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INTERFACE FOR IONTOPHORESIS

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(57) An interface composed of an aqueous solution supply portion capable of providing a fine hole for supplying an aqueous solution, a water-permeable electrode, and a water-absorbable or water-permeable film-like membrane, laminated integrally, wherein the fine hole for supplying the solution is made in the aqueous solution supply portion at the time of use, the aqueous solution is supplied through the water-permeable electrode and water-absorbable or water-permeable film-like membrane, and, when the aqueous solution reaches them, the drug or the drug-containing water-soluble layer dissolve and a locally high concentration solution of the drug is formed.

CLAIM

1. An interface for iontophoresis comprising an aqueous solution supply portion capable of providing a fine hole for supplying an aqueous solution at least when used, a water-permeable electrode, and a water-absorbable or water-permeable film-like membrane, laminated integrally.

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COMPLETE SPECIFICATION

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INVENTION TITLE:

Interface for iontophoresis

The following statement is a full description of this invention, including the best method of performing it known to me/us:-

BACKGROUND OF THE INVENTION

1. Field of the Invention

The present invention relates to an interface (or a skin contact structure) for iontophoresis.

2. Description of the Related Art

An interface for iontophoresis has a structure comprised of an assembly of a reservoir for holding a drug solution and an electrode for current dispersion.

The structure of the above-mentioned reservoir must be one which allows a predetermined amount of the drug solution to reliably reach the interface with the skin of the living body with the elapse of time. The reservoir itself is steric and contains water as the medium and thus there is dilution of the drug and, further, leakage of the drug solution, water etc. to outside the interface, causing leaks across the electrodes. A satisfactory structure has not yet been proposed.

SUMMARY OF THE INVENTION

Accordingly, the objects of the present invention are to alleviate the above-mentioned disadvantages of the conventional interfaces and to provide an interface having a structure capable of accurately administering a drug, suitable for iontophoresis.

Other advantages of the present invention will be apparent from the following description.

In accordance with the present invention, there is provided an interface for iontophoresis comprising an aqueous solution supply portion capable of providing a fine hole for supplying an aqueous solution at least when used, a

water-permeable electrode, and a water-absorbable or water-permeable film-like membrane, laminated integrally.

BRIEF DESCRIPTION OF THE DRAWINGS

The present invention will be described, by way of example only, with reference to the preferred embodiments as illustrated in the accompanying drawings, wherein:

Figure 1 is a cross-sectional view showing an embodiment of the present invention;

Figure 2 is a view showing the reverse side of the embodiment shown in Figure 1; and

Figures 3(a), (b), (c) and Figures 4(a), (b) and (c) are views for explaining other embodiments of the present invention.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

The present invention comprises an aqueous solution supply portion capable of providing one or more fine holes for supplying an aqueous solution at least when used, a water-permeable electrode, and a water-absorbable or water-permeable film-like membrane, laminated integrally. When fine holes for supplying the solution are made in the aqueous solution supply portion at the time of use, the aqueous solution is supplied through the water-permeable electrode and water-absorbable or water-permeable film-like membrane. The aqueous solution reaches and dissolves a drug or drug-containing water- soluble layer is dissolved and a solution having high local concentration of the drug is formed. Therefore, when an electric current is passed through the water-permeable electrode, the transdermic or transmucosal administration of the drug is promoted, while keeping the drug at a high concentration without diffusion or dilution of the drug solution.

Futher the drug solution or aqueous solution passes from the reservoir through the fine holes and gradually

permeates to the water-absorbing or water-permeable film-like membrane to just fill the same, so that the solution does not leak outside.

In the present invention, it is possible to keep the drug in a solid form, that is, a dried form, before use, so that the drug may be stored for a long time intact on the shelf.

Further, the drug need only be deposited on the water-absorbable or water-permeable film-like membrane in a suitable amount at a suitable time, so that effective administration of the drug becomes possible.

