BANDAGE FOR THE CONTROLLED METERING OF TOPICAL DRUGS TO THE SKIN

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Notice: The portion of the term of this patent subsequent to Aug. 10, 1988, has been disclaimed.

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Related U.S. Application Data


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Field of Search 128/260, 268, 156, 128/296, 424/22, 28

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Primary Examiner—Charles F. Rosenbaum
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ABSTRACT

Bandage for the topical administration of controlled therapeutically effective quantities of topically active drugs has a backing member, a pressure-sensitive adhesive, and a reservoir layer containing a topically active drug confined within a wall member. The wall member is formed from drug release rate controlling material to continuously meter the flow of a therapeutically effective amount of the drug through the wall to the skin at a controlled and predetermined rate over a period of time.

14 Claims, 5 Drawing Figures
3,731,683

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BANDAGE FOR THE CONTROLLED METERING OF TOPICAL DRUGS TO THE SKIN

RELATED APPLICATIONS


BACKGROUND OF THE INVENTION

This invention relates to a device for the administration of drugs and more particularly to a medical bandage for the predetermined controlled metering of the flow of topically active drugs to the skin over a period of time. Topically active drugs, as that term is used in this specification and the appended claims, are agents which primarily cause a pharmacological or physiological response at or near the site of their application. They are to be distinguished from systemically active drugs which are transported from their site of application by the recipient's circulatory system or lymphatic system, to cause a pharmacologic or physiologic response at a remote site in the body.

A large number of locally acting drugs are available to treat skin disorders or other conditions which manifest themselves in a manner such that they are susceptible to treatment via the skin. These drugs can be broadly classified as astringents, irritants, sclerosing agents, caustics, melanizing and demelanizing agents, keratolytics, mucolytics, antibacterials, anti-fungals, anti-inflammatories, antiparasitics, antiperspirants and deodorants, and the like. These drugs are conventionally topically administered to the skin with the active agent carried in the form of ointments, creams, salves, liniments, powders, dressings, and the like. The popularity of these types of formulations resides in the fact that it is quite easy to topically apply the agent to the skin in this manner. In most cases, however, it is not possible to determine how much of the preparation has been taken up or effectively administered to the skin since only non-uniform levels of the agent are available. A further undesirable feature is the unsightliness of these formulations which often discourage patients from using them during the waking hours of the day when they are most likely to be seen by others. Further, the preparations are subject to rub off onto clothing, thus causing much inconvenience and annoyance to the user.

In order to obviate some of these undesirable effects, it has been proposed to provide medicinal bandages wherein the absorbent portion to be applied to the area to be treated is further provided with drug material adherent thereto. The advantage of a bandage construction of this type, of course, resides in the elimination of the intermediate step of applying the drug. A further advantage is realized by the elimination of the possibility that the drug which is often in a liquid formulation will be lost by run-off or leakage. A significant disadvantage, however, also exists with these prior art devices for the administration of topically active drugs in that the amount of medication applied to the affected areas cannot be accurately controlled, nor is there any assurance that sufficient medication will be available for the duration of periods that it is required.

It has also been proposed to admix certain topical drugs in the adhesive materials of bandages to treat various skin conditions with improved convenience; see for example British Pat. No. 1,216,908. Further, it is known that medicaments can be incorporated into certain types of crushable microcapsules which are then incorporated in bandages; see for example Goldfarb U.S. Pat. No. 3,464,413. The microcapsules, however, merely function as drug carriers releasing the drug by rupture of the microcapsules. Therefore, these bandages are not suitable for continuously controlling the dosage of the drug administered, which is a most desirable objective of drug therapy.

SUMMARY OF THE INVENTION

Accordingly, an object of this invention is to provide a bandage for the improved continuous administration of predetermined controlled quantities of topically active drugs to the skin over a period of time.

In accomplishing these objects, this invention in its broadest aspects resides in a medicated bandage for the continuous administration of controlled quantities of topically active drugs to the skin of a patient by direct application to the affected skin area. The bandage is comprised of a laminate of: (1) a backing member defining one face surface of the bandage; (2) a pressure-sensitive adhesive adapted for contact with the skin or mucosa, the external surface of said pressure-sensitive adhesive defining the other face surface of the bandage and disposed between the face surfaces defined by (1) and (2); (3) at least one reservoir comprised of a topically active drug formulation confined within a wall member, said wall member being formed from drug release rate controlling material to continuously meter the flow of drug from the said reservoir to the skin or mucosa at a controlled and predetermined rate over a prolonged period of time.

