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(71) Applicant: **NOVA NEURA, LLC** [US/US]; 10645 N. Tatum Boulevard, Suite 200-629, Phoenix, AZ 85028 (US).

(72) Inventors: **GEORGE, David**; 5501 N Camelback Canyon Drive, Phoenix, AZ 85018 (US). **FIFE, Stuart**; 3115 Fennel Street, Savannah, GA 31404 (US). **ROSEN, Howard**; 6622 Horseshoe Lane, Huntington Beach, CA 92468 (US).

(74) Agent: **MILES, Craig, R.**; Cr Miles P.C., 405 Mason Court, Suite 119, Fort Collins, CO 80524 (US).

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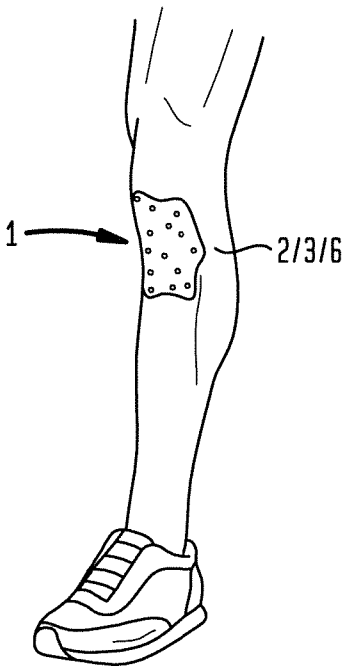
[Continued on next page]

(54) Title: PAIN RELIEVING SYSTEM

(57) Abstract: A composition for relieving pain, and methods of making and using the composition, whereby the composition comprises an amount of sugar or sugar alcohol; and an amount of vehicle; wherein the composition is formulated for transdermal administration; and wherein, upon transdermal administration, the composition is effective to relieve pain. As to particular embodiments, the composition further comprises an amount of alkalizing agent.

FIG. 1A



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— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

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PAIN RELIEVING SYSTEM

This International Patent Cooperation Treaty Patent Application is a Continuation-in-Part of United States Non-Provisional Patent Application No. 14/612,006, filed February 2, 2015, and claims the benefit of United States Provisional Patent Application No. 62/038,779, filed August 18, 2014, each hereby incorporated by reference herein.

I. BACKGROUND

Pain is one of the most frequent symptoms for which patients seek medical intervention. Pain may be classified as acute or chronic. Acute pain may be generally associated with excessive noxious stimulus resulting in a severe distressful sensation whereas chronic pain may be associated with physiological changes resulting from tissue or nerve injury leading to hyperalgesia, an increased amount of pain associated with a mild noxious stimulus, or allodynia, a pain induced by a non-noxious stimulus.

Neurogenic pain is a neurological disorder caused by insult to peripheral nerves, resulting in chronic pain and varying combinations of sensory symptoms, including paresthesia, loss of sensation, and even motor weakness. Neurogenic pain may be long-lasting, and may develop days or month following the injury. Often, this type of chronic pain may be observed in diseases affecting the peripheral nervous system, such as nerve compression syndromes, cutaneous sensory neuropathies, and polyneuropathies (of which diabetic neuropathy may be the most well-known).

Amongst the various types of chronic pain, understanding and management of neurogenic pain remains a considerably challenging task for researchers and clinicians. Despite the rapid development of neuroscience and the discovery of new pharmaceutical compounds, a need continues to exist for an effective treatment based on a basic understanding of the contributing molecular mechanisms of neurogenic pain.

Neurogenic pain involves alterations in the function of both the peripheral and central nervous systems, postulated to be caused by changes in mechano-insensitive peptidergic nociceptors referred to as “silent” or “sleeping” nociceptors, which are chemo-sensitive and respond to noxious chemicals typically released in response to tissue or nerve trauma. Once sensitized, the phenotype of the nociceptors can be altered, whereby the formerly “silent” or “sleeping” nociceptors become "polymodal" or '"awake" nociceptors (C fibers), which release significant amounts of pro-inflammatory neuropeptides, such as calcitonin gene-related peptide

(CGRP) or substance P (SP), initiating neurogenic inflammation in combination with enhancing action potentials, thereby resulting in increased nociception.

Following nerve injury, increased excitability and sensitivity is observed in the cell body of the injured dorsal root ganglia neurons and neighboring intact afferent neurons. This enhanced stimulation involving the primary afferent neurons is defined as peripheral sensitization, which is mediated by increased expression of the transient receptor potential (TRP) family of non-specific cation channels, including transient receptor potential cation channel subfamily V member 1 (TRPV1), which is expressed in C fibers and Aδ fibers. Another mechanism leading to peripheral sensitization includes the accumulation of voltage-gated sodium channels at the site of the injured nerve and at the dorsal root ganglion, resulting in abnormal ectopic excitability of afferent neurons. These changes may be perceived as spontaneous positive sensations, such as paresthesia (a sensation of tingling, burning, pricking, or numbness of skin) or dysthesia (an unpleasant, abnormal sense of touch).

Central sensitization, defined as the activation of second order nociceptive neurons in the dorsal horn of the spinal cord by peripheral nerve damage, results from the release of glutamate, SP, or other transmitters or cytokines, such as adenosine-5'-triphosphate (ATP), chemokine (C-C motif) ligand 2 (CCL2), or interferon gamma (INFγ), from the central terminals of primary nociceptive afferents in the dorsal horn. The overall effect of these changes may be prolonged excitability of the spinal cord neurons (long-term potentiation).

Further contributing factors to the development of neurogenic pain include the involvement of spinal cord microglia and astrocytes in enhancing pain, whereby ATP-activated microglial P2X4 and P2X7 receptors stimulate the p38 mitogen-activated protein kinases (p38-MAPK) signalling cascade, resulting in release of substances such as brain-derived neurotrophic factor (BNDF), down-regulation of potassium/chloride cotransporters, and diminished inhibitory neurotransmission (GABAergic inhibition).

Additionally, following an injury, various inflammatory substances such as histamines, prostaglandins, or cytokines, may be released from inflammatory cells which have migrated through the blood to the site of the injured tissue. When the injury results in nerve damage, the peripheral terminals of sensory neurons may be activated, resulting in inflammation characterized by the release of neuropeptides, such as CGRP, SP, or calcitonin, from the C fiber terminal, which can lead to vasodilation, edema, or pain. As such, neurogenic inflammation plays an integral role in the pathophysiology of neurogenic pain.

Moreover, research regarding ion channels in sensory neurons, for example in axon terminals and in cell soma, has exposed a variety of molecular mechanisms underlying how various types of stimuli may be transduced to neural signals which may then be transmitted to the brain for pain perception. Upon activation of these ion channels, inward currents or outward currents may be generated, leading to corresponding depolarization or hyperpolarization of the sensory neuron membrane which results in corresponding increased or decreased excitability of the sensory neuron.

As an example, activation of cationic channels has been found to result in excitation of sensory neurons, leading to the generation of nociceptive signals, whereby the primary channels responsible for inward currents in nociceptors are voltage-activated sodium and calcium channels while outward current is mediated largely by potassium channels. In addition, the activation of non-selective cation channels has also been implicated in the excitation of nociceptive sensory neurons. As further evidence, common cations, such as hydrogen ions and potassium ions, have been found to be associated with tissue irritation and injury, likely contributing to neurogenic pain. Thus, by regulating the expression of these channels or by modulating the activity of these channels, the excitability of the nociceptive sensory neurons may be controlled.

As but one illustrative example, the Acid Sensing Ion Channel #3 (ASIC3) senses and responds to perineural acidity, which as to particular embodiments, may be generated by an accumulation of lactic acid produced by ischemic muscle. As such, the lactic acid may contribute to neurogenic pain by acting on these ion channels, which may in part explain why painful, peripheral neurogenic sensitization is common in physical activities like running, cycling, and weight-lifting.

Additionally, post-surgical pain has likewise been shown to be associated with the presence of hydrogen ions, thereby contributing to the development of chronic pain. For example, specific research demonstrates that at a site of an incision, a downward pH shift from about 6.9 to about 6.5 may be observed.

By raising blood pH, plasma potassium ion concentrations consequently decrease. Accordingly, bicarbonate has long been advocated for the treatment of hyperkalemia, as bicarbonate raises blood pH. Also, independent of its effect on blood pH, bicarbonate can also lower plasma potassium ion concentrations. The role of potassium ion buffering in the central nervous system (CNS) is principally attributed to glial cells and by spatial buffering, which

involves the diffusion of potassium ions through the interstitial space down a concentration gradient. Of note, the former mechanism is not available in the peripheral nervous system (PNS).

Hence, successful treatment of neurogenic pain requires direct targeting of the receptors and transmitters involved. Conventional therapeutic strategies aim to reduce neuron excitability through alterations in ion channel activity, which may be targeted by compounds such as gabapentin or lidocaine, or modulate central neurotransmission, which may be targeted by compounds such as opioids or tricyclic antidepressants. Despite consistent efficacy observed in randomized trials and meta-analyses, the use of these agents may be limited due to debilitating side effects, such as sedation, somnolence, dry mouth, urinary retention, erythema, ataxia, or the like, or combinations thereof. Moreover, patients using these compounds must be closely monitored and dose tapering may be required to prevent withdrawal symptoms. Accordingly, a need exists for a novel alternative characterized by maximal therapeutic efficacy, minimal toxicity, and low incidence of side effects.

II. DISCLOSURE OF INVENTION

Accordingly, a broad object of a particular embodiment of the invention can be to provide a composition for relieving pain, and methods of making and using the composition, whereby the composition comprises an amount of sugar or sugar alcohol; and an amount of vehicle; wherein the composition is formulated for transdermal administration; and wherein, upon transdermal administration, the composition is effective to relieve pain.

Another broad object of a particular embodiment of the invention can be to provide a composition for relieving pain, and methods of making and using the composition, whereby the composition comprises an amount of sugar or sugar alcohol; an amount of alkalizing agent; and an amount of vehicle; wherein the composition is formulated for transdermal administration; and wherein, upon transdermal administration, the composition is effective to relieve pain.

Another broad object of a particular embodiment of the invention can be to provide a composition for relieving pain, and methods of making and using the composition, whereby the composition comprises an amount of sugar or sugar alcohol; and an amount of vehicle; wherein the composition is formulated for transdermal administration; wherein, upon transdermal administration, the composition is effective to relieve pain; and wherein the composition is coupled to a tape element.

Another broad object of a particular embodiment of the invention can be to provide a composition for relieving pain, and methods of making and using the composition, whereby the composition comprises an amount of sugar or sugar alcohol; an amount of alkalizing agent; and an amount of vehicle; wherein the composition is formulated for transdermal administration; wherein, upon transdermal administration, the composition is effective to relieve pain; and wherein the composition is coupled to a tape element.

Naturally, further objects of the invention are disclosed throughout other areas of the specification, drawings, and claims.

III. BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1A is an illustration of a method of using a particular embodiment of the inventive composition to alleviate one or more disorder symptoms or to treat one or more disorders.

Figure 1B is an illustration of a method of using a particular embodiment of the inventive composition coupled to a tape element to alleviate one or more disorder symptoms or to treat one or more disorders.

Figure 1C is an illustration of a method of using a particular embodiment of the inventive composition coupled to a tape element to alleviate one or more disorder symptoms or to treat one or more disorders.

Figure 2A is a top view of a particular embodiment of the inventive composition included in an inventive therapeutic tape assembly.

Figure 2B is a bottom view of a particular embodiment of the inventive composition included in an inventive therapeutic tape assembly.

Figure 3A is a side view of a particular embodiment of the inventive composition included in an inventive therapeutic tape assembly having two layers.

Figure 3B is a side view of a particular embodiment of the inventive composition included in an inventive therapeutic tape assembly having three layers.

Figure 4A is a top view of a particular embodiment of the inventive composition included in an inventive therapeutic tape assembly having a pattern on a contact layer first surface.

Figure 4B is a top view of a particular embodiment of the inventive composition included in an inventive therapeutic tape assembly having a pattern on a contact layer first surface.

Figure 4C is a top view of a particular embodiment of the inventive composition included in an inventive therapeutic tape assembly having a pattern on a contact layer first surface.

Figure 4D is a top view of a particular embodiment of the inventive composition included in an inventive therapeutic tape assembly having a pattern on a contact layer first surface.

Figure 4E is a top view of a particular embodiment of the inventive composition included in an inventive therapeutic tape assembly having a pattern on a contact layer first surface.

Figure 5A is a view of a particular embodiment of the inventive composition administered using micro-needles or nano-needles.

Figure 5B is a view of a particular embodiment of the inventive composition administered using micro-needles or nano-needles.

Figure 5C is a view of a particular embodiment of the inventive composition administered using micro-needles or nano-needles.

Figure 5D is a view of a particular embodiment of the inventive composition administered using micro-needles or nano-needles.

Figure 6A is an illustration of a method of producing a particular embodiment of the inventive therapeutic tape assembly including microstructures or nanostructures formed from the inventive composition.

Figure 6B is an illustration of a method of producing a particular embodiment of the inventive therapeutic tape assembly including microstructures or nanostructures formed from the inventive composition.

Figure 6C is an illustration of a method of producing a particular embodiment of the inventive therapeutic tape assembly including microstructures or nanostructures formed from the inventive composition.

Figure 6D is an illustration of a method of producing a particular embodiment of the inventive therapeutic tape assembly including microstructures or nanostructures formed from the inventive composition.

IV. MODE(S) FOR CARRYING OUT THE INVENTION

Now referring primarily to Figure 1A through Figure 1C, which illustrate methods of using particular embodiments of an inventive composition (1) including an amount of sugar or sugar alcohol, an amount of alkalizing agent, or combinations thereof, and an amount of vehicle; whereby the inventive composition (1) is formulated for transdermal administration; and whereby, upon transdermal administration, the inventive composition (1) is effective to relieve pain. The method of use can include transdermally administering the inventive composition (1) in an amount effective to relieve the pain.

Further, the method of use can include administering the inventive composition (1) to an external surface (2) of a body (3) to alleviate one or more disorder symptoms, for example neurogenic pain, or to treat one or more disorders, for example neurogenic inflammation, which may be associated with neurogenic pain.

The term "sugar" for the purposes of this invention means any carbohydrate or saccharide, including monosaccharides, disaccharides, oligosaccharides, or polysaccharides.

The term "sugar alcohol" for the purposes of this invention means any polyol (or polyhydric alcohol) derived from a sugar. The polyol can typically include an alcohol group (CH_2OH) in place of an aldehyde group (CHO) of the parent sugar.

The term "alkalizing agent" for the purposes of this invention means an agent capable of adjusting a pH from a lesser alkalinity toward a greater alkalinity.

The term "symptom" for the purposes of this invention means any discomfort or combination of discomforts associated with a disorder. Without limiting the breadth of the foregoing, symptoms can include: pain, dyesthesia, paresthesia, sensory loss, allodynia, hyperpathia, reduced range-of-motion, motor weakness, or the like, or combinations thereof.

The term "disorder" for the purposes of this invention means a physical or mental condition which may not be normal or healthy. Without limiting the breadth of the foregoing, a disorder can include: known compressive mononeuropathies (such as carpal tunnel syndrome, cubital tunnel syndrome, or tarsal tunnel syndrome), regional pain conditions (such as sub-

occipital neuralgia, facial neuralgias, headache, neck pain, or back pain), acute joint injury which may include a component of nerve inflammation (such as ankle sprain or strain), tendinopathies potentially promoted or aggravated by concomitant neurogenic components (such as Achilles tendonosis, lateral epicondylosis, or medial epicondylosis), isolated inflammation of any one or more peripheral nerves (such as cranial and upper cervical nerve branch derivatives of the face and cranium), or the like, or combinations thereof.

The term "topical administration or "transdermal administration" for the purposes of this invention means the administration of one or more components of a composition to and typically, but not necessarily, through at least a portion of the skin on any external surface of a body. As to particular embodiments, topical administration or transdermal administration can mean the administration of one or more components of a composition to the epidermis on any external surface of a body and typically, but not necessarily, through at least a portion of the dermis. Following topical administration or transdermal administration, one or more components of the composition may or may not be systemically bioavailable.

The term "relieve" for the purposes of this invention means lessen, reduce, decrease, or the like, or combinations thereof.

