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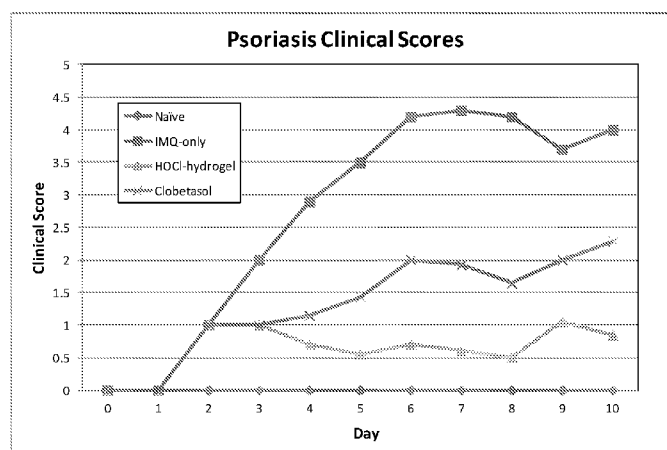
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Malvern, PA 19355 (US).(72) Inventors: **SAMPSON, Mark**; c/o Puricore, Inc., 508
Lapp Road, Malvern, PA 19355 (US). **PANICHEVA,**
Svetlana; c/o Puricore, Inc., 508 Lapp Road, Malvern, PA
19355 (US). **SCHOCKEMOEHL, Cary**; c/o Puricore,
Inc., 508 Lapp Road, Malvern, PA 19355 (US). **SO-**
LOMON, Ethan; 15 Bromley Court, Wilmington, DE
19810 (US).(74) Agents: **HAYMAN, Mark, L.** et al.; Morgan, Lewis &
Bockius LLP, 1111 Pennsylvania Avenue, NW, Washing-
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(54) Title: METHODS AND COMPOSITIONS FOR TREATING INFLAMMATORY AND IMMUNOLOGICAL DISORDERS

FIGURE 2



(57) Abstract: The present invention provides a method for treating, preventing, or managing local inflammatory symptoms, including symptoms associated with acute or chronic inflammation, and particularly for conditions that are characterized by an underlying immunological disease or condition. The invention further provides methods for controlling inflammatory processes relating to cancer and the microbial flora.

METHODS AND COMPOSITIONS FOR TREATING INFLAMMATORY AND IMMUNOLOGICAL DISORDERS

PRIORITY

5 This application claims the benefit of priority of U.S. Patent Application No. 14/670,641, filed March 27, 2015, which is hereby incorporated by reference in its entirety.

FIELD OF THE INVENTION

10 The present invention relates to compositions and methods for treating, preventing, or managing inflammatory conditions.

BACKGROUND OF THE INVENTION

15 Inflammation is part of the complex biological response of body tissues to harmful stimuli, such as pathogens, damaged cells, or irritants. Inflammation is a protective response that involves immune cells, blood vessels, and molecular mediators. The purpose of inflammation is to eliminate the initial cause of cell injury, clear out necrotic cells and tissues damaged from the original insult and the inflammatory process, and to initiate tissue repair. Chronic inflammation can lead to
20 a host of diseases, such as periodontitis, atherosclerosis, rheumatoid arthritis, dermatitis, and cancer. Inflammation is normally closely regulated by the body.

 Inflammation can be classified as either acute or chronic. Acute inflammation is the initial response of the body to harmful stimuli and is achieved by the increased movement of plasma and leukocytes from the blood into the injured
25 tissues. A series of biochemical events propagates and matures the inflammatory response, involving the local vascular system, the immune system, and various cells within the injured tissue. Prolonged or chronic inflammation leads to a progressive shift in the type of cells present at the site of inflammation, such as mononuclear cells, and is characterized by simultaneous destruction and healing of the tissue from
30 the inflammatory process.

Inflammation can be initiated by either pathogen-associated molecular patterns (or PAMPs) or damage (or danger)-associated molecular patterns (DAMPs). PAMPs are molecules associated with pathogens that are recognized by cells of the innate immune system. These molecules are recognized by Toll-like receptors (TLRs) and other pattern recognition receptors (PRRs), and activate innate immune responses to protect the host from infection. DAMPs are molecules that can initiate and perpetuate a noninfectious inflammatory response, and are often cytosolic or nuclear components that are released from the cell, for example upon cell necrosis. Innate immune responses activated by PAMPs and DAMPs include inflammatory processes/cascades such as the inflammasome, and itch and pain mediators and their respective receptors, prurireceptors and nociceptors in the skin nerve terminal. Mediators of the inflammatory cascade include various cytokines such as, α -2 macroglobulins, TNF- α , IL-2, IL-6, IL-1 β , IL-8, TSLP, IL-4, IL-13, IL-17, IL-18, IL-31, among others. When regulated and localized, these cytokines can mediate beneficial inflammatory responses as part of normal host defense response. However, when cytokine activations become disordered, these inflammatory responses can cause significant tissue injury or even death. Inflammatory symptoms, regardless of origin, share similar symptoms such as pain, heat, redness, fever, rash or swelling, and lesions, including wounds and ulcers to the skin or other tissues. Pain is often a key indicator of inflammation, because the swelling of the affected area/organ is pushing against sensitive nerve endings which then send pain and/or itch signals to the brain.

Inflammatory symptoms are often treated with topical or systemic anti-inflammatory agents, such as corticosteroids; however use of conventional agents has significant limitations including age restrictions, drug toxicity, irritation, hypersensitivity and/or other side effects that may occur or develop especially with chronic use. In addition, many treatments to control local symptoms (*e.g.*, by reducing discomfort and/or tissue damage at the affected region) provide no appreciable systemic benefits. Therefore, if there is an underlying immunological disorder that is causing the inflammatory symptoms, topical agents often do very little to improve the patient's overall condition.

It is an object of this invention to treat or manage inflammatory and/or immunological conditions, by providing relief of inflammatory symptoms, while positively affecting the underlying condition. It is also an object of the invention to provide a broadly effective and safe treatment for the prevention of diseases and conditions associated with or caused by prolonged or untreated inflammation, including cancer. It is further an object of this invention to provide compositions and methods that are safe and effective for prolonged and/or prophylactic use, by patients of all ages including pediatric and geriatric patients, and/or immunocompromised patients, for the prevention, reduction, and management of inflammation.

SUMMARY OF THE INVENTION

The present invention relates to hypochlorous acid compositions and their use for treating inflammatory or immunological conditions.

In one aspect, the present invention provides a method for treating, preventing, or managing local inflammatory symptoms, including symptoms associated with acute or chronic inflammation, and particularly for conditions that are characterized by an underlying immunological disease or condition. The invention allows for reduction, management, or prevention of local inflammatory symptoms and/or tissue damage, while providing systemic benefits that ameliorate the underlying immunological condition.

In another aspect, the invention provides for a method of treating cancer, or slowing or inhibiting the progression of cancer. Specifically, cancer relies on the inflammatory machinery to progress and to metastasize. By modulating these inflammatory processes, the invention helps to control the progression and spread of cancer, and aids the bodies repair mechanisms, particularly where the patient undergoes a primary cancer therapy that is harmful to non-cancer cells and tissues, such as chemotherapy or radiation therapy.

In another aspect, the invention provides methods for controlling or normalizing the microbiome of a patient, and particularly the microbiome of a tissue exhibiting acute or chronic inflammation. Even in the absence of overt infection,

there is a complex interplay between the microbiome and tissue inflammation. Simultaneous reduction of microbial burden and normalization of the tissue microbiome, together with a reduction of host inflammation, promotes tissue healing and normalization. Further, in some embodiments, microbial flora at remote sites
5 from administration of the hypochlorous acid are positively impacted by the treatment.

In various embodiments the method comprises administering a hypochlorous acid composition, wherein the hypochlorous acid composition has from about 100 ppm to about 5000 ppm of available free chlorine (AFC). In some embodiments, the
10 available free chlorine is at least about 70% hypochlorous acid relative to the total concentration of hypochlorous acid, hypochlorite, and Cl_2 (molecular chlorine). As disclosed herein, hypochlorous acid can exhibit anti-inflammatory properties that are dose-dependent, and can affect both local and systemic inflammatory mediators in some embodiments. The invention in various embodiments inhibits and reduces
15 inflammatory symptoms, and prevents “flare-ups” of an underlying chronic inflammatory or immunological condition. The invention in various embodiments can be used to prevent diseases or conditions caused by prolonged and/or untreated inflammation, including cancer.

In various embodiments, the invention provides for administering the
20 hypochlorous acid composition via enteral (oral, gastric and rectal), parenteral (intravenous, intra-arterial, intraosseous, intra-muscular, intrathecal, sub-cutaneous) or other route (sublingually, buccally, rectally, vaginally, intra-articular, by the ocular or otic route, nasally, cutaneously for topical or systemic effect, by inhalation or nebulization, or transdermally) or as an irrigant to one or more tissues or organs
25 (e.g., during surgery or after trauma). The application site of the hypochlorous acid composition can be exhibiting signs of local inflammation (an “affected region”), and in some embodiments, the benefits are (also) intended for remote sites, such as internal organs, vasculature, CNS, or the musculoskeletal system. For example, in various embodiments, the affected region or the region of administration is one or
30 more of the eyes, ears, nose, sinus, throat, mouth (e.g., gingiva), or skin. In other embodiments, the affected region or remote tissue or organ is one or more of the intestinal tract and/or colon, lungs, urogenital system (urinary tract or vagina),

skeletal muscle, ligaments, tendons, joints, bones, peritoneum, kidney, liver, pancreas, or vasculature. In some embodiments, the hypochlorous acid is administered topically (e.g., to the skin), with benefits exhibited systemically.

In some embodiments, the composition is used to treat local inflammatory symptoms, including but not limited to conjunctivitis, dry eye, ocular itch, sinusitis, airway hyper responsiveness, sores, ulcers, blisters and/or skin rash or lesions. In some embodiments, the method provides for systemic benefits to ameliorate an underlying immune condition, such as an autoimmune condition, genetic immune malady, or hyper allergic condition. Such conditions include, without limitation, systemic lupus erythematosus, psoriasis, atopic dermatitis, rheumatoid arthritis, celiac disease, Crohn's disease, ulcerative colitis, vasculitis, thyroiditis, severe asthma, severe allergy, diabetes mellitus, hyper immunoglobulin E syndrome, dermatomyositis, multiple sclerosis, Parkinson Disease, fibromyalgia, among others.

The invention provides a broadly effective method for treating the inflamed and/or affected regions of a patient, and in a manner relatively independent of the etiology of the inflammation, and in a manner that avoids toxicity, hypersensitivity, and other side effects of conventional agents. The methods of the invention are useful as alternatives or adjunct therapies to conventional antibiotics, antivirals, decongestants, antihistamines, immunosuppressants/immunomodulators, analgesics/anesthetics and steroid treatments, or as an alternative to therapy using a combination of conventional medicaments.

The methods of the invention are particularly suitable for prolonged and/or prophylactic use, because of the associated age restrictions, side effects, and/or drug resistance issues with alternative therapies. The methods are further suitable for individuals prone to infections or bacterial over-colonization and/or inflammatory conditions, or individuals that typically experience hypersensitivity or severe side effects with other treatments.

BRIEF DESCRIPTION OF THE FIGURES

FIG. 1 shows the ability of HOCl to reduce hyperemia in an animal model in a dose dependent fashion. Treatment with steroid (prednisolone) and antihistamine

(olopatadine) are shown as comparators. (A) 1 hour post-dose hyperemia; (B) 18 minutes post-CAC (conjunctival allergen challenge) hyperemia.

FIG. 2 shows reduction of psoriasis clinical score as compared to untreated controls and Clobetasol (corticosteroid) in imiquimod-induced psoriasis-like skin inflammation in mice.

DETAILED DESCRIPTION OF THE INVENTION

The present invention provides compositions and methods for treating, preventing, or managing an immunological and/or inflammatory condition, by administering a hypochlorous acid composition to a subject in need thereof.

Hypochlorous acid (HOCl) is an oxidant and antimicrobial that is produced by the human body's natural immune system. HOCl is generated as the final step of the Oxidative Burst Pathway, with large quantities of HOCl being released into phagocytic vesicles to destroy invading microorganisms. Hypochlorous acid may exert an antimicrobial effect by attacking the surface and plasma membrane proteins, impairing transport of solutes and the salt balance of bacterial cells (Pieterse et al., *Water SA*, 22(1): 43-48 (1996)).

In accordance with the present invention, exogenous hypochlorous acid is administered for treating or preventing immunological and/or inflammatory conditions. Without wishing to be bound by theory, it is believed that administration of hypochlorous acid treats, manages and/or prevents local inflammatory symptoms, and helps to control or modulate an underlying immune condition at a systemic level. Further, without wishing to be bound by theory, it is believed that even topically or locally applied hypochlorous acid modulates systemic inflammatory mediators in a beneficial manner, allowing for a variety of conditions characterized by chronic, systemic inflammation, to be conveniently managed and/or treated with a topical hypochlorous acid composition.

The invention in various embodiments comprises applying a hypochlorous acid formulation to ameliorate disease symptoms and/or dampen or alter inflammatory responses. For example, cells directing the immune response (which can include monocytes, macrophages, dendritic cells, Langerhans cells, fibroblasts,

and keratinocytes) secrete cytokines and other soluble factors that may include, for example, one or more of TNF, IFN γ , IL-1 β , IL-2, IL-4, IL-6, IL-8, IL-10, IL-18. Cytokine release patterns vary, both between cytokines as well as cell types. For example, many immune mediators are secreted through classical secretory pathways including regulated or constitutive exocytosis or by degranulation. In classical secretory pathways, cytokines are translated with signal peptides in the endoplasmic reticulum (ER), trafficked in vesicles to the golgi complex, and subsequently to the cell surface for release. In the case of degranulation, cytokines and/or other cargo are stored in granules for later release. On the other hand, certain cytokines, such as IL-1 β and IL-18, which are activated by the inflammasome and play a basic role in the initiation of inflammatory responses, are secreted via nonclassical secretory pathways. Specifically, these molecules are synthesized as inactive precursors, and once activated by caspase-1 cleavage, are potentially secreted either by membrane transporters, in exosomes or microvesicles, or perhaps even by cell lysis. See, for example, Lacy and Stow, Cytokine release from innate immune cells: association with diverse membrane trafficking pathways, *Blood* 118(1) (July, 2011).