The term "reservoir" as used herein refers both to microcapsules as well as distinct reservoir compartments or matrix layers.

An embodiment of the invention described above resides in a bandage comprised of a laminate of: (1) a backing member; bearing (2) a discrete middle reservoir layer containing a topically active therapeutic agent confined within a wall member, said wall member being formed from drug release rate controlling material permeable to the passage of agent, to continuously meter the flow of a therapeutically effective amount of the agent to the skin from the reservoir at a controlled and predetermined rate over a period of time; and (3) a pressure-sensitive adhesive surface adapted for contact with the skin and positioned on one wall of the reservoir remote from the backing member.

Another aspect of this invention resides in a bandage as described immediately above including a solubility membrane interposed between the wall of the reservoir and the pressure-sensitive adhesive layer.

Still, another embodiment of this invention resides in a medicated adhesive bandage comprising a laminate of: (1) a backing member; bearing (2) a pressure-sensitive adhesive on one surface thereof adapted for contact with the skin, said pressure-sensitive adhesive having distributed therethrough, (3) a plurality of discrete microcapsules, each of which microcapsules comprise a topically active therapeutic agent confined within a wall member, the wall member being formed from drug release rate controlling material, to continuously meter
the flow of a therapeutically effective amount of the agent to the skin from the microcapsules at a controlled and predetermined rate over a period of time.

Other objects, features and advantages of the invention will become more apparent from the following description when taken in conjunction with the accompanying drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

In the drawings:

FIG. 1 is a perspective view of the medical adhesive bandage of the invention wherein the topically active agent is microencapsulated with a material permeable to the passage of those agents and the microcapsules are uniformly distributed throughout the pressure-sensitive adhesive coating;

FIG. 2 is a cross-sectional view of the bandage of the invention shown in FIG. 1;

FIG. 3 is a cross-sectional view of another embodiment of the invention wherein the topically active agent is uniformly distributed throughout a matrix of material permeable to the passage of those agents and the material is laminated to a backing member. The matrix material which acts as a reservoir for the agent bears a coating of the pressure-sensitive adhesive thereon;

FIG. 4 is a cross-sectional view of still another embodiment of the invention wherein the adhesive bandage of the invention is comprised of a backing member having a reservoir on one surface thereof of topically active agent uniformly distributed throughout a matrix of material permeable to passage of agent, and on the surface of the reservoir remote from the backing member bearing a pressure-sensitive adhesive coating. A solubility membrane is interposed between the reservoir layer and the pressure-sensitive adhesive coating;

FIG. 5 is a cross-sectional view of another embodiment of the invention wherein the reservoir laminated to the backing member is a hollow container permeable to passage of agent and having the agent confined within the interior chamber thereof.

DETAILED DESCRIPTION OF THE INVENTION

In accordance with this invention there is provided a medicated bandage containing a topically active drug therein for the predetermined controlled metering of the flow of topically active drugs to the skin over a period of time.

FIG. 1 illustrates an adhesive tape 10 of the invention including a backing member 11 bearing a pressure-sensitive adhesive coating 12 on one surface thereof. Adhesive coating 12 has uniformly distributed therethrough microcapsules 13 of topically active agent encapsulated with a material permeable to passage of the drug.

Materials used to encapsulate the drug and form the microcapsules to be distributed throughout the adhesive must be permeable to the drug to permit passage of the drug, as by diffusion, through the walls of the microcapsules at a relatively low rate. Normally, the rate of passage of the drug through the walls of the microcapsules is dependent on the solubility of the drug therein or the porosity of the wall, as well as on the microcapsule wall thickness. This means that selection of appropriate encapsulating materials will be dependent on the particular drug used in the bandage. By varying the encapsulating material and the wall thickness, the dosage rate per area of bandage can be controlled and movement of drug to the adhesive regulated.

Suitable materials for use in encapsulating the drug include hydrophobic polymers such as polyvinyl chloride either unplasticized or plasticized with long-chain fatty amides or other plasticizer; plasticized nylon; unplasticized soft nylon; silicone rubber; polyethylene, and polyethylene terephthalate; and hydrophilic polymers such as esters of acrylic and methacrylic acid (as described in U.S. Pat. Nos. 2,976,576 and 3,220,960 and Belgian Pat. No. 701,813); modified collagen; cross-linked hydrophilic polyether gels (as described in U.S. Pat. No. 3,419,006); cross-linked polyvinylalcohol; and cross-linked partially hydrolyzed polyvinylacetate.