The aqueous solution supply portion may comprise a combination of a sheet composed of a plastic resin, for example PET (polyethylene telephthalate), EVA (ethylene vinyl acetate), PE (polyethylene), VC (vinylchloride) etc., having flexibility and a reservoir. The reservoir may be in the form of an ampule, sachet, container, pouch, bag, etc. which is closed by the sheet to contain the aqueous solution. As the sheet and the reservoir, mentioned may be made of ones which are formed integrally in advance or ones which are joined at the time of use.

The aqueous solution may be any which is capable of dissolving a drug.

The water-permeable electrode, may be made of a sheet or film formed partially or entirely in a meshed or porous form and having conductivity. The raw material therefor may be a sheet composed of carbon, silver, silver chloride, titanium, etc. or, for example, a composite sheet composed of a nonwoven fabric on which carbon, silver, silver chloride, or titanium paste is printed, etc. The water permeability need only be manifested at the time of use.

As the water-absorbable or water-permeable film-like

membrane it is possible to use a layer composed of a water-permeable fiber such as a laminated membrane filter, paper, nonwoven fabric, porous film (made of, for example, nylon membrane Biodyne A®, Biodyne Plus®, cellulose ester membrane or cellulose acetate membrane etc. or the like, a water-soluble polymer (e.g., PVA (polyvinyl alcohol), soluble starch, CMC (carboxymethyl cellulose), MC (methyl cellulose), hydroxypropyl cellulose, etc.) holding, adhering, or containing a predetermined drug, a PVP film, or other water-absorbing (aqueous) film. Usually, it is formed into a thin film.

The aqueous solution supply hole is a fine hole made through the reservoir of the aqueous solution supply unit. The hole suitably has a diameter of about 0.5 mm to 2 mm. A plurality of the holes may be formed and their diameter and member are suitably selected in accordance with the time by which the aqueous solution inside the aqueous solution supply unit is supposed to reach the drug and the shape and materials of the water-permeable electrode and of the water-absorbable or water-permeable film etc.

An embodiment of the present invention will now be explained in detail with reference to Figure 1.

In Figure 1, (1) is an aqueous solution supply member which has a reservoir structure of an ampule, container, pouch, or the like containing an aqueous solution (2) for dissolving a drug at the time of use and forming a conductive path.

At the bottom surface of the aqueous solution supply member (1) is adhered and affixed a meshed or porous water-permeable electrode (3). At the one end of this is attached an external connecting terminal (4).

The external connecting terminal (4) serves to connect the

water-permeable electrode (3) and an external iontophoresis output unit. At the connection portion, use is made of alligator clips, screws, etc.

Further, at the bottom surface of the water-permeable electrode (3), a water-absorbable or water-permeable film-like membrane (5) is affixed.

On the surface or inside the film-like membrane (5), there is provided a drug (6) in solid form such as dried powder or granules, which is held, adhered, or contained in the film-like membrane (5).

Reference numeral (7) indicates a fine hole. This hole is made at the time of use. The aqueous solution (2) contained in the aqueous solution supply member (1) passes through the fine hole (7) and gradually permeates to the water-permeable electrode (3) and film-like membrane (5) by capillary action, dissolves the solid drug (6), and reaches the skin surface.

Because the aqueous solution reaches the drug by capillary action, it is possible to make adjustments so that a suitable amount of aqueous solution can be supplied to the drug, without supplying excess solution, and therefore, it is possible to make the drug solution quantitatively and reliably reach inside of the body, without excessive dilution, by the aid of iontophoresis.

Another embodiment will now be explained in detail with reference to Figure 3.

In Figure 3, (1) is an aqueous solution supply member, which has a bag-like reservoir connected in an integrally formed manner at the approximate center of the sheet-like supply member. The material, as in the case of Figure 1, is a resin or plastic having flexibility and an electrical

insulation property. The reservoir is made of a similar material.

The reservoir is connected to only part of the aqueous solution supply member (1). Reference numeral (2) represents an aqueous solution, which fills the reservoir of the aqueous solution supply member (1). Reference numeral (3) is a water-permeable electrode, which is formed by printing or branding a conductive ink of carbon, silver, silver chloride, titanium, etc. on the rear surface of the aqueous solution supply member (1). Reference numeral (4) is an external connecting terminal, which has conductivity and which is for connection with an external iontophoresis output unit.