While the role of endogenous reactive oxygen species (ROS) in the inflammatory process has been somewhat clouded by conflicting data, ROS are often considered as activators of the inflammasome. See, Harijith A, et al., Reactive oxygen species at the crossroads of inflammasome and inflammation, *Front. Physiol.* 5:352 (2014). For example, endogenously generated hypochlorous acid is generally regarded as a pro-inflammatory molecule. See, Schieven GL et al., Hypochlorous acid activates tyrosine phosphorylation signal pathways leading to calcium signaling and TNF α production, *Antioxid. Redox Signal* 4(3):501-7 (2002); Pullar JL, et al., Living with a killer: the effects of hypochlorous acid on mammalian cells, *IUBMB Life*, 50(4-5):259-66 (2000). HOCl generation in vivo has been postulated to mediate inflammation in chronic inflammatory disease. Halliwell et al., Oxidants, inflammation, and anti-inflammatory drugs, *FASEB* 2:2867-2873 (1988). In contrast, the present disclosure shows that HOCl can inhibit inflammatory processes in a dose dependent fashion. Further, HOCl can reduce or alter an underlying immune condition, including reducing or altering the systemic immune response.

In accordance with the invention, hypochlorous acid (a strong oxidant) is formulated for application to tissues for treatment of acute and chronic inflammatory conditions and diseases. While topical and systemic steroids are the most commonly prescribed medications for the treatment of inflammatory diseases, there is increasing awareness to the side effects and damage that can result from long term steroid use, which include increased appetite, weight gain, sudden mood swings, muscle weakness, blurred vision, increased growth of body hair, easy bruising, lower resistance to infection, swollen, puffy face, acne, osteoporosis, worsening of diabetes, high blood pressure, stomach irritation, nervousness, restlessness, difficulty sleeping, cataracts or glaucoma and water retention or swelling, among others. Topical retinoid, topical vitamin D (and analogues thereof), antihistamine, and immunosuppressants are used for some dermatological conditions, but these agents can be associated with substantial toxicity. Further, some patients and conditions are refractory to available treatments. Thus, more effective and/or safe alternatives are desirable. The hypochlorous acid may be used as an alternative or adjunct therapy to these conventional agents.

Conventional agents often result in a large range of potential undesirable side effects that are not observed with HOCl treatment. For example, antibiotics can induce rash, diarrhea, abdominal pain, nausea/vomiting, drug fever, hypersensitivity (allergic) reactions, serum sickness, vaginal candidiasis, and photosensitivity. Common anti-virals are reported to induce nausea, vomiting, diarrhea and headache, as well as agitation, confusion, rash, anemia, muscle pain, hypersensitivity reactions, seizures, and hepatitis. Antihistamines and decongestants are known to induce drowsiness, dizziness, dry mouth/nose/throat, headache, upset stomach, constipation, and trouble sleeping. Immunosuppressants/immunomodulators are reported to induce headache, nausea, vomiting, diarrhea, and malaise, as well as decreased kidney function, hepatitis, increased risk of infections, diabetes, increased cholesterol levels, sleep problems, mild tremor, high blood pressure, swollen gums, tingling of the fingers and feet, increased facial hair, and increased risk of lymphoma. Analgesics and anesthetics, such as opioids, have shown common side effects that include sedation, dizziness, nausea, vomiting, constipation, physical dependence, tolerance, and respiratory depression. Common side effects of local anesthetics include flushing or redness of the skin, itching skin, small red or purple

spots on the skin, and unusually warm skin. Steroids are reported to induce increased appetite, weight gain, sudden mood swings, muscle weakness, blurred vision, increased growth of body hair, easy bruising, lower resistance to infection, swollen, puffy face, acne, osteoporosis, worsening of diabetes, high blood pressure, stomach irritation, nervousness, restlessness, difficulty sleeping, cataracts or glaucoma and water retention or swelling. By providing HOCl as an alternative therapy, side effects of conventional agents can be avoided.

The hypochlorous acid composition may contain a mixture of oxidizing species, but the oxidizing species are predominantly hypochlorous acid (HOCl). Hypochlorous acid and hypochlorite are in equilibrium and the position of the equilibrium is determined solely by the pH. For example, the hypochlorous acid composition may have a pH of from about 3 to about 7.5, or from about 3.5 to about 7.5, or a pH of from about 4 to about 7.5, or from about 5 to about 7.5, or a pH of from about 4 to about 7, or a pH of from about 4.5 to about 7, or a pH of from about 5 to about 7, or a pH of from about 3 to 6.5, or a pH or from about 4 to about 6.5, or from about 5 to about 6.5. For example, the hypochlorous acid composition may have a pH of from about 5 to about 6.

In certain embodiments, the hypochlorous acid composition contains at least about 70% or at least about 80% hypochlorous acid relative to the total concentration of hypochlorous acid, hypochlorite, and molecular chlorine (Cl_2) (as 100%). The hypochlorous acid composition may have at least 90%, at least 95%, or at least 98% hypochlorous acid relative to the total concentration of hypochlorous acid, hypochlorite, and molecular chlorine (Cl_2) (as 100%). Such embodiments may allow for higher levels of active chlorine to be administered, while avoiding any irritation as a result of the composition. Hypochlorite has been known for quite some time to have toxic properties on mammalian cells due to high pH in addition to required concentration of available chlorine, and thus may not be desirable for long term use or may not have a sufficient therapeutic window for some anti-inflammatory applications. Thus, in some embodiments, the level of hypochlorite in the solution or composition is limited (e.g., about 10% or less, about 5% or less, or about 3% or less relative to the total concentration of hypochlorous acid, hypochlorite, and molecular chlorine (Cl_2) (as 100%).

The hypochlorous acid composition in various embodiments contains available free chlorine (AFC) at from about 100 to about 5000 parts per million (ppm), or from about 250 to about 2000 ppm in some embodiments. In some embodiments, the composition has AFC of greater than about 500 ppm, or greater
5 than about 600 ppm, or greater than about 700 ppm, or greater than about 800 ppm, or greater than about 1000 ppm, or greater than about 1200 ppm, or greater than about 1500 ppm. For example, the composition may have AFC of from about 400 to about 3000 ppm, such as from about 500 to about 2000 ppm, or from about 500 to about 1500 ppm, or from about 500 to about 1000 ppm. In some embodiments, the
10 HOCl composition is formulated with AFC of from about 1000 to about 2000, or from about 1000 to about 1500 ppm. Hypochlorous acid displays anti-inflammatory actions that are dose dependent.

The hypochlorous acid composition can be formulated for any delivery route, selected to benefit the desired organ or tissue, with the anti-inflammatory effects
15 being local and/or systemic. In some embodiments, anti-inflammatory properties or immunomodulating properties of the composition are observed at sites that are remote from the application site.

As used herein, the term “affected area” is any tissue, organ, or part of the body in which symptoms of the inflammatory condition manifest, and which may
20 include the skin, mucus membranes, eyes, ears, nose, sinus cavity, throat, mouth (e.g., gingiva), lymph nodes, lungs, connective tissue (including skeletal muscles, ligaments, tendons, joints), nervous system (including activation or inhibition of nerve-based signaling responses such as scratching/itching or pain), intestinal tract (e.g., colon), urogenital system (including urinary tract or vagina), as well as
25 systemic inflammation affecting the vasculature, or in some embodiments the peritoneum or one or more organs such as the kidney, liver, or pancreas. The affected region in some embodiments will determine the route of administration, which will range from via enteral (oral, gastric and rectal), parenteral (intravenous, intra-arterial, intraosseous, intra-muscular, intrathecal, sub-cutaneous) or other
30 (sublingually, buccally, rectally, vaginally, intra-articular, by the ocular or otic route, nasally, cutaneously for topical or systemic effect, by inhalation or nebulization, or transdermally) or as an irrigant to one or more tissues or organs (e.g., during surgery

or trauma). In some embodiments, the affected area is one or more of skin, eyes, lungs, or mucus membranes. In some embodiments, the affected area is remote from the application site of the composition.

As used herein, the term “treating” refers to providing therapy to a patient to prevent (by means of prophylactic treatment), reduce, inhibit, ameliorate, or manage symptoms (e.g., inflammatory symptoms) of a disease, or to slow or stop progression of the disease, as well as in some embodiments, to prevent onset or re-occurrence of a condition or symptom. For example, in various embodiments the invention provides methods of treating tissues to inhibit, reduce, or prevent inflammatory processes in the tissue, or at remote sites, including acute, chronic, and delayed reactions, thereby allowing regeneration and/or healing of tissues, and/or preventing tissue damage or loss of tissue integrity.

As used herein, the term “prolonged use” refers to treatment of a chronic condition. Generally, a chronic condition is a condition that will not be eliminated even with therapy, and thus the therapy is intended to reduce, inhibit, or prevent (e.g., by means of prophylactic treatment) inflammatory symptoms, thereby managing the condition. Prolonged use generally includes treatment for at least about two months, at least about six months, at least about one year, at least about two years, or more. Prolonged use in some embodiments, is employed where systemic effects are desired, such as for treatment of an underlying autoimmune condition or cancer.

In accordance with certain embodiments of the invention, the hypochlorous acid composition may be administered, for example, once daily or more than once daily. For example, the hypochlorous acid composition may be administered from about 1 to 10 times daily (e.g., about 2 times, 3 times, 4 times, 5 times, 6 times, 7 times, 8 times, 9 times, or 10 times daily). Alternatively the hypochlorous acid composition may be administered once a week or more than once a week (e.g., about 2 to 5 times per week). In some embodiments, the hypochlorous acid composition is administered topically from one to four times daily (e.g., twice daily).

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Administration of the hypochlorous acid may be for any period of time as determined to be appropriate by, for example, a physician. In various embodiments, the hypochlorous acid composition is administered for at least one week, at least two weeks, at least three weeks, at least four weeks, at least five weeks, at least six weeks, at least seven weeks, at least eight weeks, at least nine weeks, at least ten weeks, at least eleven weeks, or at least twelve weeks. In cases of prolonged use, the hypochlorous acid composition may be administered for at least about two months, at least about three months, at least about four months, at least about five months, at least about six months, at least about seven months, at least about eight months, at least about nine months, at least about ten months, at least about eleven months, or at least about twelve months. In some embodiments, the hypochlorous acid is administered for at least about one year, or at least about two years, or more.

The inflammatory condition may be present in a human or animal patient of any age (including pediatric and geriatric patients) as well as immunocompromised patients. Exemplary animal patients include mammals such as dogs, cats, horses, lamb, cattle, goats, pigs, and guinea pigs. The present invention further contemplates preventive care (including prophylactic use) for such inflammatory conditions or prevention of such conditions where the patient is genetically or environmentally pre-disposed to such conditions, as well as conditions that don't completely resolve with antimicrobial or steroidal treatment, or treatment with retinoid, vitamin D ointment, immunosuppressant, or biologic anti-inflammatory agent. Pediatric patients include infants, children, and adolescents, and the age limit usually ranges from birth up to 18 years of age (age 21 in the United States). In some embodiments, the patient is under 12 years of age, or is an infant. Geriatric patients in accordance with this disclosure include individuals over the age of 60. Immunocompromised patients include those having an immune response attenuated by administration of immunosuppressive drugs, chemotherapy, by irradiation, by malnutrition, genetic malady, or by certain disease processes such as acquired immunodeficiency syndrome (AIDS).

The hypochlorous acid composition may be formulated as a liquid, such as an eye drop, eye wash, gargle, oral rinse, nasal rinse or throat spray, or ear drop. In still other embodiments, the composition may take the form of a paste, cream,

emulsion, gel (e.g., hydrogel), and/or foam for application to the skin, dentia, or gingiva. Such formulations may be prepared using conventional additives known in the art and/or as described herein. In embodiments employing pastes, creams, emulsions, gels, and/or foams, the solution is better contained around the site of inflammation by limiting run-off. Convenient applicators for creams, foams, and the like are known, and may be used in accordance with the present invention. Alternatively still, the composition may be formulated so as to be delivered by aerosol, mist, or steam, impregnated into wound dressings, adhesive, or dissolving strips, patches, suppositories, or encapsulated in silicon or other carriers, as nanoparticles or free-standing in liquids, suspensions, powders, pills or capsules, or particles for the purposes of release, targeted release or extended-release via enteral or parenteral administration.

The hypochlorous acid composition may also contain from about 0.1 to 2.0% w/v salt, such as NaCl. In some embodiments, the hypochlorous acid composition contains 0.4 to 1.5% w/v salt, or may be a normal saline solution (0.9% w/v NaCl). In some embodiments, the solution is isotonic with physiological fluids, such as blood, saliva or tears. In some embodiments, the solution is hypotonic with physiological fluids.

The composition in various embodiments can be administered by aerosol to the lungs or by intravenous or subcutaneous delivery of particles that encapsulate and release HOCl in the circulation, either in a sustained manner or targeted to particular tissues or organs. In some embodiments, the solution or composition is formulated for colonic, vaginal, urinary tract, or peritoneal irrigation, or is formulated for injection into joint spaces. In some embodiments, the solution or composition is formulated for irrigation of tissues or organs during or following surgery to prevent or reduce inflammatory complications, such as those that may occur post-surgery. In some embodiments, the composition is formulated for treating donor tissue or organs (e.g., kidney, liver, lung, heart, skin, and cornea) prior to or during transplantation.

