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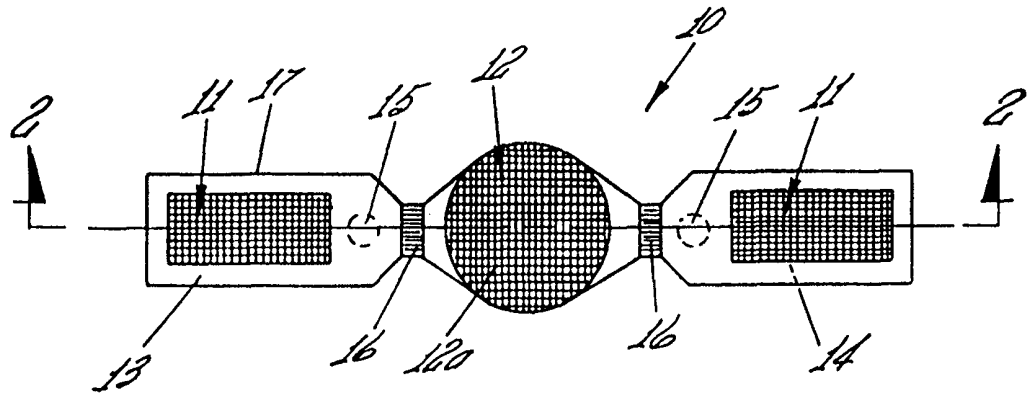


(57) Abstract

Non–reusable, medicament–dispensing applicator electrodes (10) adapted for use with an iontophoresis device or an ionosonic device for facilitating delivery of medication across the cutaneous membrane into adjacent underlying tissues, and blood vessels. The embodiments of the iontophoresis electrode include an open mesh (12) having cells (12a) in the medicament dispensing portions (11) of the electrode which retain a medicament in the form of liquid, gel or ointment. The cells are adapted to contain, to iontophoretically dispense, and deliver medicament. The medicament–dispensing electrodes (70) are composite or unitary in construction and may be useful in the treatment of acne, and also genital herpes simplex infection. The delivery electrode (71), when used in accordance with the medicated electrode, and method described herein, demonstrated >90 % treatment efficacy in clinical trials for the treatment of genital herpes. The applicator electrode may also be used with an ionosonic handpiece (40).

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# TITLE: IONTOPHORETIC DRUG DELIVERY ELECTRODES

INVENTOR: JULIAN L. HENLEY, M.D.

## SPECIFICATION

## BACKGROUND OF THE INVENTION

1. Field of the Invention:

This invention relates generally to the transdermal electrokinetic mass transfer of medication into a diseased tissue, and, more specifically, to a iontophoresis electrode for the transdermal delivery of medication into diseased tissues and blood vessels adjacent to the delivery site.

2. Prior Art:

Iontophoresis has been employed for several centuries as a means for applying medication locally through a patient's skin and for delivering medicaments to the eyes and ears. The application of an electric field to the skin is known to greatly enhance the skin's permeability to various ionic agents. This permeability change has been used, for example, to enhance transcutaneous transport of glucose for monitoring blood glucose levels. The use of iontophoretic transdermal delivery techniques has obviated the need for hypodermic injection for many medicaments, thereby eliminating the concomitant problems of trauma, pain and risk of infection to the patient.

Iontophoresis involves the application of an electromotive force to drive charged ions into the dermal layers comprising or overlying a target tissue. Particularly suitable target tissue includes tissues adjacent to the delivery site for localized treatment or tissues remote therefrom in which case the medicament enters into the circulatory system and is transported to a tissue by the blood. Positively charged ions are driven into the skin at an anode while negatively charged ions are driven into the skin at a cathode. Studies have shown increased skin penetration of

drugs at anodic or cathodic electrodes regardless of the predominant molecular ionic charge on the drug. This effect is mediated by polarization and osmotic effects.

Regardless of the charge of the medicament to be administered, a iontophoretic delivery device employs two electrodes (an anode and a cathode) in conjunction with the patient's skin to form a closed circuit between one of the electrodes (referred to herein alternatively as a "working" or "application" or "applicator" electrode) which is positioned at the site of drug delivery and a passive or "grounding" electrode affixed to a second site on the skin to enhance the rate of penetration of the medicament into the skin adjacent to the applicator electrode. Ultrasonic vibrations may be used in conjunction with iontophoresis to facilitate iontophoretic deliver of a drug. An apparatus employing both iontophoresis and ultrasonic vibrations to transdermally deliver medicament is referred to herein as an ionosonic apparatus.

Recent interest in the use of iontophoresis for the transdermal delivery of drugs to a desired cutaneous or subcutaneous treatment site has stimulated a redesign of many of such drugs with concomitant increased efficacy of the drugs when delivered transdermally. As iontophoretic delivery of medicaments become more widely used, the opportunity for a consumer/patient to iontophoretically self-administer a transdermal dosage of medicaments simply and safely at non-medical or non-professional facilities would be desirable and practical. Similarly, when a consumer/patient travels, it would be desirable to have a personal, easily transportable apparatus available which is operable for the iontophoretic transdermal delivery of a medication packaged in a single dosage applicator. A problem which presents an impediment to potential users is the necessity for reformulating medicaments for iontophoretic delivery. Such reformulations must be approved by cognizant regulatory agencies prior to sale. This requires delay and additional expense for the manufacturer, which additional expense may be passed along to consumers. The present invention provides a disposable medicament dispensing electrode for use with a portable iontophoretic medicament delivery apparatus in which the electrode is adapted for use with the apparatus for self-administering medicament. The

medicament dispensing portion of the electrode can accept, store and dispense presently approved medicament formulations.

## SUMMARY OF THE INVENTION

The present invention discloses a unit dosage medicament applicator electrode adapted for use with a portable iontophoretic transdermal or transmucoscal medicament delivery apparatus for the self-administration of a unit dose of a medicament into the skin. While the discussion to follow refers to iontophoretic devices, it is understood that an ionosonic device is included within the meaning of iontophoretic devices. The electrode and current supply apparatus is particularly suited for the localized treatment of herpes infections. The established treatment for recurrent genital herpetic lesions has been primarily supportive; including local topical application of anesthesia. Severe cases have been treated with systemic Acyclovir®, Zovirax® (Glaxo -Wellcome) or Famvir® (SmithKline Beecham). Some cases the condition is managed with prophylactic long-term dosing administration with a suitable anitviral agent at great expense. Systemic treatment of acute herpetic flare-ups may reduce the normal 10-12 day course of cutaneous symptoms into a 6-8 day episode. Topical treatment of lesions with Acyclovir® has not been as effective as in vitro studies would suggest. A compound which is not presently available to clinicians but has demonstrated significant anti herpetic activity is 5-iodo-2 deoxyuridine (IUDR). Both of those agents have shown limited clinical efficacy when applied topically to the herpetic lesion. It is the present inventor's contention that the limited efficacy of topical administration previously observed is, at least in part, due to the poor skin penetration of these medicaments when applied topically. The present invention discloses a mesh-like iontophoresis electrode, which contains and dispenses pre-approved formulations of those medicaments and provides improved transdermal delivery of these medicaments. The device and associated medicament dispensing electrodes may be used to treat such diverse conditions as herpes, warts, acne and psoriasis.