The external connecting terminal (4) is connected with the water-permeable electrode (3) and projects through the aqueous solution supply member (1). Reference numeral (5) is a film-like membrane, which consists of material having water-abosrbency or water-permeability. At the periphery of the film-like membrane (5) is formed an adhesive layer, which is connected to the aqueous solution supply member (1). Reference numeral (6) is a drug, which is deposited on a part of the film-like membrane (5). Reference numeral (8) is a peel-off membrane, which is formed from a paper, resin, etc. coated with silicone. Reference numeral (10) is a projection, which is formed integrally with the peel-off member (8) and further passes through the film-like membrane (5) and is connected to part of the reservoir of the aqueous solution supply member (1).

The method of use and operation will now be explained.

Before use, as shown in Figure 3(a), the projection (10) of the peel-off membrane (8) and part of the reservoir of the aqueous solution supply member (1) are in a connected state. The drug (6) is sandwiched in the closed space

between the peel-off membrane (8) and the film-like membrane (5). Upon use, as shown in Figure 3(b), the peel-off membrane (8) is peeled off. When it is peeled off, the projection (10) is pulled so as to break the connection between the reservoir of the aqueous solution supplying member (1) and the projection (10), whereby the fine hole (7) is made.

After the peel-off member (8) is peeled off, the interface is adhered to the surface of the skin (MM). The state of attachment is shown in Figure 3(c). The aqueous solution (2) inside the reservoir of the aqueous solution supply member (1) passes through the fine hole (7) and reaches the surface of the skin (MM). At the same time, the aqueous solution permeates inside the film-like membrane (5) and reaches the portion where the drug (6) is deposited.

The conductive terminal (4) and the external iontophoresis output unit are connected by the electric lead line (11) and the conductive metal fitting connected to the same. The drug (6) is dissolved in the aqueous solution (2) and placed under an electrical transdermal administration state while maintaining a high local concentration.

Further, the film-like membrane (5) and the surface of the skin (MM) are joined by providing an adhesive layer on the film-like membrane (5) or by applying sticking plaster.

Another embodiment will now be explained in detail with reference to Figure 4.

In Figure 4, reference numeral (12) is a reservoir, with a top surface formed by a soft portion and a side surface and bottom surface formed by a hard portion. The aqueous solution (2) is filled into the reservoir.

Reference numeral (13) is a hollow needle-like projection,

which is connected to the bottom surface of the reservoir (12).

Reference numeral (14) is a supporting member, which is composed of the same material as the aqueous solution supply member (1) explained in the previous embodiment. Reference numeral (15) is an adhesive gel which is placed around the outside periphery of the supporting member (14). The adhesive gel (15) is only required to have stickiness. Use of another adhesive agent is also possible. Reference numeral (3) is a water-permeable electrode, which consists of a nonwoven fabric on which is printed a conductive ink of carbon, silver, silver chloride, titanium, etc. Reference numeral (4) is a conductive terminal, which is formed by causing one end of the water-permeable electrode (3) to project from the supporting member (14). Reference numeral (5) is a film-like membrane of the above-mentioned materials and structure. Reference numeral (6) is a drug, which is deposited on the bottom surface of the film-like membrane (5). Reference numeral (8) is a peel-off membrane, which is of the same material and structure as in the embodiment shown in Figure 3.

An explanation will now be made on the method of use and operation of this embodiment.

Before use, as shown in Figure 4(a), the reservoir (12) is handled as a separate unit. The drug (6) is sandwiched in the closed space between the film-like membrane (5) and the peel-off membrane (8). At the time of use, as shown in Figure 4(b), the hollow projection (13) provided at the bottom surface of the reservoir (12) pierces through from the top of the supporting member (14) to reach the water-permeable electrode (3). Further, the peel-off membrane (8) is peeled off and, as shown in Figure 4(c), the interface is adhered to the skin (MM).

