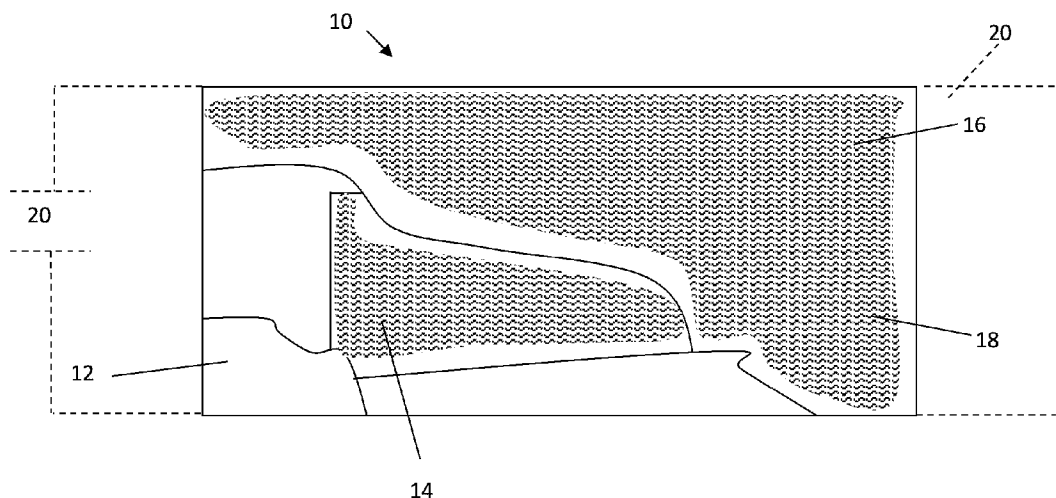




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THROUGH THE SKIN OF THE USER



(57) **Abrégé/Abstract:**

The present invention provides a device for increasing absorption of substances through the skin of an animal or human, comprising: a fabric or substrate; metal particles disposed on or exposed through at least a portion of a surface of the fabric or substrate, as a plurality of lines or dots in a specific pattern that positions the metal particles in discrete electrically isolated locations separated by a distance, wherein the fabric or substrate is configured such that said metal particles contact a skin surface of the human or animal, wherein the plurality of spaced lines are substantially evenly spaced from one other; and a layer adapted to hold a substance; wherein said fabric or substrate forms a plurality of half-cells of an air-metal battery, for ion exchange with the skin of the human or animal whereupon a substance located between the device and the skin is driven in by iontophoresis.

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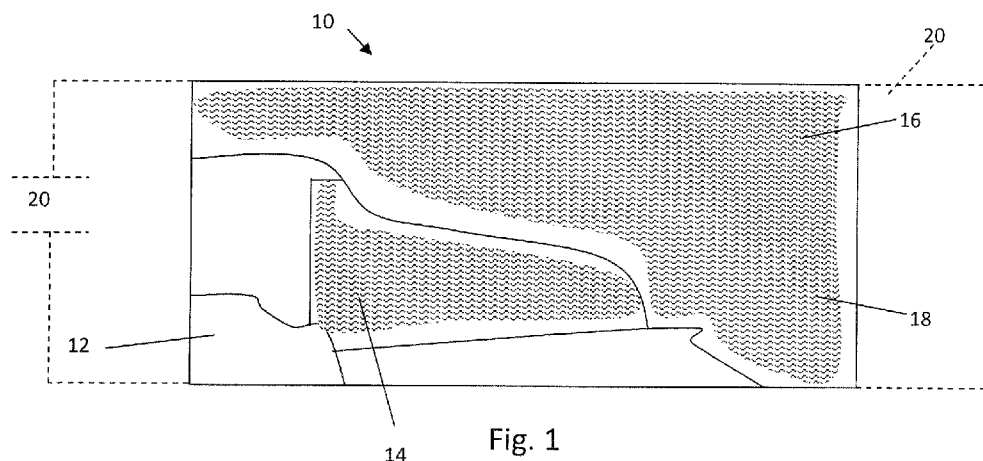
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THROUGH THE SKIN OF THE USER

Fig. 1

(57) **Abstract:** The present invention provides a device for increasing absorption of substances through the skin of an animal or human, comprising: a fabric or substrate; metal particles disposed on or exposed through at least a portion of a surface of the fabric or substrate, as a plurality of lines or dots in a specific pattern that positions the metal particles in discrete electrically isolated locations separated by a distance, wherein the fabric or substrate is configured such that said metal particles contact a skin surface of the human or animal, wherein the plurality of spaced lines are substantially evenly spaced from one other; and a layer adapted to hold a substance; wherein said fabric or substrate forms a plurality of half-cells of an air-metal battery, for ion exchange with the skin of the human or animal whereupon a substance located between the device and the skin is driven in by iontophoresis.