In certain embodiments of the present invention, the hypochlorous acid is formulated or administered in combination (e.g., administered separately) with another therapeutic or cleansing agent. Non-limiting examples of therapeutic agents

include anti-microbial agents such as antibiotics, antivirals, anti-fungal and anti-parasitics, immune-modulators/suppressants anti-inflammatory agents, anti-histamines, analgesics, local anesthetics, anti-oxidants such as vitamins, and moisturizing agents. For example, the hypochlorous acid may be formulated or
5 administered with antibiotics such as bacitracin, neomycin, neosporin, framycetin, fusidic acid, chloramphenicol, gentamicin, tobramycin, ceftriaxone, sulfacetamide, erythromycin, gentamicin, ciprofloxacin, ofloxacin, cefoxitin, cefotaxime, spectinomycin, tetracycline, doxycycline, and azithromycin; anti-virals such as acyclovir, valacyclovir, famciclovir, and oseltamivir; anti-fungals such a as
10 ketoconazole, fluconazole, itraconazole, voriconazole, terbinafine, and nystatin; anti-parasitics such as metronidazole, ivermectin, pyrantel pamoate, albendazole, and atovaquone-proguanil; immune-modulators/suppressants such as thalidomide, lenalidomide, apremilast, cyclosporine, rapamycin, prednisone and tacrolimus; corticosteroids and NSAIDs such as aspirin, ibuprofen, naproxen sodium, celecoxib;
15 anti-histamines such as diphenhydramine, loratadine, fexofenadine, cimetidine, ranitidine, ciproxifan, and cromoglycate; analgesics such as acetaminophen/paracetamol, buprenorphine, codeine, meperidine, and tramadol; local anesthetics such as epinephrine, lidocaine, bupivacaine, and benzocaine; anti-oxidants such as vitamin A & E; moisturizing agents such as silicones, emollients,
20 lanolin, mineral oil, urea, alpha-hydroxy acids, glycerine, fatty acids, ceramides, collagen or keratin. Non-limiting examples of cleansing agents include alcohol, betaine, mild soap solutions, bicarbonate or saline solutions, or electrolyzed solutions including catholytes.

The composition may comprise a pharmaceutically acceptable carrier. Non-
25 limiting examples of suitable carriers include hectorite, bentonite, laponite, oil emulsions, polyvinyl alcohol, povidone, hydroxypropyl methyl cellulose, poloxamers, carboxymethyl cellulose, hydroxyethyl cellulose, and purified water. The composition may also include various other ingredients, such as tonicity agents, buffers, surfactants, co-solvents, viscosity building agents, preservatives, and other
30 therapeutic agents.

Regarding tonicity agents, such agents may be employed to adjust the tonicity of a composition, for example, in the case of an ophthalmic composition, to

the tonicity of natural tears. For example, sodium chloride, potassium chloride, magnesium chloride, calcium chloride, dextrose and/or mannitol may be added to the composition to approximate physiological tonicity. Such an amount of tonicity agent will vary, depending on the particular agent to be added and the type of composition. In general, however, the compositions will have a tonicity agent in an amount sufficient to cause the final composition to have an acceptable osmolality. For example, for an ophthalmic composition, the composition is generally in the range of about 150 to 450 mOsm, preferably 250 to 350 mOsm.

Regarding buffers, an appropriate buffer system (such as, for example, sodium phosphates, potassium phosphates, potassium carbonate, sodium bicarbonate, sodium borate or boric acid, phosphoric acid, or HCl) may be added to the compositions to prevent pH drift under storage conditions. The particular amount of buffering agent will vary, depending on the agent employed. Preferably, however, the buffer will be chosen to maintain a target pH.

Hypochlorous acid is highly unstable, a problem made more difficult when using higher strength solutions (e.g., above a few hundred ppm AFC) as well as other formulation ingredients that can be destabilizing. Thus, in some embodiments, the formulation includes a stabilizing amount of dissolved inorganic carbon (DIC) as disclosed in US Patent 8,871,278, which is hereby incorporated by reference in its entirety. For example, the formulation may employ a stabilizing amount of DIC, which may be incorporated as a bicarbonate or carbonate salt of an alkali or alkaline earth metal, such as, for example, sodium, potassium, calcium, or magnesium. In some embodiments, the bicarbonates or carbonates are added prior to the formation of hypochlorous acid (e.g., by electrochemical treatment), and in other embodiments, the bicarbonates or carbonates are added after electrochemical treatment. For example, the bicarbonate(s) or carbonate(s) may be contained in the precursor aqueous solution (e.g., water) or dry electrolyte, and/or incorporated in the electrolyzed solution or during formulation.

The DIC is incorporated at a "stabilizing amount," which can be determined with reference to the change in the pH or AFC content of the formulation over time. Generally, the formulation is considered stabilized if the amount of AFC does not drop below about 75% of the initial value over a period of about 6 months. In certain

embodiments, the AFC content is stabilized for at least one year from the production date of the formulation. Further, the stability of the formulation may be determined with reference to the pH. Generally, the formulation is considered stabilized if the pH does not vary by 1 unit over a period of about 6 months. In certain embodiments, the pH is stabilized for at least one year from the production date of the formulation. The formulation should be stored at 25° C or at 20° C, or less for greater stability. 20° C is the reference temperature for determination of stability. For stability testing, solutions or formulations are packaged in glass or PET bottles, stored in the dark, and kept unopened. For the best stability, the formulations are stored at 4°C until use in some embodiments.

The stabilizing amount of DIC (e.g., carbonate or bicarbonate) can be determined with reference to the AFC content. For example, in certain embodiments, the stabilizing amount of the carbonate or bicarbonate is at a molar ratio of from about 5:1 to 1:5 with respect to the AFC level, or from about 3:1 to about 1:2 with respect to the AFC level. In some embodiments, the bicarbonates or carbonates are present in at least equal molar amounts with respect to the AFC content (e.g., hypochlorous acid content). In still other embodiments, the DIC (e.g., bicarbonate or carbonate) is present at about 5:1, about 4:1, about 3:1, about 2:1, about 1:1, about 1:2, about 1:3, about 1:4, or about 1:5 with respect to AFC content. In various embodiments, other buffering components such as phosphate buffers are also employed. For example, for formulation having AFC of from about 500 ppm to about 2000 ppm, carbonate or bicarbonate may be present at an amount of from about 500 mg/L to about 3000 mg/L to stabilize the formulation. In certain embodiments, the formulation is for topical treatment of skin, and has AFC in the range of 500 to 2000 ppm, and comprises sodium bicarbonate in the range of about 500 to about 2000 mg/L, has a pH in the range of 5 to 7, and comprises a fluorosilicate (e.g., sodium magnesium fluorosilicate) at from 2 to 5% (e.g., about 3% or about 4%). In some embodiments, the formulation is a hydrogel employing a silicate-based carrier such as sodium magnesium fluorosilicate or lithium magnesium fluorosilicate, comprises sodium bicarbonate (e.g., from 500 to 2000 mg/L) to stabilize the HOCl, and comprises phosphoric acid (and optionally sodium phosphate buffer) to target a slightly acidic pH (e.g., from 5 to 6.5). The formulation may have a viscosity of from about 500 to about 150,000 cP, such as

from about 1000 to about 840,000 cP, or from 1000 to about 30,000 cP. The formulation in some embodiments has a conductivity of less than 10 mS/cm, such as from about 0.5 to about 5 mS/cm, such as from 0.5 to about 3 mS/cm, or about 1 or about 2 mS/cm in some embodiments.

5 Without being bound by theory, dissolved inorganic carbon (DIC), which generally includes carbonates, bicarbonates, carbonic acid and dissolved CO₂, provides low or minimal buffering capacity in the pH range targeted by the solutions and formulations described herein. Nevertheless, these solutions are effectively
10 stabilized, such that the solutions and compositions are not dependent on “on-demand” production. The stabilizing effect can be due to, in-part, free radical scavenging ability of DIC to thereby slow the decomposition of HOCl.

The stabilized formulation may be packaged for sale, using any suitable container, such as any suitable plastic or glass bottles, or bags, tubes, or cans (e.g., spray or aerosol). Certain container materials may provide advantages in shelf-life.
15 In certain embodiments, the packaging material has minimal gas permeability (e.g., are non-permeable), including by species such as CO₂ and O₂. Thus, these containers maintain the stabilizing amount of dissolved inorganic carbon, without losing the stabilizer in the form of CO₂. The containers may be transparent, or may be opaque so that they are impenetrable by light. However, it is preferred that
20 transparent containers filter out UV light, since UV light can cause dissociation of HOCl. While the volume of the container has been considered to impact stability and shelf-life, the formulations described herein may be in the range of about 5 ml to about 20 liters, or from about 100 ml to about 1 liter. Exemplary containers have a unit volume of about 5 ml, about 16 ml, about 50 ml, about 100 ml, about 125 ml,
25 about 250 ml, about 0.5 liter, about 1 liter, about 2 liters, about 3 liters, about 4 liters, about 5 liters, or about 10 liters.

Regarding a surfactant, various surfactants useful in conventional formulations may be employed, and particularly surfactants that are resistant to oxidants such as HOCl. Surfactants include CREMOPHOR EL, lauramine oxide,
30 myristyl dimethylamine oxide, polyoxyl 20 ceto stearyl ether, polyoxyl 40 hydrogenated castor oil, polyoxyl 23 lauryl ether and poloxamer 407.

Regarding viscosity building agents, such agents may be added to HOCl compositions of the present invention to increase the viscosity of the carrier. Examples of viscosity enhancing agents include, but are not limited to: synthetic silicates, polysaccharides, such as hyaluronic acid and its salts, chondroitin sulfate
5 and its salts, dextrans, various polymers of the cellulose family; vinyl polymers; and acrylic acid polymers. For example, the composition may exhibit a viscosity of 1 to 400,000 centipoises (“cps”).

Regarding preservatives, no additional antimicrobial agent is required, since the HOCl will function as a preservative; however, in some embodiments HOCl is
10 combined with a second preservative or antimicrobial agent such as silver. In various embodiments, the HOCl is manufactured as sterile. The composition can also include other therapeutic agents such as anti-inflammatory agents, antihistamines, decongestants, antibiotics, analgesics, immune-modulators and suppressants and/or moisturizing agents known in the art.

15 In various embodiments, the inflammatory condition treated in accordance with the various embodiments is characterized, at least in part, by type I hypersensitivity, type II hypersensitivity, type III hypersensitivity, and/or type IV hypersensitivity. The inflammatory condition may be acute or chronic, and may be of autoimmune or allergic origin.

20 Type I hypersensitivity or (immediate-type hypersensitivity) is an allergic reaction provoked by re-exposure to an antigen (e.g., allergen). In type I hypersensitivity, an antigen is presented to CD4⁺ Th2 cells specific to the antigen that stimulate B-cell production of IgE antibodies also specific to the antigen. During sensitization, the IgE antibodies bind to receptors on the surface of tissue
25 mast cells and blood basophils. Later exposure to the same allergen cross-links the bound IgE on sensitized cells, resulting in degranulation and the secretion of pharmacologically active mediators such as histamine, leukotriene (LTC₄ and LTD₄), and prostaglandin that act on the surrounding tissues. The principal effects of these products are vasodilation and smooth-muscle contraction. Exemplary Type
30 I conditions for which the invention can be effective include allergic asthma (including severe asthma), allergic conjunctivitis, allergic rhinitis, anaphylaxis, angioedema, urticaria, eosinophilia, drug allergy (e.g., penicillin, cephalosporin), or

food allergy. Type I hypersensitivity can be further classified into an immediate and late-phase reaction. The immediate hypersensitivity reaction occurs minutes after exposure and includes release of vasoactive amines and lipid mediators, whereas the late-phase reaction occurs 2 to 4 hours after exposure and includes the release of
5 cytokines.

In some embodiments, the patient suffers from a hyperimmunoglobulin E syndrome, which may be characterized by recurrent staphylococcal infections, eczema-like skin rashes, severe lung infections that result in pneumatoceles (balloon-like lesions that may be filled with air or pus or scar tissue) and very high
10 concentrations of the serum antibody IgE.

In type II hypersensitivity (or cytotoxic hypersensitivity) the antibodies produced by an immune response bind to antigens on the patient's own cell surfaces. The antigens recognized may be self-antigens or extrinsic antigens that are adsorbed onto the cells during exposure to some foreign antigen. These cells are recognized
15 by macrophages or dendritic cells, which act as antigen-presenting cells. This causes a B cell response, wherein antibodies are produced against the foreign antigen. Examples of type II hypersensitivity where the invention finds use include Haemolytic Anaemia, Myasthenia Gravis, Grave's Disease, and Goodpasture's syndrome. Another form of type II hypersensitivity is called antibody-dependent
20 cell-mediated cytotoxicity (ADCC). Here, cells exhibiting the foreign antigen are tagged with antibodies (IgG or IgM). These tagged cells are then recognized by natural killer cells (NK) and macrophages which in turn kill these tagged cells.

Type III hypersensitivity occurs when antigen-antibody complexes that are not adequately cleared by innate immune cells accumulate, giving rise to an
25 inflammatory response and attraction of leukocytes. Type III hypersensitivity occurs when there is an excess of antigen, leading to small immune complexes being formed that do not fix complement and are not cleared from the circulation. Large complexes can be cleared by macrophages but macrophages have difficulty in the disposal of small immune complexes. These immune complexes insert themselves
30 into small blood vessels, joints, and glomeruli, causing symptoms. Unlike the free variant, a small immune complex bound to sites of deposition (like blood vessel walls) are far more capable of interacting with complement. Such depositions in

tissues often induce an inflammatory response, and can cause damage wherever they precipitate. The damage can result from the action of cleaved complement anaphylotoxins C3a and C5a, which, respectively, mediate the induction of granule release from mast cells, and recruitment of inflammatory cells into the tissue. Skin
5 response to type III hypersensitivity is referred to as an arthus reaction, and is characterized by local erythema and some induration. Other examples of type III hypersensitivity include Systemic lupus erythematosus (SLE) (which can involve, for example, nephritis, skin lesions, and arthritis); glomerulonephritis, systemic vasculitis, arthritis, cutaneous vasculitis, Farmer's lung (which manifests as alveolar
10 inflammation).

Type IV hypersensitivity is often called delayed-type hypersensitivity as the reaction takes two to three days to develop. Unlike the other types, it is not antibody mediated but rather is a type of cell-mediated response. CD4+ helper T cells recognize antigen in a complex with Class II major histocompatibility complex. The
15 antigen-presenting cells in this case are macrophages that secrete IL-12, which stimulates the proliferation of further CD4+ Th1 cells. CD4+ T cells secrete IL-2 and interferon gamma, further inducing the release of other Th1 cytokines, thus mediating the immune response. Activated CD8+ T cells destroy target cells on contact, whereas activated macrophages produce hydrolytic enzymes and, on
20 presentation with certain intracellular pathogens, transform into multinucleated giant cells.

