prevent them from moving independently from one another (shearing). In people born with EB, the two skin layers lack the protein anchors that hold them together, resulting in extremely fragile skin. Even minor mechanical friction (like rubbing or pressure) or trauma will separate the layers of the skin

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and form blisters and painful sores. Sufferers of EB have compared the sores with third-degree burns.

In some embodiments, when the fiber composition is applied to EB blisters, sores, wounds, or lesions, the composition will become integrated with the healing tissue
5 including the base lamina in some embodiments, and help anchor the skin. Thus, over time, the skin exhibits improved integrity as sores and blisters are treated. Further, the reduction in pain can be important for these patients to perform daily activities, such as bathing or traveling.

The thickness of fiber that is applied to the wound depends on the depth of the
10 wound, but generally just enough fibers are applied to cover the wound. The composition may be reapplied after fibers are no longer visible at the wound site. The composition may also be freshly reapplied after bathing. It is believed, without wishing to be bound by theory, that the fibers become integrated with the regenerated tissue at the wound site.

While the wound in some embodiments is not covered with any other wound
15 dressing, in some embodiments other wound dressings can be employed. For example, in some embodiments the wound is not covered (other than the fiber composition), allowing exposure of air and therefore sufficient availability of oxygen. However, for more severe wounds a dressing may be needed. Preferably, the dressing is a light covering that will not limit oxygen to the site. Generally, the fibers will not be removed. Since they are not
20 biodegradable, they will become part of the new tissue. For shallow wounds, the scaffold is likely shed along with the skin tissue that integrates with it.

In some embodiments, the wound is a skin cancer lesion, such as a melanoma or squamous cell carcinoma (SCC) or basal cell carcinoma (BCC) lesion or ulcer. By application of the fibers to the lesion, the outgrowth of malignant cells (including cancer
25 stem cells) is prevented or reduced, while normal cells are able to grow in the fiber network. Without wishing to be bound by theory, it is believed that the cancer cell phenotype is less able to populate the fiber matrix than normal cells. Further, cancers may rely on their ability to degrade collagen to grow, such that cancer cells are restricted from growing by their inability to degrade the fiber scaffold.

30 In other applications, fiber compositions in accordance with embodiments of the present invention may be added to various other compositions to improve one or more

mechanical and/or thermal properties thereof, as detailed in U.S. Provisional Patent No. 62/643,946 filed March 16, 2018, the entire disclosure of which is incorporated by reference herein. Specifically, entire silica fiber mats, or sections thereof may be utilized. In other embodiments, a silica fiber mat or portion thereof may be broken into a plurality of fragments (e.g., fibrous fragments), or even into a powder, for use as a beneficial additive with a (typically liquid or gelatinous) composition in order to impart advantageous thermal and/or mechanical properties thereto. For example, the fiber composition may be incorporated within paints or other coatings (e.g., adhesives, epoxies, etc.) in order to increase the thermal resistance per unit area (i.e., the “R-value”) of the composition once it is applied. In other embodiments, the fiber composition (e.g., in the form of a mat, mat portion, fibrous fragments, and/or powder) is added to structural compositions, such as epoxies or urethanes, in order to increase the mechanical strength and/or impact resistance of the material once it is formed (e.g., molded) into a solid object. The fiber composition may also be mixed into a liquid, which may subsequently be applied to articles such as fabrics to impart beneficial characteristics thereto. The liquid composition in such embodiments may dry onto the article and become a portion thereof or a layer thereon. For example, silica fiber-containing compositions may be applied to clothing to impart fire resistance or impact resistance thereto in the manner of a fire-resistant suit or an armored or bullet-proof vest.

Embodiments of the invention will now be described with respect to the following examples.

Examples

Example 1: Preparation of silica fiber composition

SiO₂ fibers were prepared using an electrical spinning process, where a sol-gel is spun onto a roller system creating a sheet. The sol-gel is made in two parts. First, TEOS is mixed with ethanol, and then a second mixture containing HCl, water, and ethanol is titrated into the mixture. The sol-gel is then allowed to ripen for a few days under controlled conditions before spinning.