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**METHOD AND APPARATUS FOR INCREASING ABSORPTION OF
MEDICATIONS AND COSMECEUTICALS THROUGH THE SKIN OF THE USER**

The present invention relates to a method and apparatus for increasing absorption of substances through the skin of the user. The invention has particular utility in connection with increasing absorption of medications through the skin, and will be described in connection with such utility, although other utilities, such as increasing the speed or depth of absorption of other substances including, for example, cosmeceuticals, is contemplated.

Skin comprises epidermis, dermis, and subcutaneous adipose tissue. When medicines are applied to the skin, the epidermis, i.e., the upper layer of the skin, ordinarily considers the medicines as foreign substances and hinders absorption of the medicine. As a result, due to the influence of molecular size, bio characteristics, biochemical phenomena, and the like, the amount of medicines practically absorbed into the skin is very small.

In order to overcome this problem, iontophoresis has been developed to increase absorption of medicines through the skin. Iontophoresis involves generating a micro current to flow through the skin thereby effectively increasing absorption of components contained in the medicines having electrical affinity with the skin, by electrical repulsive force. Iontophoresis may be used, for example, so that topical vitamin C, which is an anti-oxidant and a co-factor in skin growth, is absorbed into the skin providing cellular stimulation and anti-oxidant protection. Topical vitamin C is used for skin health and improvement of wrinkles. Other uses of iontophoresis can range from medication delivery, such as with prescription medications, to localized delivery without systemic side-effects.

Current iontophoresis apparatuses induce electric fields on and around the skin by attaching patches to the skin, and allowing micro current to flow from the patches into the skin. However, current iontophoresis apparatuses require a source of electricity, e.g. a battery or connection to electrical mains, wires, circuits, etc., which are costly and bulky, and are inconvenient to use, resulting in reduced patient compliance. Thus a need exists for a self-contained, low cost method and apparatus for delivering medicines for absorption through the skin. In addition to the iontophoretic effect on the skin, directed electric micro current can also stimulate the skin, enhance blood flow and tissue oxygenation, as well as an enhance cellular response with increased protein synthesis, amino acid transport and

increased ATP (mitochondrial energy) synthesis. The net effect is localized collagen stimulation addressing wrinkles, complexion and the health of the skin.

In our prior US Patent No. 9,192,761 and 9,707,172 we describe methods and devices for treating hyperhidrosis and other conditions such as neuropathic pain, peripheral artery disease and neuropathy; for surgical rehabilitation and surgical convalescence including joint surgery rehabilitation and soft tissue healing; and for physical therapy including muscle and tendon healing and stroke rehabilitation, by applying onto a skin surface of a patient in need of said treatment, a device comprising a fabric containing elemental zinc particles arranged so that the fabric forms a plurality of half-cells of an air-zinc battery, whereby to produce ion exchange with the skin of the patient. As described in our aforesaid patents, elemental zinc particles or particles of zinc salt against the skin will result in secondary reactions to form zinc complexes beneficial to the host. The ability to deliver topical zinc to the surface of the skin can have beneficial effects provided the topical zinc is in the correct elemental presentation, availability and configuration.

The unique therapeutic value of zinc, zinc oxide and zinc salt in cosmetic and medicinal ointments and creams, i.e., for treating a variety of skin conditions is well documented in the art. Also, as reported in our pending U.S. Application Serial No. 15/823,076 many of the same benefits of direct application to the skin of creams or ointments containing zinc may be achieved by bringing a fabric having elemental zinc particles printed thereon, in contact with the skin of the patient, i.e., as described in our aforesaid '761 and '172 patents.