Where trade names or trademarks are utilized herein, whether in Table 1 through Table 8, or any table, figure, or portion of the description, the trade name material or the trademark material is understood to have the chemicals or ingredients in the amounts or combinations as described below. The trade name material or trademark material or a substantially equivalent product or combination of chemicals or ingredients can be utilized in embodiments of the inventive composition (1). It is further understood that where a trade name material or trademark material is utilized in a table or figure that substantially equivalent chemicals or ingredients in the amounts and combinations as indicated below can be utilized in substitution of the trade name material or trademark material. A person of ordinary skill in the art can convert the weight percentages shown in the tables or figures to determine the amount of each chemical or ingredient to mix when the equivalent of the trade name material or trademark material is prepared.

Where the constituents of a particular trade name material or trademark material have been set out a first time in the description below, each applies to the subsequent uses of the trade name material or trademark material in the description, tables and figures.

Now referring primarily to Table 1, embodiments of the inventive composition (1) can include formulations having raw materials admixed in the exemplary weight percentages ("Weight Percent") shown in column two of Table 1. Numerous embodiments of the inventive composition (1) can be prepared by altering the weight percentages of the raw materials within the range weight percentages ("Range Weight Percent") shown in column three of Table 1 with an amount of vehicle making up the balance.

TABLE 1.

Raw Material	Weight Percent	Range Weight Percent
Sugar or Sugar Alcohol	20	1 to 40
Vehicle	80	60 to 99

As to particular embodiments, the sugar can include a monosaccharide, such as ribose (CAS No: 50-69-1), xylose (CAS No: 58-86-6), fructose (CAS No: 57-48-7), dextrose (glucose) (CAS No: 50-99-7), galactose (CAS No: 59-23-4), mannose (CAS No: 31103-86-3), sorbose (CAS No: 87-79-6), or the like, or combinations thereof, all of which can be obtained from Sigma-Aldrich, 3050 Spruce Street, St. Louis, Missouri, USA.

As to other particular embodiments, the sugar can include a disaccharide, such as sucrose (CAS No: 57-50-1), maltose (CAS No: 69-79-4), lactose (CAS No: 63-42-3), lactulose (CAS No: 4618-18-2), trehalose (CAS No: 99-20-7), cellobiose (CAS No: 528-50-7), or the like, or combinations thereof, all of which can be obtained from Sigma-Aldrich, 3050 Spruce Street, St. Louis, Missouri, USA.

The sugar can be generally included in an amount of about 1% to about 40% by weight of the inventive composition (1); however, greater or lesser weight percents of the sugar can be included depending on the disorder symptom to be alleviated or the disorder to be treated. As to particular embodiments, the amount of sugar included in the inventive composition (1) can be in a range of between about 5% to about 25% by weight of the inventive composition (1).

As to particular embodiments, the amount of sugar included in the inventive composition (1) can be selected from the group including or consisting of: between about 1% to about 5% by weight of the inventive composition (1), between about 2.5% to about 7.5% by weight of the inventive composition (1), between about 5% to about 10% by weight of the inventive composition (1), between about 7.5% to about 12.5% by weight of the inventive

composition (1), between about 10% to about 15% by weight of the inventive composition (1), between about 12.5% to about 17.5% by weight of the inventive composition (1), between about 15% to about 20% by weight of the inventive composition (1), between about 17.5% to about 22.5% by weight of the inventive composition (1), between about 20% to about 25% by weight of the inventive composition (1), between about 22.5% to about 27.5% by weight of the inventive composition (1), between about 25% to about 30% by weight of the inventive composition (1), between about 27.5% to about 32.5% by weight of the inventive composition (1), between about 30% to about 35% by weight of the inventive composition (1), between about 32.5% to about 37.5% by weight of the inventive composition (1), between about 35% to about 40% by weight of the inventive composition (1), between about 5% to about 40% by weight of the inventive composition (1), between about 10% to about 40% by weight of the inventive composition (1), between about 15% to about 40% by weight of the inventive composition (1), between about 20% to about 40% by weight of the inventive composition (1), between about 25% to about 40% by weight of the inventive composition (1), between about 30% to about 40% by weight of the inventive composition (1), and between about 35% to about 40% by weight of the inventive composition (1). As to the particular embodiment of the inventive composition (1) shown in Table 1, the amount of sugar, for example dextrose, included can be about 20% by weight of the inventive composition (1).

The amount of sugar included in the inventive composition (1) can be influenced by factors such as user anatomy, physiology, or biochemistry of the skin or underlying tissue; disorder symptom targeted for alleviation; disorder targeted for treatment; observable effect(s) of the application of the inventive composition (1); or the like; or combinations thereof; but not so much as to cause discomfort to the user or irritation to the skin or underlying tissue.

The sugar alcohol can include a polyol derived from a monosaccharide or a disaccharide, including glycerol (CAS No: 56-81-5), erythritol (CAS No: 10030-58-7), threitol (CAS No: 2418-52-2), arabitol (CAS No: 7643-75-6), xylitol (CAS No: 87-99-0), adonitol (CAS No: 488-81-3), mannitol (CAS No: 69-65-8), sorbitol (CAS No: 50-70-4), dulcitol (CAS No: 608-66-2), fucitol (CAS No: 13074-06-1), iditol (CAS No: 488-45-9), inositol (CAS No: 87-89-8), volemitol (CAS No: 30635-52-0), isomalt (CAS No: 64519-82-0), maltitol (CAS No: 585-88-6), lactitol (CAS No: 585-86-4), maltotriitol (CAS No: 32860-62-1), or the like, or combinations thereof, all of which can be obtained from Sigma-Aldrich, 3050 Spruce Street, St. Louis, Missouri, USA.

The sugar alcohol can be generally included in an amount of about 1% to about 40% by weight of the inventive composition (1); however, greater or lesser weight percents of the sugar alcohol can be included depending on the disorder symptom to be alleviated or the disorder to be treated. As to particular embodiments, the amount of sugar alcohol included in the inventive composition (1) can be in a range of between about 5% to about 25% by weight of the inventive composition (1).

As to particular embodiments, the amount of sugar alcohol included in the inventive composition (1) can be selected from the group including or consisting of: between about 1% to about 5% by weight of the inventive composition (1), between about 2.5% to about 7.5% by weight of the inventive composition (1), between about 5% to about 10% by weight of the inventive composition (1), between about 7.5% to about 12.5% by weight of the inventive composition (1), between about 10% to about 15% by weight of the inventive composition (1), between about 12.5% to about 17.5% by weight of the inventive composition (1), between about 15% to about 20% by weight of the inventive composition (1), between about 17.5% to about 22.5% by weight of the inventive composition (1), between about 20% to about 25% by weight of the inventive composition (1), between about 22.5% to about 27.5% by weight of the inventive composition (1), between about 25% to about 30% by weight of the inventive composition (1), between about 27.5% to about 32.5% by weight of the inventive composition (1), between about 30% to about 35% by weight of the inventive composition (1), between about 32.5% to about 37.5% by weight of the inventive composition (1), between about 35% to about 40% by weight of the inventive composition (1), between about 5% to about 40% by weight of the inventive composition (1), between about 10% to about 40% by weight of the inventive composition (1), between about 15% to about 40% by weight of the inventive composition (1), between about 20% to about 40% by weight of the inventive composition (1), between about 25% to about 40% by weight of the inventive composition (1), between about 30% to about 40% by weight of the inventive composition (1), and between about 35% to about 40% by weight of the inventive composition (1). As to the particular embodiment of the inventive composition (1) shown in Table 1, the amount of sugar alcohol, for example mannitol, included can be about 20% by weight of the inventive composition (1).

The amount of sugar alcohol included in the inventive composition (1) can be influenced by factors such as user anatomy, physiology, or biochemistry of the skin or underlying tissue; disorder symptom targeted for alleviation; disorder targeted for treatment; observable effect(s) of the application of the inventive composition (1); or the like; or

combinations thereof; but not so much as to cause discomfort to the user or irritation to the skin or underlying tissue.

The vehicle can include one or more excipients in which the sugar or sugar alcohol can be solubilized or suspended. As to particular embodiments, the excipient can render the inventive composition (1) suitable for topical administration or transdermal administration, whereby the vehicle can facilitate transdermal administration of a portion of the amount of sugar or sugar alcohol. As illustrative examples, the inventive composition (1) including the amount of sugar or sugar alcohol and the amount of vehicle can take the form of lotion, cream, emulsion, ointment, gel, foam, paste, oil, lipid delivery system, spray, drops, or the like, or combinations thereof.

The amount of vehicle included in the inventive composition (1) can be influenced by factors such as user anatomy, physiology, or biochemistry of the skin or underlying tissue; disorder symptom targeted for alleviation; disorder targeted for treatment; observable effect(s) of the application of the inventive composition (1); or the like; or combinations thereof; but not so much as to cause discomfort to the user or irritation to the skin or underlying tissue.

As to particular embodiments, the vehicle can include an emulsion base, which can have an oil phase. As illustrative examples, the oil phase can include vegetable oils, animal oils, mineral oils, silicone oils, synthetic oils, fatty acids, fatty alcohols, phospholipids, paraffin waxes, or the like, or combinations thereof.

As to particular embodiments, the vehicle can further include one or more solubilizing agents, such as cyclodextrins, surfactants, organic solvents, alcohols, polysorbates, or the like, or combinations thereof.

As to particular embodiments, the vehicle can further include one or more viscosity-increasing agents, such as microcrystalline cellulose, carboxymethylcellulose sodium, propylene glycol alginate, xanthan gum, polyacrylic acid, or the like, or combinations thereof.

As to particular embodiments, the vehicle can further include one or more emulsifying or co-emulsifying agents, such as non-ionic surfactants, polyethylene glycol esters, polyoxypropylene glycol ethers, sorbitan esters, ethoxylated sorbitan esters, poly esters, or the like, or combinations thereof.

As to particular embodiments, the vehicle can further include one or more emulsion stabilizing agents, such as abietic acid, hydrogenated lanolin alcohol, calcium myristate, hydroxyaluminium distearate, aluminum isostearate, aluminum stearate, 7, 8-didehydrocholesterol, aluminum magnesium hydroxide, stearic acid, lauryl alcohol, hydroxyethyl cellulose, or the like, or combinations thereof.

As to particular embodiments, the vehicle can further include one or more preservatives or preserving agents, such as sorbic acid, methyl paraben, propyl paraben, benzoic acid, sodium benzoate cetrimide, phenoxyethanol, chlorphenisin, methylchloroisothiazolinone, or the like, or combinations thereof.

As to particular embodiments, the vehicle can further include one or more penetration enhancers, such as alcohols, sulphoxides, azone, pyrrolidones, urea, disubstituted aminoacetates, glycols (for example, propylene glycol), surfactants, terpenes, terpenoids, fatty acids, esters, cyclodextrins, phospholipids, or the like, or combinations thereof.

As to particular embodiments, the vehicle can further include water (CAS No: 7732-18-5), which can be filtered, de-ionized, distilled, or water otherwise filtered or purified.

As an illustrative example, the vehicle can include PENTRAVAN®, having fatty acid alcohols, acids, esters, phospholipids, antioxidants, skin-feel enhancer, natural humectant, natural preservatives, nonionic emulsifiers, anionic emulsifiers, and buffer, which can be obtained from Fagron, 2400 Pilot Knob Road, St Paul, Minnesota 55120, USA.

As an additional illustrative example, the vehicle can include VERSATILE™, having waters, fatty acid esters, alcohols, paraffinic silicone replacement, glidant, plant-derived emollient, vitamin E, nonionic emulsifiers, pro-liposomal phospholipids, and preservatives, which can be obtained from Fagron, 2400 Pilot Knob Road, St Paul, Minnesota 55120, USA.

As yet an additional illustrative example, the vehicle can include VERSAPRO™ Cream Base, which can be obtained from Medisca, 661 Route 3, Unit C, Plattsburgh, New York 12901, USA.

As to particular embodiments, the vehicle can further include an amount of magnesium. As to particular embodiments, the amount of magnesium can be provided by magnesium chloride, magnesium sulfate, or the like, or combinations thereof.

As to particular embodiments, the vehicle can further include an amount of *Aesculus hippocastanum*. As to particular embodiments, the amount of *Aesculus hippocastanum* can be in a range of between about 0.25% to about 2% by weight of the inventive composition (1). As to particular embodiments, the amount of *Aesculus hippocastanum* can include an amount of aescin.

As to particular embodiments, the vehicle can further include an amount of quercetin. As to particular embodiments, the amount of quercetin can be in a range of between about 0.1% to about 1% by weight of the inventive composition (1).

As to particular embodiments, the vehicle can further include an amount of acetyl-L-carnitine. As to particular embodiments, the amount of acetyl-L-carnitine can be in a range of between about 0.025% to about 3% by weight of the inventive composition (1).

As to particular embodiments, the vehicle can further include an amount of zinc. As to particular embodiments, the amount of zinc can be in a range of between about 0.025% to about 3% by weight of the inventive composition (1). As to particular embodiments, the amount of zinc can be provided by zinc oxide, zinc sulfate, or the like, or combinations thereof.

As to particular embodiments, the inventive composition (1) can further include one or more colorants, fragrances, or the like, as persons of ordinary skill in the art would understand.

Now referring primarily to Table 2, embodiments of the inventive composition (1) can include formulations having raw materials admixed in the exemplary weight percentages ("Weight Percent") shown in column two of Table 2. Numerous embodiments of the inventive composition (1) can be prepared by altering the weight percentages of the raw materials within the range weight percentages ("Range Weight Percent") shown in column three of Table 2 with an amount of vehicle making up the balance.

TABLE 2.

Raw Material	Weight Percent	Range Weight Percent
Sugar or Sugar Alcohol	20	1 to 40
Alkalizing Agent	5	0.1 to 15
Vehicle	75	45 to 98.9

The sugar, sugar alcohol, and vehicle in the particular embodiment of the inventive composition (1) shown in Table 2 can be similar to the corresponding sugar, sugar alcohol, and vehicle as above described for the particular embodiment of the inventive composition (1) shown in Table 1.

Additionally, as to particular embodiments, the vehicle can include one or more excipients in which the sugar or sugar alcohol, alkalizing agent, or combinations thereof, can be solubilized or suspended. As to particular embodiments, the excipient can render the inventive composition (1) suitable for topical application or transdermal application, whereby the vehicle can facilitate transdermal administration of a portion of the amount of sugar or sugar alcohol, a portion of the amount of alkalizing agent, or combinations thereof. As illustrative examples, the inventive composition (1) including the amount of sugar or sugar alcohol, the amount of alkalizing agent, and the amount of vehicle can take the form of lotion, cream, emulsion, ointment, gel, foam, paste, oil, lipid delivery system, spray, drops, or the like, or combinations thereof.

The alkalizing agent can include any agent capable of adjusting a pH from a lesser alkalinity toward a greater alkalinity, such as sodium bicarbonate (CAS No: 144-55-8), potassium citrate (CAS No: 866-84-2), calcium carbonate (CAS No: 471-34-1), calcium acetate (CAS No: 62-54-4), or the like, or combinations thereof, all of which can be obtained from Sigma-Aldrich, 3050 Spruce Street, St. Louis, Missouri, USA.

The alkalizing agent can be generally included in an amount of about 0.1% to about 15% by weight of the inventive composition (1); however, greater or lesser weight percents of the alkalizing agent can be included depending on the disorder symptom to be alleviated or the disorder to be treated. As to particular embodiments, the amount of alkalizing agent included in the inventive composition (1) can be in a range of between about 3% to about 5% by weight of the inventive composition (1).

As to particular embodiments, the amount of alkalizing agent included in the inventive composition (1) can be selected from the group including or consisting of: between about 0.1% to about 5% by weight of the inventive composition (1), between about 1% to about 5% by weight of the inventive composition (1), between about 2.5% to about 7.5% by weight of the inventive composition (1), between about 5% to about 10% by weight of the inventive composition (1), between about 7.5% to about 12.5% by weight of the inventive composition (1), between about 10% to about 15% by weight of the inventive composition (1), between

about 1% to about 15% by weight of the inventive composition (1), between about 2.5% to about 15% by weight of the inventive composition (1), between about 5% to about 15% by weight of the inventive composition (1), between about 7.5% to about 15% by weight of the inventive composition (1), between about 10% to about 15% by weight of the inventive composition (1), and between about 12.5% to about 15% by weight of the inventive composition (1). As to the particular embodiment of the inventive composition (1) shown in Table 2, the amount of alkalizing agent, for example sodium bicarbonate, included can be about 5% by weight of the inventive composition (1).

