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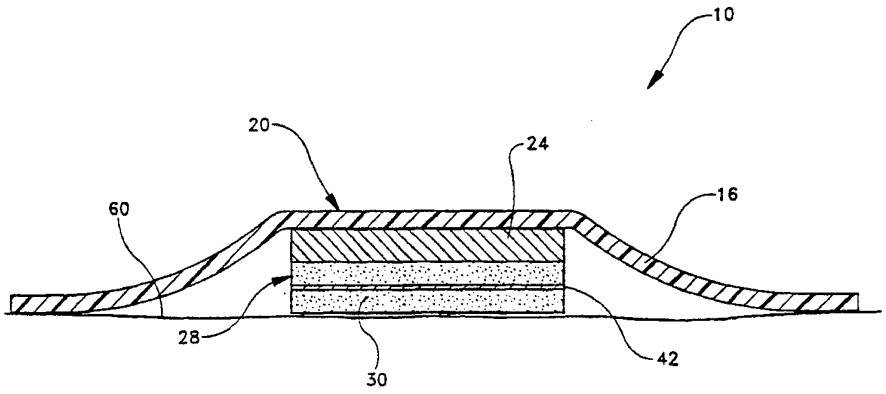

(57) Abstract

The iontophoretic drug delivery device (10) of the present invention includes an electrode assembly (12) in electrical contact with at least one reservoir (28) containing an aqueous swollen cross-linked water soluble polymer, selected from the group including polyethylene oxide (PEO), polyvinyl pyrrolidone (PVP), and polyacrylamide. The aqueous swollen water soluble polymer is cross-linked by high-energy irradiation. At least one of the reservoirs includes at least one medicament to be delivered loaded therein, and one of the reservoirs includes an electrolyte. In addition, the method of the present invention includes providing a structurally reinforcing member (42), coating the reinforcing material with the viscous water soluble polymer solution, and cross-linking the solution.

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IONTOPHORETIC DEVICE, RESERVOIR AND METHOD OF MAKING

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FIELD OF THE INVENTION

The present invention generally relates to iontophoretic systems for delivering medicaments such as therapeutic drugs and medicines to patients transdermally, i.e., through the skin, and more specifically relates to an iontophoretic drug delivery device and a reservoir for use in the same. In addition, the present invention relates to a method for making the reservoir for use in such an iontophoretic drug delivery device.

BACKGROUND OF THE INVENTION

Transdermal drug delivery systems have, in recent years, become an increasingly important means of administering drugs. Such systems offer advantages clearly not achievable by other modes of administration such as avoiding introduction of the drug through the gastro-intestinal tract or punctures in the skin to name a few.

Presently, there are two types of transdermal drug delivery systems, i.e., "Passive" and "Active." Passive systems deliver drug through the skin of the user unaided, an example of which would involve the application of a topical anesthetic to provide localized relief, as disclosed in U.S. Patent No. 3,814,095 (Lubens). Active systems on the other hand deliver drug through the skin of the user, such as a patient, using iontophoresis, which

according to Stedman's Medical Dictionary, is defined as "the introduction into the tissues, by means of an electric current, of the ions of a chosen medicament."

Conventional iontophoretic devices, such as those described in U.S. Patent Nos. 4,820,263 (Spevak et al.), 4,927,408 (Haak et al.) and 5,084,008 (Phipps), the disclosures of which are hereby incorporated by reference, for delivering a drug or medicine transdermally through iontophoresis, basically consist of two electrodes -- an anode and a cathode. Usually, electric current is driven from an external supply into the skin at the anode, and back out at the cathode. Accordingly, there has been considerable interest in iontophoresis to perform delivery of drugs for a variety of purposes. Two such examples, involve the use of Novocaine,™ which is usually injected prior to dental work to relieve pain, and Lidocaine,™ which is usually applied as a topical, local anesthetic.

Such prior devices have utilized an absorbent pad or porous solid sheet that can be filled with drug solution as the drug reservoir. These absorbent pads or porous sheets have three major disadvantages. First, they must be filled with the drug solution after removal from the package since these pads or porous sheets do not hold the drug solution as the solution is subject to removal and leakage under pressure or flexure. In addition, even after the inconvenient addition of the drug solution and after removal from the package, the absorbent pad or porous sheet

reservoir remain subject to leakage and smearing of the drug solution due to pressure or flexure upon the skin. Furthermore, absorbent pads or porous solid sheets can not provide the electrical continuity to complete intimate contact since they lack adhesivity and flexibility with the skin and its contours.

In addition, prior drug reservoirs have included pastes and unformed viscous semi-solid gels such as agar that have both solid and liquid characteristics as described, for example, in U.S. Patent No. 4,383,529 (Webster), the disclosures of which are hereby incorporated by reference.

However, several disadvantages and limitations have been associated with the use of such devices, including handleability and loadability. For example, the semi-solid reservoir disclosed in Webster flows under shear or stress. Furthermore, this disclosed reservoir may melt upon exposure to modest elevated temperatures.

Thus, there has been a need for an iontophoretic drug delivery device and a reservoir for use in the same, as well as a method for making the reservoir, which would eliminate the problems and limitations associated with the prior devices discussed above, most significant of the problems being associated with handleability and loadability of the reservoir, including chemical and thermal stability of the reservoir.