We have now found that metal particle carrying fabrics such as described in our aforesaid '761 and '172 patents and our aforesaid '076 pending application advantageously may be used as a half cell in an oxidation/reduction reaction in contact with the skin to produce an electric current that when directed into the skin alters skin membrane permeability, allowing substances such as pharmaceuticals to pass more easily into the skin. That is to say, an electric field produced by metal particle carrying fibers, in contact with the skin provides a field direction, i.e., negative in the ion fabric and positive in the tissue. As a result, substances on the fabric or skin may be absorbed into the skin towards a positive pull to the tissue of the patient, by electrical repulsive force, i.e., negative to positive attraction, similar to iontophoresis. Thus, the present invention in essence provides a self-contained

external battery-free iontophoresis apparatus for driving substances such as pharmaceuticals into the skin of the wearer.

The present invention in one aspect provides a device for increasing absorption of substances through the skin of an animal or human, comprising: a fabric or substrate; metal particles disposed on or exposed through at least a portion of a surface of the fabric or substrate, as a plurality of lines or dots in a specific pattern that positions the metal particles in discrete electrically isolated locations separated by a distance, wherein the fabric or substrate is configured such that said metal particles contact a skin surface of the human or animal, wherein the plurality of spaced lines are substantially evenly spaced from one other; and a layer adapted to hold a substance; wherein said fabric or substrate forms a plurality of half-cells of an air-metal battery, for ion exchange with the skin of the human or animal whereupon a substance located between the device and the skin of the animal or human is driven into the skin by iontophoresis.

In one aspect, the patterns conform to blood circulation patterns and/or nerve or underlying muscle patterns of the human or animal.

In another aspect, the lines or dots are evenly spaced at spacings from 0.1 to 3 mm, preferably 0.2 to 2 mm, more preferably 0.3 to 1.5 mm, most preferably 0.5 to 1 mm.

In yet another aspect, the lines or dots of lines are 0.1 mm to 5 mm wide, preferably about 0.1 to 3 mm, more preferably 0.2 to 2 mm, even more preferably 0.3 to 1 mm, most preferably 0.4 to 0.5 mm.

In still yet another aspect, the patterns cover from about 10% to 90% of the surface of the fabric or substrate, preferably from about 15% to about 75%, more preferable from about 25% to about 50%, most preferably from about 30% to about 40%.

In a preferred aspect the metal particles comprise a metal, metal oxide or metal salt, preferably elemental zinc particles, zinc oxide particles, and zinc salt particles, or aluminum, iron, copper and magnesium, and an oxide or salt thereof.

In still yet another aspect, the device includes an adhesive or adhesive tabs adapted to fix the device to the skin of the animal or human. In the case where the device is fixed to the skin by an adhesive, the metal particles may be incorporated directly into the adhesive.

The present invention also provides a method for increasing absorption of a substance through the skin of a human or animal, comprising locating the substrate adjacent

the skin of the human or animal; and disposing onto the skin of the human or animal over the substance, a device comprising: a fabric or substrate; metal particles disposed on at least a portion of a surface of the fabric or substrate, as a plurality of lines or dots in a specific pattern that positions the metal particles in discrete electrically isolated locations separated by a distance, wherein the fabric or substrate is configured such that said metal particles contact a skin surface of the human or animal, wherein the plurality of spaced lines are substantially evenly spaced from one other, wherein said fabric or substrate forms a plurality of half-cells of an air-metal battery, which alters skin membrane permeability and drives the substance into the skin.

In one aspect of the method, the patterns conform to blood circulation patterns and/or nerve or underlying muscle patterns of the human or animal.

In another aspect of the method, the lines or dots are evenly spaced at spacings from 0.1 to 3 mm, preferably 0.2 to 2 mm, more preferably 0.3 to 1.5 mm, most preferably 0.5 to 1 mm.

In yet another aspect of the method, the lines or dots of lines are 0.1 mm to 5 mm wide, preferably about 0.1 to 3 mm, more preferably 0.2 to 2 mm, even more preferably 0.3 to 1 mm, most preferably 0.4 to 0.5 mm.

In still yet another aspect of the method, the patterns cover from about 10% to 90% of the surface of the fabric or substrate, preferably from about 15% to about 75%, more preferable from about 25% to about 50%, most preferably from about 30% to about 40%.

In a preferred aspect of the method, the metal particles comprise a metal, metal oxide or metal salt, preferably elemental zinc particles, zinc oxide particles, and zinc salt particles, or aluminum, iron, copper and magnesium, and an oxide or salt thereof.

In still yet another aspect of the method, the device is fixed to the skin of the animal or human, using an adhesive or adhesive tabs. In the case where the device is fixed to the skin using an adhesive, the metal particles may be incorporated directly into the adhesive.