To provide the microcapsules, the encapsulating material can be uniformly impregnated with the drug to form microcapsules which are a matrix having the drug distributed therethrough. Alternatively, particles of drug can be encapsulated with thin coatings of the encapsulating material to form microcapsules having an interior chamber containing the drug. If desired, particles of a matrix, such as starch, gum acacia, gum tragacanth, and polyvinylchloride, can be impregnated with the drug and encapsulated with other materials such as the encapsulating materials previously described which function as a solubility membrane to meter the flow of drug to the adhesives; use of a matrix and a different solubility membrane coating can slow the passage of the drug from the microcapsules which is desirable with drugs that are released too rapidly from available encapsulating materials.

Any of the encapsulation or impregnation techniques known in the art can be used to prepare the microcapsules to be incorporated into the pressure-sensitive adhesive in accord with the embodiment of FIGS. 1 and 2. Thus, the drug can be added to the encapsulating material in liquid form and uniformly distributed therethrough by mixing and subsequently converting to a solid by curing or cooling; or solid encapsulating material can be impregnated with a drug by immersion in a bath of the drug to diffuse into the material. Subsequently, the solid material can be reduced to fine microcapsules by grinding, each of the microcapsules comprising drug coated with and distributed throughout the encapsulating material. Alternatively, fine particles of the drug can be encapsulated with the coating. One suitable technique comprises suspending dry particles of the drug in an air stream and contacting that stream with a stream containing the encapsulating material to coat the drug particles. Usually, the microcapsules have an average particle size of from 1 to 1,000 microns, although this is not critical to the invention.

Further embodiments of the adhesive bandage of the invention are illustrated in FIGS. 3, 4 and 5. As illustrated in FIG. 3, adhesive bandage 20 of the invention is comprised of topically active agent 24 uniformly distributed in a reservoir 22 which is a polymeric matrix material. The matrix material is laminated to backing member 21 and bears a pressure-sensitive adhesive coating 23 thereon. The polymeric matrix material has
a release rate for the particular drug used which continuously controls the releasing drug.

FIG. 4 illustrates a further modified form of the invention wherein the adhesive bandage 30 of the invention is comprised of a backing member 21 having a reservoir 32 on one surface thereof. A solubility member 35 is interposed between the reservoir 32 and a pressure-sensitive adhesive coating 23. Topically active agent 24 is confined in polymeric matrix material 32 which acts as the reservoir for the drug.

FIG. 5 illustrates a further form of the bandage 40 including a backing member 21 and a reservoir 42 in the form of a hollow container having an interior chamber 43 containing topically active agent 34. Wall 45 of reservoir 42, remote from backing member 21, is permeable to passage of drug 34, as by diffusion, to meter the flow of drug to pressure-sensitive adhesive layer 23 on the outer surface thereof. This form of the bandage is less preferred since it cannot conveniently be cut to fit precisely the size of skin lesions to which applied. However, it is satisfactory for application to large areas of skin.

Suitable materials for forming the reservoir, whether of the matrix or hollow container type, are those materials permeable to passage of the drug previously described as suitable encapsulating materials. The reservoir can be formed by molding into the form of a hollow container with the drug trapped therein. Alternatively, the reservoir can be in the form of an envelope formed from sheets of polymeric material permeable to passage of the drug and enclosing the drug. While the walls of the reservoir can be of any convenient thickness, usually they have a thickness of from 0.01 to 7 millimeters. When the reservoir comprises a matrix with the drug distributed therethrough, it can be prepared by adding the drug to the matrix material in liquid form or solvent solution form and subsequently converting the matrix to a solid by curing, cooling or evaporation of solvent.

Thus, the reservoir of the bandage is a hollow drug container or a solid matrix. Drug is metered from the reservoir to the adhesive layer, at a rate controlled by the composition and thickness of the reservoir or of the reservoir wall. From the adhesive layer, drug is directly transmitted to the skin to which the bandage is applied.