In one example, the first sol was made by weighing out 384 grams of (TEOS) tetraethyl orthosilicate 98% and 41.8 grams of anhydrous denatured ethanol, and pouring

together. The first sol was allowed to let stand in a beaker and a magnetic stirrer was used to create a homogenous solution. The second sol was made by weighing 41.8 grams of anhydrous denatured ethanol, 16.4 grams of distilled water, and 0.34 grams of hydrochloric acid, which was then poured together and mixed for 8 seconds with a
5 magnetic stirrer until a homogenous second sol was formed.

The second sol was then poured into the titration device, which was placed above a beaker containing the first sol. The titration device then dripped about 5 drops per second until a third sol was formed mixing the first sol and the second sol. During the dripping process, the first sol continues to be mixed with a magnetic stirrer while the
10 second sol is dripped into the first sol.

The combined third sol was then placed into an enclosure box. A low pressure vacuum is provided by a fan on medium speed to remove fumes. In the experiment, the air temperature within the box was 72° F with 60% humidity. In the experiment, the third sol was allowed to sit and process for about three (3) days. By ripening the sol-gel slowly
15 over several days, the sol-gel will transition slowly such that the ideal time to electrospin can be identified.

The mixtures were agitated daily to reduce the build-up of crystalline structures. The third sol begins to transition to sol-gel with evaporation of the alcohol solvent. Sol-gel may be monitored to determine an approximate amount of C₂H₄ (ethylene) in the
20 vapors, which can be in the range of about 10-20% relative to the original sol before ripening. Upon proper gelatinization, the sol-gel is loaded into the electrospinning machine or is frozen to preserve for electrospinning. Proper gelatinization occurs when the total mass of the sol-gel was between about 100 grams and about 180 grams.

The above example can be scaled appropriately to produce desirable structures. To
25 further identify the ideal time to electrospin, portions of the gel can be dripped into the electric field to evaluate the properties of the resulting fibers.

FIGS. 1A-1D are scanning electron microscopy (SEM) images of fibers spun in accordance with this disclosure (50, 100, 200, and 500 micron scales shown). As shown, the fibers are flexible, smooth, dense, and continuous (not fractured). Material with these
30 properties is ideal for treating wounds and animal tissues (e.g., as a collagen mimetic).

FIGS. 2A-2D are SEM images of fibers that were electrospun at a non-optimal time (before the sol-gel was fully ripened) (50, 100, 200, and 500 micron scale shown). The fibers appear rigid, with many fractures visible, and with formation of clumps. FIG. 3 shows an SEM image (20 micron scale is shown) of fibers from a similar material, where the fibers are clearly rigid with many fractures clearly evident.

FIG. 4 shows a fiber mat spun in accordance with the disclosure. The flexibility and continuity of the fibers allows mats to be spun at a thickness of 1/4 inch or more. The mat has a soft, flexible texture, and allows for layers of fibers to be easily separated for covering a wound bed. FIGS. 5A and 5B compare a silica fiber mat that was electrospun when the sol-gel was ripened in accordance with this disclosure (FIG. 5A) to a fiber mat that was spun too early, before the sol-gel was optimally ripened (FIG. 5B). The material in FIG. 5A has a soft texture, is very flexible, and can be spun at a thickness that is easily handled for application of fiber layers to a wound. The material in FIG. 5B is brittle, inflexible, thin, and layers of fiber cannot be easily separated for covering the surface area of a wound.

Example 2: Treatment of Burns

Fibers were applied to first and second degree burns to the face of an adult male. The amount applied was just enough to cover the wound sites, with the thickness of the fibers based on the depth of the wound. After initial application of the fibers, additional fibers were added once fibers were no longer visible. After 4 days burns were barely visible.