SUMMARY OF THE INVENTION

In contrast to the prior devices discussed above, it has been found that a iontophoretic drug delivery device particularly suited for use to deliver at least one medicament, particularly in a high dose efficiency, can be constructed in accordance with the present invention by the incorporation of an aqueous swollen cross linked water soluble polymeric drug delivery reservoir. In addition, the device of the present invention can easily fit over any contour of the body and provide excellent electro coupling with the electrode and the skin, while still being capable of flexing and adhering to the skin. Also the device of the present invention can be applied over a range of temperatures and is stable for over two years at controlled room temperature to provide a commercially suitable shelf-life.

The iontophoretic drug delivery device of the present invention for delivering at least one medicament to an applied area of a patient, such as the skin, mucus membrane and the like, includes electrode assembly means for driving a medication into the applied area of the patient to be absorbed by the body of the patient and a reservoir situated in electrically conductive relation to the electrode assembly means, with the reservoir including an aqueous swollen cross linked water soluble polymer, with the reservoir containing the at least one medicament.

In the preferred embodiment, the device of the present invention also includes a structurally reinforcing

member situated within the reservoir including the aqueous swollen cross linked water soluble polymer, with the structurally reinforcing member having an open area. In addition, the structurally reinforcing member is a thermoplastic polymeric scrim and the aqueous swollen cross linked water soluble polymer is cross linkable by high energy irradiation. Also, the aqueous swollen cross linked water soluble polymer is selected from the group including polyethylene oxide, polyvinyl pyrrolidone, polyvinyl alcohol and polyacrylamide. Further, in the preferred embodiment, the at least one medicament includes Lidocaine and the reservoir includes a vasoconstrictor, stabilizers and glycerin. In addition, the reservoir further includes additives and conductive salts, with the additives selected from the group including glycerin, propylene glycol and polyethylene glycol.

In alternative embodiments, the composition of the polyethylene oxide is from 1% to 6% and the composition of the polyvinyl pyrrolidone is from 15% to 40%, with the compositions being irradiation cross linked in aqueous solution.

The reservoir of the present invention for use in an iontophoretic drug delivery device having an electrode assembly for delivering at least one medicament through an applied area of a patient, such as the skin, mucus membrane and the like, includes a layer of a aqueous swollen cross linked water soluble polymer material capable of being electrically conductive with the electrode assembly and the

aqueous swollen cross linked water soluble polymer material including at least one medicament for delivery through an applied area of a patient, such as the skin, mucus membrane and the like.

In the preferred embodiment, the reservoir also includes a structurally reinforcing member situated within the layer of aqueous swollen cross linked water soluble polymer material, with the structurally reinforcing member having an open area. In addition, the structurally reinforcing member is a scrim of a aqueous insoluble thermoplastic polymeric material and the aqueous swollen cross linked water soluble polymer material is cross linked by high energy irradiation. Also, the aqueous swollen cross linked water soluble polymer is selected from the group including polyethylene oxide, polyvinyl pyrrolidone, polyvinyl alcohol and polyacrylamide. The at least one medicament in the reservoir of the preferred embodiment is Lidocaine and the aqueous swollen cross linked water soluble polymer includes a vasoconstrictor, stabilizers and glycerin. Further, the reservoir includes additives and conductive salts, with the additives selected from the group including glycerin, propylene glycol and polyethylene glycol.

In alternative embodiments, the composition of the polyethylene oxide is from 1% to 6% and the composition of the polyvinyl pyrrolidone is from 15% to 40%, with the compositions being irradiation cross linked in aqueous solution.

The method of the present invention for making a reservoir for use in an iontophoretic drug delivery device includes the steps of providing a structurally reinforcing member, coating the reinforcing member with a viscous water soluble polymer solution, and cross linking the layer by high energy irradiation.

In the preferred embodiment of the method, the step of coating includes the steps of applying a layer of the viscous solution to one side of the reinforcing member, applying a layer of the viscous solution to one side of a release liner and laminating the release liner and the reinforcing material together such that both surfaces of the reinforcing member are coated with the viscous solution. Also, the viscous solution is applied to the reinforcing member and the release liner to a thickness of Ca. 5 mil to 30 mil. In addition, the method includes the step of applying a final release liner to the remaining exposed viscous solution coated surface of the reinforcing member to form a laminate and cross linking the viscous solution and includes the step of replacing the final release liner with an electrode. Also, the method includes the step of adding at least one medicament to the viscous water soluble polymer solution, with the medicament including Lidocaine and the polymer includes a vasoconstrictor, stabilizers and glycerin. Further, the method includes the step of cutting the laminate into a suitable shape and area for use in the iontophoretic drug delivery device.

BRIEF DESCRIPTION OF THE DRAWINGS

The various features, objects, benefits, and advantages of the present invention will become more apparent upon reading the following detailed description of the preferred embodiment along with the appended claims in conjunction with the drawings, wherein like reference numerals identify corresponding components, and:

Figure 1 is a schematic view of the iontophoretic drug delivery device of the present invention illustrating placement of the device on a user;

Figure 2 is a cross sectional view of the device of the present invention;

Figures 3A, 3B, 3C and 3D are schematic views of the various steps of the method for making the reservoir of the present invention; and

Figure 4 is a logic flow diagram depicting the various steps of the method for making the reservoir of the present invention.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

The iontophoretic drug delivery device of the present invention is illustrated in Figures 1 and 2, and generally includes the designation 10. Referring to Figures 1 and 2, the device 10 of the present invention includes an electrode assembly 12, having at least one electrode and at least one reservoir, with the reservoir and electrode held or contained within a suitable structure 16, with a skin adhesive 18. Also, as is well known in the

art, a power source 19 is provided in circuit with the electrode assembly 12 for supplying a source of electrical current. It should be appreciated that a return electrode and reservoir may be combined into a single electrode assembly 12 or separately provided as illustrated in Figure 1.