The amount of alkalizing agent included in the inventive composition (1) can be influenced by factors such as user anatomy, physiology, or biochemistry of the skin or underlying tissue; disorder symptom targeted for alleviation; disorder targeted for treatment; observable effect(s) of the application of the inventive composition (1); or the like; or combinations thereof; but not so much as to cause discomfort to the user or irritation to the skin or underlying tissue.

As to particular embodiments, the amount of alkalizing agent included in the inventive composition (1) can be sufficient to provide the inventive composition (1) with a pH of between about 8 to about 10.

As to particular embodiments, the amount of alkalizing agent included in the inventive composition (1) can be sufficient to provide the inventive composition (1) with a pH selected from the group including or consisting of: between about 8 to about 8.5, between about 8.25 to about 8.75, between about 8.5 to about 9, between about 8.75 to about 9.25, between about 9 to about 9.5, between about 9.25 to about 9.75, and between about 9.5 to about 10.

As to particular embodiments, the alkalizing agent can include a salt.

As to particular embodiments, the salt can include a monovalent cation, a divalent cation, or a trivalent cation, including but not limited to sodium, calcium, potassium, zinc, iron, magnesium, or the like, or combinations thereof.

As to other particular embodiments, the salt can include an anion, including but not limited to chloride, acetate, ascorbate, bicarbonate, citrate, formate, fumarate, phosphate, succinate, borate, gluconate, lactate, malate, trimalate, panthothenate, thiocyanate, glycinate, sulphate, or the like, or combinations thereof.

As to particular embodiments, the salt can be selected from the group including or consisting of: sodium chloride, sodium acetate, sodium bicarbonate, sodium citrate, sodium phosphate, sodium dihydrogen phosphate, sodium hydrogen phosphate, sodium succinate, sodium borate, sodium gluconate, sodium citrate, sodium lactate, calcium citrate, calcium chloride, calcium pantothenate, calcium gluconate, calcium phosphate, potassium chloride, monopotassium phosphate, dipotassium phosphate, tripotassium phosphate, potassium gluconate, magnesium sulphate, magnesium chloride magnesium gluconate, magnesium acetate, magnesium malate, magnesium glycinate, magnesium lactate, zinc chloride, zinc sulphate and zinc acetate. Other exemplary salts may be formed from any combination of anions and cations listed above and may include, anhydrous, hydrates, dehydrates, or the like, or combinations thereof.

As to particular embodiments, one or more components of the inventive composition (1) can be activated for transdermal administration by the application of pressure, heat, cold, electricity, perspiration, chemical activation, mechanical action, or the like, or combinations thereof. To facilitate activation, one or more components of the inventive composition (1) can be coupled with delivery agents, transport agents, binders, or the like, or combinations thereof. As to particular embodiments, the inventive composition (1) can be activated for delivery at a predetermined delivery rate.

As to particular embodiments, transdermal administration of the inventive composition (1) can be facilitated by one or more physical skin penetration enhancement techniques. As to particular embodiments, the skin penetration enhancement technique can be selected from the group including or consisting of: phonophoresis, sonophoresis, iontophoresis, electroporation, radiofrequency-driven skin microchanneling, micro-needles, nano-needles, massage, occlusion, heating, cooling, or the like, or combinations thereof.

As to particular embodiments, upon transdermal administration, the inventive composition (1) can be effective to decrease neurogenic pain, decrease neurogenic inflammation, or combinations thereof.

As to particular embodiments, upon transdermal administration, the inventive composition (1) can be effective to alkalize a perineural environment proximate a nerve. As to particular embodiments, alkalization of the perineural environment can include adjusting a pH of the perineural environment from a lesser alkalinity toward a greater alkalinity.

As to particular embodiments, upon transdermal administration, the inventive composition (1) can be effective to decrease an amount of cations in a perineural environment proximate a nerve.

As to particular embodiments, upon transdermal administration, the inventive composition (1) can be effective to decrease an amount of hydrogen ions (H+) in a perineural environment proximate a nerve. Research suggests an association between tissue acidity and neurogenic inflammation whereby hydrogen ions (H+) may prime the transient receptor potential cation channel subfamily V member (TrpV1), thereby increasing neurogenic inflammation and associated neurogenic pain. Accordingly, decreasing the amount of hydrogen ions (H+) by adjusting the perineural environment from a lesser alkalinity toward a greater alkalinity may be beneficial for alleviating neurogenic pain or treating neurogenic inflammation.

As to particular embodiments, upon transdermal administration, the inventive composition (1) can be effective to decrease a viscosity of hyaluronic acid (also known as hyaluronan, hyaluronate, or HA), which is an anionic, nonsulfated glycosaminoglycan widely distributed throughout connective, epithelial, and neural tissues. Particularly, hyaluronic acid can be found between fascial layers, acting as a lubricant to facilitate fascial glide. As peripheral nerves, especially superficial sensory nerves, can typically be enveloped between fascial layers, decreasing the viscosity of hyaluronic acid may decrease friction or mechanical irritation of the nerves by the fascia enveloping the nerve.

Research suggests that adjusting the pH of a perineural environment from a lesser alkalinity toward a greater alkalinity may result in a conformational change in the hyaluronic acid molecule resulting from a degradation of attraction forces between hyaluronic acid molecules, thereby increasing the flexibility of the hyaluronic acid polymer and correspondingly decreasing the viscosity of hyaluronic acid.

As to particular embodiments, upon transdermal administration, the inventive composition (1) can be effective to provide an amount of energetic substrate to a nerve, whereby as to particular embodiments, the energetic substrate can be a sugar, for example dextrose. Research suggests that normal mitochondrial function in Schwann cells is imperative for maintaining axon-glial interactions which are necessary for long-term support of axons and normal peripheral nerve function. As peripheral neurogenic inflammation may contribute to compartmental edema and consequently, to local sequestration of superficial sensory nerves

which may lead to energy substrate deprivation, for example by impaired axoplasmic interstitial flow and impaired perineural interstitial flow, the delivery of an amount of energetic substrate to the nerve may promote nerve function, thereby decreasing neurogenic pain, decreasing neurogenic inflammation, or combinations thereof.

Now referring primarily to Figure 1B through Figure 5E, as to particular embodiments, the inventive composition (1) can be coupled to a tape element (4), together forming an inventive therapeutic tape assembly (5). The tape element (4) can be configured to couple to a user (6), for example by adhering to the external surface (2) of a portion of the body (3) of the user (6) or by surrounding the external surface (2) of a portion of the body (3) of the user (6). In addition to providing a medium for the inventive composition (1), the tape element (4) can provide mechanical stimulation to the body (3) of the user (6) in the form of pressure or friction, which can enhance the delivery of the invention composition (1) into the skin. Also, the mechanical stimulation provided by the tape element (4) can enhance lymphatic drainage, local blood flow, or the like, or combinations thereof. Furthermore, the tape element (4) can provide mechanical support to the body (3) of the user (6), thereby enhancing performance, comfort, or the like, or combinations thereof.

Now referring primarily to Figure 2A and Figure 2B, as to particular embodiments, the tape element (4) can be configured as a non-elastic tape element (4) having dimensions which can be generally non-stretchable. As to other particular embodiments, the tape element (4) can be configured as an elastic tape element (4) having dimensions which can stretchably adjust between an unstretched condition and a stretched condition, whereby, in the stretched condition, the dimensions of the elastic tape element (4) can be up to 200% greater than the dimensions of the elastic tape element (4) when in the unstretched condition (not shown).

As to particular embodiments, the tape element (4) can be configured to stretch or deform in only one dimension. For example, the tape element (4) can be configured to stretch longitudinally while remaining non-elastic laterally. Conversely, the tape element (4) can be configured to stretch laterally while remaining non-elastic longitudinally. As to other particular embodiments, the tape element (4) can be configured to stretch both longitudinally and laterally. As to yet other particular embodiments, one or more portions of the tape element (4) can be configured to be elastic while one or more other portions of the tape element (4) can be configured to be non-elastic.

As an illustrative example, the elastic tape element (4) can be configured as elastic therapeutic tape or kinesiology tape (also known as "kinesio tape"). As to particular embodiments, tape elements (4) which may be useful in particular embodiments of the inventive therapeutic tape assembly (5) can include RockTape, which can be obtained from Rocktape, 1610 Dell Avenue, Campbell, CA 95008, USA; KT TAPE®, which can be obtained from LUMOS INC., 7 South 1550 West #600, Lindon, UT 84042, USA; or the like.

Now referring primarily to Figure 3A and Figure 3B, as to particular embodiments, the tape element (4) can include a plurality of layers, such as an exterior layer (7) and a contact layer (8) which can be configured for contact with the external surface (2) of the body (3) of the user (6) to administer the inventive composition (1) to the user (6). The tape element (4) can further include a generally impermeable layer (10) disposed between the contact layer (8) and the exterior layer (7), the generally impermeable layer (10) capable of precluding components of the inventive composition (1) from diffusing from the contact layer (8) toward the exterior layer (7). The tape element (4) can further include perspiration channels to divert perspiration, for example to maintain the efficacy of the inventive composition (1).

As to particular embodiments, a layer can be formed from any of a numerous and wide variety of materials, depending on the application, including synthetic materials, natural materials, or combinations thereof, which can be formed from any of a correspondingly numerous and wide variety of processes, depending upon the application, including fabrication, press molding, injection molding, printing, three-dimensional printing, or the like, or combinations thereof, as one layer or assembled from a plurality of layers into an embodiment of the tape element (4). As an illustrative example, a layer can include nylon (for example, nylon 6/12) or cotton configured as a porous mesh. The porous mesh can be configured to receive a solvent, which can be capable of solubilizing the inventive composition (1) to facilitate delivery of the inventive composition (1) into the skin.

As to particular embodiments of the inventive therapeutic tape assembly (5) including a plurality of layers, the layers can be coupled together by mechanical fasteners (for example stitches, clips, hook and loop fasteners, or the like), adhesives, lamination, thermal bonding, cryo bonding, compression, or the like, or combinations thereof.

To form particular embodiments of the inventive therapeutic tape assembly (5), the inventive composition (1) can be infused, impregnated, integrated, or otherwise coupled to the tape element (4) by any of a numerous and wide variety of processes including infusing,

impregnating, integrating, injecting, permeating, printing, coating, spraying, soaking, baking, searing, or otherwise coupling to the tape element (4).

The inventive composition (1) can be formulated as a liquid, a solid, or any other form which allows one or more therapeutic components of the inventive composition (1) to diffuse into the skin from the contact layer (8) of the tape element (4). As to particular embodiments, one or more therapeutic components of the inventive composition (1) can further diffuse into the dermis, subcutaneous layer, muscle, adipose tissue, tendons, ligaments, joints, local circulation, or systemic circulation.

Now referring primarily to Figure 2A through Figure 3B, as to particular embodiments, the inventive composition (1) can be integrated with an adhesive (10) which can be coupled to the contact layer (8) of the tape element (4) to form a composition-adhesive admixture (11). As to particular embodiments, the inventive composition (1) and the adhesive (10) can be admixed during production or manufacturing. The composition-adhesive admixture (11) can then be coupled to one or more surfaces of the tape element (4). As an illustrative example, the composition-adhesive admixture (11) can be coupled to a contact layer first surface (12) of the tape element (4) (as shown in the example of Figure 2A, Figure 3A, and Figure 3B).

As illustrative examples, adhesives (10) which can be used in particular embodiments of the inventive therapeutic tape assembly (5) can include acrylics, silicones, polyisobutylenes, epoxies, styrene block co-polymers, bioadhesives, pressure-sensitive adhesives, or the like, or combinations thereof, which can be obtained from Dow Corning Corporation, PO Box 994, Midland, Michigan 48686, USA; Scapa, 111 Greta Pond Drive, Windsor, Connecticut 06095, USA; Ethicon Endo-Surgery Inc, 4545 Creek Road, Blue Ash, Ohio 45242, USA; or Johnson & Johnson, One Johnson & Johnson Plaza, New Brunswick, New Jersey 08933, USA. As to particular embodiments, the adhesive (10) can take the form of a liquid, gel, solid, film, or the like, or combination thereof. As to particular embodiments, the adhesive (10) can include hydrocolloid, hydrophilic, hydrophobic, or electrically conductive adhesives.

Now referring primarily to Figure 2A through Figure 4E, as to particular embodiments, the composition-adhesive admixture (11) can be disposed on an entire surface of the tape element (4), for example the contact layer first surface (12). As to other particular embodiments, the composition-adhesive admixture (11) can be disposed on a portion of a surface of the tape element (4), for example in a point (13) or series of points (13), a strip (14) or series of strips (14), a pattern, or the like, or combinations thereof.

Now referring primarily to Figure 4A through Figure 4E, as to particular embodiments, the inventive therapeutic tape assembly (5) can include a pattern having inventive composition elements (15), adhesive elements (16), or combinations thereof, whereby the pattern can facilitate the distribution of the inventive composition (1) to particular portions of a user's skin.

Now referring primarily to Figure 4A and Figure 4C, the pattern can include points (13) or series of points (13) of either the inventive composition (1), adhesive (10), or combinations thereof, disposed on the contact layer first surface (12).

Now referring primarily to Figure 4B, Figure 4D, and Figure 4E, the pattern can include strips (14) or series or strips (14) of either the inventive composition (1), adhesive (10), or combinations thereof, disposed on the contact layer first surface (12).

In relation to the length of the tape element (4), the series of points (13) or one or more strips (14) can be disposed longitudinally, laterally, diagonally, or in any of a numerous and wide variety of patterns, including structured patterns or random patterns. As to particular embodiments, the points (13) or strips (14) can extend outwardly or be recessed inwardly from the contact layer first surface (12).

As to particular embodiments, the inventive composition (1) can be included in a delivery system having microstructures (such as micro-needles) or nanostructures (such as nano-needles) for administering the inventive composition (1) into the skin. For example, the microstructures or nanostructures can embed into the skin upon contact to facilitate transdermal administration of the inventive composition (1). As to particular embodiments, the microstructures or nanostructures can be configured to be non-irritating to the skin. As to other particular embodiments, the microstructures or nanostructures can be configured to be absorbed by the skin during or following administration of the inventive composition (1).

Now referring primarily to Figure 5A, as to particular embodiments, the micro-needles (17) or nano-needles (17) can include solid micro-needles (17) or nano-needles (17), which can be used as a skin pretreatment. For example, after inserting and removing the micro-needles (17) or nano-needles (17) to form corresponding micro-scale pores (18) or nano-scale pores (18) in the skin surface, the inventive composition (1) can be applied to the skin for diffusion of the inventive composition (1) through the pores (18) and into the skin.

Now referring primarily to Figure 5B, as to particular embodiments, the micro-needles (17) or nano-needles (17) can be coated with the inventive composition (1). After insertion of

micro-needles (17) or nano-needles (17) into the skin, the inventive composition (1) can dissolve from the micro-needles (17) or nano-needles (17) and diffuse into the skin, after which the micro-needles (17) or nano-needles (17) can be removed.

Now referring primarily to Figure 5C, as to particular embodiments, the micro-needles (17) or nano-needles (17) can be formed from water-soluble or biodegradable polymer which can encapsulate the inventive composition (1) within the micro-needle (17) or nano-needle (17) matrix. As such, the micro-needles (17) or nano-needles (17) can completely dissolve or degrade in the skin, thereby releasing the encapsulated inventive composition (1) with no residual micro-needle (17) or nano-needle (17) waste.

Now referring primarily to Figure 5D, as to particular embodiments, the micro-needles (17) or nano-needles (17) can include hollow micro-needles (17) or nano-needles (17), which can be used for infusion of liquid formulations into the skin or, alternatively, for diffusion into the skin through the needle bore.

Now referring primarily to Figure 6A through Figure 6D, which provide an illustrative example of a method of forming micro-needles (17) or nano-needles (17) from the inventive composition (1) on the contact layer first surface (12). The contact layer (8) can be disposed on a surface including a plurality of micro-points (19) or nano-points (19) having terminal elements (20) which can engage with and extend through the contact layer (8) to protrude from the contact layer first surface (12) (as shown in the example of Figure 6A and Figure 6B). Following, the terminal elements (20) can be coated by the inventive composition (1) (as shown in the example of Figure 6C). Upon solidification of the inventive composition (1), the micro-points (19) or nano-points (19) can be disengaged from the contact layer (8), resulting in micro-needles (17) or nano-needles (17) formed from the inventive composition (1) on the contact layer first surface (12), whereby the surface of the micro-needle (17) or nano-needle (17) bounds a hollow interior (21) (as shown in the example of Figure 6D). The contact layer (8) can be integrated into an inventive therapeutic tape assembly (5). Upon application to a user (6), the micro-needles (17) or nano-needles (17) can pierce the skin. Subsequently, fluid can be applied to the inventive therapeutic tape assembly (5), whereby the fluid can travel into the hollow interior (21) of the micro-needle (17) or nano-needle (17), solubilizing the micro-needle (17) or nano-needle (17) formed from the inventive composition (1) such that the inventive composition (1) can be delivered into the skin.