Examples of type IV hypersensitivity include the following. Diabetes mellitus type 1 affects pancreatic beta cells, leading to beta cell destruction and/or insulinitis. Multiple sclerosis results from an attack on oligodendrocyte proteins, and
25 resulting in demyelinating disease, perivascular inflammation, paralysis, and/or ocular lesions. Rheumatoid arthritis (RA) results from an attack on antigen in synovial membrane, and leading to chronic arthritis. RA often leads to the destruction of articular cartilage and bone (which can also involve type III hypersensitivity). Peripheral neuropathy which can result from attack on Schwann
30 cell antigen, leading to neuritis or paralysis. Hashimoto's Thyroiditis results from attack on thyroglobulin antigen, leads to hypothyroidism, goiter, and/or follicular thymitis. Crohn's disease involves inflammation of the ileum and colon. Allergic

contact dermatitis results from contact with environmental chemicals including poison ivy and nickel, and manifests as itching and can include exposure to radiation, whether by exposure to artificial or natural UV in the course of living (leading to UV-damaged/aged skin), and/or exposure to radiation for the purposes of cancer
5 treatment or for interventional procedures. Other examples include celiac disease, graft-versus-host disease, and chronic transplant rejection.

In various embodiments, administration of the hypochlorous acid composition results in a systemic reduction of pro-inflammatory cytokines, such as one or more of IL-1 β , IL-2, IL-4, IL-6, IL-8, IL-18, and TNF- α , as well as other
10 soluble or cellular factors such as α -2 macroglobulin and NF- κ B.

In various embodiments, the HOCl composition is applied to prevent diseases or conditions caused by or associated with prolonged and/or untreated inflammation, including those conditions mentioned above. Examples of these diseases or conditions include: cancer (e.g. bowel cancer, lung cancer, skin cancer,
15 ovarian cancer, breast cancer among others); cardiovascular disease; diabetes; and metabolic disease.

In some embodiments, the hypochlorous acid is administered to a cancer patient, to slow or inhibit the progression of cancer. Specifically, cancer relies in the inflammatory machinery to progress and to metastasize. By modulating these
20 inflammatory processes, the invention helps to control the progression and spread of cancer, and aids the bodies repair mechanisms, particularly where the patient undergoes a primary cancer therapy that is harmful to non-cancer cells and tissues (including but not limited to mucosa, skin, and GI), such as chemotherapy or radiation therapy.

As used herein, cancer refers to any uncontrolled growth of cells that may interfere with the normal functioning of the bodily organs and systems, and includes both primary and metastatic tumors. Primary tumors or cancers that migrate from their original location and seed vital organs can eventually lead to the death of the subject through the functional deterioration of the affected organs. A metastasis is a
25 cancer cell or group of cancer cells, distinct from the primary tumor location, resulting from the dissemination of cancer cells from the primary tumor to other
30

parts of the body. Metastases may eventually result in death of a subject. For example, cancers can include benign and malignant cancers, polyps, hyperplasia, as well as dormant tumors or micrometastases. In some embodiments, the cancer is stage I or stage II cancer. In other embodiments, the cancer is stage III or stage IV.

5 Illustrative cancers that may be treated include, but are not limited to, basal cell carcinoma, biliary tract cancer; bladder cancer; bone cancer; brain and central nervous system cancer; breast cancer; cancer of the peritoneum; cervical cancer; choriocarcinoma; colon and rectum cancer; connective tissue cancer; cancer of the digestive system; endometrial cancer; esophageal cancer; eye cancer; cancer of the
10 head and neck; gastric cancer (including gastrointestinal cancer); glioblastoma; hepatic carcinoma; hepatoma; intra-epithelial neoplasm; kidney or renal cancer; larynx cancer; leukemia; liver cancer; lung cancer (*e.g.*, small-cell lung cancer, non-small cell lung cancer, adenocarcinoma of the lung, and squamous carcinoma of the lung); melanoma; myeloma; neuroblastoma; oral cavity cancer (lip, tongue, mouth, and pharynx); ovarian cancer; pancreatic cancer; prostate cancer; retinoblastoma;
15 rhabdomyosarcoma; rectal cancer; cancer of the respiratory system; salivary gland carcinoma; sarcoma; skin cancer; squamous cell cancer; stomach cancer; testicular cancer; thyroid cancer; uterine or endometrial cancer; cancer of the urinary system; vulval cancer; lymphoma including Hodgkin's and non-Hodgkin's lymphoma, as well as B-cell lymphoma (including low grade/follicular non-Hodgkin's lymphoma (NHL); small lymphocytic (SL) NHL; intermediate grade/follicular NHL; intermediate grade diffuse NHL; high grade immunoblastic NHL; high grade lymphoblastic NHL; high grade small non-cleaved cell NHL; bulky disease NHL; mantle cell lymphoma; AIDS-related lymphoma; and Waldenstrom's
20 Macroglobulinemia; chronic lymphocytic leukemia (CLL); acute lymphoblastic leukemia (ALL); Hairy cell leukemia; chronic myeloblastic leukemia; as well as other carcinomas and sarcomas; and post-transplant lymphoproliferative disorder (PTLD), as well as abnormal vascular proliferation associated with phakomatoses, edema (*e.g.* that associated with brain tumors), and Meigs' syndrome.

30 In various embodiments, cancers that may be treated include, but are not limited to, skin cancer, cutaneous melanoma, breast cancer, colon cancer, lung cancer, testicular cancer, cervical cancer, lymphoma, parathyroid cancer, penile

cancer, rectal cancer, small intestine cancer, thyroid cancer, uterine cancer, Hodgkin's lymphoma, lip and oral cancer, leukemia or multiple myeloma. In an embodiment, the cancer is a cutaneous cancer such as basal cell carcinoma or squamous cell carcinoma. In an embodiment, the cancer is breast cancer. In another
5 embodiment, the cancer is a cancer of the mouth, throat, or sinus. In a further embodiment, the cancer is lung cancer.

In some embodiments, the hypochlorous acid composition is administered directly to the tumor or to tissue or organ harboring the tumor. For example, in some embodiments, the hypochlorous acid composition is administered during
10 surgical removal of the cancer. In other embodiments, the location of the tumor will instruct the most appropriate route of delivery, including by topical administration, pulmonary administration, colonic irrigation, catheter, intra-tumoral injection, or delivery to the oral cavity or sinus cavity. In some embodiments, the hypochlorous acid composition is administered topically, whether or not the cancer is cutaneous in
15 origin, or proximal to the skin. In some embodiments, the hypochlorous acid provides systemic effects upon topical delivery, allowing for even remote cancers (such as liver, pancreatic, bladder, colorectal, and others) to be effectively treated using this route. In some embodiments, prolonged treatment with the hypochlorous acid composition is employed for the treatment of cancer.

In various embodiments, the HOCl composition is applied to treat or prevent lesions caused by inflammatory conditions by inhibiting the inflammatory processes and/or by maintaining skin homeostasis or by stimulating cell (e.g., skin cell) proliferation to heal lesion wounds. Thus, in some embodiments, the patient has an inflammatory condition that manifests as skin or mucosa lesions, and the HOCl
20 formulation protects intact skin (e.g., from developing lesions) and/or promotes closing of wounds once developed. In some embodiments, the patient may have a condition that predisposes the patient to skin lesions, and is characterized by microbial infection or burden, inflammation, itch, high pH, and compromised barrier. HOCl as described herein acts in a multi-modal fashion to inhibit various stages of
25 the condition, including reduction of the microbial burden, normalizing the pH, reducing itch, while reducing inflammatory mediators.
30

In some embodiments the invention provides methods for controlling or normalizing the microbiome of a tissue, including but not limited to skin, eyes, mouth, gingiva, nasal passages, sinus cavity, urogenital system, vagina, intestine, etc. In some embodiments, the tissue is affected by acute or chronic inflammation, and
5 in some embodiments, is characterized by microbial over-colonization, or is characterized by the presence of one or more microbes associated with an inflammatory or immunological condition.

Even in the absence of overt infection, there is a complex interplay between the microbiome and tissue inflammation. See, McDermott and Huffnagle, The
10 microbiome and regulation of mucosal immunity, *Immunology* Vol. 142(1): 24–31 (2014). Simultaneous reduction of microbial burden and normalization of the tissue microbiome, together with a reduction of local inflammation, can promote tissue healing and normalization. In some embodiments, the microflora from the inflamed tissue, or other region, is determined (e.g., by rRNA gene sequencing). In
15 embodiments where microbes (or populations or profiles of microbes) associated with immunological or inflammatory conditions are present, the hypochlorous acid composition can be administered to normalize the microbial flora.

In some embodiments, topically applied HOCl, especially with prolonged use, helps to maintain a healthy microflora (including skin, mucosal membranes, gut,
20 etc.), which is beneficial for controlling chronic inflammation.

In various embodiments, the inflammatory condition involves as an affected region, one or more of the eyes, ears, nose, sinus, throat, mouth, gingiva, or skin. In other embodiments, the inflammatory condition may have as an affected region, one or more of the intestinal tract/ colon, lungs, urogenital system (e.g., urinary tract,
25 vagina), skeletal muscle, ligaments, tendons, joints, bones, kidney, liver, pancreas, or vasculature.

Various localized inflammatory conditions or symptoms that may be treated in accordance with the invention include: conditions of the eye such as allergic conjunctivitis, blocked glands, chalazion, stye, red eye, dry eye disease, uveitis,
30 inflammation after eye surgery, dry or wet age-related macular degeneration (AMD); conditions of the nose or sinus cavity such as rhinitis, rhinorrhea, sinusitis, nasal

congestion; conditions of the mouth or throat such as stomatitis, xerostomia, gingivitis, or pharyngitis; and conditions of the skin such as keratitis, dermatitis, acne, psoriasis, Netherton Syndrome, Ichthyosis, bullous disease of the skin (e.g., epidermolysis bullosa), Bullous Pemphigoid, Actinic Keratosis, pruritis, rash, lesions, blisters, and bumps.

Additional inflammatory conditions to be treated in various embodiments, which can affect a particular target tissue, or affect multiple tissues, organs, or systems, are as follows. Exemplary conditions that affect the lungs include allergic asthma, occupational asthma, bronchitis, chronic obstructive pulmonary disease (COPD), idiopathic pulmonary fibrosis (IPF), cystic fibrosis, Goodpasture Syndrome, or Farmer's Lung. Exemplary conditions that affect the skin include contact dermatitis, acne, angioedema, urticaria, Systemic lupus erythematosus (SLE), psoriasis, sarcoidosis, rosacea, dermatitis herpetiformis, sun-burn, and cutaneous vasculitis. Exemplary conditions that affect the colon or intestinal tract include Crohn's disease, celiac disease, ulcerative colitis, and hemorrhoids. Exemplary conditions that affect the joints or bones include arthritis (e.g., rheumatoid arthritis or osteoarthritis), multifocal osteomyelitis, traumatic knee injury, SLE, and gout. Exemplary conditions that affect the kidneys include Goodpasture Syndrome, SLE, glomerulonephritis, and kidney stones. Other exemplary conditions involving inflammation of an organ, system, or systemic inflammation include eosinophilia, drug allergy, food allergy, hemolytic anemia, myasthenia gravis, systemic vasculitis, diabetes mellitus type 1 and 2, Hidradenitis suppurativa, multiple sclerosis (MS), myelitis, peripheral neuropathy, Parkinson's Disease, hepatitis, renal failure, pancreatitis, Hashimoto's Thyroiditis, adult onset Still's disease, systemic onset juvenile idiopathic arthritis (SJIA) Schnitzler syndrome, Behcet's disease, SAPHO syndrome, macrophage activation syndrome, Familial Mediterranean Fever (FMF), cryopyrin-associated periodic syndrome (CAPS), TNF receptor associated periodic syndrome (TRAPS), Hyper-IgD syndrome, periodic fever, aphthous stomatitis, pharyngitis and adenitis (PFAPA), deficiency of interleukin-1 (IL-1) receptor antagonist (DIRA), Giant cell arteritis, graft versus host disease, amyloidosis, recurrent pericarditis, and neuromyelitis optica, amyotrophic lateral sclerosis, myeloma, and chronic transplant rejection.

In some embodiments, the HOCl is applied to the skin, either to reduce or inhibit inflammation, or to prevent inflammation in a patient with an acute or chronic inflammatory condition. For example, the affected areas of the skin may be characterized by an alkaline pH as compared to normal healthy skin. In such
5 embodiments, the weak - acidic pH of the hypochlorous acid helps bring the skin to a pH that is more conducive to healing and healthy regeneration. Further, in some embodiments, application to intact but inflamed skin promotes healthy skin regeneration and barrier integrity, by inhibiting or reducing the tissue-damaging inflammatory response, thereby allowing the cells (e.g., dermal fibroblasts and/or
10 keratinocytes) to proliferate in a manner consistent with the healing process. Further still, HOCl is not cytotoxic to these cells at the levels applied. The healing environment is further aided by reducing the microbial burden of the inflamed tissue, where otherwise infection might spawn due to loss of barrier integrity. Thus, in various embodiments, the hypochlorous acid formulation results in one or more of a
15 reduction of microbial burden, a reduction of inflammation, reduced pruritis, enhanced skin cell regeneration, and normalized skin pH. In some embodiments, the patient has a condition characterized by microbial bioburden (e.g., over-colonization) or infection, inflammation, itch, lesions, and high skin pH at the affected region. In some embodiments, the patient has a condition characterized by
20 skin lesions, with or without active lesions. While the HOCl formulation promotes healing of active lesions and normalization of the skin, new lesions are prevented from forming.

In some embodiments, the subject has an underlying immunological condition that affects a plurality of organs or tissues, including the skin. In these
25 embodiments, the hypochlorous acid composition relieves inflammatory symptoms at affected regions of the skin, while dampening or altering the underlying systemic immunological condition, which may have an autoimmune or hypersensitivity component.