In the embodiment of the invention illustrated in FIG. 4, metering of the drug from the reservoir to the adhesive is further controlled by interposing a further solubility membrane therebetween. The solubility membrane is formed of a material in which the drug is soluble and capable of diffusing through. Any of the materials previously mentioned for use in microencapsulation may be used as the solubility membrane. Of course, in each instance, the solubility membrane will have different characteristics than the reservoir wall of the particular device. This use of a pair of solubility membranes, that is, the reservoir wall and the further solubility membrane, allows for precise metering of drug to the adhesive layer; for the thickness and composition of both membranes can be varied to provide for wide range of dosage levels for a given area of bandage. It will be appreciated that this solubility membrane can be used with either the matrix or container type of reservoir.

In practicing this invention one can employ a wide variety of topically active drugs consistent with their known dosages and uses. Suitable drugs include, without limitation: Antiperspirants, e.g. aluminum chloride; Deodorants, e.g. hexachlorophene, methylbenzethonium chloride; Astringents, e.g. tannic acid; Irritants, e.g. methyl salicylate, camphor, cantharidin; Keratolytics, e.g. benzoic acid, salicylic acid, resorcin, iodochlorhydroxyquin; Antifungal Agents such as tolnaftate, griseofulvin, nystatin and amphotericin; Anti-Inflammatory Agents, such as corticosteroids, e.g. hydrocortisone, hydrocortisone acetate, prednisolone, methylprednisolone, triamcinolone acetonide, fluocortisone, flurandrenolone, flumethasone, dexamethasone sodium phosphate, betamethasone valerate, fluocinolone acetonide; fluorometholone; and pramoxine HCl; and Antibacterial Agents, such as bacitracin, neomycin, erythromycin, tetracycline HCl, chlorotetracycline HCl, chloramphenicol, oxytetracycline, polymyxin B, nitrofurazone, mafenide (alpha-p-toluenesulfonamide), hexachlorophene, benzalkonium chloride, cetylalkonium chloride, methylbenzethonium chloride, and neomycin sulfate.

In addition to the aforementioned drugs, simple pharmacologically acceptable derivatives of the drugs, such as ethers, esters, amides, acetals, salts, etc., or formulations of these drugs, having the desired polymeric permeability or transport properties can be prepared and used in practicing the invention. Drugs mentioned above can be used alone or in combination with others and each other.

The amount of topically active agent to be incorporated in the bandage to obtain the desired therapeutic effect will vary depending upon the desired dosage, the permeability of the polymeric materials of the bandage which are employed to the particular agent to be used, and the length of time the bandage is to remain on the skin. The effective rate or release of the active agent to the skin can be in the range of from 0.5 to 1,000 micrograms per square centimeter of bandage per day. The exact amount will depend on the desired dosage as well as the area of the skin to be treated. These effective rates of release of active agent to the skin can be obtained by altering the permeability and thickness of the release rate controlling barrier. In the case of the microencapsulated active agent, the release rate can also be controlled by varying the number of microcapsules present in a given volume of the matrix of the device. This is a particular desirable feature of this aspect of the invention. Additionally, the duration of action of the device can be altered by controlling the amount of active agent initially incorporated consistent with the release rate. Further, the release rate of drug as well as the duration of release of the drug from the device can be predetermined to be in consonance with the optimum therapeutic values. Once this dosage level in micrograms per square centimeter of bandage has been determined, the total amount of drug to be incorporated in the bandage can be established by obtaining the release rate of the agent in the particular material or materials which are to be used.

Those skilled in the art can readily determine the rate of permeation of agent through a polymeric material or selected combinations of polymeric materials. One method that has been found to be eminently
well suited is to cast or hot press a film of the material to a thickness in the range of 2 to 60 mils. The film is used as a barrier between a rapidly stirred (e.g., 150 r.p.m.) saturated solution of the drug containing excess solid drug (or a concentrated solution of the drug) and a rapidly stirred solvent bath, both maintained at constant temperature (typically 37°C). Samples are periodically withdrawing from the solvent bath and analyzed for drug concentration. By plotting drug concentration in the solvent bath versus time, the permeability constant \( P \) of the membrane is determined by the Fick’s First Law of Diffusion.