By pressing down the top surface of the reservoir (12), the aqueous solution (2) is pushed to the outside through the hollow projection (13). Further, the aqueous solution (2) permeates through the water-permeable electrode (3) and the film-like membrane (5) to reach the drug (6) and the surface of the skin (MM), whereby a conductive pathway is formed between the water-permeable electrode (3) and the surface of the skin (MM).

The electrical output from the external iontophoresis output unit is supplied to the water-permeable electrode (3) through the electrical lead line (11), so that the drug (6) dissolved in the aqueous solution (2) and maintained at a high local concentration is placed in an electrical transdermal administration state.

The above-mentioned three embodiments illustrate the case where the main electrode and the counter electrode were separate and an iontophoresis electrical output unit was provided externally, but it is also possible to have an integral construction by placing the main electrode and counter electrode on the same electrically insulating member and attaching an iontophoresis electrical output unit to the same.

The above-mentioned drug is not limited in terms of its molecular weight or other physical qualities, and the interface of the present invention is particularly useful for insulin and other peptide type drugs which, despite being used in small quantities, have to be held at as high a concentration as possible and yet be sufficiently liquid for efficient iontophoresis. Examples of the drugs are given below:

Local anaesthetics: Lidocaine hydrochloride;
Antitussive expectorants: Sodium cromoglicate;
ketotifen fumarate;
Bronchial vasodilators: Formoterol fumarate;

Analgesics: Nalbuphine hydrochloride, pentazocine lactate, Diclofenac sodium; Cardiacs; Dopamine hydrochloride; Psychoneurotic stabilizers: Perphenazine, phenothiazine; Antibiotics: Cefotetan disodium, dibekacin sulfate, amikacin sulfate, netilmicin sulfate, sisomicin sulfate; Anti-malignant tumor agents.

Adriamycin, mitomycin C, belomycin hydrochloride, lentinan, picibanil, vincristine sulfate, cisplatin; Circulatory function ameliorators: Nicametate citrate, meclofenoxate hydrochloride, lisuride maleate, calcium hopantenate; Gout therapeutic agents: Allopurinol

Other peptides: LHRH, enkephalin, endorphin, interferon, insulin, calcitonin, TRH, oxytocin, lypressin vasopressin, glucagon, pituitary hormones (HGH, HMG, HCG, desmopressin acetate), follicular luteinizing hormones, growth hormone releasing factors and analogues.

As mentioned in detail above, the present invention enables sufficient aqueous solution to be supplied, without the drug solution being diluted and enables long-term storage without deterioration, decomposition, etc. since the drug remains in a dry state before use. Further, since the drug is only present at the interface with the skin, once dissolved, highly efficient drug utilization can be achieved under electric current with minimum leakage from the application site. Thus, this invention is particularly suitable for administration of drugs which are highly potent and very expensive.

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. An interface for iontophoresis comprising an aqueous solution supply portion capable of providing a fine hole for supplying an aqueous solution at least when used, a water-permeable electrode, and a water-absorbable or water-permeable film-like membrane, laminated integrally.

2. An interface for iontophoresis as claimed in claim 1, wherein the aqueous solution supply portion comprises a sheet composed of a plastic film and a reservoir.

3. An interface for iontophoresis as claimed in claim 1 or claim 2, wherein the water-permeable electrode is composed of a sheet or film formed partially or entirely in a meshed or porous form and having conductivity.

4. An interface for iontophresis as claimed in any one of claims 1 to 3, wherein the film-like membrane is composed of a laminated membrane, paper, nonwoven fabric, porous film or water soluble polymer.

5. An interface for iontophoresis substantially as hereinbefore described with reference to the drawings.

DATED this 29th day of March, 1994.