In the preferred embodiment, the device is divided or otherwise separated into two portions 20 and 22, with the electrode assembly 12 including two electrodes 24 and 26. One portion 20 (first) includes the electrode 24 and a reservoir 28, with the reservoir being situated adjacent and coupled to the electrode 24 and holding at least one medicament or drug 30, preferably in ionized or ionizable forms, to be delivered iontophoretically. The other portion 22 (second) includes the electrode 26 and a reservoir 32, with the reservoir being situated adjacent to the electrode 26 and holding an electrolyte 34. The particular electrolyte is not essential to the present invention and is merely a matter of choice. However, in this embodiment the electrolyte may include sodium chloride in an aqueous solution, matrix or the like as explained in greater detail hereinbelow.

A schematic diagram of the first portion 20 of the device 10 is illustrated in Figure 2. In this case, the medicament 30 to be delivered through the skin is a cation and the reservoir 28 is connected to the electrode 24, which acts as an anode. The return electrode 26 (cathode) may be constructed in the manner as the working electrode

24. If the drug is an anion, then the drug containing reservoir would be connected to the cathode and the return reservoir would be connected to the anode.

As is well known within the field, the device can be situated on the area of the patient to which the medicament is to be applied (the applied area) and a voltage impressed across the electrodes 24, 26 of the electrode assembly 12 to cause current to flow through the skin 60 of the patient to drive the ionic medicament locally into the skin and the tissue or to be absorbed systematically by the body of the patient. It should also be appreciated that the device of the present invention can be applied to other areas of the body such as mucus membranes and the like depending upon the desired therapy and medicaments to be delivered.

In order to transport the medicament through intact skin 60 at least the reservoir 28 containing the medicament includes an aqueous swollen cross linked water soluble polymer, which for simplicity is hereinafter referred to as a cross linked water soluble polymer. The cross linked water soluble polymer can be incorporated into the reservoir as a homogeneous solid cut or molded sheet 40 of suitable shape and area which can be attached to the electrode as illustrated in Figures 1 and 2. However, it should be appreciated that the reservoir 32 (cathode) may also be made of the same material as the reservoir 28 containing the medicament, i.e., to include the cross linked water soluble polymer sheet 40 illustrated in

Figures 3A-3D. Accordingly, the cross linked water soluble polymer sheet 40 containing either the medicament and/or the electrolyte serves as the reservoirs 28, 32 and the electrical coupling to the skin while being able to conform to all contours of the body. In addition, the reservoir may include additives selected from the group including glycerin, propylene glycol and polyethylene glycol and conductive salts.

The particular cross linked water soluble polymer material may be made from a variety of commercially available water soluble polymers known to those skilled in the art as long as it is of low bioburden, is electrically conductive, readily conforms to the contours of the body, is capable of being cross linked and can hold or otherwise retain the drug solution under pressure and flexure.

Cross linked water soluble polymers are preferred reservoirs as they provide a comfortable interface with good electrical coupling and excellent biocompatibility. Examples of such cross linked water soluble polymers are irradiated cross linked polyethylene oxide (PEO), with from 94% to 99% water, polyvinyl pyrrolidone (PVP), polyvinyl alcohol (PVA), and polyacrylamide. The cross linked water soluble polymer sheet 40 by nature of its preparation by irradiation cross linking is of low bioburden and is non toxic, non irritating and non sensitizing to the skin. This is particularly assured by the fact that no chemical cross linking agents or organic solvents are required to synthesize the cross linked water soluble polymer material.

It should be appreciated, that the techniques of irradiation cross linking the water soluble polymer material are well known in the art.

In the preferred embodiment, the cross linked water soluble polymer sheet 40 may include a netting material 42 such as an inert polyethylene scrim of the type known as Delnet™, which is commercially available from Applied Extrusion Technologies Inc. The scrim utilized for this application is preferably an open web, water insoluble material that does not change the conductivity or ionic flow of the materials in the water soluble polymer. In this way, the cross linked water soluble polymer sheet 40 can be formed from a solution 44 of premixes after dispersion and full solution, with the solution then applied on both sides of the scrim 42 to a thickness of Ca. 5 mil to 30 mil and then cross linked by high energy irradiation such as for example, electron beam or gamma irradiation to form covalent cross links. The particular thickness of the cross linked water soluble polymer sheet may vary depending upon, e.g., the medicament to be delivered, the applied area and the like, from a very thin sheet, i.e., film, for high drug efficiency to a very thick sheet for minimization of sensation when an electrical current is applied.

As illustrated in Figures 3A, 3B, 3C and 3D, and the flow diagram illustrated in Figure 4, preferably the cross linked water soluble polymer sheet 40 is formed by providing the release liner 46 and the scrim 42,

applying or otherwise coating a release liner or other backing material 46 with one-half of the viscous solution 44 of water soluble polymer to form a layer 44A (Figure 3B) and coating or otherwise applying the other half of the viscous solution 44 to one side of the scrim 42 to form a layer 44B (Figure 3C). The coated liner 46 is then laminated to the coated scrim 42 such that the scrim has the viscous solution on both sides (Figure 3D). Next, a final liner or other backing material 48 is then applied to the exposed surface, with the cross linked water soluble polymer sheet 40 sandwiched between the two release liners 46, 48 to form a laminate 50, which in the preferred embodiment is then exposed to high energy irradiation to cross link the water soluble polymer solution. In the alternative, to provide ease of handling, the final release liner 48 can be applied to the coated scrim prior to lamination with the coated liner 46.