For example, in some embodiments, the subject has Systemic Lupus
30 Erythematosus (SLE). SLE or lupus, is a systemic autoimmune disease in which the body's immune system attacks healthy tissues. SLE often affects the heart, joints, skin, lungs, blood vessels, liver, kidneys, and nervous system. Lupus patients can

present with skin lesions/rash. The three main categories of lesions are chronic cutaneous (discoid) lupus, subacute cutaneous lupus, and acute cutaneous lupus. Discoid lupus exhibits as thick, red scaly patches on the skin. Similarly, subacute cutaneous lupus manifests as red, scaly patches of skin but with distinct edges.

5 Acute cutaneous lupus manifests as a rash. The hypochlorous acid composition in some embodiments ameliorates and/or relieves skin lesions or rashes, while providing systemic anti-inflammatory benefits. Thus, other tissues and organs commonly affected in Lupus can benefit from cutaneous treatment with HOCl as described herein.

10 In other embodiments, the subject has psoriasis, such as plaque psoriasis, erythrodermic psoriasis, pustular psoriasis, scalp psoriasis, guttate psoriasis, or inverse psoriasis. While psoriasis manifests heavily as skin lesions, psoriasis can also affect joints and surrounding connective tissue, eyes, and mucous membranes (including ears and nasal passages). The hypochlorous acid composition in some

15 embodiments ameliorates and/or relieves psoriatic skin lesions, while providing systemic anti-inflammatory benefits. Thus, other tissues affected in psoriasis can benefit from cutaneous treatment with HOCl as described herein.

In some embodiments, the subject has rheumatoid arthritis (RA). RA is a chronic inflammatory disorder that affects joint linings causing painful swelling that

20 may eventually result in bone erosion and joint deformity. In addition to causing joint problems, RA can affect other organs of the body including the skin. For example, some RA patients experience rheumatoid nodules on the skin, vasculitis, rash, ulcers, blisters, and bumps. In addition, RA can also induce skin conditions including Pyoderma gangrenosum, Sweet's syndrome, erythema nodosum, lobe

25 panniculitis, atrophy of finger skin, palmar erythema, and diffuse thinning and skin fragility (often worsened by corticosteroid use). In various embodiments, the hypochlorous acid composition prevents, ameliorates and/or relieves skin symptoms associated with RA, while providing systemic anti-inflammatory benefits for RA patients.

30 In some embodiments, the subject has celiac disease. Celiac disease is an autoimmune disorder that occurs in genetically predisposed subjects who develop an immune reaction to eating gluten. Patients with celiac disease exhibit

gastrointestinal symptoms including diarrhea, abdominal pain, and cramping. In addition, celiac disease can also affect other organ systems such as the skin resulting in symptoms such as mouth ulcers or sores. About 15-25% of celiac disease patients also develop dermatitis herpetiformis which is manifested as an extremely itchy skin rash with bumps and blisters. In various embodiments, the hypochlorous acid composition prevents, ameliorates and/or relieves mouth ulcers, sores, and skin rash (when topically applied) associated with celiac disease as well as providing systemic benefits to the condition as a whole.

In some embodiments, the subject has Crohn's disease. Crohn's disease is a type of inflammatory bowel disease causing inflammation of the linings of the digestive tract. The inflammation caused by Crohn's disease often leads to severe abdominal pain, diarrhea, fatigue, weight loss, and malnutrition. Crohn's disease can also cause other complications outside of the gastrointestinal tract including the skin. For example, Crohn's disease can cause skin symptoms including mouth ulcers or sores, erythema nodosum manifested as raised red nodules on the skin, and pyoderma gangrenosum which causes painful ulcerating skin nodules. In various embodiments, administration of the hypochlorous acid composition prevents or ameliorates the dermatological symptoms associated with Crohn's disease and provides additional systemic benefits to other organs or tissues affected by the disease.

In some embodiments, the subject has ulcerative colitis. Similar to Crohn's disease, ulcerative colitis is also a type of inflammatory bowel disease. The disease causes inflammation and ulcers in the colon causing symptoms such as diarrhea. Additionally, ulcerative colitis can cause dermatological symptoms such as mouth ulcers or sores, erythema nodosum, and pyoderma gangrenosum. The hypochlorous acid composition (applied locally) in some embodiments prevents, ameliorates and/or relieves the mouth ulcers, sores, and painful or necrotic ulcers associated with ulcerative colitis, while providing systemic anti-inflammatory benefits. Thus, other tissues and organs affected in ulcerative colitis can benefit from cutaneous treatment with HOCl as described herein.

In some embodiments, the subject has vasculitis. Vasculitis is a condition that involves inflammation of the blood vessels, and can cause skin complications.

For example, patients with vasculitis often develop skin rash as well as skin hemorrhage or discoloration due to palpable purpura and livedo reticularis. In some embodiments, the hypochlorous acid composition prevents, ameliorates and/or relieves these skin symptoms while providing systemic anti-inflammatory benefits.

5 In some embodiments, the subject has thyroiditis, which is an inflammation of the thyroid gland. Thyroiditis can cause a variety of symptoms due to either hypothyroidism or hyperthyroidism. For example, thyroiditis often causes dry skin, which may be prevented or relieved by applying the hypochlorous acid composition. Application of the hypochlorous acid composition may also provide systemic effects
10 by providing relief to other tissues and organs affected by thyroiditis such as the eyes and muscles.

 In some embodiments, the subject has type I diabetes. Diabetes can affect every part of the body, including the skin, and many people with diabetes develop a skin disorder caused or affected by diabetes. In some cases, skin problems can be
15 the first sign that a person has diabetes. Some common skin conditions in people with diabetes include, acanthosis nigricans, skin rashes, bumps, or blisters, dry and/or itchy skin, diabetic dermopathy which can cause scaly patches on the skin, digital sclerosis, disseminated granuloma annulare, eruptive xanthomatosis, necrobiosis lipidica diabetorum, scleroderma diabetorum, and vitiligo. In
20 various embodiments, application of the hypochlorous acid composition prevents, ameliorates and/or relieves the various skin symptoms associated with diabetes as well as providing benefit to the other tissues or organs affected or caused by diabetes.

 In some embodiments, the subject has dermatomyositis. Dermatomyositis is an inflammatory disease marked by muscle weakness and a distinctive skin rash.
25 Patients with this disease often exhibit a red-purple scaly rash on the face and eyelids, and in areas around the nails, knuckles, elbows, knees, chest, and back. In various embodiments, applying the hypochlorous acid composition to the skin may prevent, ameliorate and/or relieve the rash associated with this disorder while providing systemic anti-inflammatory benefits. Thus, other tissues such as the
30 muscles affected in dermatomyositis can also benefit from treatment with HOCl as described herein.

The doses used for the above described purposes can be determined by a physician or other qualified medical personnel and can depend, for example, on the type of skin condition and underlying immune condition, the frequency of administration (i.e. for chronic or acute use), the severity of the condition, the age and overall health of the patient, the dosage form of the hypochlorous acid, and other factors. For example, in one non-limiting embodiment, the HOCl composition may be administered 1 to 10 times per day. In another embodiment, the composition is administered 1 to 4 times per day (e.g., about twice daily) to affected areas of the skin. The hydrogel composition described herein can be administered in these embodiments, and may be administered for a prolonged period as described.

In certain embodiments, the present invention relates to treating an ocular condition. The ocular condition may affect any portion of the eye or surrounding areas, such as the conjunctiva, uvea, eyelid, oil glands, and lacrimal ducts. Exemplary ocular conditions include: red eye; dry eye (including dry eye syndrome); conjunctivitis of bacterial, viral, or allergic origin; uveitis, blepharitis; external or internal hordeolum; canaliculitis; dacrocystitis; and chalazions.

The invention includes the treatment and prevention of ocular infections caused by a variety of pathogens, such as, for example, a bacterial agent, a viral agent, a parasitic agent, and/or a fungal agent. Non-limiting examples of bacterial agents include *Streptococcus spp.* (e.g. pneumoniae), *Staphylococcus spp.* (e.g., aureus), *Haemophilus spp.* (e.g., influenzae), *Pseudomonas spp.* (e.g., aeruginosa), *Chlamydia spp.* (e.g., trachomatis, psittaci, pecorum), *Neisseria spp.* (e.g. gonorrhoeae), and *Actinomyces* species. Non-limiting examples of viral agents include adenovirus, respiratory syncytial virus (RSV), influenza (including parainfluenza), coxsackie virus, rhinovirus, coronavirus, and herpes simplex virus. Non-limiting examples of fungal agents include *Candida* species, *Fusarium* species, and *Aspergillus* species. A non-limiting example of a parasitic agent is an eyeworm. Certain bacterial agents may be more common in certain patient subpopulations. For example, different strains of *Chlamydia psittaci* and *Chlamydia pecorum* cause significant eye infection in cats, lambs, goats, and guinea pigs. These infections are occasionally transmitted to humans. Further, eyeworms are common parasites of horses and cattle, goats, pigs, dogs and cats. Thus, the invention provides further

provides additional benefits in the farming industry where antibiotics and other active agents should be used sparingly.

These microbial agents may be involved in various ocular infections including blepharitis; hordeola, such as external hordeolum and internal hordeolum; 5 conjunctivitis, such as viral conjunctivitis or bacterial conjunctivitis, conjunctivitis in newborns (ophthalmia neonatorum) due to *Chlamydia trachomatis* or *Neisseria gonorrhoeae*, chlamydial disease in adults such as inclusion conjunctivitis and trachoma, or gonococcal conjunctivitis in adults; iridocyclitis and panophthalmitis caused by *Bacillus subtilis*; lacrimal system infections such as canaliculitis and 10 dacrocystitis; keratitis, such as viral keratitis (herpes simplex virus), bacterial keratitis and fungal keratitis (e.g., *Fusarium*), including among soft contact lens wearers; toxoplasmosis, including in dogs and cats; feline herpes virus, which is a common cause of eye and upper respiratory infections in cats; uveitis, including in large animals, such as cattle, caused by *Listeria*; and eye infections caused by avian 15 flu or other eye conditions and infections secondary to other medical conditions.

In certain embodiments, the ocular condition involves an inflammatory disorder or hypersensitivity reaction (including types I, II, III, and/or IV). For example, the ocular condition may involve an immediate-type hypersensitivity reaction such as allergic conjunctivitis. In other embodiments, the condition may 20 result from a blocked gland or chronic inflammatory condition, including styes and chalazions, which may also develop an acute bacterial infection. Such conditions may be recurring or may be difficult to completely clear. Other inflammatory ocular conditions that may or may not involve microbial infection include uveitis.

In some embodiments, the ocular condition (including but not limited to dry 25 eye) is associated with an underlying immunological condition. In these embodiments, the hypochlorous acid composition not only relieves the local ocular symptoms, but also dampens or positively alters the underlying systemic immunological condition, which is an autoimmune condition in some embodiments.

For example, in some embodiments, the subject may be afflicted with SLE 30 and exhibit ocular symptoms. These symptoms include, but are not limited to, dry eyes, scleritis (which is inflammation in the white scleral layer of the eye), retinal

vascular lesions, and skin lesions around the eye lids. SLE may also cause nerve damage to the eyes thus affecting eye movement and vision. In various embodiments, the hypochlorous acid solution prevents or ameliorates some or all of the local ocular symptoms associated with SLE, while providing systemic anti-inflammatory effects to benefit the other organs and systems affected with SLE.

In some embodiments, the present hypochlorous acid composition effectively treats the ocular symptoms associated with psoriasis. For example, uveitis and iritis are often complications of psoriasis. In addition, psoriatic patients may also present with flare-up around the eye resulting in scales and dryness around the eyelids. Hypochlorous acid solutions may be applied to the eye and surrounding regions to prevent or relieve these local inflammatory symptoms, while potentially providing systemic benefits.

In some embodiments, the hypochlorous acid composition is used to treat the ocular symptoms associated with rheumatoid arthritis (RA). In RA patients, inflammation may also cause damages to the eyes. For example, these patients may experience episcleritis and scleritis, which involve inflammation of the sclera. RA patients may also experience uveitis, which involves inflammation of the uvea. In addition, RA patients may present with keratoconjunctivitis sicca (also known as dry eyes syndrome), glaucoma, and/or cataracts. Further, some RA patients develop Sjögren's syndrome, which is a chronic, autoinflammatory condition causing extreme dryness to the eyes, nose, and mouth. In various embodiments, hypochlorous acid composition may be applied to the local region to prevent or relieve these symptoms as well as to ameliorate systemic symptoms.

In some embodiments, the subject has Crohn's disease. In various embodiments, the hypochlorous acid composition may be administered to treat or prevent the local ocular symptoms associated with Crohn's disease including for the treatment of uveitis, episcleritis, and scleritis, while potentially providing systemic improvement of the overall condition.

In some embodiments, the subject has ulcerative colitis. Patients with ulcerative colitis may also develop ocular symptoms including uveitis, iritis, and episcleritis. The hypochlorous acid composition may be applied locally to these

patients to prevent or ameliorate and/or relieve these ocular inflammatory symptoms, while providing systemic anti-inflammatory benefits.

In some embodiments, the subject has vasculitis. Vasculitis can affect many organs and tissues including the eye. For example, some patients with vasculitis
5 may experience inflammation of the eye which can cause reduced visual acuity and vision loss. In various embodiments, hypochlorous acid composition applied to the eye to prevent or relieve these symptoms while providing systemic effects to treat the underlying inflammatory condition.

In some embodiments, the subject has thyroiditis. In these patients, eye
10 symptoms often develop. For example, these patients may develop thyroid eye disease which is an eye condition in which the eye muscles and fatty tissue behind the eye become inflamed. This can cause the eyes to be pushed forward ('staring' or 'bulging' eyes) and the eyes and eyelids to become swollen and red. In some cases there is swelling and stiffness of the muscles that move the eyes so that the eyes are
15 no longer in line with each other; this can cause double vision. The hypochlorous acid composition of the invention may be used to prevent or relieve these local eye symptoms as well as additional systemic symptoms affecting other tissues or organs.