KABUSHIKI KAISYA ADVANCE
By its Patent Attorneys
DAVIES COLLISON CAVE

INTERFACE FOR IONTOPHORESIS

ABSTRACT OF THE DISCLOSURE

An interface composed of an aqueous solution supply portion capable of providing a fine hole for supplying an aqueous solution, a water-permeable electrode, and a water-absorbable or water-permeable film-like membrane, laminated integrally, wherein the fine hole for supplying the solution is made in the aqueous solution supply portion at the time of use, the aqueous solution is supplied through the water-permeable electrode and water-absorbable or water-permeable film-like membrane, and, when the aqueous solution reaches them, the drug or the drug-containing water-soluble layer dissolve and a locally high concentration solution of the drug is formed.

Fig. 1

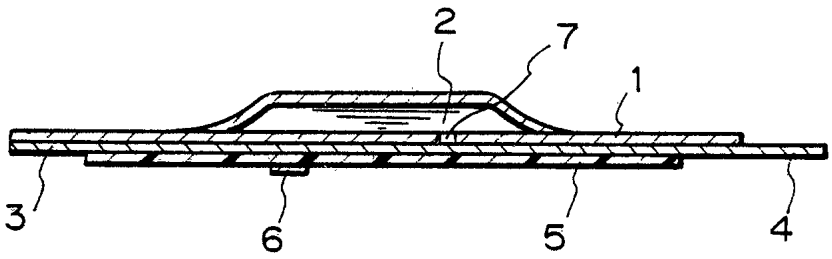

Fig. 2

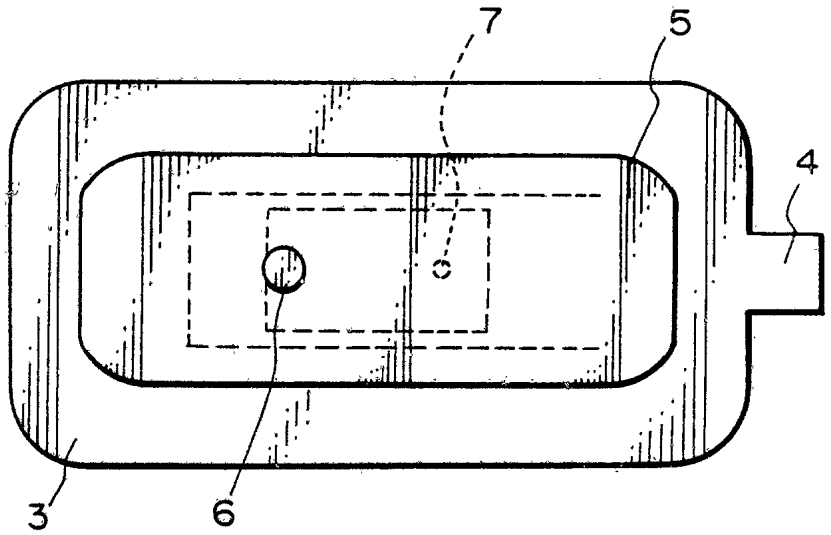

Fig. 3(a)

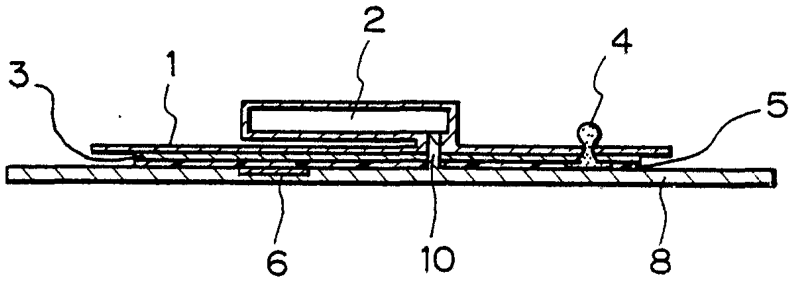

Fig. 3(b)