Slope of plot = \( Q_1 - Q_2/t_1 - t_2 = p (AC/h) I \)

wherein

\[ Q_1 = \text{cumulative amount of drug in solvent in micrograms at } t_1 \]
\[ Q_2 = \text{cumulative amount of drug in solvent in microgram at } t_2 \]
\[ t_1 = \text{elapsed time to first sample i.e. } Q_1 \]
\[ t_2 = \text{elapsed time to second sample i.e. } Q_2 \]
\[ A = \text{area of membrane in cm}^2 \]
\[ C = \text{saturation concentration of drug in solution} \]
\[ h = \text{thickness of membrane in cm} \]

By determining the slope of the plot i.e. \( Q_1 - Q_2 / t_1 - t_2 \) and solving the equation using the known or measured values of \( A, C, \) and \( h \), the permeability constant \( P \) constant in \( \text{cm}^2/\text{time of the material or membrane for a given compound} \) is readily determined. Of course, this permeability constant is an inherent characteristic of the material for a given compound.

Using the above technique, the permeability constant \( P \) of hydrocortisone from isotonic solution through different membranes into isotonic solution at 37°C was found to be:

<table>
<thead>
<tr>
<th>Membrane</th>
<th>Permeability Constant (cm²/hr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Silicone Rubber 1</td>
<td>835</td>
</tr>
<tr>
<td>Aromatic Polyamide 2</td>
<td>10</td>
</tr>
<tr>
<td>Down Corning – HH0717</td>
<td></td>
</tr>
<tr>
<td>Allied Chemical – Capron</td>
<td></td>
</tr>
</tbody>
</table>

Using the above technique and data, the permeability constant \( P \) for a select membrane and drug can be determined. These data can then be employed to design a device of the invention to release the agent to the skin in the desired dosage range. Similarly, this experimental procedure or others known to those skilled in the art can be used to determine release rates for the suitable polymeric materials as above disclosed in order to design the bandage of this invention.


Any of the well-known dermatologically acceptable permeable pressure-sensitive adhesives which permit drug migration can be used in practicing this invention. Exemplary adhesives include acrylic or methacrylic resins such as polymers of esters of acrylic or methacrylic acid with alcohols such as n-butanol, n-pentanol, 2-methyl butanol, 1-methyl butanol, 1-methyl pentanol, 2-methyl pentanol, 3-methyl pentanol, 2-ethyl butanol, isooctanol, n-decanol, or n-dodecanol, alone or copolymerized with ethylenically unsaturated monomers such as acrylic acid, methacrylic acid, acrylamide, methacrylamide, N-alkoxymethyl acrylamides, N-alkoxymethyl methacrylamides, N-tert. butylacrylamide, itaconic acid, vinylacetate, N-branched alkyl maleic acids wherein the alkyl group has 10 to 24 carbon atoms, glycol diacrylates, or mixtures of these; natural or synthetic rubbers such as silicone rubber, styrene-butadiene, butyl-ether, neoprene, polyisobutylenne, polybutadiene, and polysisoprene; polyurethane elastomers; vinyl polymers, such as polyvinylalcohol, polyvinyl ethers, polyvinyl pyrrolidone, and polyvinylacetate; ureaformaldehyde resins; phenolformaldehyde resins; resorcinol formaldehyde resins; cellulose derivatives such as ethyl cellulose, methyl cellulose, nitrocellulose, cellulose acetatebutyrate, and carboxymethyl cellulose; and natural gums such as guar, acacia, pectins, starch, dextrin, albumin, gelatin, casein, etc. The adhesives may be compounded with tackifiers and stabilizers as is well known in the art.

Various occlusive and non-occlusive, flexible or nonflexible backing members can be used in the adhesive bandage of the invention. Suitable backings include cellophane, cellulose acetate, ethylcellulose, plasticized vinylacetate-vinylchloride copolymers, polyethylene terephthalate, nylon, polyethylene, polypropylene, polyvinylidenchloride, paper, cloth, and aluminum foil. Preferably, a flexible occlusive backing is employed to conform to the shape of the body member to which the adhesive tape is applied and to enhance administration of the agent to the skin.

To prevent passage of the drug away from the exposed surface of the pressure-sensitive adhesive prior to use, the adhesive surface of the tape generally is covered with a protective release film or foil, such as waxed paper. Alternatively, the exposed rear surface of the backing member can be coated with a low-adhesion backsize and the bandage rolled about itself. To enhance stability of the active compounds, the therapeutic bandage usually is packaged between hermetically sealed polyethylene terephthalate films under an inert atmosphere, such as gaseous nitrogen.