The scrim 42 itself imparts structural support and mechanical strength to the final cross linked water soluble polymer sheet to prevent shearing. Thereafter, the laminate 50 can be easily handled and cut or otherwise formed into the desired shape for the particular reservoir 28, 32. In this way, the release liner 46 can be subsequently removed and the exposed surface of the cross linked water soluble polymer adhered to the electrode 24, 26, or removed and the medicament 30 added and the release liner replaced or adhered to the electrode. Also, the release liner 48 can remain until being removed for

application of the device 10 to the applied area of the patient.

In the alternative, the release liner 48 (or 46) can be replaced by the electrode in the form of a thin metal sheet or polymer sheet coated with a conductive ink or metal foil laminated to the polymeric sheet. In this way, the reservoir can be coupled to the electrode in one step. It should also be appreciated that a conductive scrim may be incorporated into the reservoir with the scrim being placed asymmetrically with in the reservoir by placing different thicknesses of the viscous solution on each side of the scrim.

The use of an easily handled cross linked water soluble polymer sheet as the reservoir 28, 32 to replace a paste, semi-solid gel or an absorbent pad has many advantages over existing coupling reservoirs. The cross linked water soluble polymer is solid and shape retaining and it exhibits no leakage of medicament or electrolyte under flexure or applied pressure. It is also drapeable and flexible and adhesive to the skin. This assures that the cross linked water soluble polymer maintains the required medicament and electrolyte concentration as well as reproducible delivery by its adherence and conformability to the contours of the skin or other applied area.

Due to its high water content, the cross linked water soluble polymer is highly conductive to ionic transport, yet it possesses sufficient mechanical strength

for processing and use. Also, despite its high water content, the cross linked water soluble polymer is a single phase solid solution which does not synerese liquid upon applied pressure or flexure.

The ability of the cross linked water soluble polymer to retain aqueous solution and its stability over extremes of ambient temperature, allow the iontophoretic drug delivery device 10 to be prepackaged and stored as a ready to use device, eliminating the need for loading a drug solution after opening and assembly.

In addition, the various reservoirs 28, 32 formed from the cross linked water soluble polymer sheet 40 are easily and stably coupled with the electrically conductive electrodes 14, 26 to form a highly electrically conductive electrode assembly 12. Also, because of the handleability of the cross linked water soluble polymer, the medicament can either be added to the viscous water soluble polymer solution or subsequently added after cross linking depending upon the application and/or the medicament to be administered.

As previously discussed, the two portions of the device 20, 22 are placed over the applied area, i.e., the portion of the skin where the medicament is to be delivered such as the arm as illustrated in Figure 1 with other electrode 32, i.e., the return electrode, placed on the skin 60 at an appropriate location relative to the first or working electrode 14.

Further, the cross linked water soluble polymer 40 in the preferred embodiment of the present invention is self-adhering to the skin of the patient and therefore provides intimate contact for ionic transport. Accordingly, the cross linked water soluble polymer sheet 40 contained in the drug reservoir 28 and used for the electrolyte reservoir 32 may also act as an adhesive, eliminating the need in prior devices for an adhesive layer or the like.

The following formulations for the cross linked water soluble polymer sheet 40 were used in connection with the device of the present invention for the reservoirs in the iontophoretic delivery of a topical anesthetic and a vasoconstrictor, with the device 10 including one active electrode 24 having a surface area between 2-10 cm^2 and one to three return electrodes 26 having a total surface area between 1-5 cm^2. The electrode reservoir 28 was comprised of the following active and inert components to a thickness of between 10-50 mils by making a viscous stock solution containing the medicaments and the excipients that was 3 times more concentrated than the intended final formulation. The stock solution was then added to preexisting sheets and allowed to diffuse and equilibrate in the sheets.

EXAMPLE 1

% w/w	Active Components	Mass per 2.5 cm^2 (mg)	
10.00	Lidocaine hydrochloride HCl U.S.P.	45.00	
0.10	L-Adrenaline free base U.S.P.	1.35	
% w/w	Inert Components	Mass per 2.5 cm^2 (mg)	
10.00	Glycerin U.S.P.	45.00	
2.67	Cross linked Polyethylene oxide (PEO) NF	12.02	
0.05	Sodium metabisulphite U.S.P.	0.23	
0.03	Hydrochloric acid U.S.P.	0.14	
0.01	EDTA disodium U.S.P.	0.05	
77.14	Water	346.23	
Trace	Sodium hydroxide U.S.P. (<.01% w/w)		
100		450	TOTAL

In the preferred embodiment, the Lidocaine is an anesthetic, the L-Adrenaline is a vasoconstrictor, and the composition of polyethylene oxide (PEO) is 2.67% and known as WSR-301 from Union Carbide Corp. However, it should be appreciated that the concentration of the PEO may vary from approximately 1-6% w/w. In addition, it should be appreciated that Epinephrine can be substituted for the L-Adrenaline.

EXAMPLE 2

Same as Example 1, however, polyvinyl pyrrolidone (PVP) was substituted for the PEO with the preferred

concentration being around 20%, however, it should be appreciated that the concentration of the PVP may varying from approximately 10-40% w/w.

EXAMPLE 3

Same as Example 1, with polyvinyl alcohol (PVA) being substituted for the PEO, and the preferred concentration of the PVA varying from approximately 10-30% w/w.

Each of the above applications involved the use of devices for the delivery of Lidocaine and Epinephrine for short application times, i.e., less than 10 minutes.

Drug, medication, medicament and active compound have been used herein to mean any pharmaceutical agent, such as therapeutic compounds, diagnostic agents and the like.