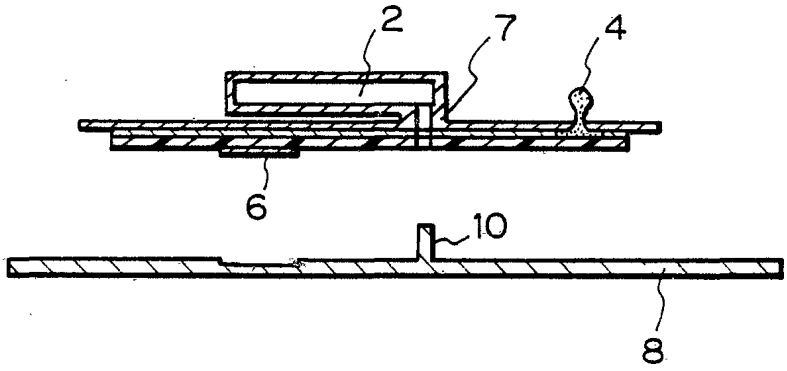

Fig. 3(c)

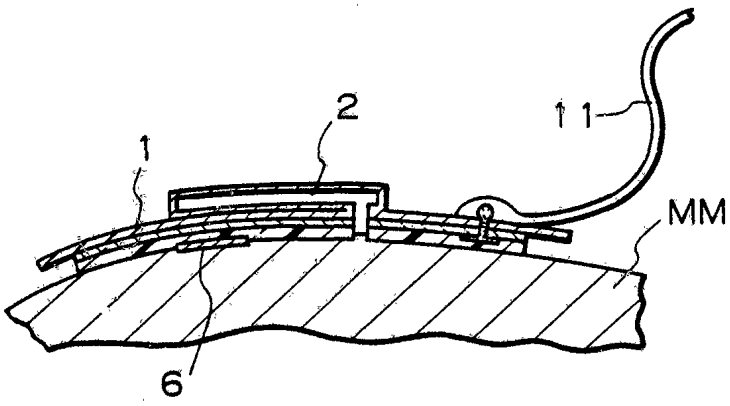

Fig. 4(a)

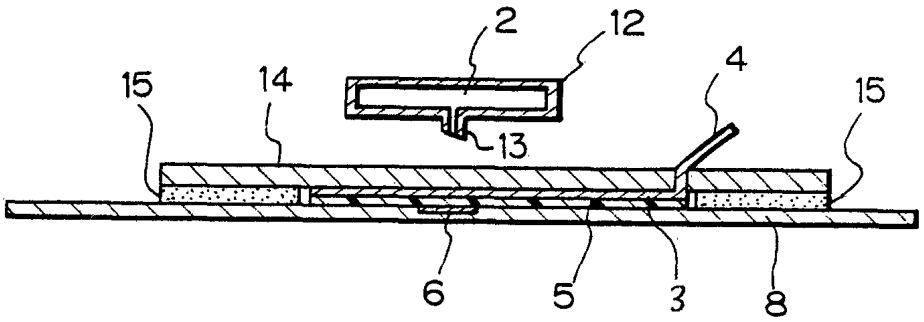

Fig. 4(b)

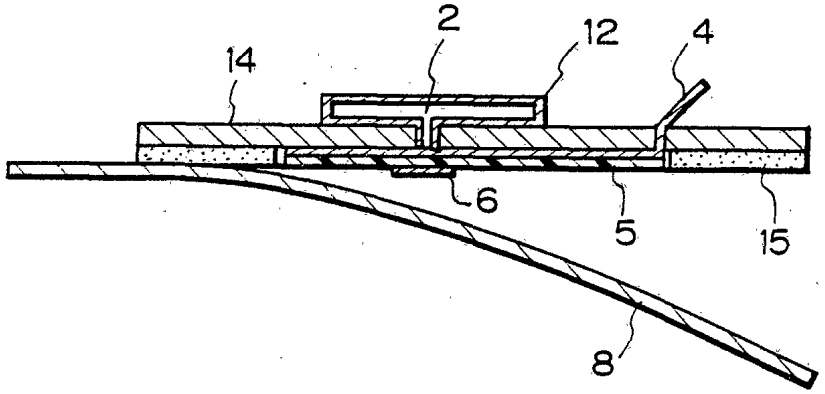

Fig. 4(c)