Genital herpes (usually herpes simplex II infection) afflicts many people, cause discomfort, shame, and may contribute to more severe and costly illnesses such as

cervical cancer, prostate cancer, and perinatal blindness from herpetic conjunctivitis. Certain formulations containing anti-viral and/or anti-microbial drugs have been approved for topical application by the cognizant regulatory agency. Reformulation of such compositions for iontophoretic transdermal drug delivery entails significant delays before such technology is available to the public for general use. The present invention discloses a medicated iontophoresis electrode for the portable transdermal delivery of Acyclovir® (9-[(2-hydroxyethoxy)methyl]guanine) or similar anti-viral agent formulations which have already received (or may in the future receive) regulatory approval to greatly benefit these afflicted patients. In a second preferred embodiment of the invention, the medicament delivery electrode is attached to a user-wearable glove having one or more fingers or merely a finger cot covering at least a portion of one or more fingers of a user's hand.

It is an object of the present invention to provide an iontophoretic medicament delivery electrode which is adapted to be used with an iontophoresis device operable for self-administration of medicament into the skin of a person.

It is another object of the present invention to provide an improved iontophoretic transdermal drug delivery apparatus having a medicament-containing application electrode which dispenses and transdermally delivers a single dosage and which is disposable and non-reusable.

It is a further object of the present invention to provide an iontophoresis electrode meeting the above objectives which can receive and retain a previously approved drug formulation for dispensation by ionosonic transdermal delivery.

It is still another advantage of the present invention to provide an improved disposable iontophoretic medicament applicator which meets the above objectives and which is inexpensive, safe to use and greatly increases the therapeutic efficacy of a medicament administered thereby.

The medicament-containing electrode in accordance with the present invention, together with an iontophoresis or ionosonic apparatus, provides a means for transdermally administering medicament dispersed in a variety of previously approved formulations directly and with high efficiency into a diseased tissue thereby providing a novel method for treating clinical conditions presenting cutaneous and/or

mucocutaneous symptoms such as warts, acne, superficial fungus infections, hyperproliferative diseases such as psoriasis, and particularly mucocutaneous Herpes simplex viral eruptions and sequelle associated therewith.

The above objects, features and advantages of the invention are realized by the improved iontophoretic medicament applicator electrode of the present invention. The objects, features and advantages of the invention will become apparent upon consideration of the following detailed disclosure of the invention, especially when it is taken in conjunction with the accompanying drawings wherein:

## BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a top plan view of a first embodiment of the disposable iontophoretic medicament containing applicator electrode adapted for attachment to an iontophoresis handpiece wherein the medicament dispensing portion of the electrode is an open mesh.

FIG. 2 is a side elevational view of a preferred embodiment of the disposable non-reusable iontophoretic applicator electrode for use with an iontophoresis handpiece adapted for self-administration.

FIG. 3 is a top plan view of the iontophoresis applicator electrode in accordance with claim 2.

FIG. 4 is a horizontal cross-sectional plan view of an iontophoresis handpiece adapted for use with the embodiments of the medicament dispensing applicator electrode of the present invention shown in Figures 1 - 3.

FIG. 5 is a perspective view showing the applicator electrode of Figures 1 - 3 releasably affixed to an iontophoresis handpiece in accordance with Figure 4.

FIG. 6 shows a patient preparing to self-administer medicament to a treatment site.

FIG. 7 is a top plan view of an embodiment of a medicament dispensing applicator electrode having unitary construction and an open mesh medicament dispensing portion similar to the embodiment shown in Figures 1 - 3 and adapted for attachment to the skin of a patient.

FIG. 8 is a horizontal cross-sectional view of the applicator electrode of Figure 7 taken along section line 8-8.

FIG. 9 is a bottom plan view of the applicator electrode of Figure 7.

FIG. 10 is a perspective view of an embodiment of an iontophoresis device and a medicament dispensing applicator electrode adapted to be releasably affixed to a finger of a patient wherein the medicament dispensing portion of the electrode is an open mesh.

FIG. 11 is a perspective view of the iontophoresis device and applicator electrode of Figure 10 wherein the thimble-like applicator electrode has been removed from the patient's finger.

FIG. 12 is a partially cut-away view of the iontophoresis applicator electrode of Figures 10 and 11 showing the relationship between the applicator electrode, an insulating finger cot and a wrist-worn adaptation of the iontophoresis device shown in Fig. 4.

FIG. 13 is a plan view of a glove embodiment of the applicator electrode in accordance with the present invention having a large area for medicament delivery.

FIG. 14 is a perspective view of a patient using the glove embodiment of FIG. 13 to self-administer a medicament to a relatively large portion of skin underlying the glove, as in, for example, the treatment of acne.

FIG. 15 is a schematic elevational view of a hand-held ionosonic handpiece having an applicator electrode in accordance with the present invention attached thereto.

## DESCRIPTION OF THE PREFERRED EMBODIMENT

FIG 1 shows, in top plan view, a first preferred embodiment of the hand-held iontophoretic transdermal medicament delivery apparatus of the present invention. The first preferred embodiment of the iontophoretic medicament-containing application electrode is shown at 10. The application electrode 10 is preferably disposable and non-reusable. The electrode 10 is suitable, for example, for transdermally delivering anti-viral agents such as Acyclovir® for the treatment of cold sores or genital herpes. The applicator electrode 10 is adapted for use with an

iontophoresis handpiece such as the handpiece shown in Figures 4 and 5. In use, the applicator electrode 10 is detachably affixed to a hand-held iontophoresis handpiece 40 which handpiece presents a first electrically conductive surface 41 and a second electrically conductive surface 42. The handpiece 40 comprises a current driver 45 which receives an electrical voltage from a voltage multiplier 46 which is in electrical communication with one electrode 47 of an electrical power source 48 such as a battery. The other electrode 49 of the battery is in electrical communication with a tactile electrode 42 on the surface of the handpiece 40 which electrode is, in use, in contact with the skin of one or more fingers of a user. The electrical current from the current driver 45 is conducted through a wire or conductive strip 44 to the first electrically conductive surface 41. When the applicator electrode 10 is attached to the handpiece 40, the current passes through the conductive applicator electrode to the skin of the user, returning to the second electrically conductive element 42, or "tactile electrode" to drive the medicament 23 through the mesh-like matrix material 12 and into the user's skin. The medicament or treatment agent is contained within a viscous fluid vehicle which, in turn, is contained within a plurality of cellular apertures 12a comprising the mesh 12.