In addition, while the present invention has been described in connection with iontophoresis, it should be appreciated that it may be used in connection with other principles of electroactive introduction, i.e., motive forces, such as electrophoresis which includes the movement of particles in an electric field toward one or other electric pole, anode, or cathode and electro-osmosis which includes the transport of uncharged compounds due to the bulk flow of water induced by an electric field. Also, it should be appreciated that the patient may include humans as well as animals.

While the preferred embodiments of the present invention have been described so as to enable one skilled

in the art to practice the device and method of the present invention, it is to be understood that variations and modifications may be employed without departing from the concept and intent of the present invention as defined in the following claims. The preceding description is intended to be exemplary and should not be used to limit the scope of the invention. The scope of the invention should be determined only by reference to the following claims.

What is claimed is:

CLAIMS

1. An iontophoretic drug delivery device for delivering at least one medicament to an applied area of a patient, such as the skin, mucus membrane and the like, comprising:

electrode assembly means for driving a medication into the applied area of the patient to be absorbed by the body of the patient; and

a reservoir situated in electrically conductive relation to the electrode assembly means, with said reservoir including an aqueous swollen cross linked water soluble polymer, with said reservoir containing at least one medicament.

2. A device as defined in claim 1, further comprising a structurally reinforcing member situated within said reservoir including said aqueous swollen cross linked water soluble polymer, with said structurally reinforcing member having an open area.

3. A device as defined in claim 2, wherein said structurally reinforcing member is a thermoplastic polymeric scrim and said aqueous swollen cross linked water soluble polymer is cross linkable by high energy irradiation.

4. A device as defined in claim 1, wherein said aqueous swollen cross linked water soluble polymer is

selected from the group including polyethylene oxide, polyvinyl pyrrolidone, polyvinyl alcohol and polyacrylamide.

5. A device as defined in claim 1, wherein said aqueous swollen cross linked water soluble polymer is polyethylene oxide which is irradiation cross linked in aqueous solution.

6. A device as defined in claim 5, wherein the composition of said polyethylene oxide is from 1% to 6%.

7. A device as defined in claim 1, wherein said aqueous swollen cross linked water soluble polymer is polyvinyl pyrrolidone which is irradiation cross linked in aqueous solution.

8. A device as defined in claim 5, wherein the composition of said polyvinyl pyrrolidone is from 15% to 40%.

9. A device as defined in claim 5, wherein said at least one medicament includes Lidocaine and the reservoir also includes a vasoconstrictor, stabilizers and glycerin.

10. A device as defined in claim 1, wherein said reservoir further includes additives and conductive salts,

with said additives selected from the group including glycerin, propylene glycol and polyethylene glycol.

11. A reservoir for use in an iontophoretic drug delivery device having an electrode assembly for delivering at least one medicament through an applied area of a patient, such as the skin, mucus membrane and the like, comprising:

a layer of a aqueous swollen cross linked water soluble polymer material capable of being electrically conductive with said electrode assembly; and

said aqueous swollen cross linked water soluble polymer material including said at least one medicament for delivery through an applied area of a patient, such as the skin, mucus membrane and the like.

12. A reservoir as defined in claim 11, further comprising a structurally reinforcing member situated within said layer of aqueous swollen cross linked water soluble polymer material, with said structurally reinforcing member having an open area.

13. A reservoir as defined in claim 11, wherein said structurally reinforcing member is a scrim of a aqueous insoluble thermoplastic polymeric material and said aqueous swollen cross linked water soluble polymer material is cross linked by high energy irradiation.

14. A reservoir as defined in claim 11, wherein said aqueous swollen cross linked water soluble polymer is selected from the group including polyethylene oxide, polyvinyl pyrrolidone, polyvinyl alcohol and polyacrylamide.

15. A reservoir as defined in claim 11, wherein said aqueous swollen cross linked water soluble polymer is polyethylene oxide which is irradiation cross linked in aqueous solution.

16. A reservoir as defined in claim 15, wherein the composition of said polyethylene oxide is from 1% to 6% and its molecular weight is above about 0.6×10^6.

17. A reservoir as defined in claim 11, wherein said aqueous swollen cross linked water soluble polymer is polyvinyl pyrrolidone which is irradiation cross linked in aqueous solution.

18. A reservoir as defined in claim 17, wherein the composition of said polyvinyl pyrrolidone is from 15% to 40% and its molecular weight is above about 0.5×10^6.

19. A reservoir as defined in claim 15, wherein said at least one medicament includes Lidocaine and said aqueous swollen cross linked water soluble polymer material includes a vasoconstrictor, stabilizers and glycerin.

20. A reservoir as defined in claim 11, further comprising additives and conductive salts, with said additives selected from the group including glycerin, propylene glycol and polyethylene glycol.

21. A method of making a reservoir for an iontophoretic drug delivery device, comprising the steps of:

providing a structurally reinforcing member;

coating said reinforcing member with a viscous water soluble polymer solution; and

cross linking said layer by high energy irradiation.

22. A method as defined in claim 21, wherein said step of coating includes the steps of applying a layer of said viscous solution to one side of said reinforcing member, applying a layer of said viscous solution to one side of a release liner and laminating the release liner and the reinforcing material together such that both surfaces of said reinforcing member are coated with said viscous solution.

23. A method as defined in claim 22, wherein said viscous solution is applied to said reinforcing member and said release liner to a thickness of about Ca. 5 mil to 30 mil.

24. A method as defined in claim 22, further comprising the step of applying a final release liner to the remaining exposed viscous solution coated surface of said reinforcing member to form a laminate and cross linking said viscous solution.