As to particular embodiments, the contact layer (8) can be covered with a removable backing layer which can be removed for application of the inventive therapeutic tape assembly (5) to the user (6). The backing layer can preclude the adhesive (10), the inventive composition (1), or combinations thereof, from contamination, oxidation, degradation, or the like, prior to application of the inventive therapeutic tape assembly (5).

Although the tape element (4) of inventive therapeutic tape assembly (5) can be described above as having a tape-like configuration with an elongate length in relation to the width, the invention need not be so limited. As such, the tape element (4) can include any element comprising the inventive composition (1) coupled to a contact layer (8) capable of coupling to the external surface (2) of the body (3) for transdermal administration of the inventive composition (1), such as a patch, a brace, or the like.

A method of making a particular embodiment of the inventive composition (1) includes include combining an amount of sugar or sugar alcohol and an amount of vehicle; and formulating the inventive composition (1) for transdermal administration; whereby, upon transdermal administration, the inventive composition (1) is effective to relieve pain.

As used herein, the term "combination or combining" refers to any method of putting two or more materials together. Such methods include, but are not limited to, mixing, blending, commingling, concocting, homogenizing, ultrasonic homogenizing, incorporating, intermingling, fusing, joining, shuffling, stirring, coalescing, integrating, confounding, joining, uniting, creating a stable suspension of two immiscible liquids via any number of means such as emulsions, or the like.

The method of making a particular embodiment of the inventive composition (1) can further include combining the sugar or sugar alcohol and the vehicle, whereby each can be combined in an amount as above-described.

The method of making a particular embodiment of the inventive composition (1) can further include combining an amount of alkalizing agent with the amount of sugar or sugar alcohol and the amount of vehicle.

The method of making a particular embodiment of the inventive composition (1) can further include combining the sugar or sugar alcohol, the alkalizing agent, and the vehicle, whereby each can be combined in an amount as above-described.

The method of making a particular embodiment of the inventive composition (1) can further include combining one or more additional components to formulate the inventive composition (1), whereby the one or more additional components can be as above-described above or can be other additional components.

As an exemplary embodiment, an inventive composition (1) can be produced by combining dextrose in an amount of 20% by weight of the inventive composition (1) and sodium bicarbonate in an amount of 5% by weight of the inventive composition (1) and vehicle in an amount of 75% by weight of the inventive composition (1), whereby the vehicle can include PENTRAVAN®, VERSATILE™, VERSAPRO™, or the like, in an amount of 91% by weight of the vehicle composition and propylene glycol in an amount of 9% by weight of the vehicle composition.

The method of making a particular embodiment of the inventive composition (1) can further include coupling the composition to a tape element (4). As to particular embodiments, the method can further include configuring the tape element (4) to couple to an external surface (2) of a body (3) of a user (6).

As to particular embodiments, the method of making the inventive composition (1) can further include configuring the tape element (4) as non-elastic, having dimensions which are generally non-stretchable. As to other particular embodiments, the method of making the inventive composition (1) can further include configuring the tape element (4) as elastic, having dimensions which are stretchably adjustable between unstretched and stretched conditions.

The method of making a particular embodiment of the inventive composition (1) can further include configuring the tape element (4) to have an exterior layer (7) and a contact layer (8), the contact layer (8) configured for contact with the external surface (2) of the body (3) of the user (6).

The method of making a particular embodiment of the inventive composition (1) can further include integrating the inventive composition (1) with an adhesive (10) coupled to the contact layer (8).

The method of making a particular embodiment of the inventive composition (1) can further comprise including the inventive composition (1) in a delivery system having microstructures or nanostructures. As to particular embodiments, the method can further

include configuring the microstructures or nanostructures as corresponding micro-needles (17) or nano-needles (17).

Now referring primarily to Figure 1A through Figure 1C, a method for relieving pain includes obtaining the inventive composition (1) comprising: an amount of sugar or sugar alcohol; and an amount of vehicle; whereby the inventive composition (1) is formulated for transdermal administration; and whereby, upon transdermal administration, the inventive composition (1) is effective to relieve pain; and transdermally administering the inventive composition (1) in an amount effective to relieve the pain. As to particular embodiments, the inventive composition (1) can further include an amount of alkalizing agent.

The method for relieving pain can further include transdermally administering the inventive composition (1) to alleviate one or more disorder symptoms, for example to lessen neurogenic pain, or to treat one or more disorders, for example to lessen neurogenic inflammation.

The method for relieving pain can further include transdermally administering the inventive composition (1) along a nerve pathway of a nerve to lessen neurogenic pain or to lessen neurogenic inflammation.

The method for relieving pain can further include transdermally administering the inventive composition (1) to alkalize a perineural environment proximate the nerve. As to particular embodiments, alkalization of the perineural environment includes adjusting a pH of the perineural environment from a lesser alkalinity toward a greater alkalinity.

The method for relieving pain can further include transdermally administering the inventive composition (1) to decrease an amount of cations in a perineural environment proximate the nerve.

The method for relieving pain can further include transdermally administering the inventive composition (1) to decrease a viscosity of hyaluronic acid. As to particular embodiments, decreasing the viscosity of hyaluronic acid can decrease mechanical irritation of the nerve by fascia enveloping the nerve.

The method for relieving pain can further include transdermally administering the inventive composition (1) to provide an amount of energetic substrate to the nerve. As to particular embodiments, the energetic substrate can be a sugar, for example dextrose.

The method for relieving pain can further include transdermally administering the inventive composition (1) formulated as a fluid selected from the group including or consisting of: lotion, cream, emulsion, ointment, gel, foam, paste, oil, lipid delivery system, spray, drops, or the like, or combinations thereof.

The method for relieving pain can further include administering one or more physical skin penetration enhancement techniques before, during, or after transdermal administration of the inventive composition (1). As to particular embodiments, the skin penetration enhancement technique can be selected from the group including or consisting of: phonophoresis, sonophoresis, iontophoresis, electroporation, radiofrequency-driven skin microchanneling, micro-needles, nano-needles, massage, occlusion, heating, cooling, or the like, or combinations thereof.

The method for relieving pain can further include transdermally administering the inventive composition (1) coupled to a tape element, whereby the tape element (4) is configured to couple to an external surface (2) of a body (3) of a user (6).

The method for relieving pain can further include adhering the tape element (4) to the external surface (2) of the body (3) of the user (6).

The method for relieving pain can further include surrounding the external surface (2) of the body (3) of the user (6) with the tape element (4).

Now referring primarily to Figure 1C, the method for relieving pain can further include coupling the tape element (4) to an external surface (2) of a body (3) of a user (6) along a nerve pathway of a nerve.

As an illustrative example, the tape element (4) can be coupled to the posterior lower leg along the pathway of the tibial nerve to alleviate one or more disorder symptoms associated with the tibial nerve or to treat one or more disorders associated with the tibial nerve.

As an additional illustrative example, the tape element (4) can be coupled to the dorsolateral wrist and forearm along the pathway of the superficial radial nerve to alleviate one or more disorder symptoms associated with the superficial radial nerve or to treat one or more disorders associated with the superficial radial nerve.

Now referring primarily to Table 3A and Table 3B, which evidences the results of a method of transdermally administering a particular embodiment of the inventive composition

(1) to twenty-six subjects (indicated in column 1 as "Subject Number") who presented with various pain-related complaints (indicated in column 2 as "Primary Complaint"). As to this particular embodiment, the inventive composition (1) included dextrose in an amount of about 20% by weight of the inventive composition (1), sodium bicarbonate in an amount of about 5% by weight of the inventive composition (1), and vehicle in an amount of about 75% by weight of the inventive composition (1).

TABLE 3A.

Subject Number	Primary Complaint	Pre-Admin Pain Level	5 Minutes Post-Admin Pain Level	Percent Reduction in Pain Level
1	Post-surgical knee pain	4	0	100%
2	Idiopathic knee pain	3	0	100%
3	Radiating leg pain	4	0	100%
4	Post-surgical knee pain	8	0	100%
5	Iliotibial band pain	2	0	100%
6	Post-surgical hip pain	3	0	100%
7	Elbow pain	4	0	100%
8	Severe low back & leg pain	8	0	100%
9	Neck pain & face paresthesia	8	0	100%
10	Elbow/forearm pain	4	0	100%
11	Shoulder pain	4	0	100%
12	Post-surgical knee pain	8	2	75%
13	Post-surgical back pain	9	2	78%
14	Plantar fasciitis	4	0	100%
15	Plantar fasciitis	3	0	100%
16	Post-surgical knee pain	7	0	100%
17	Acute lower back pain	6	0	100%
18	Severe low back & leg pain	10	2	80%
19	Shoulder pain & restriction	4	0	100%
20	Post-surgical shoulder pain	5	0	100%
21	Chronic shoulder pain	5	0	100%
22	Acute upper back pain	6	0	100%

23	Acute shoulder pain	6	2	67%
24	Chronic shoulder pain	9	1	89%
25	Neck & shoulder pain	8	1	88%
26	Chronic headache/migraine	6	0	100%

TABLE 3B.

Subject Number	Primary Complaint	Pre-Admin Pain Level	24 Hours Post-Admin Pain Level	Percent Reduction in Pain Level
1	Post-surgical knee pain	4	1	75%
2	Idiopathic knee pain	3	1	67%
3	Radiating leg pain	4	1	75%
4	Post-surgical knee pain	8	2	75%
5	Iliotibial band pain	2	0	100%
6	Post-surgical hip pain	3	0	100%
7	Elbow pain	4	0	100%
8	Severe low back & leg pain	8	1	88%
9	Neck pain & face paresthesia	8	0	100%
10	Elbow/forearm pain	4	1	75%
11	Shoulder pain	4	1	75%
12	Post-surgical knee pain	8	2	75%
13	Post-surgical back pain	9	2	78%
14	Plantar fasciitis	4	1	75%
15	Plantar fasciitis	3	1	67%
16	Post-surgical knee pain	7	1	86%
17	Acute lower back pain	6	0	100%
18	Severe low back & leg pain	10	3	70%
19	Shoulder pain & restriction	4	0	100%
20	Post-surgical shoulder pain	5	0	100%
21	Chronic shoulder pain	5	0	100%
22	Acute upper back pain	6	0	100%

23	Acute shoulder pain	6	2	67%
24	Chronic shoulder pain	9	3	67%
25	Neck & shoulder pain	8	3	63%
26	Chronic headache/migraine	6	0	100%

Again referring primarily to Table 3A and Table 3B, the method of transdermally administering the particular embodiment of the inventive composition (1) included: i) identifying the site of one or more symptoms, typically pain, and having the subject assess their perceived pain level on a scale ranging from 0 to 10, with 0 being the least amount of pain and 10 being the greatest amount of pain (indicated in column three as "Pre-Admin Pain Level"); ii) determining the cutaneous nerve branch(es) or main nerve trunk(s) liable for the one or more symptoms; iii) confirming the liability of the cutaneous nerve branch(es) or main nerve trunk(s) for the one or more symptoms by palpation; and iv) transdermally administering the inventive composition (1) along the nerve pathway of the cutaneous nerve branch(es) or main nerve trunk(s) liable for the one or more symptoms, focusing on areas where the cutaneous nerve branch(es) or main nerve trunk(s) emerge superficially from deeper regions. Generally, the inventive composition (1) was transdermally administered for a time period of about sixty seconds. Following, the subject reassessed their perceived pain level at about five minutes after the transdermal administration of the inventive composition (1) (indicated in Table 3A, column four as "5 Minutes Post-Admin Pain Level") and again at about twenty-four hours after the transdermal administration of the inventive composition (1) (indicated in Table 3B, column four as "24 Hours Post-Admin Pain Level").

Again referring primarily to Table 3 and Table 3B, the mean pre-administration perceived pain level was 5.7/10 whereas the mean five minutes post-administration perceived pain level was 0.4/10, resulting in a mean 95% reduction in perceived pain level (each subject's percent reduction in perceived pain level indicated in Table 3A, column five as "Percent Reduction in Pain Level") in relation to the pre-administration perceived pain level. The mean twenty-four hour post-administration perceived pain level was 1/10, resulting in a mean 84% reduction in perceived pain level (each subject's percent reduction in perceived pain level indicated in Table 3B, column five as "Percent Reduction in Pain Level") in relation to the pre-administration perceived pain level.

Now referring primarily to Table 4, which evidences the results of a method of transdermally administering a particular embodiment of the inventive composition (1) to twelve

subjects (indicated in column 1 as "Subject Number") who presented with various pain-related complaints (indicated in column 2 as "Primary Complaint"). As to this particular embodiment, the inventive composition (1) included dextrose in an amount of about 20% by weight of the inventive composition (1), sodium bicarbonate in an amount of about 5% by weight of the inventive composition (1), and vehicle in an amount of about 75% by weight of the inventive composition (1).

TABLE 4.

Subject Number	Primary Complaint	Pre-Admin Pain Level	1 Minute Post-Admin Pain Level	Percent Reduction in Pain Level
1	Abdominal pain	6	1	83%
2	Knee pain	6	1	83%
3	Metacarpal-phalangeal joint pain	6	0.5	92%
4	Carpal tunnel pain	6	0	100%
5	Supraspinatus tendon pain	10	2	80%
6	Wrist rheumatoid arthritis	3	3	0%
7	Lower back pain	9	3	67%
8	Foot complex regional pain syndrome	3.4	1.5	56%
9	Knee pain	5	0	100%
10	Achilles tendon pain	6	1	83%
11	Wrist pain	9	0	100%
12	Lower back pain	7	1.5	79%
Mean		6.4	1.2	77%

Again referring primarily to Table 4, the method of transdermally administering the particular embodiment of the inventive composition (1) included: i) identifying the site of one or more symptoms, typically pain, and having the subject assess their perceived pain level on a scale ranging from 0 to 10, with 0 being the least amount of pain and 10 being the greatest amount of pain (indicated in column three as "Pre-Admin Pain Level"); ii) determining the cutaneous nerve branch(es) or main nerve trunk(s) liable for the one or more symptoms; iii) confirming the liability of the cutaneous nerve branch(es) or main nerve trunk(s) for the one or more symptoms by palpation; and iv) transdermally administering the inventive composition (1) along the nerve pathway of the cutaneous nerve branch(es) or main nerve trunk(s) liable for

the one or more symptoms, focusing on areas where the cutaneous nerve branch(es) or main nerve trunk(s) emerge superficially from deeper regions. Generally, the inventive composition (1) was transdermally administered for a time period of about sixty seconds. Following, the subject reassessed their perceived pain level at about one minute after the transdermal administration of the inventive composition (1) (indicated in column four as "1 Minute Post-Admin Pain Level").

Again referring primarily to Table 4, the mean pre-administration perceived pain level was 6.4/10 whereas the mean one minute post-administration perceived pain level was 1.2/10, resulting in a mean 77% reduction in perceived pain level (each subject's percent reduction in perceived pain level indicated in column five as "Percent Reduction in Pain Level") relative to the pre-administration perceived pain level.

Now referring primarily to Table 5, which evidences the results of a method of transdermally administering a particular embodiment of the inventive composition (1) to nine subjects (indicated in column 1 as "Subject Number") who presented with various pain-related complaints (indicated in column 2 as "Primary Complaint"). As to this particular embodiment, the inventive composition (1) included dextrose in an amount of about 20% by weight of the inventive composition (1), sodium bicarbonate in an amount of about 5% by weight of the inventive composition (1), and vehicle in an amount of about 75% by weight of the inventive composition (1).

TABLE 5.