In some embodiments, the subject has allergic asthma, which is an inflammatory disorder triggered by allergens. During an asthmatic attack, the
20 subject's airways become inflamed, narrow, and swell, making it difficult to breathe. The subject may also experience itchy, glassy, or water eyes. In various embodiments, the hypochlorous acid composition may be applied to the eyes of these subjects to prevent or relieve local eyes symptoms in addition to mediating systemic anti-inflammatory effects, which can be observed in terms of less frequent
25 attacks, or attacks of reduced severity.

In some embodiments, the subject has type I diabetes. In some embodiments, the hypochlorous acid composition is used to treat diabetic eye disease. Diabetic eye disease refers to a group of eye conditions that affect people with diabetes. These conditions include diabetic retinopathy, diabetic macular edema (DME),
30 cataract, and glaucoma. All forms of diabetic eye disease have the potential to cause severe vision loss and blindness. Diabetic retinopathy involves changes to retinal

blood vessels that can cause them to bleed or leak fluid, thereby distorting vision. DME is a consequence of diabetic retinopathy that causes swelling in the area of the retina called the macula. Diabetes may also cause cataract, which is a clouding of the eye's lens, as well as glaucoma, which is associated with elevated pressure
5 inside the eye causing damage to the optic nerve. Application of the hypochlorous acid composition to the eye may prevent or relieve one or more symptoms of the diabetic eye disease as well as other systemic symptoms.

In some embodiments, the hypochlorous acid composition of the invention may be used to treat one or more ocular symptoms associated with dermatomyositis.
10 Subjects with dermatomyositis may be afflicted with local inflammation of the eyes, resulting in swollen or puffy eyes due to edema. The hypochlorous acid composition may be applied to the eyes to prevent or ameliorate these local eye symptoms while providing systemic anti-inflammatory benefits.

In some embodiments, the subject has conjunctivitis, commonly known as
15 pink eye. Conjunctivitis is an inflammation of the conjunctiva, the outer-most layer of the eye that covers the sclera. While many of the signs and symptoms of conjunctivitis are relatively non-specific, there are several etiologies that may be causative in a given case. The three most common causes of conjunctivitis are bacterial infection, viral infection, or an allergic reaction.

In some embodiments, the composition is applied to treat or prevent
20 blepharitis, chalazion, or hordeola. Blepharitis is an inflammation of the eyelid margins, and is usually caused by an infection of *Staphylococcus aureus*. Blepharitis can lead to a chalazion, or lead to a sty (hordeolum). A chalazion is a cyst in the eyelid caused by inflammation of a blocked meibomian gland, usually on
25 the upper eyelid. A chalazion may spawn bacterial infection. When the condition does not resolve on its own, a chalazion may be injected with corticosteroid or be surgically removed. Hordeola include both external hordeolum, or "stye", and internal hordeolum (acute meibomianitis). Styes are lesions at the base of the eyelashes and are predominantly caused by infection of *Staphylococcus aureus*.

30 In some embodiments, the composition is applied to treat or prevent infection and/or inflammation of the lacrimal system, such as canaliculitis and

dacrocystitis. Canaliculitis can be caused by *Actinomyces* infection. Dacrocystitis is often due to streptococci or *Staphylococcus aureus*.

In certain embodiments, the ocular condition is prevention of infection and/or inflammation resulting from an eye surgery or trauma to the eye.

5 In certain other embodiments, the hypochlorous acid composition is administered prophylactically, especially where eye infections are likely to occur or be transmitted among persons. Thus, in this embodiment, the invention involves administering the hypochlorous acid before an infection and/or inflammation develops. Such prophylactic care might include routine cleaning of the eyes and
10 surrounding areas, such as the eyelids, with the hypochlorous acid, or routine rinsing of contact lenses by applying the hypochlorous acid to the contact lenses to decontaminate and clear debris and biofilm. Such embodiments can result in the prevention of an ocular infection, can prevent the worsening of an existing ocular infection caused by contaminated lenses, or can prevent irritation of the eyes caused
15 by bacterial biofilm. In other embodiments, the invention involves administering hypochlorous acid to the environment via fogging, misting, or humidifying, to prevent the transfer of pathogens from air droplets into the eyes of susceptible individuals.

In certain embodiments, the ocular condition may result from an acute or
20 chronic inflammatory condition, which may develop an acute infection. In these embodiments, the hypochlorous acid is administered to treat both the infection and the underlying inflammation. Thus, the hypochlorous acid may be administered instead of steroidal drops or systemic steroidal medications, or antibiotics, thereby avoiding the potential adverse reactions of such treatments. In certain other
25 embodiments, the hypochlorous acid composition is administered to clean the region during the duration of steroidal and/or antibiotic treatment. In one embodiment, hypochlorous acid is administered to the eye of a patient inflicted with uveitis, during the duration of steroid treatment. For example, the hypochlorous acid may be used in conjunction with glucocorticoid steroids, either as topical eye drops (such
30 as betamethasone, dexamethasone or prednisolone) or oral therapy with prednisolone tablets. Likewise, when the condition has an allergic origin, such as allergic conjunctivitis, the hypochlorous acid may be used alongside an

antihistamine to more effectively inhibit release of inflammatory mediators from mast cells.

In certain embodiments, the hypochlorous acid solution may be administered to two or more sites in the ocular system of a patient. For example, the
5 hypochlorous acid may be administered as drops to the eye or eye wash, and as a cleanser for the eye lids and/or eyelid margins.

The hypochlorous acid and compositions of the present invention may be administered in any appropriate dosage form such as a liquid, aerosol, gas, or semi-solid including a solution, suspension, viscous or semi-viscous gel, ointment, cream,
10 or other types of compositions. Preferably, the solution is administered topically either dropwise into the eye or to the tissue surrounding the eye. The solution or composition comprising the solution can also be formulated into a sterile solution for administration by intracameral injection into the anterior chamber of the eye or directly into the trabecular meshwork of the eye (e.g., for the treatment of dry or wet
15 AMD). The doses used for the above described purposes can be determined by a physician or other qualified medical personnel and can depend, for example, on the type of ocular condition, the frequency and/or duration of treatment (i.e. for chronic or acute use), the severity of the condition, the age and overall health of the patient, the dosage form of the hypochlorous acid, and other factors. For example, when
20 applying as drops to the eyes, in one non-limiting embodiment, 1 to 2 drops of an HOCl solution is administered 1 to 10 times per day. In another embodiment, the solution (e.g., about 1 or 2 drops per eye) is administered 1 to 4 times per day (e.g., about twice daily). This regimen may be employed for a prolonged period of time, as described.

25 The present invention provides treatments as well as preventive care for conditions characterized by inflammation of the ears (including the outer ear, middle ear, and inner ear), nose (including sinus care), mouth, and throat. Exemplary conditions include: rhinitis, rhinorrhea, nasal congestion, otitis media, external otitis, pharyngitis, and stomatitis, and may be present in a human or animal patient. The
30 present invention further provides preventive care for such conditions, especially where such conditions are recurring, such as recurring ear infection, sinus infection, sore throat, or mouth ulcer.

In various embodiments, the present invention provides sinus/nasal treatments for subjects with an inflammatory condition. In various embodiments, administration of the hypochlorous acid compositions ameliorates and relieves the local sinus and nasal symptoms while providing systemic anti-inflammatory benefits.

5 In some embodiments, the present invention provides relief of local sinus and nasal symptoms in a subject with systemic lupus erythematosus. In such embodiments, the hypochlorous acid composition may be administered to the subject to prevent or provide relief for nasal ulcers or nasal sores. In various
10 embodiments, application of the hypochlorous acid composition also dampens or alters systemic inflammation in the subject.

In some embodiments, the composition is used to treat subjects with psoriasis. Psoriatic patients may develop scales inside their nose which can be prevented or ameliorated by applying the hypochlorous acid composition.

15 In some embodiments, the composition is used to treat subjects with rheumatoid arthritis. For example, the composition may be applied to a RA subject to prevent or provide local relief to the excessive dry nose in those RA subjects that secondarily develops due to Sjögren's syndrome.

20 In some embodiments, the hypochlorous acid composition is administered to a subject with vasculitis. For example, the composition may be applied to the nose to prevent or provide relief for nose bleeds.

25 In some embodiments, the composition is used to treat a subject with allergic asthma. For example, the composition may be applied to the nose or sinuses to prevent or provide relief for congestion. In various embodiments, administration of the hypochlorous acid composition not only treats these nasal symptoms, but also provides systemic benefits to other tissues and organs.

30 In some embodiments, the hypochlorous acid composition is used to treat sinusitis and/or sinus infections in a subject afflicted with diabetes such as type 1 diabetes. In various embodiments, administration of the hypochlorous acid composition prevents or ameliorates the local sinus inflammation as well as any systemic inflammation in these subjects.

In some embodiments, the composition is applied to treat or prevent rhinitis, rhinorrhea, or nasal congestion. Rhinitis, an inflammation of the nasal mucous membrane, may produce nasal decongestion and rhinorrhea. Rhinitis is typically of viral origin, but may involve secondary bacterial infection. Rhinorrhea and nasal
5 congestion are typically of viral or allergic origin. In certain instances, congestion is observed as an after-effect of topical decongestants (rhinitis medicamentosa). While topical or oral decongestants (e.g., pseudoephedrine) can prevent or provide some symptomatic relief, prolonged use is not recommended.

In some embodiments, the present hypochlorous acid composition is
10 administered to treat the ear symptoms associated with various inflammatory conditions. Administration of the composition can prevent and ameliorate the local symptoms in the ear and provide systemic anti-inflammatory benefits.

For example, in some embodiments, the hypochlorous acid composition is administered to a subject with systemic lupus erythematosus. SLE subjects may
15 present local inflammation in the ear passages leading to ringing the ears due to, for example, peripheral nerve damage. Administration of the composition prevents or provides relief to these local ear symptoms as well as other systemic symptoms affecting other tissues and organs. In some embodiments, the composition is administered to treat the ear symptoms of subjects with psoriasis. Psoriatic patients
20 may develop scales that build up in the ear passages. The composition may be applied to these patients to prevent or ameliorate scale build up.

In some embodiments, the composition is administered to treat or prevent otitis media or external otitis. Otitis media, inflammation of the middle ear structures, can lead to loss of equilibrium and deafness. Otitis media is generally of
25 bacterial or viral origin. Viral infections may spawn secondary bacterial infections, including infections of *Streptococcus pneumonia*, *Moraxella catarrhalis*, and non-typable *Haemophilus influenzae*. External otitis is an acute or chronic inflammation of the external ear canal, and may involve bacterial (e.g., *Pseudomonas aeruginosa*, *Proteus vulgaris*, and *Staphylococcus aureus*) or fungal (e.g., *Aspergillus* and
30 *Candida*) infection.

In still other embodiments, the composition is administered to treat or prevent pharyngitis (sore throat) or stomatitis. Pharyngitis is characterized by pain and swelling in the posterior pharynx. Pharyngitis is commonly caused by bacterial (e.g., Streptococcal) or viral infection. Stomatitis is a painful ulcer or inflammation of the oral mucosa. Stomatitis may be caused, for example, by infection (bacterial, viral, or fungal), chemical irritant, or allergic reaction, and may be common for patients having Xerostomia. Some common infectious agents include herpes simplex virus, varicella zoster, Epstein-Barr virus, influenza, cytomegalovirus, Gonorrhea, and Candida.

10 In certain embodiments, the condition may involve a bacterial infection that produces a discharge, for example, external otitis or otorrhea. In these embodiments, the hypochlorous acid effectively cleans discharge, biofilm, or debris from the ear in a manner that reduces the risk of spreading infection.

In addition to the skin, ear, nose, mouth, and/or throat, many inflammatory conditions affect other organs and tissues as well. For example, as expected in a multisystem disease, the entire pulmonary system is vulnerable to injury. The pulmonary manifestations are diverse, affecting all anatomic locations of the respiratory tract (*i.e.*, airways, alveoli, blood vessels, and pleura). In various embodiments, administration of the hypochlorous acid composition of the invention provides local as well as systemic anti-inflammatory benefits to various tissues and organs including the lungs.

In some embodiments, the composition may be used to treat or prevent the pulmonary symptoms associated with systemic lupus erythematosus. Pulmonary involvement is frequent in SLE, and can affect the pleura, pulmonary vasculature, and parenchyma. In various embodiments, the composition may be used to prevent or treat one or more of, pleuritis, unilateral or bilateral pleural effusion, pulmonary hemorrhage, pulmonary emboli, pulmonary fibrosis, lupus pneumonitis, interstitial lung disease, pulmonary hypertension, and shrinking lung syndrome associated with SLE.

30 In some embodiments, the composition may be used to treat or prevent local pulmonary symptoms in patients with rheumatoid arthritis. Lung disease is a

leading cause of death in RA, second only to infection. Pulmonary complications of RA include pleural effusion, nodular lung disease, diffuse interstitial fibrosis, pulmonary vasculitis, alveolar hemorrhage, obstructive pulmonary disease, pulmonary hypertension, interstitial lung disease, pulmonary arteritis, and infections.

- 5 In various embodiments, administration of the hypochlorous acid composition may prevent, ameliorate, or relieve one or more of these pulmonary symptoms associated with RA.

In some embodiments, the composition may be used to prevent or treat the pulmonary symptoms of a subject with Crohn's disease or ulcerative colitis.

- 10 Pulmonary complications of these disorders include inflammation of small and large airways, pulmonary parenchymal disease, serositis, and pulmonary embolism. In various embodiments, methods of the invention prevent or ameliorate one or more of these symptoms.

In some embodiments, the hypochlorous acid composition is used to treat a subject with allergic asthma, including severe and/or uncontrolled asthma. Asthma is a chronic condition characterized by inflammation of the air passage that results in a temporary narrowing of the airways. This results in asthmatic symptoms including coughing, wheezing, shortness of breath, fast breathing, and tightening of the chest. The hypochlorous acid composition can provide relief to one or more of these symptoms while reducing inflammation systemically. In some embodiments, the severity and/or frequency of attacks is reduced.

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Pulmonary delivery of the HOCl composition can be conducted by nebulizer, for example. For example, in one non-limiting embodiment, the HOCl composition may be administered 1 to 4 times per day. In another embodiment, the composition is administered 1 or 2 times per day.