25. A method as defined in claim 24, further comprising the step of replacing said final release liner with an electrode in flexible sheet form.

26. A method as defined in claim 21, further comprising the step of adding at least one medicament to the cross linked water soluble polymer.

27. A method as defined in claim 25, wherein said at least one medicament includes Lidocaine and the cross linked water soluble polymer includes a vasoconstrictor, stabilizers and glycerin.

28. A method as defined in claim 24, further comprising the step of cutting said laminate into a suitable shape and area for use in an iontophoretic drug delivery device.

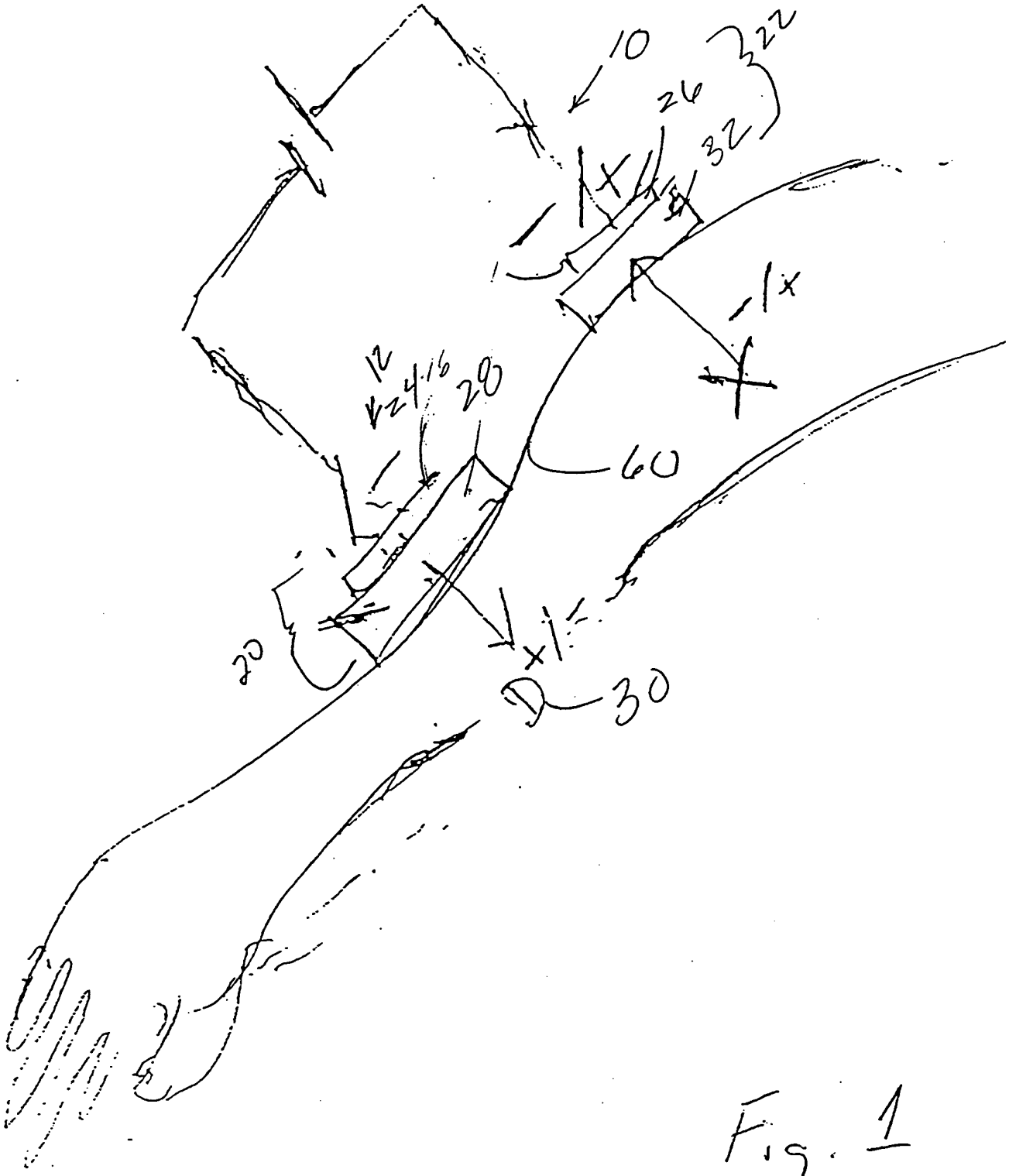


Fig. 1

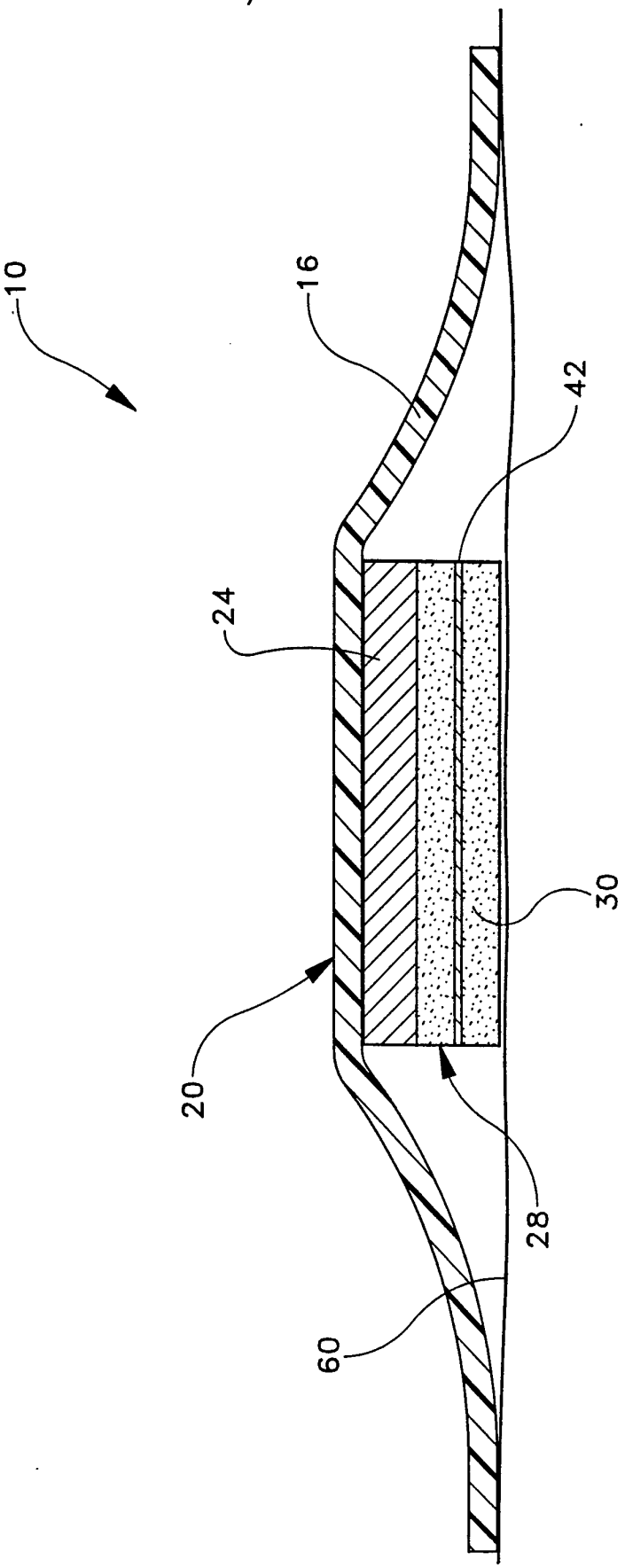


FIG-2

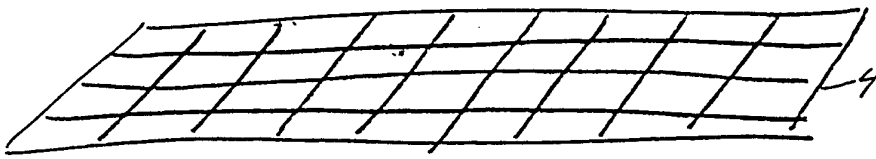


Fig. 3A

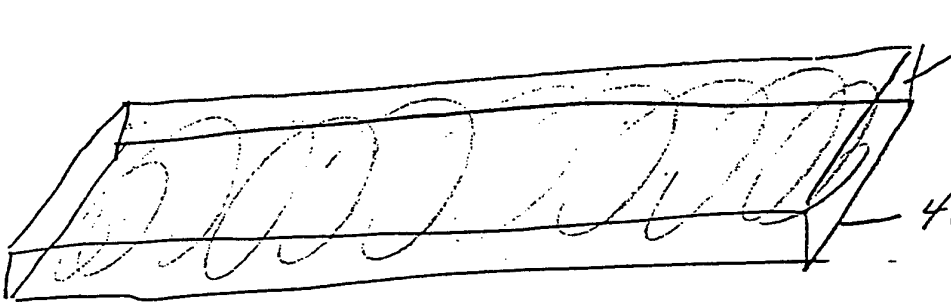


Fig. 3B

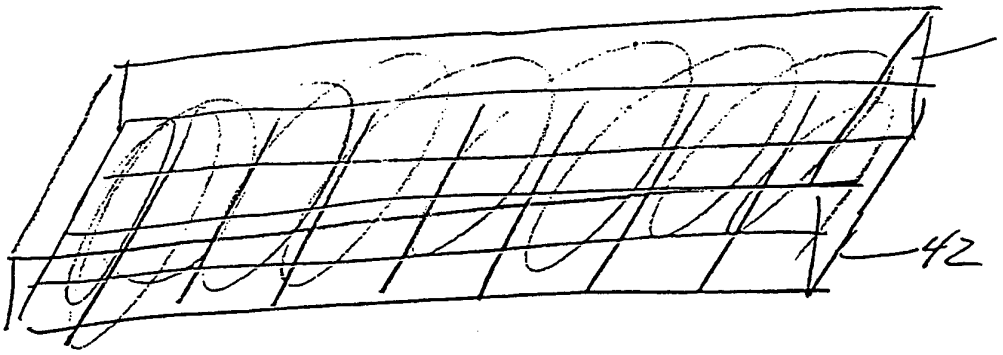
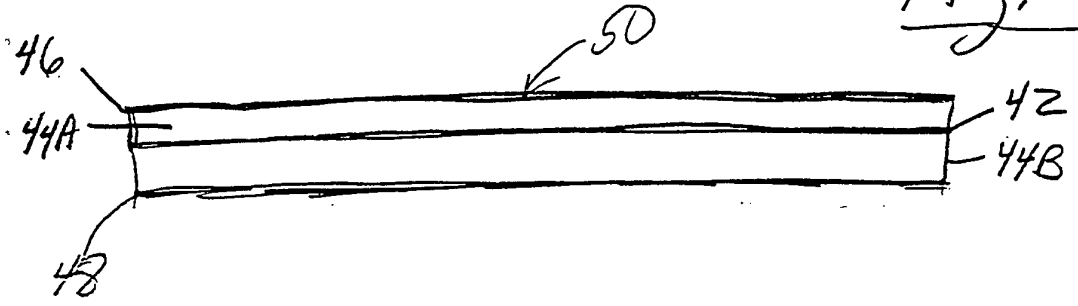