The present invention also provides a method for increasing absorption of a substance through the skin of a human or animal, comprising: disposing the substance in contact with the skin of a human or animal; and covering the substance with a fabric device comprising: a fabric or substrate; metal particles disposed on at least a portion of a surface of the fabric or substrate, as a plurality of lines or dots in a specific pattern that positions the

metal particles in discrete electrically isolated locations separated by a distance, wherein the fabric or substrate is configured such that said metal particles contact a skin surface of the human or animal, wherein the plurality of spaced lines are substantially evenly spaced from one other, wherein said fabric or substrate forms a plurality of half-cells of an air-metal
5 battery with the skin of the human or animal, whereupon the metal particles in the fabric form a first half cell of a battery circuit, while the body of the human or animal forms a second half cell of the battery circuit with oxygen from the host, whereupon the substance is driven into the skin of the human or animal by iontophoresis.

10 In one aspect of the latter method, the patterns conform to blood circulation patterns and/or nerve or underlying muscle patterns of the human or animal. Alternatively, the patterns may also conform to meridians and the focal points of meridians as defined by Asian medicine.

In another aspect of the latter method, the lines or dots are evenly spaced at spacings from 0.1 to 3 mm, preferably 0.2 to 2 mm, more preferably 0.3 to 1.5 mm, most preferably
15 0.5 to 1 mm.

In yet another aspect of the latter method, the lines or dots of lines are 0.1 mm to 5 mm wide, preferably about 0.1 to 3 mm, more preferably 0.2 to 2 mm, even more preferably 0.3 to 1 mm, most preferably 0.4 to 0.5 mm.

In still yet another aspect of the latter method, the patterns cover from about 10% to
20 90% of the surface of the fabric or substrate, preferably from about 15% to about 75%, more preferable from about 25% to about 50%, most preferably from about 30% to about 40%.

In a preferred aspect of the latter method, the metal particles comprise a metal, metal oxide or metal salt, preferably elemental zinc particles, zinc oxide particles, and zinc salt particles, or aluminum, iron, copper and magnesium, and an oxide or salt thereof.

25 In still yet another aspect of the latter method, an adhesive or adhesive tabs are used adapted to fix the device to the skin of the animal or human.

Further features and advantages of the present invention will be seen from the following detailed description, taken in conjunction with the accompanying drawings, wherein;

30 Fig. 1 is a top plan view, in partial a cross section, of a self-contained iontophoresis pad in accordance with the present invention;

Fig. 2 is a flow chart diagrammatically illustrating a process for forming a self-contained iontophoresis pad in accordance with the present invention; and

Fig. 2A is an enlarged view of an intermediate product formed by the process of Fig. 2.

5 In the following description, the term “metal particles” may include elemental metal particles of metals capable of forming metal-air electrochemical cells, and oxides and salts thereof. Preferred are zinc metal particles and oxides and salts thereof, although other metals and oxides and salts thereof may be used including aluminum, iron, copper, or magnesium.

10 The term “fibers” may comprise both natural and synthetic fibers, filaments and threads, although synthetic fibers are preferred, in particular, fibers formed of thermoplastic or thermosetting plastic materials, and/or adhesive-coated fibers.

Referring to Fig. 1, a self-contained, battery-free iontophoresis apparatus or device 10 in accordance with the present invention takes the form of a patch comprising a sandwich of a flexible substrate 12 formed of a sheet material such as an air permeable or non-air permeable textile or fabric which may include an adhesive-coated textile or fabric, a pharmaceutical carrier such as a gauze 14 and a cover 16 formed of a second sheet material carrying a plurality of spaced lines or lines of dots of metal particles, e.g. as described in our aforesaid ‘761 and ‘172 patents or as described in our ‘076 pending application. Preferably the metal particles are zinc particles and have an average particle size of between 1 and 100 nanometers, more preferably 1 to 10 microns, and even more preferably about 5 microns. The metal particles may be printed on the substrate 16, or extruded or melt spun at the time of fiber formation as taught by our aforesaid patents and pending application. Polyethylene is a material of choice for forming the fibers for releasing zinc ions. The amount of zinc and the surface area of the zinc or other metal used is a function of particle size and availability to create the battery. The amount of total zinc per unit volume will decide the capacity of the battery. When the zinc runs out the battery will also die out, unless there is recharging going on, e.g. due to ions present in the skin.