Subject Number	Primary Complaint	Pre-Admin Pain Level	1 Minute Post-Admin Pain Level	Percent Reduction in Pain Level
1	Neck pain	6	1	83%
2	Plantar fasciitis	6	0	100%
3	Carpal tunnel pain	6	0	100%
4	Plantar fasciitis pain	6	2	67%
5	Bilateral ankle pain	4	0	100%
6	Carpal tunnel pain	4	0	100%
7	Extensor ligament pain	4	0	100%
8	Achilles tendon pain	8	1	88%

9	Knee pain	6	0	100%
Mean		5.6	0.4	93%

Again referring primarily to Table 5, the method of transdermally administering the particular embodiment of the inventive composition (1) included: i) identifying the site of one or more symptoms, typically pain, and having the subject assess their perceived pain level on a scale ranging from 0 to 10, with 0 being the least amount of pain and 10 being the greatest amount of pain (indicated in column three as "Pre-Admin Pain Level"); ii) determining the cutaneous nerve branch(es) or main nerve trunk(s) liable for the one or more symptoms; iii) confirming the liability of the cutaneous nerve branch(es) or main nerve trunk(s) for the one or more symptoms by palpation; iv) transdermally administering the inventive composition (1) along the nerve pathway of the cutaneous nerve branch(es) or main nerve trunk(s) liable for the one or more symptoms, focusing on areas where the cutaneous nerve branch(es) or main nerve trunk(s) emerge superficially from deeper regions; and v) administering ultrasound to enhance skin penetration of the inventive composition (1). Generally, the inventive composition (1) was transdermally administered for a time period of about sixty seconds and ultrasound was administered for a time period of about five minutes. Following, the subject reassessed their perceived pain level at about one minute after the ultrasound administration (indicated in column four as "1 Minute Post-Admin Pain Level").

Again referring primarily to Table 5, the mean pre-administration perceived pain level was 5.6/10 whereas the mean one minute post-administration perceived pain level was 0.4/10, resulting in a mean 93% reduction in perceived pain level (each subject's percent reduction in perceived pain level indicated in column five as "Percent Reduction in Pain Level") relative to the pre-administration perceived pain level.

Now referring primarily to Table 6, which evidences the results of the transdermal administration of a particular embodiment of the inventive composition (1), a first compound, a second compound, and a third compound (as detailed in column one) to a subject who presented with lower back pain in four distinct regions (a first region, a second region, a third region, and a fourth region) along superior cluneal nerves, as detailed in column two. The inventive composition (1), first compound, second compound, and third compound were transdermally administered to the first, second, third, and fourth regions, respectively.

As to this particular embodiment, the inventive composition (1) included dextrose in an amount of about 20% by weight of the inventive composition (1), sodium bicarbonate in an

amount of about 5% by weight of the inventive composition (1), and vehicle in an amount of about 75% by weight of the inventive composition (1).

The first compound included dextrose in an amount of about 10% by weight of the first compound, tannic acid in an amount of about 2% by weight of the first compound, aloe vera in an amount of about 0.75% by weight of the first compound, and vehicle in an amount of about 87.25% by weight of the first compound.

The second compound included mannitol in an amount of about 20% by weight of the second compound and vehicle in an amount of about 80% by weight of the second compound.

The third compound included dextrose in an amount of about 20% by weight of the third compound and vehicle in an amount of about 80% by weight of the third compound.

Table 6.

Inventive Composition and Compounds	Distinct Region	Pre-Admin Pain Level	5 Minutes Post-Admin Pain Level	Percent Reduction in Pain Level	15 Minutes Post-Admin Pain Level	Percent Reduction in Pain Level
Inventive Composition	First Region	9	1	89%	1	89%
First Compound	Second Region	10	5	50%	5	50%
Second Compound	Third Region	9	4	56%	3	66%
Third Compound	Fourth Region	10	3	70%	2	80%

Again referring primarily to Table 6, the method of transdermally administering the particular embodiment of the inventive composition (1) and each of the first, second, and third compounds included: i) identifying the first, second, third, and fourth regions of pain symptoms; ii) applying 2.5 kg/cm^2 of pressure via an algometer to each of the first, second, third, and fourth regions of pain symptoms and having the subject assess their perceived pain level on a scale ranging from 0 to 10, with 0 being the least amount of pain and 10 being the greatest amount of pain (indicated in column three as "Pre-Admin Pain Level"); iii) determining the cutaneous nerve branch(es) or main nerve trunk(s) liable for the pain symptoms in each of the first, second, third, and fourth regions; iv) confirming the liability of the cutaneous nerve branch(es) or main nerve trunk(s) for the pain symptoms in each of the first,

second, third, and fourth regions by palpation; and v) transdermally administering the inventive composition (1) along the nerve pathway liable for the pain symptoms proximate the first region; vi) transdermally administering the first compound along the nerve pathway liable for the pain symptoms proximate the second region; vii) transdermally administering the second compound along the nerve pathway liable for the pain symptoms proximate the third region; and viii) transdermally administering the third compound along the nerve pathway liable for the pain symptoms proximate the fourth region. Generally, the inventive composition (1) and each of the first, second, and third compounds were transdermally administered for a time period of about sixty seconds. Following, 2.5 kg/cm^2 of pressure was applied via an algometer to each of the first, second, third, and fourth regions of pain symptoms at about five minutes after the transdermal administration and the subject reassessed their perceived pain level (indicated in column four as "5 Minutes Post-Admin Pain Level") and again at about fifteen minutes after the transdermal administration, 2.5 kg/cm^2 of pressure was applied via an algometer to each of the first, second, third, and fourth regions of pain symptoms and the subject reassessed their perceived pain level (indicated in column six as "15 Minutes Post-Admin Pain Level").

Again referring primarily to Table 6, regarding the inventive composition (1) transdermally administered to the first region, the subject reported an 89% reduction in perceived pain level at five minutes post-administration (indicated in column five as "5 Minutes Post-Admin Pain Level") in relation to the pre-administration perceived pain level and an 89% reduction in perceived pain level at fifteen minutes post-administration (indicated in column five as "15 Minutes Post-Admin Pain Level") in relation to the pre-administration perceived pain level. Regarding the first compound transdermally administered to the second region, the subject reported a 50% reduction in perceived pain level at five minutes post-administration (indicated in column five as "5 Minutes Post-Admin Pain Level") in relation to the pre-administration perceived pain level and a 50% reduction in perceived pain level at fifteen minutes post-administration (indicated in column five as "15 Minutes Post-Admin Pain Level") in relation to the pre-administration perceived pain level. Regarding the third compound transdermally administered to the third region, the subject reported a 56% reduction in perceived pain level at five minutes post-administration (indicated in column five as "5 Minutes Post-Admin Pain Level") in relation to the pre-administration perceived pain level and a 66% reduction in perceived pain level at fifteen minutes post-administration (indicated in column five as "15 Minutes Post-Admin Pain Level") in relation to the pre-administration perceived pain level. Regarding the fourth compound transdermally administered to the fourth region, the subject reported a 70% reduction in perceived pain level at five minutes post-administration

(indicated in column five as "5 Minutes Post-Admin Pain Level") in relation to the pre-administration perceived pain level and an 80% reduction in perceived pain level at fifteen minutes post-administration (indicated in column five as "15 Minutes Post-Admin Pain Level") in relation to the pre-administration perceived pain level. Overall, of the inventive composition (1), and first, second, and third compounds, the greatest percent reduction in perceived pain level at both five minutes post-administration and fifteen minutes post-administration was observed following transdermal administration of the inventive composition (1).

Now referring primarily to Table 7, which evidences the results of the transdermal administration of a particular embodiment of the inventive composition (1), the first compound, the second compound, and the third compound (as detailed in column one) to a subject who presented with knee pain in four distinct regions (a first region, a second region, a third region, and a fourth region) along cutaneous branches of the femoral nerve, as detailed in column two. Upon presentation, the subject was medicating with oxycodone/acetaminophen (5/325 milligrams every four to six hours), yet still reported significant perceived pain. The inventive composition (1), first compound, second compound, and third compound were transdermally administered to the first, second, third, and fourth regions, respectively.

As to this particular embodiment, the inventive composition (1) included dextrose in an amount of about 20% by weight of the inventive composition (1), sodium bicarbonate in an amount of about 5% by weight of the inventive composition (1), and vehicle in an amount of about 75% by weight of the inventive composition (1).

The first compound included dextrose in an amount of about 10% by weight of the first compound, tannic acid in an amount of about 2% by weight of the first compound, aloe vera in an amount of about 0.75% by weight of the first compound, and vehicle in an amount of about 87.25% by weight of the first compound.

The second compound included mannitol in an amount of about 20% by weight of the second compound and vehicle in an amount of about 80% by weight of the second compound.

The third compound included dextrose in an amount of about 20% by weight of the third compound and vehicle in an amount of about 80% by weight of the third compound.

TABLE 7.

Inventive Composition and Compounds	Distinct Region	Pre-Admin Pain Level	5 Minutes Post-Admin Pain Level	Percent Reduction in Pain Level	15 Minutes Post-Admin Pain Level	Percent Reduction in Pain Level
Inventive Composition	First Region	10	1	90%	0	100%
First Compound	Second Region	8	4	50%	4	50%
Second Compound	Third Region	7	2	72%	2	72%
Third Compound	Fourth Region	7	1	86%	1	86%

Again referring primarily to Table 7, the method of transdermally administering the particular embodiment of the inventive composition (1) and each of the first, second, and third compounds included: i) identifying the first, second, third, and fourth regions of pain symptoms; ii) applying 2.5 kg/cm^2 of pressure via an algometer to each of the first, second, third, and fourth regions of pain symptoms and having the subject assess their perceived pain level on a scale ranging from 0 to 10, with 0 being the least amount of pain and 10 being the greatest amount of pain (indicated in column three as "Pre-Admin Pain Level"); iii) determining the cutaneous nerve branch(es) or main nerve trunk(s) liable for the pain symptoms in each of the first, second, third, and fourth regions; iv) confirming the liability of the cutaneous nerve branch(es) or main nerve trunk(s) for the pain symptoms in each of the first, second, third, and fourth regions by palpation; and v) transdermally administering the inventive composition (1) along the nerve pathway liable for the pain symptoms proximate the first region; vi) transdermally administering the first compound along the nerve pathway liable for the pain symptoms proximate the second region; vii) transdermally administering the second compound along the nerve pathway liable for the pain symptoms proximate the third region; and viii) transdermally administering the third compound along the nerve pathway liable for the pain symptoms proximate the fourth region. Generally, the inventive composition (1) and each of the first, second, and third compounds were transdermally administered for a time period of about sixty seconds. Following, 2.5 kg/cm^2 of pressure was applied via an algometer to each of the first, second, third, and fourth regions of pain symptoms at about five minutes after the transdermal administration and the subject reassessed their perceived pain level (indicated in column four as "5 Minutes Post-AdminPain Level") and again at about fifteen minutes after the transdermal administration, 2.5 kg/cm^2 of pressure was applied via an algometer to each of the

first, second, third, and fourth regions of pain symptoms and the subject reassessed their perceived pain level (indicated in column six as "15 Minutes Post-Admin Pain Level").

Again referring primarily to Table 7, regarding the inventive composition (1) transdermally administered to the first region, the subject reported a 90% reduction in perceived pain level at five minutes post-administration (indicated in column five as "5 Minutes Post-Admin Pain Level") in relation to the pre-administration perceived pain level and a 100% reduction in perceived pain level at fifteen minutes post-administration (indicated in column five as "15 Minutes Post-Admin Pain Level") in relation to the pre-administration perceived pain level. Regarding the first compound transdermally administered to the second region, the subject reported a 50% reduction in perceived pain level at five minutes post-administration (indicated in column five as "5 Minutes Post-Admin Pain Level") in relation to the pre-administration perceived pain level and a 50% reduction in perceived pain level at fifteen minutes post-administration (indicated in column five as "15 Minutes Post-Admin Pain Level") in relation to the pre-administration perceived pain level. Regarding the third compound transdermally administered to the third region, the subject reported a 72% reduction in perceived pain level at five minutes post-administration (indicated in column five as "5 Minutes Post-Admin Pain Level") in relation to the pre-administration perceived pain level and a 72% reduction in perceived pain level at fifteen minutes post-administration (indicated in column five as "15 Minutes Post-Admin Pain Level") in relation to the pre-administration perceived pain level. Regarding the fourth compound transdermally administered to the fourth region, the subject reported an 86% reduction in perceived pain level at five minutes post-administration (indicated in column five as "5 Minutes Post-Admin Pain Level") in relation to the pre-administration perceived pain level and an 86% reduction in perceived pain level at fifteen minutes post-administration (indicated in column five as "15 Minutes Post-Admin Pain Level") in relation to the pre-administration perceived pain level. Overall, of the inventive composition (1), and first, second, and third compounds, the greatest percent reduction in perceived pain level at both five minutes post-administration and fifteen minutes post-administration was observed following transdermal administration of the inventive composition (1).

Now referring primarily to Table 8, which evidences the results of the transdermal administration of a first inventive composition (1), a second inventive composition (1), a first compound, and a second compound (as detailed in column one) to a subject who presented with lower back pain in four distinct regions (a first region, a second region, a third region, and a fourth region), as detailed in column two. Upon presentation, the subject was having a

trochanteric shot administered every four weeks. In addition, the subject was medicating with a steroid pak, celecoxib (200 milligrams every twenty-four hours), and oxycodone/acetaminophen (10/325 milligrams every four hours), yet still reported significant perceived pain. The first inventive composition (1), the second inventive composition (1), the first compound, and the second compound were transdermally administered to the first, second, third, and fourth regions, respectively.

As to this particular embodiment, the first inventive composition (1) included dextrose in an amount of about 25% by weight of the first inventive composition (1), sodium bicarbonate in an amount of about 2.5% by weight of the first inventive composition (1), and vehicle in an amount of about 72.5% by weight of the first inventive composition (1).

The second inventive composition (1) included dextrose in an amount of about 20% by weight of the second inventive composition (1), sodium bicarbonate in an amount of about 10% by weight of the second inventive composition (1), and vehicle in an amount of about 70% by weight of the second inventive composition (1).

The first compound included sodium bicarbonate in an amount of about 2.5% by weight of the first compound and vehicle in an amount of about 97.5% by weight of the first compound.

The second compound included mannitol in an amount of about 2.5% by weight of the second compound and vehicle in an amount of about 97.5% by weight of the second compound.

TABLE 8.

Inventive Composition and Compounds	Distinct Region	Pre-Admin Pain Level	5 Minutes Post-Admin Pain Level	Percent Reduction in Pain Level	15 Minutes Post-Admin Pain Level	Percent Reduction in Pain Level
First Inventive Composition	First Region	7	3	57%	3	57%
Second Inventive Composition	Second Region	6	1	83%	1	83%
First Compound	Third Region	9	8	11%	7	22%

Second Compound	Fourth Region	6	3	50%	3	50%

Again referring primarily to Table 8, the method of transdermally administering the particular embodiment of the inventive composition (1) and each of the first, second, and third compounds included: i) identifying the first, second, third, and fourth regions of pain symptoms; ii) applying 2.0 kg/cm^2 of pressure via an algometer to each of the first, second, third, and fourth regions of pain symptoms and having the subject assess their perceived pain level on a scale ranging from 0 to 10, with 0 being the least amount of pain and 10 being the greatest amount of pain (indicated in column three as "Pre-Admin Pain Level"); iii) determining the cutaneous nerve branch(es) or main nerve trunk(s) liable for the pain symptoms in each of the first, second, third, and fourth regions; iv) confirming the liability of the cutaneous nerve branch(es) or main nerve trunk(s) for the pain symptoms in each of the first, second, third, and fourth regions by palpation; and v) transdermally administering the inventive composition (1) along the nerve pathway liable for the pain symptoms proximate the first region; vi) transdermally administering the first compound along the nerve pathway liable for the pain symptoms proximate the second region; vii) transdermally administering the second compound along the nerve pathway liable for the pain symptoms proximate the third region; and viii) transdermally administering the third compound along the nerve pathway liable for the pain symptoms proximate the fourth region. Generally, each of the first inventive composition (1), the second inventive composition (1), the first compound, and the second compound were transdermally administered for a time period of about sixty seconds. Following, 2.5 kg/cm^2 of pressure was applied via an algometer to each of the first, second, third, and fourth regions of pain symptoms at about five minutes after the transdermal administration and the subject reassessed their perceived pain level (indicated in column four as "5 Minutes Post-Admin Pain Level") and again at about fifteen minutes after the transdermal administration, 2.5 kg/cm^2 of pressure was applied via an algometer to each of the first, second, third, and fourth regions of pain symptoms and the subject reassessed their perceived pain level (indicated in column six as "15 Minutes Post-Admin Pain Level").