Fig. 3C

Fig. 3D



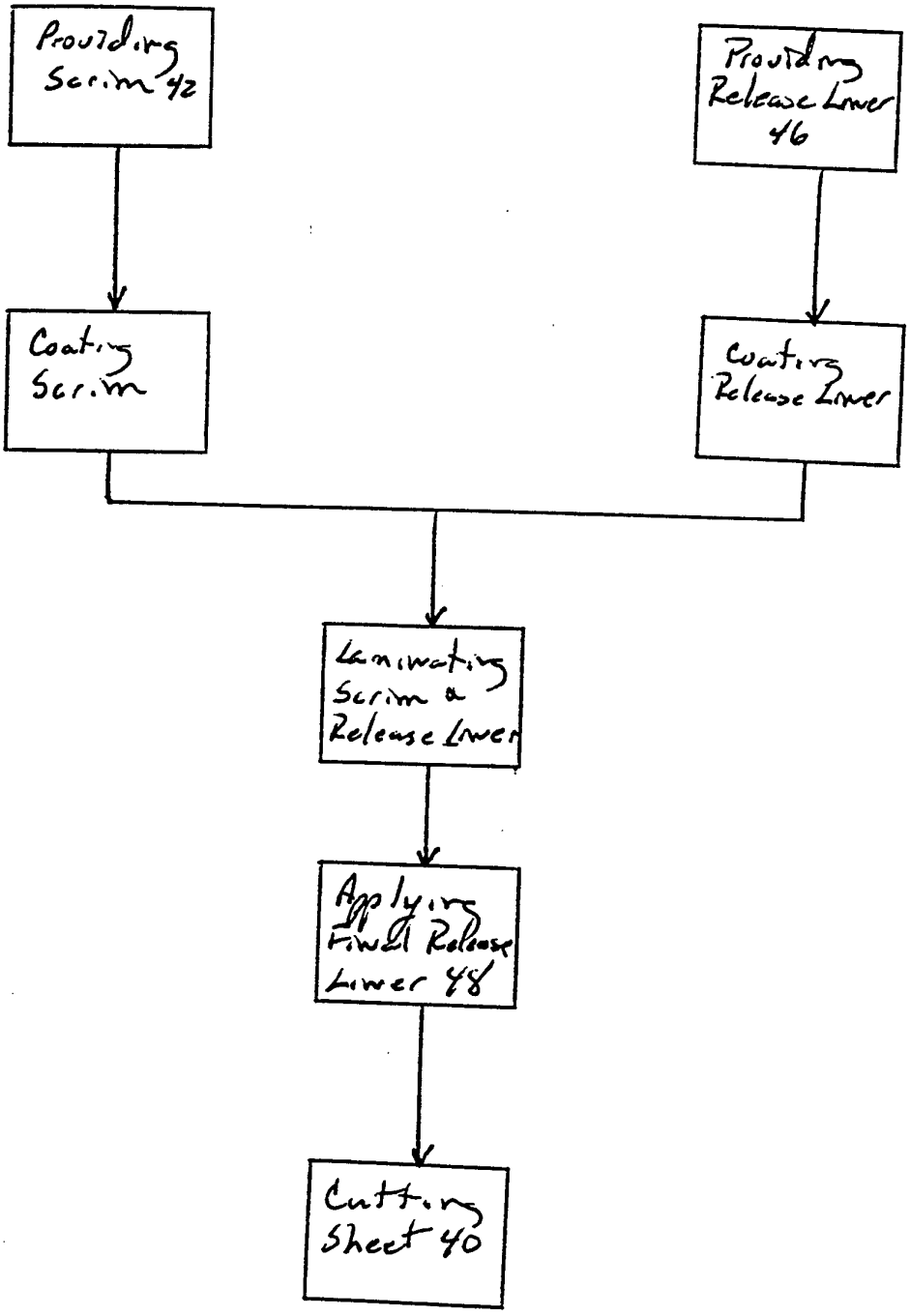

Providing Scrim 42
Providing Release Liner 46
Coating Scrim
Coating Release Liner
Laminating Scrim & Release Liner
Applying Final Release Liner 48
Cutting Sheet 40

Fig. 4

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US94/10960

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :A61N 1/30
US CL :604/20

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. : 607/149-153

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

NONE

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

NONE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	US, A, 4,786,277, (POWERS ET AL.), 22 November 1988. See entire document.	1, 4, 11, 14 --- 2, 3, 5-10, 12, 13, 15-28
Y	US, A, 5,006,108, (LAPRADE), 09 April 1991. See matrix materials.	10, 20
Y	US, A, 5,087,242, (PETELENZ ET AL.), 11 February 1992. See column 3, lines 34-62.	2, 3, 5, 6, 12, 13, 15, 16
Y	US, A, 4,706,680, (KEUSCH ET AL.), 17 November 1987. See column 13, lines 24-68.	2, 3, 5, 6, 12, 13, 15, 16

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

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be part of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"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
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search	Date of mailing of the international search report
23 DECEMBER 1994	09 JAN 1995
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer FOR MARK BOCKELMAN Telephone No. (703) 308-2112

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

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US, A, 5,224,928, (SIBALIS ET AL.), 06 July 1993. See column 10, lines 57-62.	9, 19
Y, P	US, A, 5,250,022, (CHIEN ET AL.), 05 October 1993. See column 13, lines 1-6.	9, 19