The applicator electrode 10 comprises a substantially flat elongate strip having lateral ends extending from a central medicament dispensing portion 12. The central medicament dispensing portion 12 is of mesh-like construction and has vertical cells dimensioned to accommodate a viscous fluid within the confines of the cellular structures. The viscous fluid contained within each of the plurality of cells 12a includes a medicament (not shown) which is in a form suitable for transport under the influence of an electrical current. The lateral ends of the applicator electrode 10 may include a mesh-like tactile conductive portion 11 which contains an electrically conductive gel therewithin. The applicator electrode 10 has a skin-facing surface 13 and a device-facing surface 14. One or a plurality of cells 12a form one or a plurality of apertures between the upper skin-facing surface 13 and the lower device-facing surface 14. The device-facing surface 14 may further include an adhesive layer 18 applied thereto suitable for releasably adhering the applicator electrode 10 to the positive (anode) or negative (cathode) pole of a iontophoresis handpiece. The

positioning of the electrode's tactile conductive portion 11 on the surface of the handpiece is such that tactile conductive portion 11 makes electrical contact with the tactile electrode 42 on the handpiece. When the applicator electrode 10 is correctly positioned on the handpiece, the medicament dispensing reservoir 12 is in electrical communication with the electrically contacting element 41 on the handpiece. In addition, one or more small magnets 15 disposed within the applicator electrode 10 may be positioned on the handpiece to activate a switch within said handpiece which turns the handpiece on and/or off. The relatively narrow, flexible areas 16 on the electrode 10 enable the applicator electrode 10 to be bent and formed around the handpiece. Figure 2 shows a cross-sectional view of the applicator electrode 10 of Figure 1 taken along section lines 2-2. The material 17 forming the structural portion of the applicator electrode 10 is preferably a non-electrically conducting elastomer. A bottom view of the applicator electrode 10 of Figures 1 and 2 is shown in Figure 3.

Figure 5 is a perspective view of the applicator electrode 10 attached to the handpiece 40 in position for use. Figure 6 shows a patient preparing to use the iontophoresis device for administering medicament to herpes lesions on the face. The patient 60 grasps the tactile electrode 42 with a finger 61 to make electrical communication therewith. The patient then touches the tip 12 of the applicator electrode 10 to the lesion 63 thereby completing the electrical circuit and the resulting current flow driving the medicament into the skin.

Turning next to Figure 7, a second preferred embodiment of a medicament dispensing applicator electrode in accordance with the present invention is shown at 70. The centrally located medicament dispensing portion 71 has cells 72 therewithin which cells provide an aperture between the upper surface 73 and the lower, skin-contacting surface 74 of the electrode 70. The applicator electrode 70 is shown in cross-section along section lines 8-8 in Figure 8. The central medicament dispensing portion 71 of the electrode 70 is mesh-like in construction. A plurality of vertical cells 72 are molded within the elastomer strip comprising the applicator electrode to form apertures which communicate between the upper surface 73 and the lower surface 74. A fluid or semi-fluidic vehicle containing a medicament is placed within the cells 72 which cells are dimensioned to retain the medicament therewithin until an electrical

current is passed therethrough. An adhesive layer 75 is coated upon the lower surface 74 of the applicator electrode. The adhesive is chosen to be hypoallergenic, biocompatible and to releasably affix the electrode 70 to the skin.

A bottom view of the applicator electrode 70 of Figures 7 and 8 is shown in Figure 9. In use, the embodiment of the applicator electrode 70 shown in Figures 7 - 9 is affixed to the skin via the adhesive surface 75. The iontophoresis handpiece 40 is grasped between the fingers of the patient such that the tactile electrode (42 in Fig. 5) is in contact with at least one of the patient's fingers. The handpiece is then advanced to the medicament dispensing portion 71 of the applicator electrode 70 until it makes contact therewith. The circuit formed between the fingers grasping the tactile electrode 42 portion of the handpiece 40 and the lesion is made through the mesh surface of the medicament dispensing portion of the applicator electrode. Current flows through the handpiece to the medicament dispensing electrode and into the skin of the patient to return to the handpiece via the fingers and the tactile electrode to close the circuit. As the current flows through the medicament dispensing electrode the current drives the medicament into the skin of the patient.

Turning now to Figure 10, a thimble-like medicament dispensing applicator electrode 100 is shown attached to a finger 105 of a patient. The applicator electrode 100 is in electrical communication with one pole (cathode or anode) of a wrist-worn, bipolar iontophoresis device 101 by means of a wire 102. The bottom 106 or wrist-facing, skin-contacting surface of the bipolar iontophoresis device 101 is the other pole (anode or cathode) comprising a conductive electrode. The iontophoresis device 101 is releasably affixed to the wrist by means of a strap 103. The iontophoresis device 101 may be constructed similarly to the iontophoresis handpiece 40 except that the working electrode 41 is attached to the wire 102 and the tactile electrode 42 replaced with a conductive electrode 106 forming the skin-contacting portion of the device 101 which is in contact with the wrist of the patient. The applicator electrode 100 is electrically isolated from the finger 105 by means of an insulating finger cot 104. Current from the iontophoresis device 101 passes through the conductive wire 102 to an inner electrically conductive thimble 110 (Figure 11) to which the wire is conductively attached by means of solder. The electrically conductive thimble 110 has

an overlying silicone elastomeric thimble 111. The elastomeric thimble 111 is homogenous in composition and has an upper surface 112 and a lower surface 113 which comprises a mesh 113a. The mesh 113a has integral therewith a plurality of retaining cells 114 which cells extend between the electrically conductive thimble 110 and the lower surface 113 and are dimensioned to contain a medicament. In operation, current from the iontophoresis device 101 passes through the wire 102 to the electrically conductive thimble 110 of the applicator electrode. The voltage applied to the surface of the electrically conductive thimble 110 drives medicament contained within the cells 114 of the mesh 113 into the skin of a user's body. The current passes through the user's body to the conductive electrode (not shown) which comprises the wrist-facing portion of the iontophoresis device 101. The iontophoresis device 101 preferably includes a power source, a voltage multiplier, a driver and an on/off switch as shown in the handpiece 40, but reconfigured to be worn on the wrist. An enlarged perspective view of the applicator electrode 100 overlying a finger cot is shown in structural relationship in Figure 12.