Fibers were applied to second degree burns to the arm of an adult male. Application of thin sections of material to the burn wound is shown in FIG. 6.

Fibers were applied to 2nd degree burns on the feet of an adult woman, with substantial healing shown in a four-day period. After initial application of the fibers, additional fibers were added once fibers were no longer visible. Fibers were also reapplied after bathing. A picture of the burns pretreatment and pictures taken in 4-day intervals (during treatment) are shown in FIGS. 7A, 7B, 7C, and 7D.

Example 3: Treatment of Amputation Wound

The fiber scaffolding was applied to a gangrenous wound site where the toe had been amputated. The wound was a diabetic wound, which are extremely hard to heal, and difficult to stop the necrotic processes.

5 The wound healed in about 5 to 6 weeks with application of the fiber matrix. Prior to treatment, the foot was at risk of needing amputation. However, after treatment with the fibers, the foot was ultimately saved.

Example 4: Treatment of Animal Wounds

10 The fiber scaffolding was applied to a deep wound on a dog's leg, which was recommended for amputation. After treatment for 2-3 weeks, the wound was fully healed, and a full covering of fur developed over the wound within 3 months. Pictures of the wound with fiber graft are shown (FIG. 8A), and again after about 3 months of treatment (FIG. 8B).

15 The fiber scaffolding was applied to a deep wound on a horse's leg, which was ripped open by a fence. The wound was causing the horse to limp badly. Wounds on horses are very hard to heal, especially wounds on their legs. The fibers were applied at night while the horse was in the barn (FIG. 9A). The next morning the horse was trotting limp-free, suggesting that the horse no longer had the same pain sensations from the wound site. The same wound is shown after 4 days of treatment in FIG. 9B. That wound
20 is now fully healed (FIG. 9C).

Example 5: Treatment of pressure sores

A paraplegic adult male with a severe bed sore on his lower back was treated with the fibers. The wound was a chronic wound that existed for at least 17 months. When a
25 paralyzed person has a wound, instead of feeling pain, they tend to sweat profusely. When the fibers were added to the wound, the subject stopped sweating. After treatment for several months the wound is nearly healed.

Example 6: Treatment of Epidermolysis Bullosa (EB) wounds

30 A child with Epidermolysis Bullosa (EB) was treated by applying the fibers to open sores and blisters. Application of the fibers allowed the child to take a bath without pain,

eliminating the need for pain drugs during bath time. Application of the fibers to a severe open wound on the child's hand is shown in FIG. 10A. The same hand after healing is shown in FIG. 10B. When a rub test (to induce a blister) is conducted on the healed site with the fibers, the skin does not blister.

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Example 7: Treatment of Burns

Fibers were applied to second degree burns to the arm of an adult male. FIGS. 11A and 11B show the fibers applied to the wound a few days after commencement of treatment. The pain due to the burn subsided considerably within one day of the initial
10 treatment. FIGS. 11C and 11D show the healed wound eight days after the burn occurred. Healthy skin is evident across the entire wound site. New hair growth from the skin is also evident, and no evidence of scarring or scar tissue is present.

The terms and expressions employed herein are used as terms and expressions of
15 description and not of limitation, and there is no intention, in the use of such terms and expressions, of excluding any equivalents of the features shown and described or portions thereof. In addition, having described certain embodiments of the invention, it will be apparent to those of ordinary skill in the art that other embodiments incorporating the concepts disclosed herein may be used without departing from the spirit and scope of the
20 invention. Accordingly, the described embodiments are to be considered in all respects as only illustrative and not restrictive.