Many immune conditions also affect muscles and joints resulting in muscle and joint pain and swelling. In various embodiments, administration of the hypochlorous acid composition, for example, topically, relieves one or more of these musculoskeletal symptoms and provides systemic anti-inflammatory benefits.

- 30 In some embodiments, the composition treats musculoskeletal symptoms in a subject with systemic lupus erythematosus. Involvement of the musculoskeletal

system is very common in patients with SLE. Arthralgia, arthritis (pain with or without swelling), osteonecrosis (avascular necrosis of bone), and myopathy are the principal manifestations. In various embodiments, the composition of the invention prevents or treats the local musculoskeletal symptoms while providing systemic
5 anti-inflammatory effects.

In some embodiments, the subject is a psoriatic patient who has developed psoriatic arthritis. There are several types of psoriatic arthritis depending on the joints being affected. Symmetric psoriatic arthritis affects several joints in pairs on both sides of the body and can be disabling. Asymmetric psoriatic arthritis typically
10 affects only a few joints. Distal interphalangeal predominant (DIP) psoriatic arthritis mainly affects small joints at the ends of the fingers and toes, as well as the nails. Spondylitis affects the backbone and can cause inflammation and stiffness between the vertebrae, including the bones of the neck, spine, lower back, and pelvis. Arthritis mutilans is the most severe and destructive form of psoriatic arthritis and
15 often results in deformity of the fingers and toes. Administration of the hypochlorous acid composition can prevent or treat one or more forms of psoriatic arthritis by relieving local as well as systemic inflammatory symptoms.

In some embodiments, the composition effectively prevents or treats one or more symptoms of rheumatoid arthritis. Such symptoms include local inflammation
20 of the synovial membrane causing the affected joints to become swollen, warm, painful, and stiff. Inflammation is mostly associated with small joints of the hands, feet, and cervical spine, but larger joints like the shoulder and knees can also be involved. In various embodiments, the hypochlorous acid composition effectively prevents or ameliorates the local and systemic inflammatory symptoms of RA. In
25 some embodiments, the hypochlorous acid composition (gel or lotion) is applied at least once per day (e.g., 1 to 4 times per day) to the hands and/or feet of a patient with RA, thereby slowing progression of RA, relieving RA symptoms, and/or reducing inflammation in the joints of the hands and feet.

In some embodiments, the composition is administered to prevent or relieve
30 the musculoskeletal symptoms of subjects with Crohn's disease or ulcerative colitis. In an embodiment, the composition is administered to provide relief to arthritis in these subjects. In another embodiment, the composition is administered to prevent

or treat spondyloarthritis, which is a type of arthritis that attacks the spine and sometimes the joints of the arms and legs.

In some embodiments, the composition is administered to prevent or treat one or more musculoskeletal symptoms in subjects afflicted with vaculitis. For example, the composition may be administered to prevent or treat one or more of myalgia or myositis, arthralgia or arthritis.

In some embodiments, the composition is administered to prevent or treat the musculoskeletal complications associated with diabetes such as type I diabetes. Diabetic patients may experience localized inflammation of the nerves and joints resulting in conditions such as stiff hands syndrome, carpal tunnel syndrome, adhesive capsulitis of the shoulder, trigger finger, neuropathic joints, peripheral neuropathy, and reflex sympathetic dystrophy syndrome. Administration of the hypochlorous acid composition may provide prevent or relief to one or more of these symptoms while providing systemic anti-inflammatory effects.

In certain embodiments, the condition may result from an acute or chronic immune condition such as an autoimmune condition, which may develop an acute infection. In these embodiments, the hypochlorous acid is administered to prevent or treat both the infection and the underlying immune condition. Thus, the hypochlorous acid may be administered instead of steroidal drops or systemic steroidal medications, or antibiotics, thereby avoiding the potential adverse reactions of such treatments. In certain other embodiments, the hypochlorous acid is used to clean the region during the duration of steroidal and/or antibiotic treatment. In one embodiment, hypochlorous acid is administered to the nasal passages and/or sinuses of an allergic patient, during the duration of steroid treatment. For example, the hypochlorous acid may be used in conjunction with steroid treatment, or alongside an antihistamine to more effectively inhibit release of inflammatory mediators from mast cells.

EXAMPLES

Evaluation of Inflammation Reduction

In an investigator – blinded, randomized study, hypochlorous acid composition in the form of gel was evaluated for reduction of inflammation, by means of itching reduction. 30 subjects aged 12 to 75 years old with mild to moderate atopic dermatitis participated over a period of 3 days. The patients, 20 subjects, treated with hypochlorous acid composition, ≤ 450 ppm AFC, were compared to 10 untreated control subjects. The evaluation included an assessment of tolerability by investigator and participant.

Overall irritation, stinging, burning and itching on a 5-point ordinal scale were evaluated on day 1 (baseline visit), day 2 and day 3. Investigator assessment was calculated as the mean of 5-point scale for erythema, desquamation, lichenification, overall irritation, and excoriation. Subject queries were based on stinging, burning and itching at day 1, day 2, and day 3. Incidence of all adverse events, including serious adverse events, local skin reaction, and adverse events leading to discontinuation, were documented.

Treatment with the HOCl composition effectively reduced itch in subjects with mild to moderate atopic dermatitis as early as day 1.

The HOCl treatment group had significantly reduced itch compared with the Untreated group at Day 3 ($p=0.007$).

Treatment with the HOCl composition at least BID was very well tolerated, and there were no serious adverse events and no treatment-related discontinuations.

Case Study Evaluation of Inflammation Reduction

An evaluation of inflammation reduction by means of itching reduction and skin quality improvement was conducted on a 4 year old male treated with HOCl gel. The patient had eczema of the palmar aspect of the patient's hands and plantar aspect of the feet. The patient experienced severe itching, severe erythema (beet redness) to eschar formation, cracking, yellow plaques/ hardening of skin and peeling of the skin over the course of two months. As a first line of therapy, the patient was prescribed Hydrocortisone Valerate Ointment USP, 0.2%, a topical

corticosteroid twice daily to the affected areas. After 4 weeks of treatment twice daily with corticosteroids, the patient had no resolution of symptoms.

The patient was taken off the topical corticosteroid and instead treated with hypochlorous acid composition ≤ 450 ppm AFC, twice daily to the affected areas.

- 5 Treatment with HOCl composition effectively reduced symptoms in a subject with moderate eczema as early as Day 1.

At both Day 1 and Day 3, the patient exhibited marked reduction of symptoms including: reduction of itch, reduction of erythema (reduction of redness), skin wound healing (reduction of cracks), softening of plaques and movement
10 towards normal skin color, and reduction of peeling.

Treatment with HOCl composition at least BID was very well tolerated.

The patient went on to complete resolution of all symptoms over the course of two weeks BID treatment.

- There were no serious adverse events and no treatment related
15 discontinuations.

The patient and guardian reported increased “ease-of-use” with the HOCl composition in form of gel vs treatment with corticosteroids, as there were no warnings regarding getting the product in/or near the eyes, nose or mouth, which is difficult when the product must be applied to the hands and fingers.

20 Reduction in hyperemia in an animal model

- HOCl solution was studied for topical treatment of redness and itching associated with allergic conjunctivitis in systemic sensitization model. In this model, a systemic sensitization with an allergen (Short Ragweed, SRW) was followed by topical challenge with the same allergen. The objective of this study was to evaluate
25 the effectiveness of three hypochlorous acid formulations in reducing the signs and symptoms associated with ocular allergic conjunctivitis.

The results of this study indicate the hypochlorous acid was able to reduce hyperemia in this model of allergic conjunctivitis in a dose dependent manner. The

500 ppm and 1000 ppm hypochlorous acid significantly reduced redness in the eyes of balb/c mice similar to that of a steroid (prednisolone, 1%). The controls in this study worked as they should, with the vehicle control producing a high amount of hyperemia post challenge and the prednisolone group maintaining low redness scores throughout all challenges. As expected, the mast cell stabilizer group (olopatadine) was able to significantly reduce hyperemia after the first challenge, but loses efficacy over time. The high concentration hypochlorous acid groups were able to significantly reduce hyperemia throughout the entire challenge process, whereas the lowest concentration of 100 ppm could not reduce redness.

10 Efficacy of Hypochlorous Acid (HOCl) hydrogel on imiquimod (IMQ)-induced psoriasis-like skin inflammation mouse model

A study was conducted to determine the efficacy of HOCl hydrogel, containing 1000 parts per million (ppm) of free available chlorine, on a mouse model of psoriasis. Psoriasis was induced by the application of IMQ cream to the shaved backs of BALB/c mice. Animals treated with IMQ developed clinical signs of psoriasis such as erythema and plaques on affected areas. Application of HOCl hydrogel reduced the clinical symptoms of psoriasis more significantly than an untreated control and animals treated with clobetasol (corticosteroid). Results indicated that treatment with HOCl hydrogel reduced clinical symptoms of psoriasis in a mouse model.

Psoriasis-like skin inflammation was induced by daily application of 31.25 mg of imiquimod (IMQ) on the shaved back of BALB/c mice (Harlan Laboratories). IMQ cream is used to treat several skin conditions such as warts and basal cell carcinoma. Application of IMQ to the healthy skin of mice has been demonstrated to result in clinical symptoms of psoriasis and is therefore used as a model to determine efficacy of topical treatment.

The study was conducted over the course of 10 days and consisted of four treatment groups: naïve (untreated), animals treated with IMQ only, clobetasol treated, and HOCl hydrogel treated. IMQ cream was applied each day at 4 PM to the backs of each mouse in the 3 treated groups. The clobetasol group was treated at 2 PM daily with 50 mg of clobetasol. The HOCl hydrogel group was dosed twice

daily (10 AM and 3 PM) with 200 mg on the back of each animal. Psoriasis clinical scores were determined daily by visual inspection. Treatments were compared to naïve animals as a negative control.

5 Treatment with HOCl-hydrogel and clobetasol cream resulted in significantly reduced clinical scores compared to animals receiving IMQ only (FIG. 2). The reduction in clinical scores were significant at the $p=0.01$ level. In addition, the clinical scores of HOCl-treated animals were lower than those treated with clobetasol from day 4 of the study onward through day 10. Collectively, these results demonstrate that HOCl-hydrogel containing 1000 ppm of free available
10 chlorine was able to significantly reduce the clinical symptoms of psoriasis in a mouse model.

Modifications of the disclosed embodiments incorporating the spirit and substance of the invention may occur to persons skilled in the art and such modifications are within the scope of the present invention. All references cited
15 herein are incorporated by reference in their entirety.

CLAIMS:

1. A method for treating or preventing inflammation local inflammatory symptoms in a patient having an underlying immunological or inflammatory disorder, the method comprising: administering a hypochlorous acid composition to an area affected by local inflammation, wherein the hypochlorous acid composition has from 100 to 5000 ppm of available free chlorine.
2. The method of claim 1, wherein the immunological disorder is characterized by one or more of type I hypersensitivity, type II hypersensitivity, type III hypersensitivity, and type IV hypersensitivity.
3. The method of claim 1, wherein the underlying immunological disorder is an autoimmune condition.
4. The method of any one of claims 1 to 3, wherein the underlying immunological condition is systemic lupus erythematosus, psoriasis, atopic dermatitis, rheumatoid arthritis, celiac disease, Crohn's disease, ulcerative colitis, vasculitis, thyroiditis, severe asthma, diabetes mellitus, hyper immunoglobulin E syndrome, dermatomyositis, or multiple sclerosis.
5. The method of any one of claims 1 to 3, wherein the underlying immunological or inflammatory disorder is eosinophilia, drug allergy, food allergy, hemolytic anemia, myasthenia gravis, systemic vasculitis, diabetes mellitus, multiple sclerosis (MS), fibromyalgia, myelitis, peripheral neuropathy, Parkinson's Disease, hepatitis, renal failure, pancreatitis, thyroiditis, graft versus host disease, chronic transplant rejection, Hidradenitis suppurativa, adult onset Still's disease, systemic onset juvenile idiopathic arthritis (SJIA) Schnitzler syndrome, Behcet's disease, SAPHO syndrome, macrophage activation syndrome, Familial Mediterranean Fever (FMF), cryopyrin-associated periodic syndrome (CAPS), TNF receptor associated periodic syndrome (TRAPS), Hyper-IgD syndrome, periodic fever, aphthous stomatitis, pharyngitis and adenitis (PFAPA), deficiency of interleukin-1 (IL-1) receptor antagonist (DIRA), Giant cell arteritis, amyloidosis, recurrent pericarditis, neuromyelitis optica, amyotrophic lateral sclerosis, gout, glomerulonephritis, myeloma, Netherton Syndrome, Ichthyosis, and Epidermolysis Bullosa.

6. The method of any one of claims 1 to 5, wherein the local inflammatory symptoms include one or more of conjunctivitis, dry eye, ocular itch, uveitis, wet or dry AMD, sinusitis, rhinorrhea or nasal congestion, stomatitis, pharyngitis, gingivitis, xerostomia, airway hyper responsiveness, skin or mucosal sores or ulcers, urticaria, blisters and/or skin rash or lesions.
7. The method of any one of claims 1 to 6, wherein the local inflammatory symptoms affect one or more of skin, eyes, nose, sinus cavity, ears, mouth or throat.
8. The method of any one of claims 1 to 6, wherein the local inflammatory symptoms affect one or more of skin, colon, lungs, urinary tract, vagina, skeletal muscle, ligaments, tendons, joint space, bone, peritoneum, kidney, liver, pancreas, and vasculature.
9. The method of any one of claims 1 to 8, wherein the hypochlorous acid composition is administered from 1 to 10 times per day.
10. The method of claim 9, wherein the hypochlorous acid composition is administered from 1 to 4 times per day.
11. A method for treating an immunological or inflammatory disorder, comprising, administering a hypochlorous acid composition to the patient, the immunological or inflammatory disorder being selected from: eosinophilia, drug allergy, food allergy, hemolytic anemia, angioedema, myasthenia gravis, Grave's Disease, Goodpasture's Syndrome, Farmer's Lung, asthma, chronic obstructive pulmonary disease (COPD), idiopathic pulmonary fibrosis (IPF), cystic fibrosis, systemic vasculitis, diabetes mellitus, multiple sclerosis (MS), myelitis, peripheral neuropathy, Parkinson's Disease, hepatitis, osteomyelitis, renal failure, pancreatitis, thyroiditis, graft versus host disease, chronic transplant rejection, Hidradenitis suppurativa, adult onset Still's disease, systemic onset juvenile idiopathic arthritis (SJIA) Schnitzler syndrome, Behcet's disease, SAPHO syndrome, macrophage activation syndrome, Familial Mediterranean Fever (FMF), cryopyrin-associated periodic syndrome (CAPS), TNF receptor associated periodic syndrome (TRAPS), Hyper-IgD syndrome, Hyper-IgE syndrome, periodic fever, aphthous stomatitis, pharyngitis and adenitis (PFAPA), deficiency of interleukin-1 (IL-1) receptor antagonist (DIRA), Giant cell arteritis, amyloidosis, recurrent pericarditis,

neuromyelitis optica, amyotrophic lateral sclerosis, gout, glomerulonephritis, Netherton Syndrome, Ichthyosis, Epidermylosis Bullosa, or myeloma.