The simple design is capable of retaining and dispensing existing medicament formulations in various viscosities because the size of the retaining cells 72 in the mesh portion of the electrode may be varied. The structural matrix of the applicator electrode is a flexible, preferably hypoallergenic, nonelectrically-conductive material. A suitable material is Silastic®, a silicone elastomer which is biocompatible, non-conductive, flexible and possessing sufficient structural rigidity to contain medicaments and a delivery vehicle within the retaining cells 114. Further, Silastic silicone elastomer is inert so that medicaments will not oxidize or otherwise have their chemical structures damaged. An electrode constructed from silicone elastomer has a prolonged shelf-life, is soft and pleasant on contact, is hypoallergenic and sufficiently flexible to adhere to any anatomical contour such as presented by a thimble. Such anatomical plasticity is a key advantage to the foregoing design. Other polymers, such as polyurethane, are suitable as well. A hydrated hydrophilic cotton layer (not shown) may be interposed between the medicament dispensing portion 71 and the electrically conductive surface 41 of the handpiece 40 to provide pretreatment hydration of the

medicament dispensing portion or the mesh may be hydrated by the patient immediately prior to use.

With reference to the embodiment of an iontophoresis applicator electrode shown in Figures 7 - 9, the electrode is easily manufactured using mold technology wherein uncured silicone elastomer is either poured into a complementary mold or pressure-mold injected. The lower surface 74 of the non-medicament dispensing portion of the electrode is coated with skin adhesive. The medicament dispensing portion 71 functions as a medicament reservoir and is preferably between 1mm and 4mm thick, depending upon the amount of medicament required to be stored in the cells 72. The medicament-retaining cells 72, which are preferably a hexagonal, honey comb-like structure, retain the medicament therein through their surface tension. Hexagonal cells also lessen cross channel conductivity by means of their vertical orientation. The size and geometry of these cells can vary. The smallest cells, for instance, would be more suited to retaining liquid medicaments while the larger cells are better adapted to retain ointment-based medicaments. Medium cells are more suited to retaining and dispensing gel medicaments and lotions. The silicone walls of the cells can be chemically modified to change the hydrophobic surface characteristics thereof and further improve retention of specially formulated liquid medicaments. For additional cell stability and retention capabilities, the skin-facing surface of the cells can be covered with non-wicking, fibrous and porous materials commonly used in electrodes. A composite or unitary construction from a single mold can be used depending on production cost, it is inexpensive to manufacture and it offers both a compartment for storage of existing formulations as well as a structural backbone for the application electrode. The surface treatments of the retaining material bounding each of the cells to create hydrophilic or hydrophobic surface effects depending on the formulation to be utilized is well known in the art. An example of such technology is disclosed, for example, in US patent 5,589,563. For ointments and hydrophobic materials, silicone is preferred. For water or gel medicaments, surface treatment such as doping the elastomeric cell surface with hydrophilic molecules can be of additional benefit, as described herein. The embodiments disclosed herein present the following advantages:

Inexpensive manufacture;

Use of either injection or pour molding production;

Use of composite sheet cutout assembly;

Anatomically conforming;

Elastomer surface modification for optimum retention of medicament;

Variable retaining cell size;

Variable retaining cell geometry;

Ability to utilize existing medicament formulations;

May use a cotton or (other hydrophilic matrix) layer for rapid pre-treatment hydration.

May be used with single or multi-channel dispersive iontophoretic drivers; and

May be used with iontophoretic or ionosonic devices.

An embodiment of the present invention adapted for delivering medicament to a large area of skin is shown in Figure 13. The iontophoresis electrode is contained within a glove adapted to conform to and be worn upon a patient's hand. The glove embodiment 130 of the iontophoresis drug delivery electrode comprises an elastomeric glove 131 having a plurality of holes or open pores 132 in the palmar surface 133 thereof. Underlying the palmar surface 133 and disposed within the glove between the skin 134 and glove is an electrically insulating sheet 135 having an inner surface 136 and an outer surface 137, both of which surfaces are coated with an electrically conductive layer 138. The inner conductive layer 136 is, in use, in electrical communication with the skin. The outer conductive layer 137 is in contact with the interior surface of the glove and the pores 132. A medicament 139 capable of iontophoretic transdermal delivery is contained within the pores. A bipolar power source 140 has a working electrode 141 in electrical communication with the outer conductive layer 137 coating the electrically insulating sheet 135, and a ground electrode (not shown) which is in electrical communication with the inner conductive layer coating the electrically insulating sheet. When the power source 140 is energized, an electrical current flows between the inner conductive layer and the outer conductive layer, which layers are separated by the electrically insulating sheet, via the patient's skin. The polarity and amplitude of the current flowing through pores into

the user's skin facilitates entry of the medicament into the skin. The glove embodiment, shown in use in Figure 14, is particularly useful for transdermally delivering medicament to large areas of skin.

The advantages of a unitary iontophoresis electrode and a glove and finger cot embodiment of an iontophoresis electrode for drug delivery have been presented. It is noted that similarly constructed electrodes may be employed for non-invasively collecting molecular species from the blood. For example, the mesh may be impregnated with an electrically conductive gel. The polarity of the gel, with respect to the skin, may be employed to transport blood components through the skin into the gel where such components may be detected and/or quantitated. Such measurements are useful for monitoring blood levels of compounds such as glucose or drugs.

The hand held iontophoretic device 40 (Figure 4)may be modified to include a piezoelectric element operable for imparting ultrasonic vibrational motion to the applicator electrode 12 to further facilitate transdermal delivery of certain iontophoretically transportable compounds. A schematic view of such a modified handpiece similar to the handpiece 40 of Figure 4 is shown at 150 in Figure 15. The applicator electrode 160 includes all embodiments of the applicator electrode described for the iontophoresis handpiece discussed above. One side of an annular ultrasonic piezoelectric element 151 is disposed rearwardly to the applicator electrode 160 containing a medicament. Power is supplied to energize the piezoelectric element 151 by means of conductive elements 157 and 152 which are in electrical communication with an ultrasonic driver 163. An optional current sensitive switching element (not shown) may be used to energize the piezoelectric element only when current passes through the applicator electrode circuit. The applicator electrode 160 may include any applicator electrode heretofore described for use with an iontophoretic handpiece. The applicator electrode 160 may contain an ionic medicament or a biologically inactive ionic solution which penetrates the skin and opens clogged pores under the influence of iontophoretically driven transport assisted by ultrasonic waves in the cutaneous tissue. Stephen et al. have shown in US Patent 4,979,938 that the iontophoretic delivery of hydroxyl ions into the skin can be used to treat acne. The ionosonic delivery of a similar anion may provide improved opening

of pores in the skin for treating acne. The combination of iontophoretic delivery of a compound into a tissue, together with inducing ultrasonic vibration in the tissue, may enable the removal of coloration (such as a blemish, freckle or tattoo) within the skin by the delivery of a suitable bleaching agent

While the invention has been described above with references to specific embodiments thereof, it is apparent that many changes, modifications and variations in the materials, arrangements of parts and steps can be made without departing from the inventive concept disclosed herein. For example, an impregnated conductive gel can also be used to as medicament containing medium to increase the physical stability and the tissue adhering characteristics of the electrode. The applicator electrode described herein, when used with an ionosonic or iontophoretic handpiece can deliver medicaments for treating diverse medical conditions including, but not limited to acne, hyperproliferative diseases of the skin, superficial fungal infections, warts, and herpes type viral infections. Accordingly, the spirit and broad scope of the appended claims is intended to embrace all such changes, modifications and variations that may occur to one of skill in the art upon a reading of the disclosure. All patent applications, patents and other publication cited herein are incorporated by reference in their entirety.