Preferably, but not necessarily, fabric 16 comprises a woven textile, although fabric 16 may be a non-woven textile, a fibrous mesh, a non-fibrous mesh, which may include an adhesive coated textile or fabric, mesh or the like.

Preferably, but not necessarily, opposite ends of the device 10 may include adhesive or adhesive tabs shown in phantom at 20 so that the iontophoresis device may be fixed to the skin of a user. Alternatively, the iontophoresis device 10 may be held in place by a wrap or the like.

5 As taught in our aforesaid '761 and '172 patents or as described in our '076 pending application, and as shown in Fig. 1, the metal particles are discontinuously and substantially uniformly distributed on the surface of fabric 16, in imaginary spaced lines or lines of dots, across the surface area of the fabric 16, at least in part. Typically, the lines or lines of dots are evenly spaced at spacings from 0.1 to 3 mm, preferably 0.2 to 2 mm, more preferably 0.3
10 to 1.5 mm, most preferably 0.5 to 1.0 mm. The concentration of metal such as zinc in the binder or in the extruded fibers that forms the lines or dots determines the amount of metal available for the "battery". Preferred concentration is 30% of the surface area of the fabric; however, the concentration of zinc may range from about 1% to about 99%. A mixture of binder and zinc metal may be formed as a paste and applied by silk screening e.g., as
15 described in our aforesaid '761 and '172 patents. A 30% by weight zinc-to-binder is preferred for this. The line or dot width and length also determines the amount of metal in the deposition since the wider and longer the line, the more metal is available. Preferred line dots width is 1 mm width but width can vary from 0.1 mm up to 5 mm width. Since the deposition is on a fabric or carried in the adhesive, the amount of binder/metal applied also
20 can be varied. In certain embodiments, the fabric being coated can be coated twice or more times over the same pattern whereupon the thickness of the deposition can be increased as desired. In certain embodiments, the metal deposition area patterns cover from about 10% to about 90% of the surface area of the fabric. In other embodiments, the metal deposition areas cover from about 20% to about 80%, from about 15% to about 75%, from about 25%
25 to about 50%, or from about 30% to about 40% of the surface area of the fabric or anywhere in between. Although Fig. 1 shows the plurality of metal deposition areas 18 substantially uniformly distributed on the surface of the fabric, in other embodiments, the plurality of metal deposition areas may be randomly distributed on the surface of the fabric. Typically, the lines have a thickness of 0.1 to 3 mm, preferably 0.2 to 2 mm, more preferably 0.3 to
30 1.0, most preferably 0.4 to 0.5 mm. The spaced lines may be continuous and may take various forms including straight, curved and various angular shapes as shown, for example,

straight continuous lines; straight broken lines; continuous saw-shaped; continuous wavy lines; broken wavy lines, etc, as described in our aforesaid '761 and '172 patents and our '076 pending application. The actual shape of the lines is not important. Preferably, but not necessarily, the lines are approximately equal in thickness and are evenly spaced.

5 Referring to Figs. 2 and 2A, a self-contained external battery-free iontophoresis apparatus in accordance with the present invention is formed following the teachings of our aforesaid '076 application as follows: Metal particles, specifically elemental zinc particles, previously formed by grinding or precipitated out of suspension, and having an average particle size between 1 and 100 nanometers, more preferably 1 - 10 microns, even more
10 preferably about 5 microns are mixed with a thermal plastic material such as polyethylene in a heated mixing vat 30 to melt the material, and the mixture extruded or melt spun at spinning station 32 to form fibers 34, having metal particles 36 contained therein. Polyethylene is the polymer of choice for releasing of electrons from the metal. The porosity of the fiber also is believed to play a part. Polyacrylic or polyester fibers also may
15 be used however the result is a slower ion release. The metals containing fibers may then be cabled or twisted at a cabling station 38, and woven at a weaving or knitting station 40 into a sheet or cloth. The resulting metal particle impregnated sheet or cloth is cut to size at a cutting station 42, assembled together with a gauze pad impregnated with a medicine and a base sheet 12 as previously described at an assembly station 44, and the assembled package
20 laminated together to form a self-contained battery-free iontophoresis apparatus at a laminating station 46. Lamination may be by application of glue on the border of base 12 and a metal-containing fabric 16, or by melt fusing the edges of the assembly.

There is thus provided a self-contained, external battery-free iontophoresis apparatus.