12. The method of claim 11, wherein a hypochlorous acid composition is administered to one or more of skin, colon, lungs, urinary tract, vagina, skeletal muscle, ligaments, tendons, joints or joint space, bone, peritoneum, kidney, liver, pancreas, and vasculature.

13. The method of claim 11, wherein the hypochlorous acid composition is administered to the skin, eyes, nasal passages, or by injection.

14. A method for treating a condition selected from allergic asthma, occupational asthma, bronchitis, chronic obstructive pulmonary disease (COPD), idiopathic pulmonary fibrosis (IPF), cystic fibrosis, Goodpasture Syndrome, or Farmer's Lung; comprising, administering a hypochlorous acid composition to the lungs, the hypochlorous acid composition having from 100 to 5000 ppm of available free chlorine.

15. A method for treating a condition selected from contact dermatitis, radiation dermatitis, ageing skin, sunburn, angioedema, urticaria, Systemic lupus erythematosus, sarcoidosis, rosacea, dermatitis herpetiformis, Netherton Syndrome, Ichthyosis, Epidermylosis Bullosa, or cutaneous vasculitis, and hemorrhoids; wherein the hypochlorous acid composition is administered to affected portions of the skin as a hydrogel having from 100 to 5000 ppm of available free chlorine.

16. A method for treating a patient having cancer, comprising, administering a hypochlorous acid composition to the patient, wherein the hypochlorous acid composition has from 100 to 5000 ppm of available free chlorine.

17. The method of claim 16, wherein the hypochlorous acid composition slows
5 or inhibits the progression or metastasis of the cancer.

18. The method of claim 16 or 17, wherein the hypochlorous acid composition reduces damage to, or lesions in, one or more of mucosa, skin, and gastrointestinal tract, which results from one or more or of chemotherapy or radiation therapy.

19. The method of any one of claims 16 to 18, wherein the cancer is stage I or stage II cancer.
20. The method of any one of claims 16 to 18, wherein the cancer is stage III or stage IV.
- 5 21. The method of any one of claims 16 to 20, wherein the cancer is basal cell carcinoma, biliary tract cancer, bladder cancer, bone cancer, brain and central nervous system cancer, breast cancer, cancer of the peritoneum, cervical cancer, choriocarcinoma, colon and rectum cancer, connective tissue cancer, cancer of the digestive system, endometrial cancer, esophageal cancer, eye cancer, cancer of the
10 head and neck, gastric or intestinal cancer, glioblastoma, hepatic carcinoma, hepatoma, intra-epithelial neoplasm, kidney or renal cancer, larynx cancer, leukemia, liver cancer, lung cancer, melanoma, myeloma, neuroblastoma, oral cavity cancer, ovarian cancer, pancreatic cancer, prostate cancer, retinoblastoma, rhabdomyosarcoma, rectal cancer, salivary gland carcinoma, sarcoma, skin cancer,
15 squamous cell cancer, testicular cancer, thyroid cancer, uterine or endometrial cancer, cancer of the urinary system, vulval cancer, and lymphoma.
22. The method of any one of claims 16 to 20, wherein the cancer is skin cancer, cutaneous melanoma, breast cancer, colon cancer, lung cancer, testicular cancer, cervical cancer, lymphoma, parathyroid cancer, penile cancer, rectal cancer, small
20 intestine cancer, thyroid cancer, uterine cancer, Hodgkin's lymphoma, lip and oral cancer, leukemia or multiple myeloma.
23. The method of claim 22, wherein the cancer is a cutaneous cancer.
24. The method of claim 22, wherein the cancer is breast cancer.
25. The method of claim 22, wherein the cancer is a cancer of the mouth, throat,
25 or sinus.
26. The method of claim 22, wherein the cancer is lung cancer.
27. The method of any one of claims 16 to 26, wherein the hypochlorous acid is administered for at least about 2 months.

28. The method of any one of claims 16 to 27, wherein the hypochlorous acid composition is administered directly to a tumor.
29. The method of any one of claims 16 to 27, wherein the hypochlorous acid composition is administered topically.
- 5 30. A method for normalizing the microbial flora in a patient with an inflammatory condition, comprising administering a hypochlorous acid composition to the patient, wherein the hypochlorous acid composition has from 100 to 5000 ppm of available free chlorine.
- 10 31. The method of claim 30, wherein the hypochlorous acid composition is applied at least once per day for at least one week, or optionally at least one month.
32. The method of claim 30, wherein normalization of the microbial flora of a tissue is determined by rRNA gene sequencing.
- 15 33. The method of any one of claims 30 to 32, wherein the hypochlorous acid composition is applied to the skin, oral or nasal mucosa, gastrointestinal tract, or urogenital system.

FIGURE 1

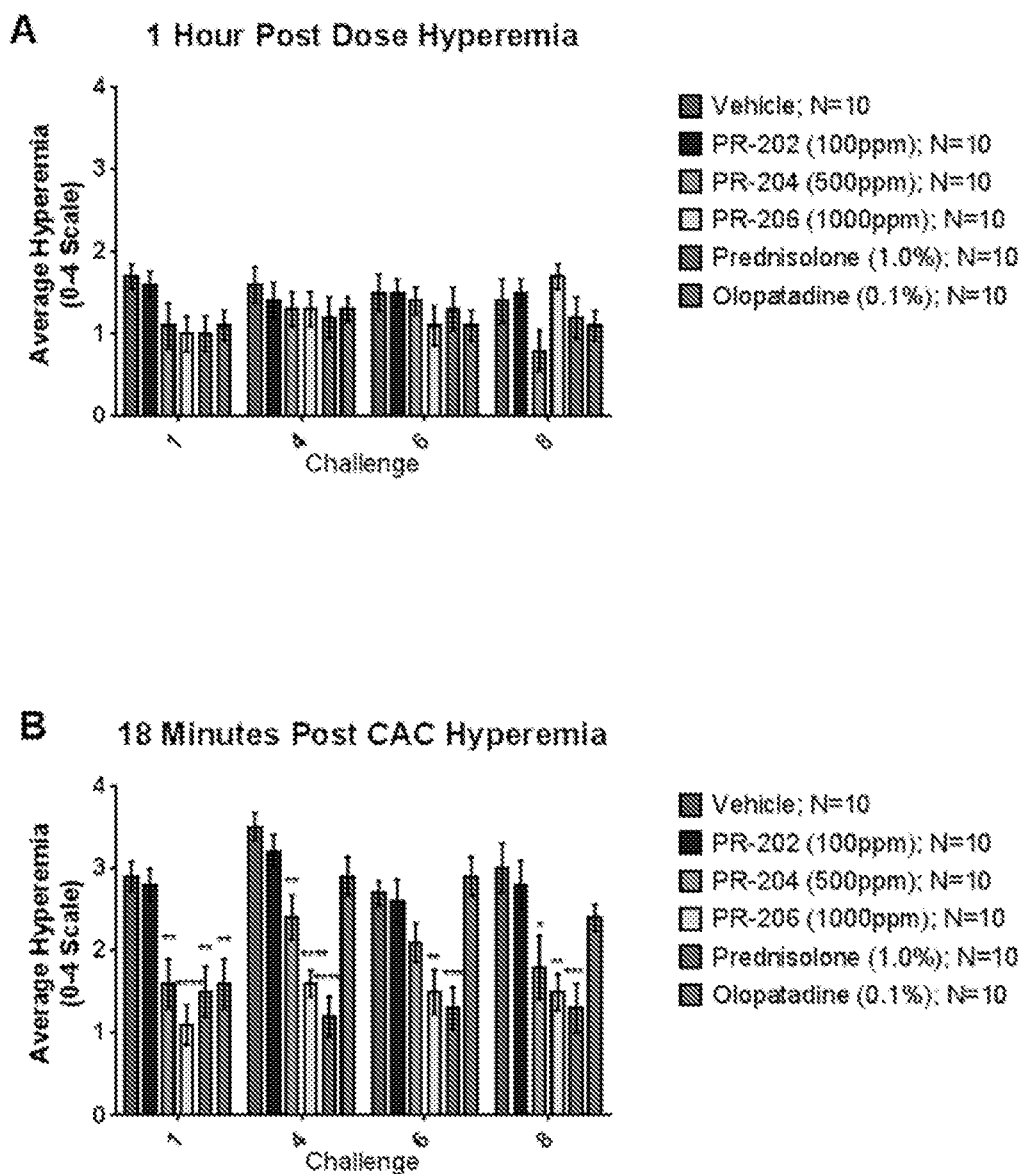
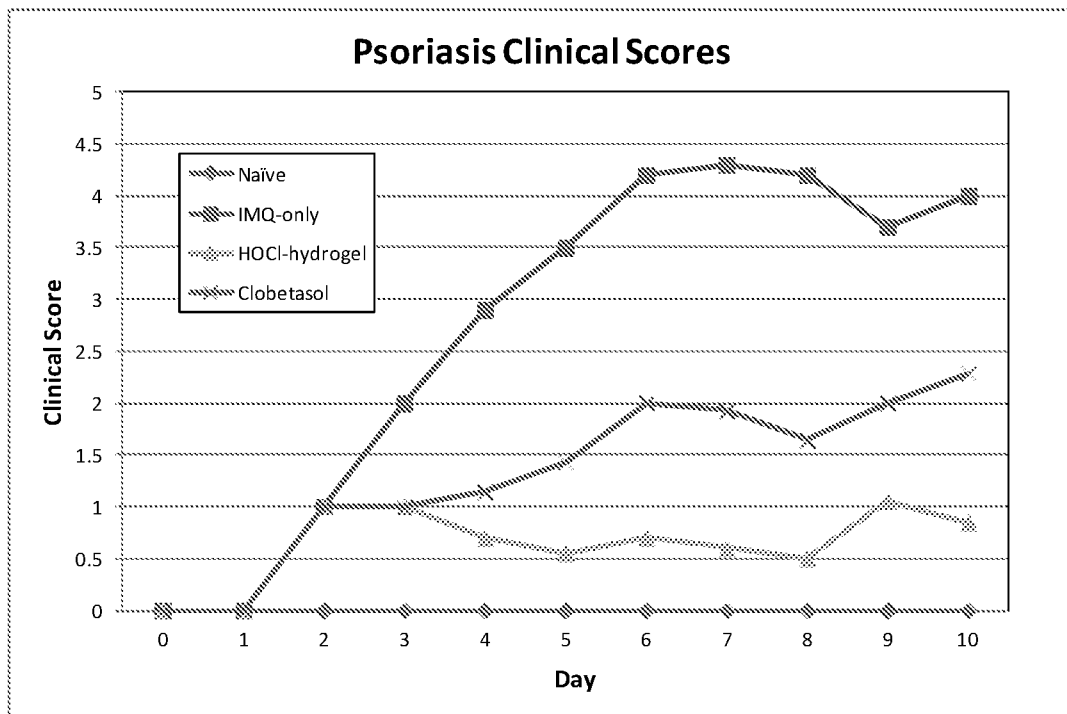


FIGURE 2



INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 16/24453

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61K 33/20 (2016.01)

CPC - A61K33/20; A61K8/21; A61K9/08

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

CPC: A61K33/20; A61K8/21; A61K9/08

IPC(8): A61K 33/20 (2016.01)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC: 424/661; 604/290 (See Search Words Below)

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

PATBASE: Full-text = AU BE BR CA CH CN DE DK EP ES FI FR GB IN JP KR SE TH TW US WO

Google: Patents/Scholar: orp hydrogel chlorine hypochlorous inflammatory condition skin lungs hepatitis allergy hypersensitivity tissue cancer metastasis autoimmune dermatitis arthritis microbial flora rRNA gene sequencing mucosa asthma

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	US 2012/0251631 A1 (ALIMI et.al.) 04 October 2012 (04.10.2012) para [0010];[0011];[0035];[0038];[0040];[0041];[0047];[0049];[0055];[0064];[0105];[0108];[0148];[0197] [0198]	1-5;11-14; 16-18 ----- 15; 30-33
Y	US 6,333,054 B1 (ROGOZINSKI) 25 December 2001 (25.12.2001) Col 3, ln 3-8; Col 4, ln 22-28	15
Y	US 2009/0305267 A1 (KRAUSE et.al.) 10 December 2009 (10.12.2009) para [0004];[0030]; [0070];[0088];[0089]	30-33

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

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

22 May 2016 (22.05.2016)

Date of mailing of the international search report

30 JUN 2016

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US, Commissioner for Patents

P.O. Box 1450, Alexandria, Virginia 22313-1450

Facsimile No. 571-273-8300

Authorized officer:

Lee W. Young

PCT Helpdesk: 571-272-4300

PCT OSP: 571-272-7774

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 16/24453

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☒ Claims Nos.: 6-10 and 19-29
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

摘要

本发明提供了用于治疗、预防或控制局部炎性症状(包括与急性或慢性炎症相关的症状)，特别是以潜在免疫疾病或病症为特征的病症的方法。本发明还提供了用于控制与癌症和微生物菌群相关的炎症过程的方法。