What I claim is:

# CLAIMS

1. A medicament dispensing applicator electrode adapted for use with an iontophoresis device comprising a unitary strip consisting of an elastomeric substrate having an upper surface and a lower surface, said strip having a medicament dispensing portion comprising a cell or a plurality of cells forming an aperture or a plurality of apertures between said upper surface and said lower surface and wherein said cell or plurality of cells contain a medicament.

2. The applicator electrode of Claim 1 further comprising a layer of adhesive covering at least a portion of said upper surface of said strip, said adhesive layer being operable for releasably attaching said strip to an iontophoresis device.

3. The applicator electrode of Claim 1 further comprising a layer of adhesive covering at least a portion of said lower surface of said strip, said adhesive layer being operable for releasably attaching said strip to skin.

4. The applicator electrode of Claim 2 further comprising a tactile conductive portion having a second cell or a plurality of cells electrically insulated from said medicament dispensing portion, said second cell or plurality of cells containing an electrically conductive fluid.

5. The applicator electrode of Claim 3 further comprising a tactile conductive portion having a second cell or plurality of cells electrically insulated from said medicament dispensing portion, said second cell or plurality of cells containing an electrically conductive fluid.

6. An iontophoresis device comprising, in combination:

(a) a current source having an anode and a cathode and a source of electrical power; and

(b) the medicament dispensing applicator electrode of claim 4 wherein said medicament dispensing portion of said applicator electrode is in electrical connection with either of said anode or said cathode and said tactile conductive portion is in electrical connection with either of said cathode or said anode, respectively.

7. A medicament dispensing iontophoresis applicator electrode comprising a generally thimble-shaped electrically conductive member and an

overlying medicament dispensing portion of an electrically non-conducting elastomer having a cell or plurality of cells in at least a portion thereof and wherein said thimble-shaped conductive portion is dimensioned to fit over and conform to the shape of the distal end of a finger.

8. The applicator electrode of Claim 7 wherein said cell or plurality of cells contain a medicament.

9. The applicator electrode of Claim 8 further comprising an electrically insulating layer underlying said thimble-shaped electrically conductive member.

10. The applicator electrode of Claim 8 wherein said thimble-shaped electrically conductive member has a first end of an electrically conductive wire affixed thereto.

11. The applicator electrode of Claim 10 wherein said electrically conductive wire has a second end in opposition to said first end and includes means for attaching said second end to a pole of a current source.

12. The applicator electrode of claim 8 wherein said medicament dispensing portion further comprises a hydrophilic matrix layer overlying said cell or plurality of cells for pre-treatment hydration by a user immediately prior to use when used with non-ionic medicament formulation.

13. The applicator electrode of claim 12 wherein said hydrophilic matrix layer is hydrated.

14. A method for treating lesions associated with cold sore and genital herpes comprising the steps of:

(a) presenting a hand-held iontophoretic device comprising an electrode and a medicament dispensing reservoir containing an antiviral agent, said reservoir being in electrical communication with said electrode of the iontophoretic device; and

(b) bringing the medicament dispensing reservoir into contact with said lesions; then

(c) applying a voltage gradient between the electrode and the lesion.

15. The method of claim 14 wherein said medicament comprises (2 amino-1, 9-dihydro-9-[(2-hydroxyethoxy) methyl]-6H-purin-6-one) or iontophoretically transportable analogs thereof.

16. A method for treating lesions associated with cold sore and genital herpes comprising the steps of:

(a) presenting a hand-held ionosonic device comprising an electrode and a medicament dispensing reservoir containing an antiviral agent, said reservoir being in electrical communication with said electrode; and

(b) bringing the medicament dispensing reservoir into contact with said lesions; then

(c) inducing ultrasonic vibration in a tissue comprising the lesion; and

(d) applying a voltage gradient between the electrode and the lesion.

17. The method of claim 16 wherein said medicament comprises (2 amino-1, 9-dihydro-9-[(2-hydroxyethoxy) methyl]-6H-purin-6-one) or ionosonically transportable analogs thereof.

18. A method for treating lesions associated with acne comprising the steps of:

(a) presenting a hand-held ionosonic device comprising an electrode and a medicament dispensing reservoir containing an ionic compound in electrical communication with said electrode; and

(b) bringing the medicament dispensing reservoir into contact a said lesion; then

(c) inducing ultrasonic vibration in a tissue comprising the lesion; then

(d) applying a voltage gradient between the electrode and the lesion

19. The method of claim 18 wherein said ionic compound is anionic.

20. The method of claim 18 wherein said ionic compound is a hydroxyl ion.

21. The method of claim 18 wherein said ionic compound is cationic.

22. A disposable medicament dispensing applicator electrode for an iontophoretic drug delivery device adapted for the self-administration of a medicament into a person's skin, said device comprising a base assembly having an active terminal adapted to receive and make electrical contact with a detachable medicament dispensing applicator electrode wherein said base assembly comprises; a case having an elongate, substantially cylindrical outer surface having a size and shape adapted to be comfortably grasped within a person's hand and wherein at least a portion of said outer surface is a tactile electrode formed of an electrically conductive material; and a bipolar electrical power means having a first pole and a second pole; said electrical power means being enclosed within said case and wherein said first pole is in electrical communication with said tactile electrode; wherein said medicament dispensing applicator electrode comprises: a module containing unit dose of medicament, an electrically conductive working electrode and means thereon adapted for releasably attaching said working electrode to said second pole of said electrical power means wherein said working electrode further comprises an elongate strip constructed of a substantially electrically non-conductive substrate material, said strip having a central portion containing a medicament in an electrically conductive substrate and laterally symmetric end portions having cutouts therewithin.

23. The disposable medicament dispensing applicator electrode of claim 22 wherein said cutouts in said laterally symmetric end portions contain an electrically conductive material.

24. The disposable medicament dispensing applicator electrode of claim 23 wherein said electrically conductive material is a gel.