To use the adhesive bandage of the invention, it is applied directly to skin, to release a therapeutically effective amount of the agent to the affected area. By use of this invention, one ensures that an accurately measured quantity of the active drug is available when the bandage is applied to the skin.

The following examples will serve to illustrate the invention without in any way being limiting thereon.

**EXAMPLE 1**

2-hydroxyethyl methacrylate (100 grams) is diluted with water (100 grams) and mixed with tertiary butyl peroctoate (0.20 gram). Ethylene glycol dimethacrylate (0.20 gram) is added along with 4 grams of sodium bicarbonate as a foaming agent. The mixture is heated to 70°C under an atmosphere of nitrogen and the resulting solid, friable polymeric foam is ground into fine powder of 20 micron average particle size. The polymeric powder (10 grams) is mixed with neomycin (2 grams) dissolved in a mixture of ethyl alcohol: water
(50:50) and the resultant mixture placed on a mechanical roller until the polymeric powder has absorbed the drug. The solution is then filtered.

The resulting microcapsules of neomycin are mixed with 100 grams of a 22 percent solution in hexane: isopropylacetate (70:30) of a viscoelastic copolymer of isocytacrylate and acrylic acid (94:6) adhesive to uniformly distribute the microcapsules throughout the adhesive solution. The resulting slurry is coated onto a cellophane sheet 10 centimeters in width by 100 centimeters in length and the solvent removed by evaporation from the coated film.

When applied to the infected skin area of a subject, the resulting bandage is effective to control the continuous administration of a daily therapeutically effective dosage of neomycin to the skin.

**EXAMPLE II**

Liquid dimethyl silicone polymeric rubber (100 grams, Dow-Corning Silastic) is mixed with 5 grams of nitrofurazone. After uniformly mixing the drug with unvulcanized silicone rubber, 0.5 gram of stannous octoate catalyst is added and the rubber cured at room temperature. The resulting silicone rubber body is reduced to an average particle size of 100 microns. Pressure-sensitive adhesive composition is prepared by adding to 100 milliliters of hexane the following:

- 20 grams of polyvinylpyrrolidone (reduced viscosity = 5.0 ± 0.5)
- 4 grams of polyvinylpyrrolidone (reduced viscosity = 0.3 ± 0.1)
- 4 grams of glycerol ester of hydrogenated rosin and 2 grams polyethylene glycol 400

Ten grams of the resulting nitrofurazone capsules are mixed with pressure-sensitive adhesive prepared above to uniformly distribute the microcapsules throughout the adhesive. Immediately thereafter, the adhesive mixture is coated onto one surface of a 1,000 square centimeter Mylar sheet. The resulting bandage can be used for control of skin infections.

**EXAMPLE III**

Ten milligrams of betamethasone is placed on a sheet of dimethyl silicone rubber having a thickness of 0.13 millimeters. The sheet is folded to provide a surface area of 100 square centimeters on each face and the flaps sealed with silicone adhesive to provide a thin envelope containing the drug.

Pressure-sensitive adhesive is prepared by mixing together, 90 grams of polycrystalline solution (ethy lactate: hexane:5:1) containing 25 percent non-volatile matter, (obtained by the catalytic polymerization of isomethylacrylate and acrylic acid in the ratio of 95:5 in ethylactate and then diluting with hexane), 5 grams polyvinylpyrrolidone (reduced viscosity = 0.3 ± 0.1), 1 gram castor oil (USP) and 4 grams polyethylene glycol 400.

One face surface of the envelope is bonded to a sheet of cellophane while the other is coated with adhesive prepared above to a thickness of 2 millimeters. The adhesive face surface of the bandage has an area of 100 square centimeters. The bandage is effective to release a therapeutically effective daily dosage of the drug when applied to the skin for control of psoriasis.

Thus, this invention provides a reliable and easy to use device for administering topical drugs directly to the skin. Uncertainties resulting from topical application of these agents, from creams and solutions, are not encountered; and a precisely determined amount of the drug is applied in a controlled manner.

Although the product of this invention has been referred to as an adhesive bandage, those skilled in the art will appreciate that the term “adhesive bandage” as used herein includes any product having a backing member and a pressure-sensitive adhesive face surface. Such products can be provided in various sizes and configurations, including tapes, bandages, sheets, plasters, and the like.