Again referring primarily to Table 8, regarding the first inventive composition (1) transdermally administered to the first region, the subject reported a 57% reduction in perceived pain level at five minutes post-administration (indicated in column five as "5 Minutes Post-Admin Pain Level") in relation to the pre-administration perceived pain level and a 57% reduction in perceived pain level at fifteen minutes post-administration (indicated in column

five as "15 Minutes Post-Admin Pain Level") in relation to the pre-administration perceived pain level. Regarding the second inventive composition (1) transdermally administered to the second region, the subject reported an 83% reduction in perceived pain level at five minutes post-administration (indicated in column five as "5 Minutes Post-Admin Pain Level") in relation to the pre-administration perceived pain level and an 83% reduction in perceived pain level at fifteen minutes post-administration (indicated in column five as "15 Minutes Post-Admin Pain Level") in relation to the pre-administration perceived pain level. Regarding the first compound transdermally administered to the third region, the subject reported an 11% reduction in perceived pain level at five minutes post-administration (indicated in column five as "5 Minutes Post-Admin Pain Level") in relation to the pre-administration perceived pain level and a 22% reduction in perceived pain level at fifteen minutes post-administration (indicated in column five as "15 Minutes Post-AdminPain Level") in relation to the pre-administration perceived pain level. Regarding the second compound transdermally administered to the fourth region, the subject reported a 50% reduction in perceived pain level at five minutes post-administration (indicated in column five as "5 Minutes Post-Admin Pain Level") in relation to the pre-administration perceived pain level and a 50% reduction in perceived pain level at fifteen minutes post-administration (indicated in column five as "15 Minutes Post-Admin Pain Level") in relation to the pre-administration perceived pain level. Overall, of the first inventive composition (1), the second inventive composition (1), the first compound, and the second compound, the greater percent reduction in perceived pain level at both five minutes post-administration and fifteen minutes post-administration was observed following transdermal administration of the first and second inventive compositions (1)(1), with the greatest percent reduction in perceived pain level at both five minutes post-administration and fifteen minutes post-administration observed following transdermal administration of the second inventive composition (1).

As can be easily understood from the foregoing, the basic concepts of the present invention may be embodied in a variety of ways. The invention involves numerous and varied embodiments of a pain relieving system and methods for making and using such pain relieving systems, including the best mode.

As such, the particular embodiments or elements of the invention disclosed by the description or shown in the figures or tables accompanying this application are not intended to be limiting, but rather exemplary of the numerous and varied embodiments generically encompassed by the invention or equivalents encompassed with respect to any particular

element thereof. In addition, the specific description of a single embodiment or element of the invention may not explicitly describe all embodiments or elements possible; many alternatives are implicitly disclosed by the description and figures.

It should be understood that each element of an apparatus or each step of a method may be described by an apparatus term or method term. Such terms can be substituted where desired to make explicit the implicitly broad coverage to which this invention is entitled. As but one example, it should be understood that all steps of a method may be disclosed as an action, a means for taking that action, or as an element which causes that action. Similarly, each element of an apparatus may be disclosed as the physical element or the action which that physical element facilitates. As but one example, the disclosure of a "combination" should be understood to encompass disclosure of the act of "combining" -- whether explicitly discussed or not -- and, conversely, were there effectively disclosure of the act of "combining", such a disclosure should be understood to encompass disclosure of a "combination" and even a "means for combining". Such alternative terms for each element or step are to be understood to be explicitly included in the description.

In addition, as to each term used it should be understood that unless its utilization in this application is inconsistent with such interpretation, common dictionary definitions should be understood to be included in the description for each term as contained in the Random House Webster's Unabridged Dictionary, second edition, each definition hereby incorporated by reference.

All numeric values herein are assumed to be modified by the term "about", whether or not explicitly indicated. For the purposes of the present invention, ranges may be expressed as from "about" one particular value to "about" another particular value. When such a range is expressed, another embodiment includes from the one particular value to the other particular value. The recitation of numerical ranges by endpoints includes all the numeric values subsumed within that range. A numerical range of one to five includes for example the numeric values 1, 1.5, 2, 2.75, 3, 3.80, 4, 5, and so forth. It will be further understood that the endpoints of each of the ranges are significant both in relation to the other endpoint, and independently of the other endpoint. When a value is expressed as an approximation by use of the antecedent "about," it will be understood that the particular value forms another embodiment. The term "about" generally refers to a range of numeric values that one of skill in the art would consider equivalent to the recited numeric value or having the same function or result. Similarly, the antecedent "substantially" means largely, but not wholly, the same form, manner or degree and

the particular element will have a range of configurations as a person of ordinary skill in the art would consider as having the same function or result. When a particular element is expressed as an approximation by use of the antecedent "substantially," it will be understood that the particular element forms another embodiment.

Moreover, for the purposes of the present invention, the term “a” or “an” entity refers to one or more of that entity unless otherwise limited. As such, the terms “a” or “an”, “one or more” and “at least one” can be used interchangeably herein.

Thus, the applicant(s) should be understood to claim at least: i) each of the pain relieving systems herein disclosed and described, ii) the related methods disclosed and described, iii) similar, equivalent, and even implicit variations of each of these devices and methods, iv) those alternative embodiments which accomplish each of the functions shown, disclosed, or described, v) those alternative designs and methods which accomplish each of the functions shown as are implicit to accomplish that which is disclosed and described, vi) each feature, component, and step shown as separate and independent inventions, vii) the applications enhanced by the various systems or components disclosed, viii) the resulting products produced by such systems or components, ix) methods and apparatuses substantially as described hereinbefore and with reference to any of the accompanying examples, x) the various combinations and permutations of each of the previous elements disclosed.

The background section of this patent application provides a statement of the field of endeavor to which the invention pertains. This section may also incorporate or contain paraphrasing of certain United States patents, patent applications, publications, or subject matter of the claimed invention useful in relating information, problems, or concerns about the state of technology to which the invention is drawn toward. It is not intended that any United States patent, patent application, publication, statement or other information cited or incorporated herein be interpreted, construed or deemed to be admitted as prior art with respect to the invention.

The claims set forth in this specification are hereby incorporated by reference as part of this description of the invention, and the applicant expressly reserves the right to use all of or a portion of such incorporated content of such claims as additional description to support any of or all of the claims or any element or component thereof, and the applicant further expressly reserves the right to move any portion of or all of the incorporated content of such claims or any element or component thereof from the description into the claims or vice-versa as necessary to

define the matter for which protection is sought by this application or by any subsequent application or continuation, division, or continuation-in-part application thereof, or to obtain any benefit of, reduction in fees pursuant to, or to comply with the patent laws, rules, or regulations of any country or treaty, and such content incorporated by reference shall survive during the entire pendency of this application including any subsequent continuation, division, or continuation-in-part application thereof or any reissue or extension thereon.

Additionally, the claims set forth in this specification, if any, are further intended to describe the metes and bounds of a limited number of the preferred embodiments of the invention and are not to be construed as the broadest embodiment of the invention or a complete listing of embodiments of the invention that may be claimed. The applicant does not waive any right to develop further claims based upon the description set forth above as a part of any continuation, division, or continuation-in-part, or similar application.

V. CLAIMS

1. A composition for relieving pain, said composition comprising:
an amount of sugar or sugar alcohol; and
an amount of vehicle;
wherein said composition is formulated for transdermal administration; and
wherein, upon said transdermal administration, said composition is effective to relieve pain.

2. The composition of claim 1, wherein said amount of sugar or sugar alcohol is in a range of between about 1 to about 40% by weight of said composition.

3. The composition of claim 1, wherein said amount of sugar or sugar alcohol is in a range selected from the group consisting of: between about 1% to about 5% by weight of said composition, between about 2.5% to about 7.5% by weight of said composition, between about 5% to about 10% by weight of said composition, between about 7.5% to about 12.5% by weight of said composition, between about 10% to about 15% by weight of said composition, between about 12.5% to about 17.5% by weight of said composition, between about 15% to about 20% by weight of said composition, between about 17.5% to about 22.5% by weight of said composition, between about 20% to about 25% by weight of said composition, between about 22.5% to about 27.5% by weight of said composition, between about 25% to about 30% by weight of said composition, between about 27.5% to about 32.5% by weight of said composition, between about 30% to about 35% by weight of said composition, between about 32.5% to about 37.5% by weight of said composition, between about 35% to about 40% by weight of said composition, between about 5% to about 40% by weight of said composition, between about 10% to about 40% by weight of said composition, between about 15% to about 40% by weight of said composition, between about 20% to about 40% by weight of said composition, between about 25% to about 40% by weight of said composition, between about 30% to about 40% by weight of said composition, and between about 35% to about 40% by weight of said composition.

4. The composition of claim 1, wherein said sugar comprises one or more compounds selected from the group consisting of: ribose, xylose, fructose, dextrose, galactose, mannose, sorbose, sucrose, maltose, lactose, lactulose, trehalose, and cellobiose.

5. The composition of claim 1, wherein said sugar comprises dextrose.

6. The composition of claim 1, wherein said sugar alcohol comprises one or more compounds selected from the group consisting of: glycerol, erythritol, threitol, arabitol, xylitol, adonitol, mannitol, sorbitol, dulcitol, fucitol, iditol, inositol, volemitol, isomalt, maltitol, lactitol, and maltotriitol.

7. The composition of claim 1, wherein said sugar alcohol comprises mannitol.

8. The composition of claim 1, further comprising an amount of alkalizing agent.

9. The composition of claim 8, wherein said amount of alkalizing agent is in a range of between about 0.1% to about 15% by weight of said composition.

10. The composition of claim 8, wherein said amount of alkalizing agent is in a range selected from the group consisting of: between about 0.1% to about 5% by weight of said composition, between about 1% to about 5% by weight of said composition, between about 2.5% to about 7.5% by weight of said composition, between about 5% to about 10% by weight of said composition, between about 7.5% to about 12.5% by weight of said composition, between about 10% to about 15% by weight of said composition, between about 1% to about 15% by weight of said composition, between about 2.5% to about 15% by weight of said composition, between about 5% to about 15% by weight of said composition, between about 7.5% to about 15% by weight of said composition, between about 10% to about 15% by weight of said composition, and between about 12.5% to about 15% by weight of said composition.

11. The composition of claim 8, wherein said amount of alkalizing agent is in a range of between about 3% to about 5% by weight of said composition.

12. The composition of claim 8, wherein said amount of alkalizing agent is sufficient to provide said composition with a pH of between about 8 to about 10.

13. The composition of claim 8, wherein said amount of alkalizing agent is sufficient to provide said composition with a pH selected from the group including or consisting of: between about 8 to about 8.5, between about 8.25 to about 8.75, between about 8.5 to about 9, between about 8.75 to about 9.25, between about 9 to about 9.5, between about 9.25 to about 9.75, and between about 9.5 to about 10.

14. The composition of claim 8, wherein said alkalizing agent comprises one or more compounds selected from the group consisting of: sodium bicarbonate, potassium citrate, calcium carbonate, and calcium acetate.

15. The composition of claim 8, wherein said alkalizing agent comprises sodium bicarbonate.

16. The composition of claim 8, wherein said alkalizing agent comprises a salt.

17. The composition of claim 16, wherein said salt comprises a cation selected from the group consisting of: sodium, calcium, potassium, zinc, iron, and magnesium.

18. The composition of claim 16, wherein said salt comprises an anion selected from the group consisting of: chloride, acetate, ascorbate, bicarbonate, citrate, formate, fumarate, phosphate, succinate, borate, gluconate, lactate, malate, trimalate, panthothenate, thiocyanate, glycinate, and sulphate.

19. The composition of claim 16, wherein said salt comprises a compound selected from the group consisting of: sodium chloride, sodium acetate, sodium bicarbonate, sodium citrate, sodium phosphate, sodium dihydrogen phosphate, sodium hydrogen phosphate, sodium succinate, sodium borate, sodium gluconate, sodium citrate, sodium lactate, calcium citrate, calcium chloride, calcium pantothenate, calcium gluconate, calcium phosphate, potassium chloride, monopotassium phosphate, dipotassium phosphate, tripotassium phosphate, potassium gluconate, magnesium sulphate, magnesium chloride, magnesium gluconate, magnesium acetate, magnesium malate, magnesium glycinate, magnesium lactate, zinc chloride, zinc sulphate and zinc acetate.

20. The composition of claim 1, wherein said amount of sugar or sugar alcohol is solubilized in said vehicle.

21. The composition of claim 1, wherein said amount of sugar or sugar alcohol is suspended in said vehicle.

22. The composition of claim 1, wherein said vehicle facilitates said transdermal administration of a portion of said amount sugar or sugar alcohol.

23. The composition of claim 8, wherein said amount of sugar or sugar alcohol, said amount of alkalizing agent, or combinations thereof, are solubilized in said vehicle.

24. The composition of claim 8, wherein said amount of sugar or sugar alcohol, said amount of alkalizing agent, or combinations thereof, are suspended in said vehicle.

25. The composition of claim 8, wherein said vehicle facilitates said transdermal administration of a portion of said amount sugar or sugar alcohol, a portion of said amount of alkalizing agent, or combinations thereof.

26. The composition of claim 1 or claim 8, wherein said vehicle comprises an emulsion base.

27. The composition of claim 26, wherein said emulsion base comprises an oil selected from the group consisting of: vegetable oils, animal oils, mineral oils, silicone oils, synthetic oils, fatty acids, fatty alcohols, phospholipids, and paraffin waxes.

28. The composition of claim 1 or claim 8, were said vehicle comprises a solubilizing agent.

29. The composition of claim 28, wherein said solubilizing agent is selected from the group consisting of: cyclodextrins, surfactants, organic solvents, alcohols, and polysorbates.

30. The composition of claim 1 or claim 8, wherein said vehicle comprises a viscosity-increasing agent.

31. The composition of claim 30, wherein said viscosity-increasing agent is selected from the group consisting of: microcrystalline cellulose, carboxymethylcellulose sodium, propylene glycol alginate, xanthan gum, and polyacrylic acid

32. The composition of claim 1 or claim 8, wherein said vehicle comprises an emulsifying agent.

33. The composition of claim 32, wherein said emulsifying agent is selected from the group consisting of: non-ionic surfactants, polyethylene glycol esters, polyoxypropylene glycol ethers, sorbitan esters, ethoxylated sorbitan esters, and poly esters.

34. The composition of claim 1 or claim 8, wherein said vehicle comprises an emulsion stabilizing agent.

35. The composition of claim 34, wherein said emulsion stabilizing agent is selected from the group consisting of: abietic acid, hydrogenated lanolin alcohol, calcium myristate, hydroxyaluminium distearate, aluminum isostearate, aluminum stearate, 7, 8-didehydrocholesterol, aluminum magnesium hydroxide, stearic acid, lauryl alcohol, and hydroxyethyl cellulose.

36. The composition of claim 1 or claim 8, wherein said vehicle comprises a preserving agent.

37. The composition of claim 36, wherein said preserving agent is selected from the group consisting of: sorbic acid, methyl paraben, propyl paraben, benzoic acid, sodium benzoate cetrimide, phenoxyethanol, chlorphenisin, and methylchloroisothiazolinone.

38. The composition of claim 1 or claim 8, wherein said vehicle comprises a penetration enhancer.

39. The composition of claim 38, wherein said penetration enhancer is selected from the group consisting of: alcohols, sulphoxides, azone, pyrrolidones, urea, disubstituted aminoacetates, glycols (for example, propylene glycol), surfactants, terpenes, terpenoids, fatty acids, esters, cyclodextrins, and phospholipids.

40. The composition of claim 1 or claim 8, wherein said vehicle comprises water.

41. The composition of claim 1 or claim 8, wherein said vehicle comprises fatty acid alcohols, acids, esters, phospholipids, antioxidants, skin-feel enhancer, natural humectant, natural preservatives, nonionic emulsifiers, anionic emulsifiers, and buffer.

42. The composition of claim 1 or claim 8, wherein said vehicle comprises waters, fatty acid esters, alcohols, paraffinic silicone replacement, glidant, plant-derived emollient, vitamin E, nonionic emulsifiers, pro-liposomal phospholipids, and preservatives.

43. The composition of claim 1 or claim 8, further comprising an amount of magnesium.

44. The composition of claim 43, wherein said amount of magnesium is provided by magnesium chloride or magnesium sulfate.

45. The composition of claim 1 or claim 8, furthering comprising an amount of *Aesculus hippocastanum*.

46. The composition of claim 45, wherein said amount of *Aesculus hippocastanum* is in a range of between about 0.25% to about 2% by weight of said composition.