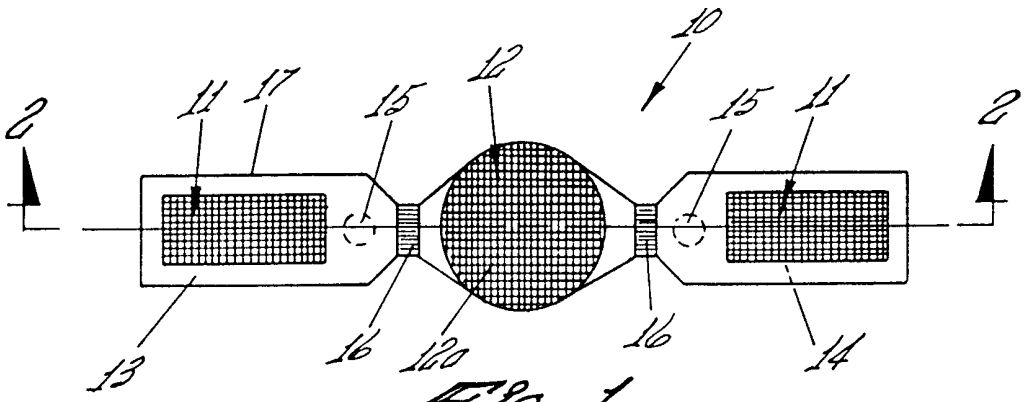


Fig 1

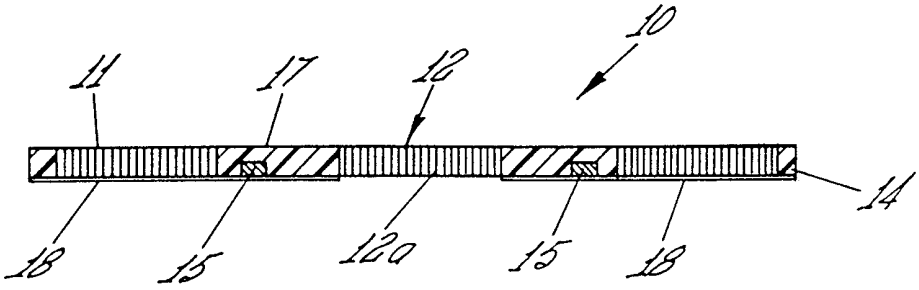


Fig 2

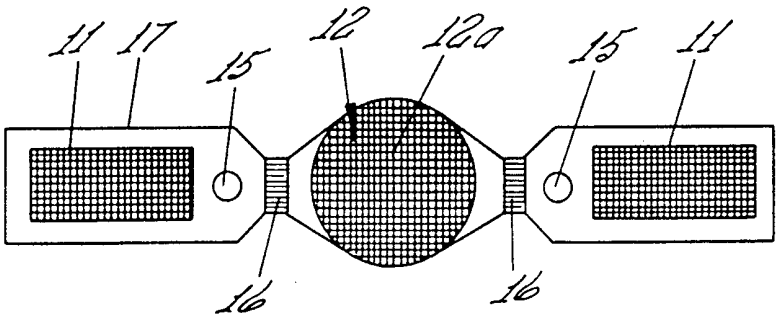


Fig 3

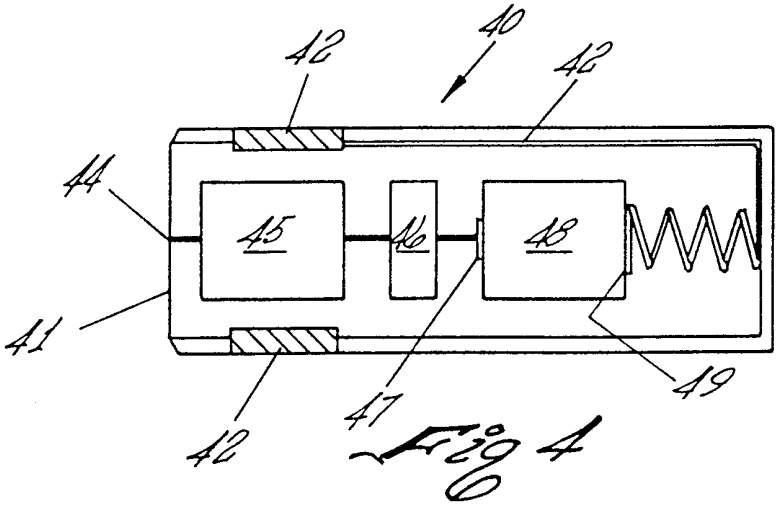


Fig 4

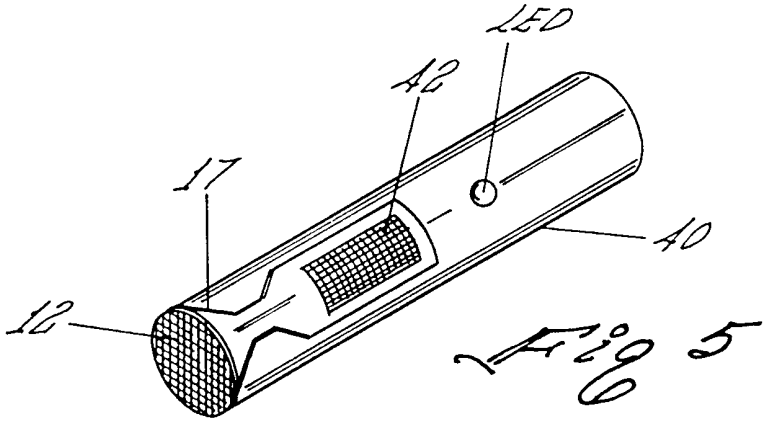


Fig 5


Fig 6

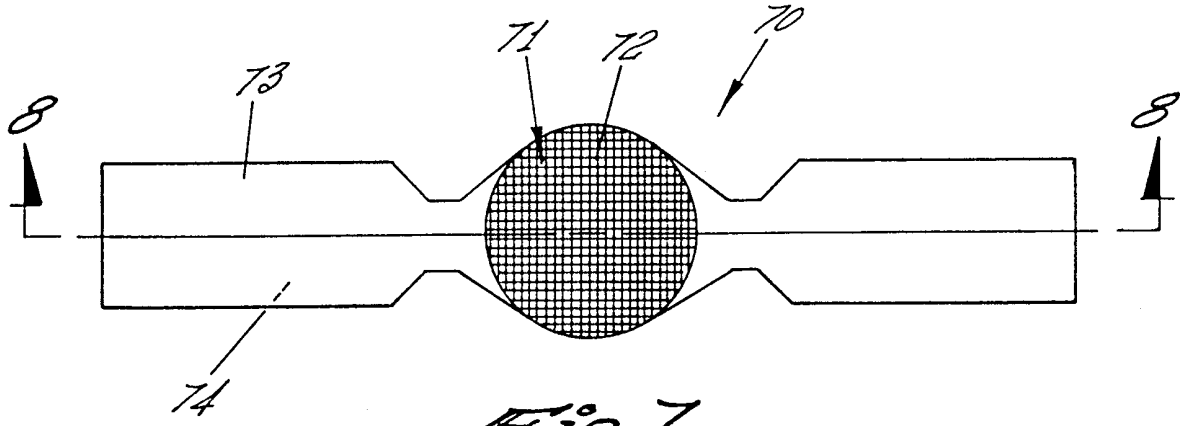


Fig 7

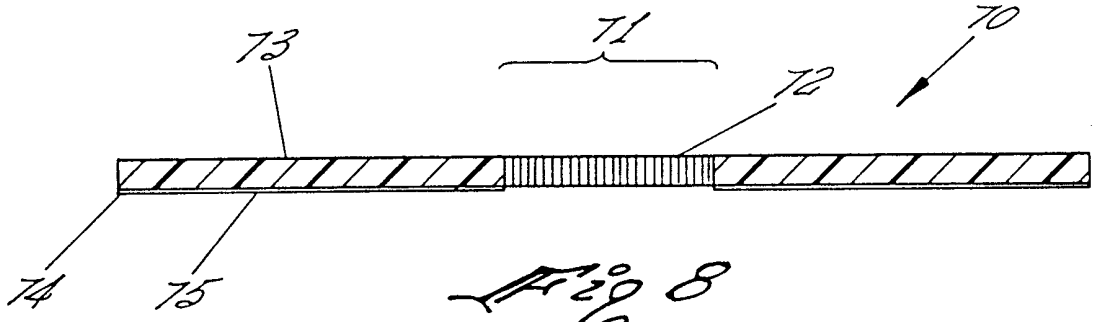


Fig 8

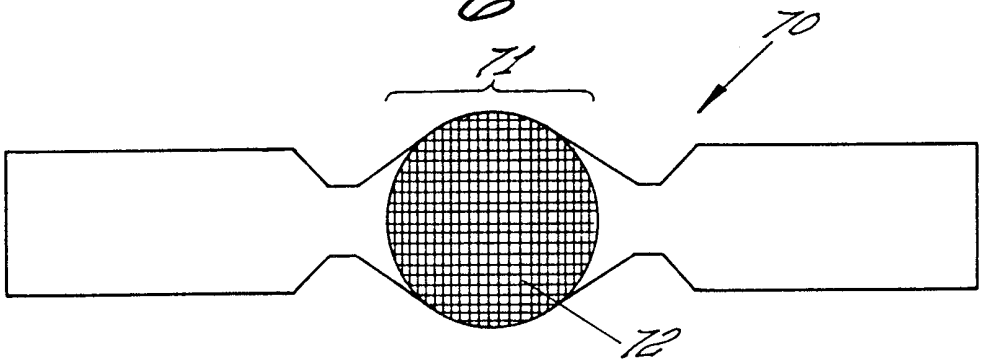


Fig 9

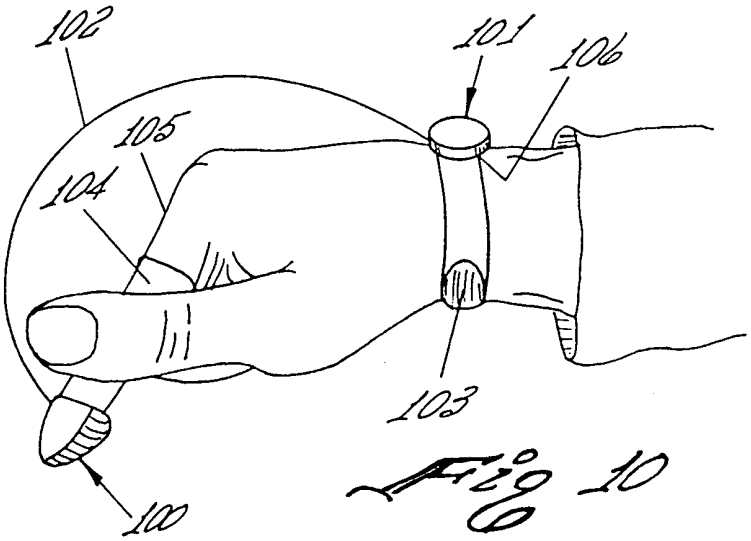


Fig 10

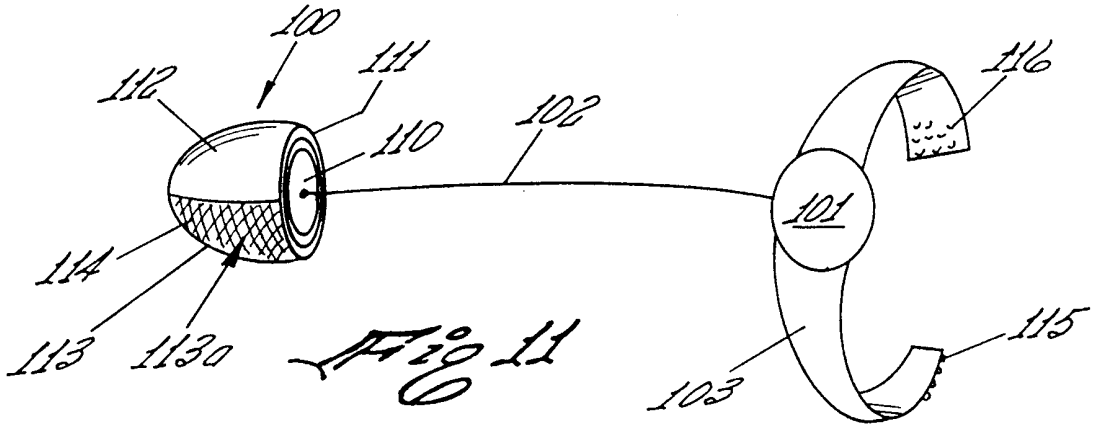


Fig 11

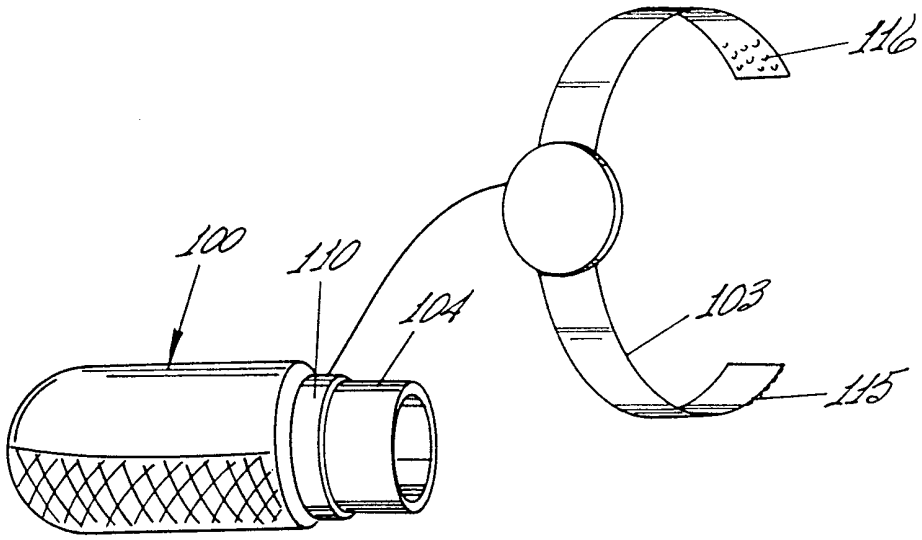
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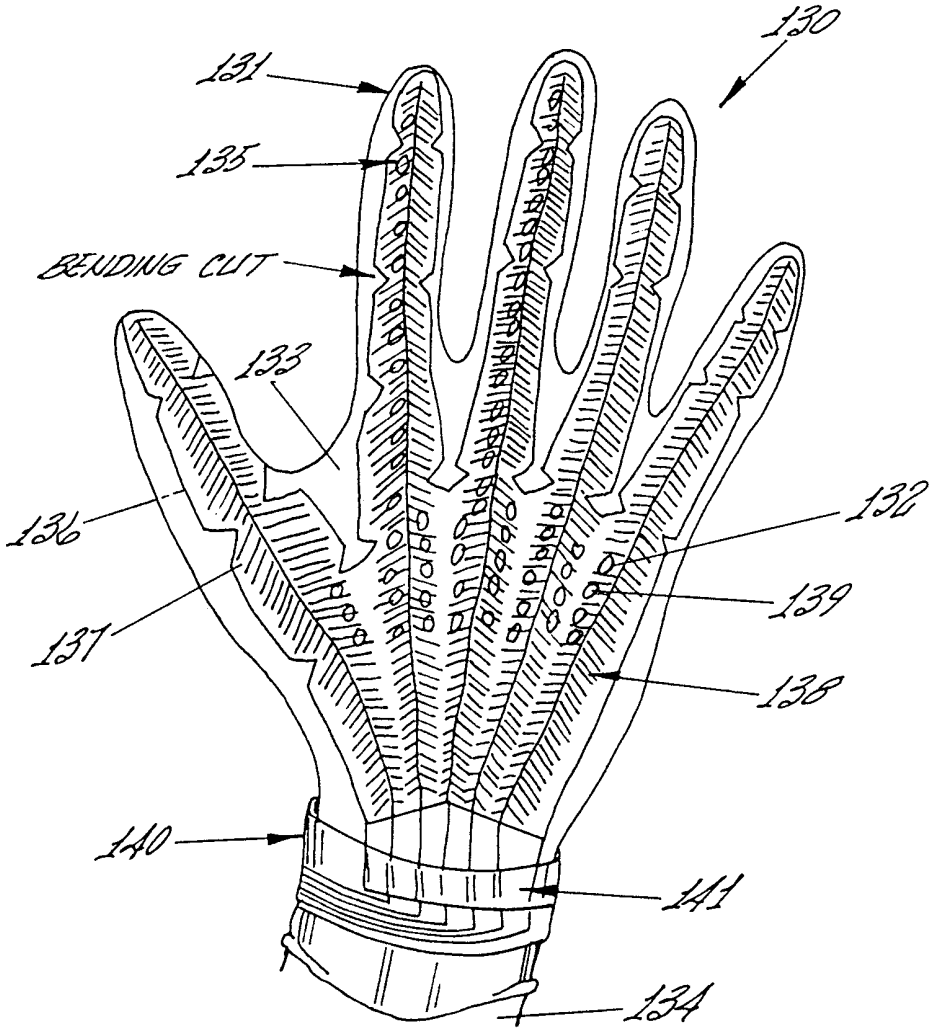
Fig 12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BENDING CUT
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Fig 13