CLAIMS

1. A method for making a silica fiber composition, comprising:
preparing a sol that contains 70% to 90% tetraethyl orthosilicate (TEOS) by weight, 8% to 25% ethanol by weight, an acid catalyst, and the balance water;
transitioning the sol to a sol-gel for 2 to 7 days under conditions where humidity is within the range of 40% to 80%, and the temperature is within the range of 50 to 90° F; and
electrospinning the sol-gel into a silica fiber mat.
2. The method of claim 1, wherein the sol is not exposed to heat over 150° F.
3. The method of claim 2, wherein the sol is not exposed to heat over 100° F.
4. The method of claim 1, wherein the sol contains 75% to 85% by weight TEOS, 15% to 20% by weight ethanol, and 2% to 5% by weight water.
5. The method of claim 1, wherein the sol contains 70% to 90% by weight TEOS, 8% to 25% by weight ethanol, and 1% to 10% by weight water.
6. The method of claim 1, wherein the acid catalyst is HCl.
7. The method of claim 1, wherein the sol contains less than about 0.1% by weight of the acid catalyst.
8. The method of claim 7, wherein the sol contains from 0.02% to 0.08% by weight of the acid catalyst.
9. The method of claim 1, wherein the sol does not contain an organic polymer.
10. The method of claim 1, where the composition consists essentially of SiO₂.

11. The method of claim 1, wherein the sol is allowed to transition for 2 to 4 days.
12. The method of claim 11, wherein the sol is allowed to transition for about 3 days.
13. The method of claim 1, wherein the humidity is 50 to 70%.
14. The method of claim 13, wherein the temperature is 60 to 80° F.
15. The method of claim 1, wherein the conditions further comprise a fan exhausting gases from the sol.
16. The method of claim 1, wherein the sol-gel is electrospun when the weight is at from 20% to 40% of the starting weight of the sol.
17. The method of claim 1, wherein the sol-gel is electrospun when the production of ethylene vapor is 10% to 20% relative to the peak production of ethylene vapors from the sol.
18. The method of claim 1, wherein the mat has a thickness of at least about 1/8 inch.
19. The method of claim 18, wherein the mat has a thickness of at least about 1/4 inch.
20. The method of claim 1, further comprising combining at least a portion of the silica fiber mat with a liquid or gelatinous composition.
21. The method of claim 20, wherein the liquid or gelatinous composition comprises a paint, an epoxy, a urethane, or an adhesive.

22. The method of claim 20, wherein the at least a portion of the silica fiber mat is processed into a plurality of fragments or a powder for combination with the liquid or gelatinous composition, whereby a modified composition is formed.
23. The method of claim 22, further comprising applying the modified composition as a coating to a solid object or a fabric.
24. The method of claim 22, further comprising molding the modified composition into a solid object.
25. A silica fiber mat composition, comprising silica fibers prepared by electrospinning a sol-gel prepared with tetraethyl orthosilicate (TEOS), an alcohol solvent, and acid catalyst, the sol-gel having been allowed to transition for at least 2 days under conditions where humidity is within the range of about 40% to about 80%, and the temperature is within the range of 50° F to 90° F.
26. The composition of claim 25, wherein the sol-gel is electrospun when the weight is at from 20% to 40% of the starting weight before transitioning.
27. The composition of claim 25, wherein the sol-gel is electrospun when the production of ethylene vapor therefrom is 10% to 40% relative to the sol-gel before transitioning.
28. The composition of claim 25, wherein the fibers have a diameter of from about 50 nm to about 5 μ m.
29. The composition of claim 25, wherein the fibers have a variable diameter of from about 200 nm to about 1000 nm.
30. The composition of claim 25, wherein the composition consists essentially of SiO₂.

31. The composition of claim 25, wherein the sol-gel is prepared with 70% to 90% TEOS by weight, 8% to 25% ethanol by weight, an acid catalyst, and the balance water.
32. The composition of claim 25, further comprising a topical carrier.
33. The composition of claim 32, wherein the topical carrier is a lotion, ointment, paste, cream, foam, or gel.
34. The composition of claim 32, wherein the topical carrier further comprises one or more pharmaceutical or antimicrobial agents.
35. The composition of claim 32, wherein the topical carrier comprises an antibiotic or antiseptic.
36. The composition of claim 32, wherein the topical carrier comprises an anti-inflammatory agent or immunosuppressant