47. The composition of claim 45, wherein said amount of *Aesculus hippocastanum* comprises aescin.

48. The composition of claim 1 or claim 8, furthering comprising an amount of quercetin.

49. The composition of claim 48, wherein said amount of quercetin is in a range of between about 0.1% to about 1% by weight of said composition.

50. The composition of claim 1 or claim 8, further comprising an amount of acetyl-L-carnitine.

51. The composition of claim 50, wherein said amount of acetyl-L-carnitine is in a range of between about 0.025% to about 3% by weight of said composition.

52. The composition of claim 1 or claim 8, further comprising an amount of zinc.

53. The composition of claim 52, wherein said amount of zinc is in a range of between about 0.025% to about 3% by weight of said composition.

54. The composition of claim 52, wherein said amount of zinc is provided by zinc oxide or zinc sulfate.

55. The composition of claim 1 or claim 8, wherein said transdermal administration is facilitated by one or more physical skin penetration enhancement techniques.

56. The composition of claim 55, wherein said skin penetration enhancement technique is selected from the group consisting of: phonophoresis, sonophoresis, iontophoresis, electroporation, radiofrequency-driven skin microchanneling, micro-needles, nano-needles, massage, occlusion, heating, and cooling.

57. The composition of claim 1 or claim 8, wherein, upon said transdermal administration, said composition is effective to decrease neurogenic pain.

58. The composition of claim 1 or claim 8, wherein, upon said transdermal administration, said composition is effective to decrease neurogenic inflammation.

59. The composition of claim 57 or claim 58, wherein, upon said transdermal administration, said composition is effective to alkalize a perineural environment proximate a nerve.

60. The composition of claim 59, wherein alkalization of said perineural environment comprises adjusting a pH of said perineural environment from a lesser alkalinity toward a greater alkalinity.

61. The composition of claim 57 or claim 58, wherein, upon said transdermal administration, said composition is effective to decrease an amount of cations in a perineural environment proximate a nerve.

62. The composition of claim 57 or claim 58, wherein, upon said transdermal administration, said composition is effective to decrease a viscosity of hyaluronic acid.

63. The composition of claim 62, wherein a decrease in said viscosity of said hyaluronic acid decreases mechanical irritation of a nerve by fascia enveloping said nerve.

64. The composition of claim 57 or claim 58, wherein, upon said transdermal administration, said composition is effective to provide an amount of energetic substrate to a nerve.

65. The composition of claim 64, wherein said energetic substrate comprises said sugar.

66. The composition of claim 65, wherein said sugar comprises dextrose.

67. The composition of claim 1 or claim 8, wherein said composition is coupled to a tape element.

68. The composition of claim 67, wherein said tape element is configured to couple to an external surface of a body of a user.

69. The composition of claim 68, wherein said tape element is non-elastic, having dimensions which are generally non-stretchable.

70. The composition of claim 68, wherein said tape element is elastic, having dimensions which are stretchably adjustable between unstretched and stretched conditions.

71. The composition of claim 68, wherein said tape element comprises an exterior layer and a contact layer, said contact layer configured for contact with said external surface of said body of said user.

72. The composition of claim 71, wherein said composition is integrated with an adhesive coupled to said contact layer.

73. The composition of claim 67, wherein said composition is included in a delivery system having microstructures or nanostructures.

74. The composition of claim 73, wherein said microstructures or nanostructures comprise corresponding micro-needles or nano-needles.

75. A method of making a composition for relieving pain, said method comprising:
combining an amount of sugar or sugar alcohol and an amount of vehicle; and
formulating said composition for transdermal administration;
wherein, upon said transdermal administration, said composition is effective to relieve pain.

76. The method of claim 75, further comprising combining an amount of alkalizing agent with said amount of sugar or sugar alcohol and said amount of vehicle.

77. The method of claim 75 or claim 76, further comprising coupling said composition to a tape element.

78. The method of claim 77, further comprising configuring said tape element to couple to an external surface of a body of a user.

79. The method of claim 78, further comprising configuring said tape element as non-elastic, having dimensions which are generally non-stretchable.

80. The method of claim 78, further comprising configuring said tape element as elastic, having dimensions which are stretchably adjustable between unstretched and stretched conditions.

81. The method of claim 78, further comprising configuring said tape element to have an exterior layer and a contact layer, said contact layer configured for contact with said external surface of said body of said user.

82. The method of claim 81, further comprising integrating said composition with an adhesive coupled to said contact layer.

83. The method of claim 77, further comprising including said composition in a delivery system having microstructures or nanostructures.

84. The method of claim 83, further comprising configuring said microstructures or nanostructures as corresponding micro-needles or nano-needles.

85. A method for relieving pain, said method comprising:

obtaining a composition comprising:

an amount of sugar or sugar alcohol; and

an amount of vehicle;

wherein said composition is formulated for transdermal administration; and

wherein, upon said transdermal administration, said composition is effective to relieve pain; and

transdermally administering said composition in an amount effective to relieve said pain.

86. The method of claim 85, wherein said composition further comprises an amount of alkalizing agent.

87. The method of claim 85 or claim 86, further comprising transdermally administering said composition to decrease neurogenic pain.

88. The method of claim 87, further comprising transdermally administering said composition along a nerve pathway of a nerve to decrease said neurogenic pain.

89. The method of claim 85 or claim 86, further comprising transdermally administering said composition to decrease neurogenic inflammation.

90. The method of claim 89, further comprising transdermally administering said composition along a nerve pathway of a nerve to decrease said neurogenic inflammation.

91. The method of claim 88 or claim 90, further comprising transdermally administering said composition to alkalize a perineural environment proximate said nerve.

92. The method of claim 91, wherein alkalization of said perineural environment comprises adjusting a pH of said perineural environment from a lesser alkalinity toward a greater alkalinity.

93. The method of claim 88 or claim 90, further comprising transdermally administering said composition to decrease an amount of cations in a perineural environment proximate said nerve.

94. The method of claim 88 or claim 90, further comprising transdermally administering said composition to decrease a viscosity of hyaluronic acid.

95. The method of claim 94, wherein a decrease in said viscosity of said hyaluronic acid decreases mechanical irritation of said nerve by fascia enveloping said nerve.

96. The method of claim 88 or claim 90, further comprising transdermally administering said composition to provide an amount of energetic substrate to said nerve.

97. The method of claim 96, wherein said energetic substrate comprises said sugar.

98. The method of claim 97, wherein said sugar comprises dextrose.

99. The method of claim 85 or claim 86, further comprising transdermally administering said composition formulated as a fluid selected from the group consisting of: lotion, cream, emulsion, ointment, gel, foam, paste, oil, lipid delivery system, spray, and drops.

100. The method of claim 85 or claim 86, further comprising administering one or more physical skin penetration enhancement techniques before, during, or after transdermal administration of said composition.

101. The method of claim 100, wherein said skin penetration enhancement technique is selected from the group consisting of: phonophoresis, sonophoresis, iontophoresis, electroporation, radiofrequency-driven skin microchanneling, micro-needles, nano-needles, massage, occlusion, heating, and cooling.

102. The method of claim 85 or claim 86, further comprising transdermally administering said composition coupled to a tape element.

103. The method of claim 102, wherein said tape element is configured to couple to an external surface of a body of a user.

104. The method of claim 103, further comprising adhering said tape element to said external surface of said body of said user.

105. The method of claim 103, further comprising surrounding said external surface of said body of said user with said tape element.