While there have been shown and described and pointed out the fundamental novel features of the invention as applied to the preferred embodiment, it will be understood that various omissions and substitutions and changes in the form and details of the adhesive tape illustrated may be made by those skilled in the art without departing from the spirit of the invention. It is the intention, therefore, to be limited only as indicated by the scope of the following claims.

What is claimed is:

1. A medical bandage for the continuous administration to the skin or mucosa of controlled quantities of topically active drugs over a prolonged period of time, said bandage comprising a laminate of (1) a backing member defining one face surface of the bandage; (2) a pressure-sensitive adhesive adapted for contact with the skin or mucosa, the external surface of said pressure-sensitive adhesive defining the other face surface of the bandage and disposed between the face surfaces defined by (1) and (2); (3) at least one reservoir comprised of a topically active drug formulation confined within a wall member, said wall member being formed from drug release rate controlling material to continuously meter the flow of drug from the said reservoir to the skin or mucosa at a controlled and predetermined rate over a prolonged period of time.

2. The medical bandage of claim 1, wherein said bandage comprises a laminate of: (1) a backing member; bearing (2) a pressure-sensitive adhesive on one surface thereof adapted for contact with the skin, said pressure-sensitive adhesive having distributed therethrough; (3) a plurality of discrete microcapsules, each of which microcapsules comprises a topically active drug formulation confined within a wall member, said wall member being formed from drug release rate controlling material to continuously meter the flow of a therapeutically effective amount of the drug in the skin through the wall of said microcapsules at a controlled and predetermined rate over a period of time.

3. The bandage as defined by claim 2, wherein each of said microcapsules (3) is comprised of a topically active drug formulation microencapsulated with the drug release rate controlling material.

4. The bandage as defined by claim 2, wherein each of said microcapsules (3) is comprised of a matrix of the drug release rate controlling wall material, said matrix having the topically active drug formulation distributed therethrough.

5. The bandage as defined by claim 2, wherein the drug formulation includes a pharmacologically acceptable solvent.
6. The medical bandage of claim 1, wherein said bandage comprises a laminate of: (1) a backing member; bearing (2) a discrete, middle reservoir layer, which reservoir layer is comprised of topically active drug formulation confined within a wall member, said wall member being formed from drug release rate controlling material to continuously meter the flow of a therapeutically effective amount of the drug to the skin through the wall at a controlled and predetermined rate over a period of time; and (3) a pressure-sensitive adhesive adapted for contact with the skin and carried by the reservoir remote from the backing member.

7. The bandage as defined by claim 6, wherein the reservoir layer (2) is comprised of a walled container having an interior chamber containing the topically active drug formulation.

8. The bandage as defined by claim 6, wherein the reservoir layer (2) is comprised of a matrix of the drug release rate controlling wall material, said matrix having the topically active drug formulation distributed therethrough.

9. The bandage as defined by claim 6, wherein the drug formulation includes a pharmacologically acceptable solvent.

10. The bandage as defined by claim 6, further comprising a solubility membrane (4) interposed between said reservoir layer (2) and said surface of pressure-sensitive adhesive (3).

11. The bandage as defined by claim 2, wherein the rate release controlling material is silicone rubber.

12. The bandage as defined by claim 6, wherein the rate release controlling material is silicone rubber.

13. The bandage as defined by claim 2, wherein the rate release controlling material is a hydrophilic polymer of an ester of an olefinic acid.

14. The bandage as defined by claim 6, wherein the rate release controlling material is a hydrophilic polymer of an ester of an olefinic acid.
UNITED STATES PATENT OFFICE
CERTIFICATE OF CORRECTION

Inventor(s) Alejandro Zaffaroni

It is certified that error appears in the above-identified patent and that said Letters Patent are hereby corrected as shown below:

Column 3, lines 33, 34, and 35, "...agent, and on the surface of the reservoir remote from the backing member bearing a..." should read --...agent, and bearing on the surface of the reservoir remote from the backing member a...--;
Column 4, line 27, "acadia" should read --acacia--; Column 5, line 7, "member" should read --membrane--; Column 5, line 54, add after "and" and before "capable" the following: --through which the drug is--; same column and line, delete the word "through" after the word "diffusing"; Column 7, line 8, "withdrawing" should read --withdrawn--.

Signed and sealed this 17th day of September 1974.

(SEAL)
Attest:

McCoy M. Gibson Jr. C. Marshall Dann
Attesting Officer Commissioner of Patents