Fig 14

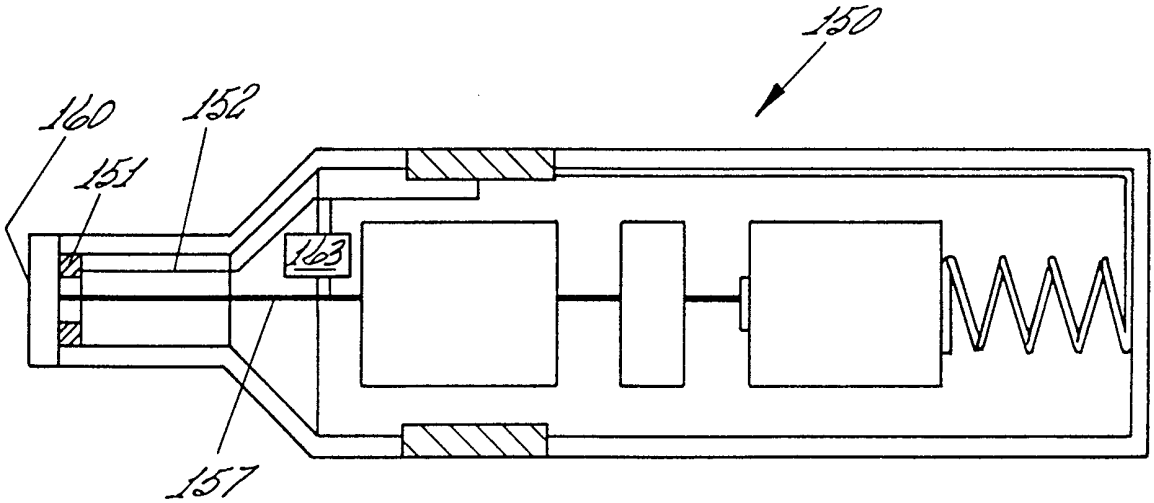


Fig 15

# INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/11440

A. CLASSIFICATION OF SUBJECT MATTER
IPC(6) :A61B 17/20; A61M 31/00; A61N 1/30
US CL :604/20, 22, 501
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 604/19- 20, 22, 48, 501; 607/75, 111, 145

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

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| A | US 279,524 A (BEATY) 19 June 1883, all. | 7-13 |
| A | US 3,163,166 A (BRANT et al.) 29 December 1964, all. | 22 |
| A | US 4,838,273 A (CARTNELL) 13 June 1989, col. 4 line 3 to col. 5 line 5. | 1-13, 22 |
| A | US 4,953,565 A (TACHIBANA et al.) 04 September 1990, all. | 16, 18 |
| X | US 5,458,569 A (KIRK, III et al.) 17 October 1995, Figs. 5 and 6, col.3 line 42 to col. 7 line 30. | 1-6 |
| A | US 5,658,247 A (HENLEY) 19 August 1997, all. | 1-24 |

[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

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

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"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
28 JUNE 1999

Date of mailing of the international search report
08 JUL 1999

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Form PCT/ISA/210 (second sheet)(July 1992)*

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/11440

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| A | US 5,676,648 A (HENLEY) 14 October 1997, all. | 1-24 |
| A, P | US 5,879,323 A (HENLEY) 09 March 1999, all. | 1-24 |