106. The method of claim 103, further comprising coupling said tape element along a nerve pathway of a nerve.

FIG. 1A

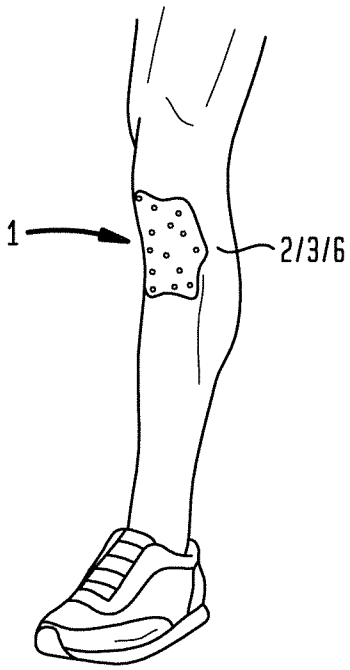


FIG. 1B

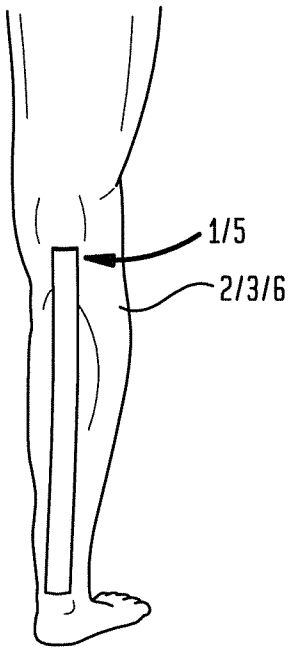


FIG. 1C

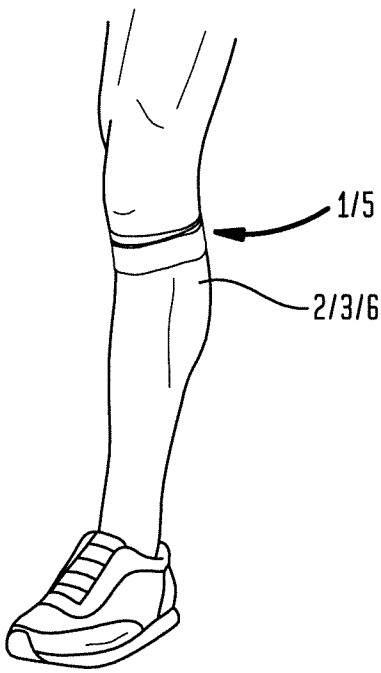


FIG. 2A

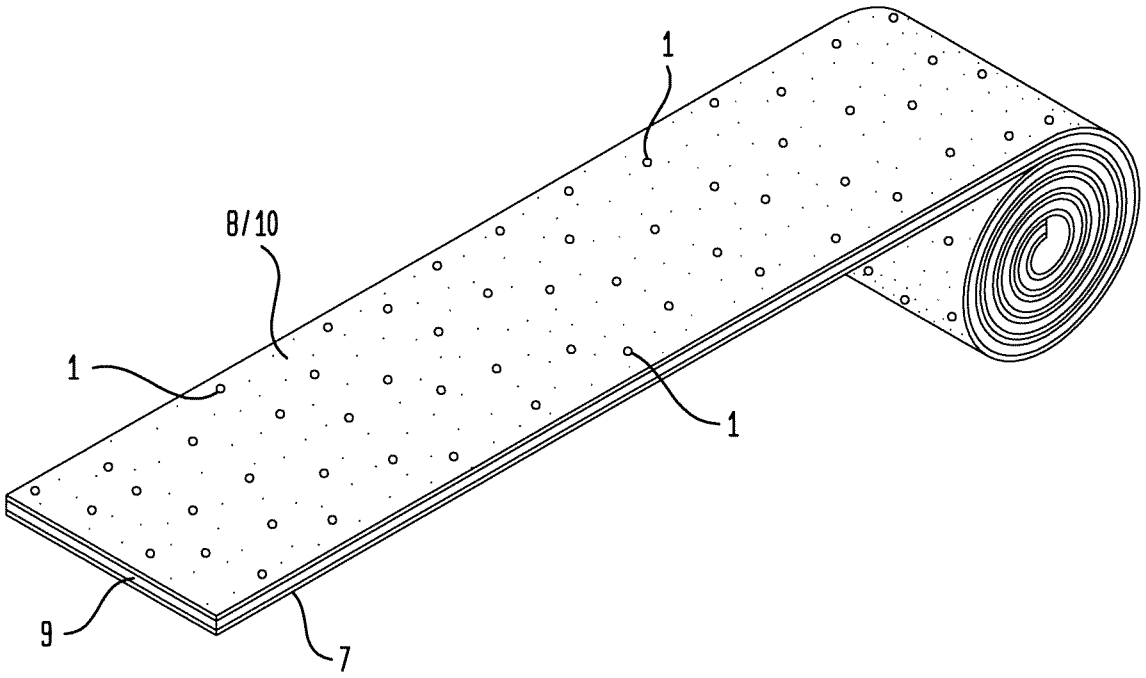


FIG. 2B

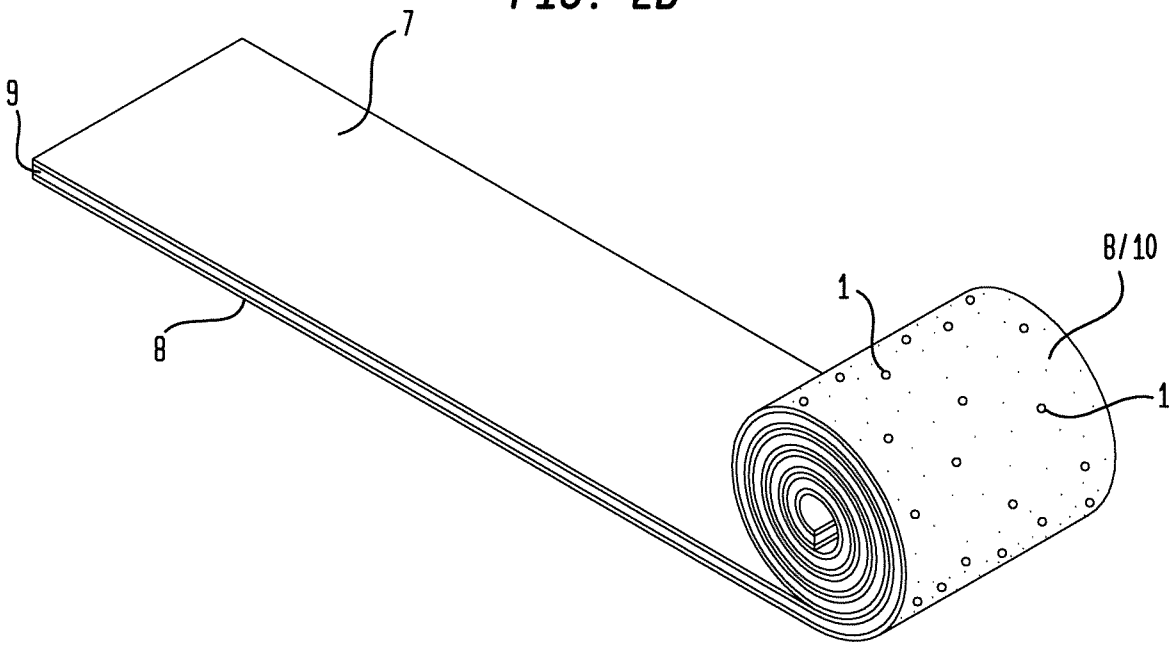


FIG. 3A

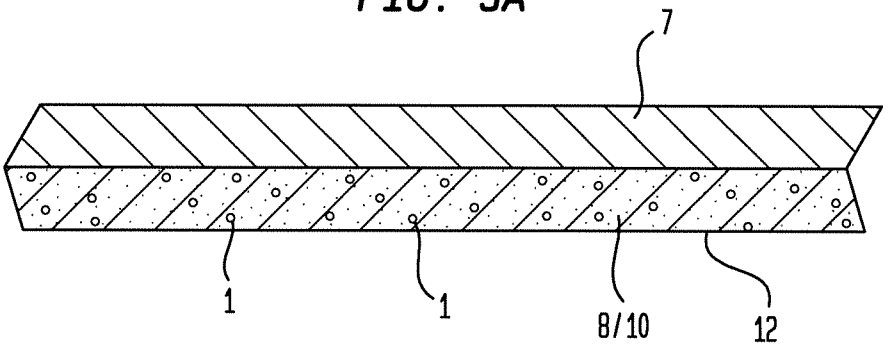


FIG. 3B

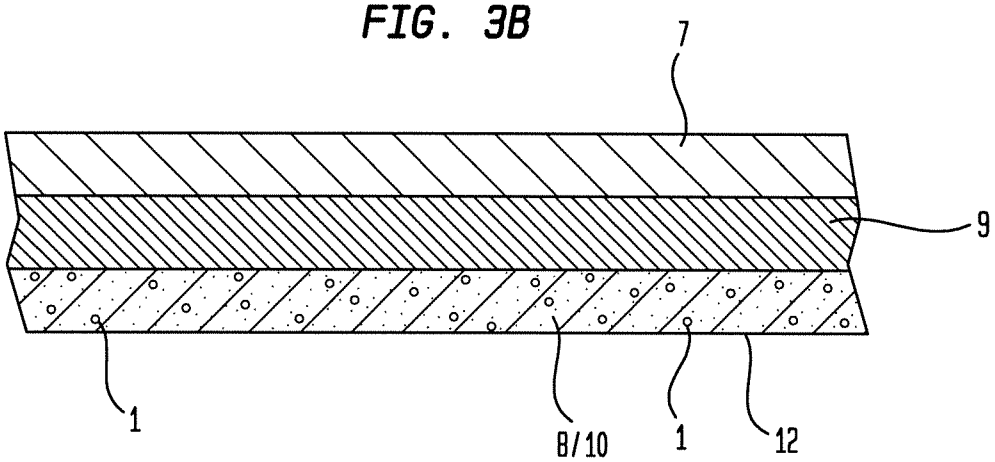


FIG. 4A

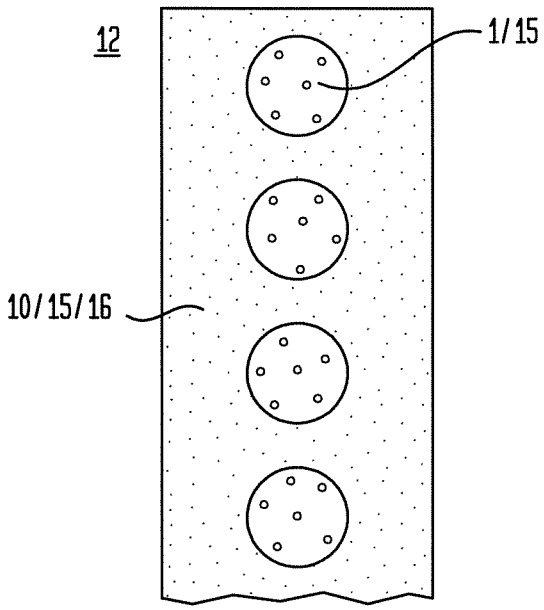


FIG. 4B

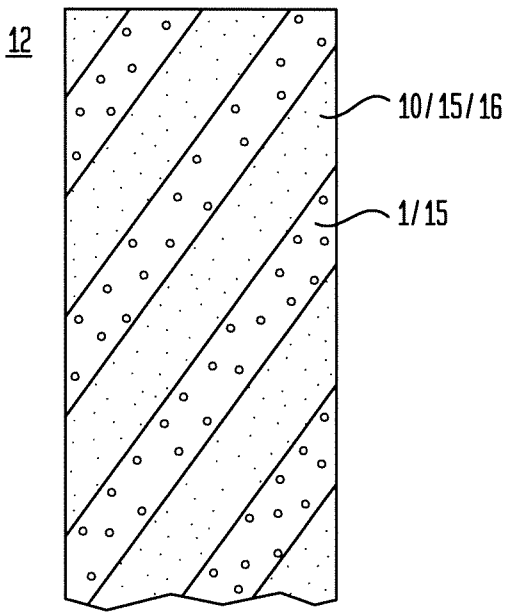


FIG. 4C

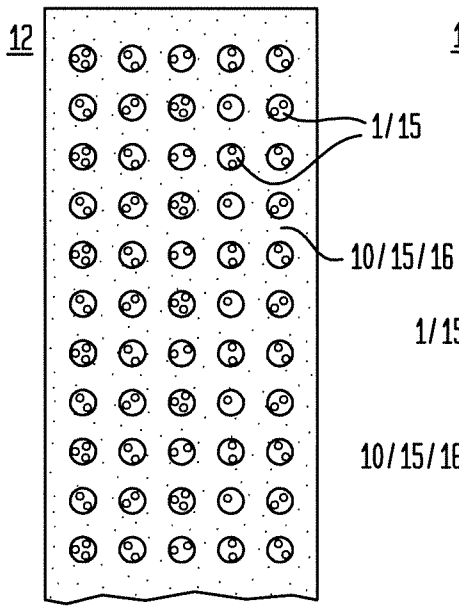


FIG. 4D

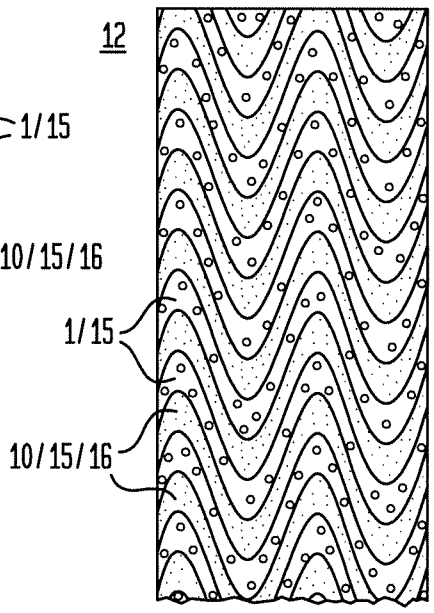
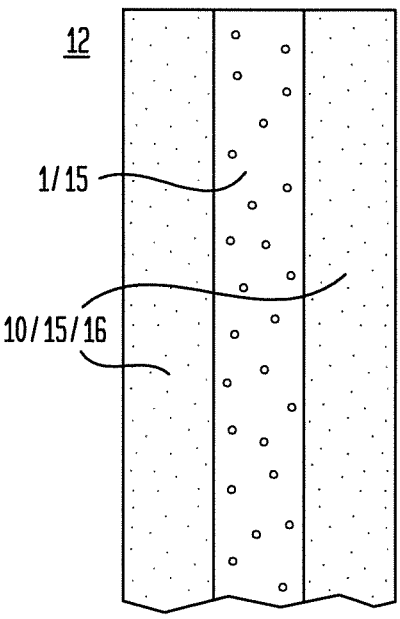


FIG. 4E



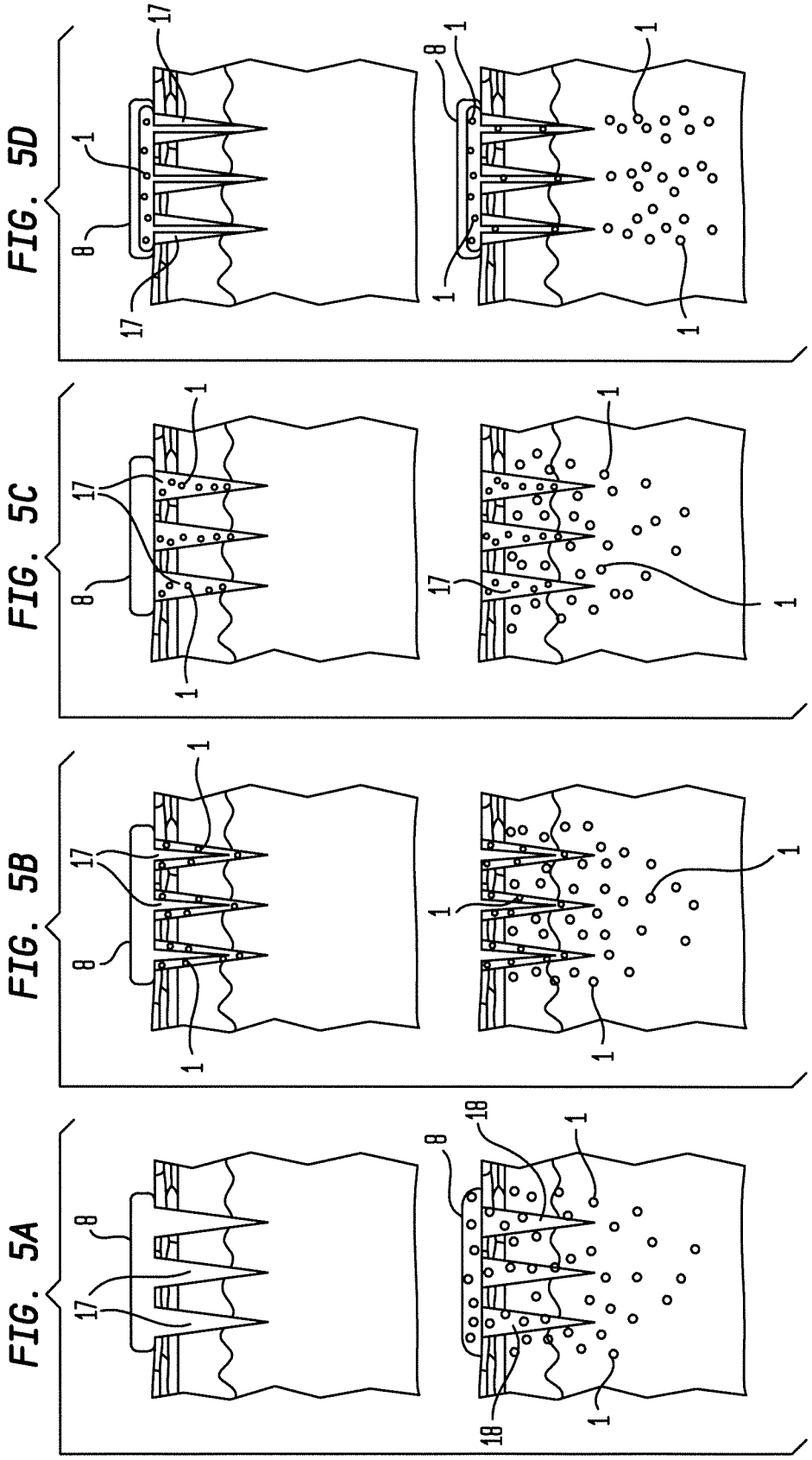


FIG. 5A
FIG. 5B
FIG. 5C
FIG. 5D
8
17
1
18

FIG. 6A

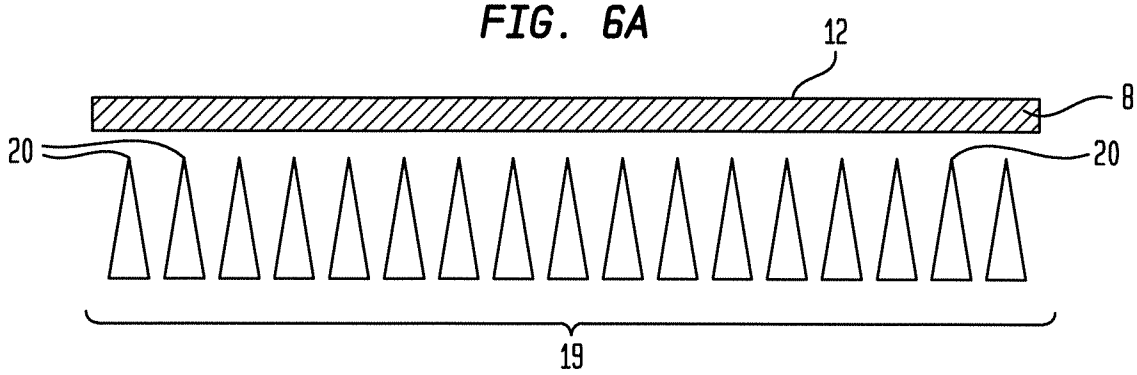


FIG. 6B

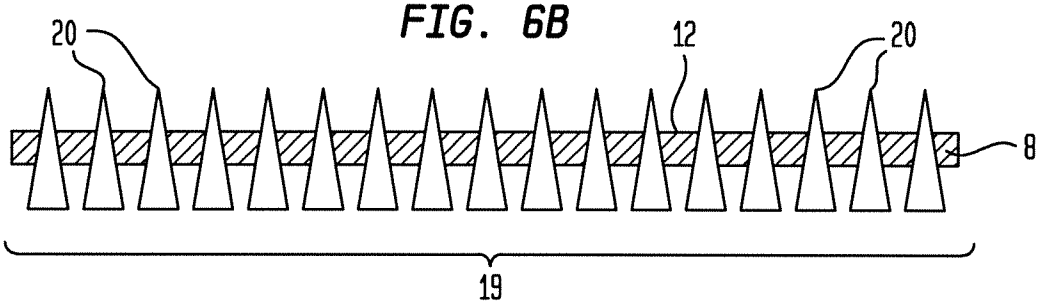


FIG. 6C

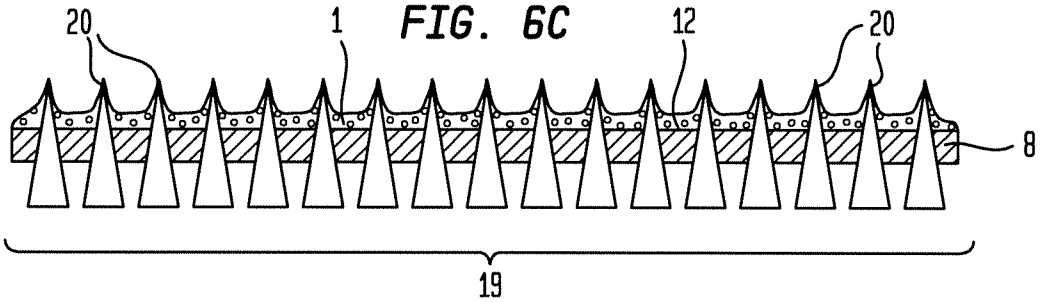
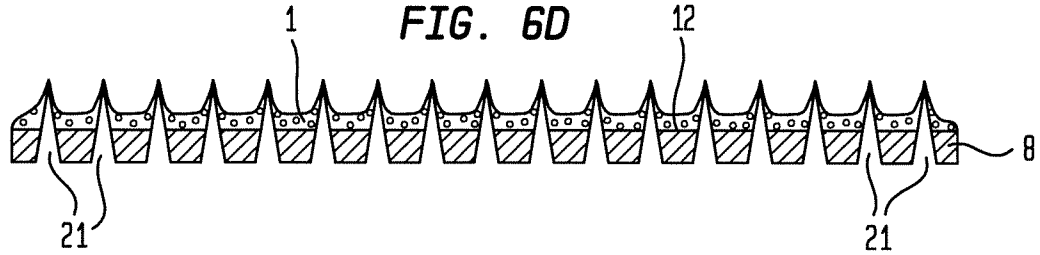


FIG. 6D



INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 15/45753

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61K 31/70; A61K 31/047; A61P 25/00 (2015.01)
CPC - A61K 31/70; C07D309/10
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)
IPC(8) - A61K 31/70; A61K 31/047; A61P 25/00 (2015.01)
CPC - A61K 31/70; C07D309/10

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
UC - 514/23; 536/1.11

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Minesoft patbase, Google Scholar; keywords: sugar/dextrose, sugar alcohol/mannitol, pain relieving system, transdermal, sodium bicarbonate; PA = (NOVA w2 NEURA)

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 2013/0236577 A1 (ROSEN) 12 September 2013 (12.09.2013) abstract, [0005]-[0014], [0033], [0053], [0056]-[0070]	1-7, 20, 21, 38-40, 55-56, 75, 85, 99-101 ---------- 8-19, 22-37, 41-54, 57,58, 67-74, 76-84, 86-98, 102-106
Y	US 2002/0032240 A1 (Hsu et al.) 14 March 2002 (14.03.2002)abstract, [0057], [0058], [0059], [0068]	8-19, 22-37, 41-44, 76, 86, 91-95
Y	US 2010/0062067 A1 (Tonge et al.) 11 March 2010 (11.03.2010) para [0017], [0239]-[0241]; [0243]-[0244]; [0248]	45-47
Y	US 2008/0070875 A1 (Majewski et al.) 20 March 2008 (20.03.2008) para [0071], [0095]	48-49
Y	US 6585987 A (Fransoni) 01 July 2003 (01.07.2003) abstract; col 1, lines 20-25; col 13, lines 40 -45	50-51
Y	US 2002/0037314 A1 (Meisner) 28 March 2002 (28.03.2002) para [0051]	52-54
Y	US 2011/0274743 A1 (Lyftogt) 10 November 2011 (10.11.2011) abstract, para [0029], [0031]	57, 58, 87-98

☒ 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	Date of mailing of the international search report
15 October 2015 (15.10.2015)	23 NOV 2015
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

Form PCT/ISA/210 (second sheet) (January 2015)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 15/45753

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2004/0009180 A1 (Donovan) 15 January 2004 (15.01.2004) para [0065]-[0066], [0075]-[0076], [0079]	67-74, 83, 84
Y	US 2011/0174650 A1 (Kimball) 21 July 2011 (21.07.2011) para [0036], [0051], [0053]	69, 70, 77-84, 102-106

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 15/45753

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.: 59-66
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.