Various changes may be made in the above invention without departing from the
25 spirit and scope thereof. For example, the amount of zinc in the fabric or adhesive coating can be increased or decreased to change the battery capacity. Adding too much zinc to a fiber may weaken the fiber so we can employ a bi-component concept where only the outside layer has the zinc and the inner core is polyester or another polymer that has more strength. By this method we can process the fiber differently than a polyethylene fiber
30 loaded with zinc alone.

What is claimed:

1. A device for increasing absorption of substances through the skin of an animal or human, comprising, in order:

a substrate layer;

a treatment substance carrying layer holding a treatment substrate, carried on said substrate layer; and

a cover layer disposed over said treatment substance carrying layer, said cover layer having metal particles disposed on or exposed through at least a portion of said cover layer as a plurality of lines or dots in a specific pattern that positions the metal particles in discrete electrically isolated locations separated by a distance, or disposed in or on an adhesive coating on said cover layer in said plurality of lines or dots in said specific pattern that positions the metal particles in discrete electrically isolated locations separated by said distance, wherein said cover layer is configured such that said metal particles are exposed at least in part, wherein said metal particles on said cover layer or carried by said adhesive coating form a plurality of half-cells of an air-or oxygen-metal battery, for ion exchange with the skin of the human or animal whereupon the treatment substance may be driven into the skin by iontophoresis.

2. The device of claim 1, wherein the patterns conform to blood circulation patterns and/or nerve or underlying muscle patterns of the human or animal.

3. The device of claim 1, wherein the lines or dots are evenly spaced from one another at spacings from 0.1 to 3 mm, preferably 0.2 to 2 mm, more preferably 0.3 to 1.5 mm, most preferably 0.5 to 1 mm.

4. The device of claim 1, wherein the lines or dots of lines are 0.1 mm to 5 mm wide, preferably about 0.1 to 3 mm, more preferably 0.2 to 2 mm, even more preferably 0.3 to 1 mm, most preferably 0.4 to 0.5 mm.

5. The device of claim 1, wherein the patterns cover from about 10% to 90% of the surface of the cover layer, preferably from about 15% to about 75%, more preferable from about 25% to about 50%, most preferably from about 30% to about 40%.

6. The device of claim 1, wherein the metal particles comprise a metal, metal oxide or metal salt, wherein the metal particles preferably are selected from the group consisting of elemental zinc particles, zinc oxide particles, and zinc salt particles, or elemental aluminum, iron,

copper or magnesium particles, aluminum, iron, copper or magnesium oxide particles, or aluminum, iron, copper or magnesium salt particles.

7. The device of claim 1, further including an adhesive pad or adhesive tabs adapted to fix the substrate layer.

8. A use of the device as claimed in claim 1 for increasing absorption of a substance through the skin of a human or animal, comprising:

disposing the device in contact with the skin of a human or animal, wherein the metal particles exposed through said cover layer or adhesive coating form said plurality of half-cells of said air-or oxygen-metal battery with the skin of the human or animal, whereupon the metal particles form a first half cell of a battery circuit, while the body of the human or animal forms a second half cell of the battery circuit with oxygen, whereupon the substance is driven into the skin of the human or animal by iontophoresis.

9. The use of claim 8, wherein the patterns conform to blood circulation patterns and/or nerve or underlying muscle patterns of the human or animal.

10. The use of claim 8, wherein the lines or dots are evenly spaced at spacings from 0.1 to 3 mm, preferably 0.2 to 2 mm, more preferably 0.3 to 1.5 mm, most preferably 0.5 to 1 mm.

11. The use of claim 8, wherein the lines or dots of lines are 0.1 mm to 5 mm wide, preferably about 0.1 to 3 mm, more preferably 0.2 to 2 mm, even more preferably 0.3 to 1 mm, most preferably 0.4 to 0.5 mm.

12. The use of claim 8, wherein the patterns cover from about 10% to 90% of the surface of the cover layer, preferably from about 15% to about 75%, more preferable from about 25% to about 50%, most preferably from about 30% to about 40%.

13. The use of claim 8, wherein the metal particles comprise a metal, metal oxide or metal salt, preferably wherein the metal particles are selected from the group consisting of elemental zinc particles, zinc oxide particles, and zinc salt particles, or elemental aluminum, iron, copper or magnesium particles, aluminum, iron, copper or magnesium oxide particles, or aluminum, iron, copper or magnesium salt particles.

14. The use of claim 8, further including fixing the device to the skin of the animal or human using adhesive.

