

PATENT SPECIFICATION

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NO DRAWINGS

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(54) MEDICATED ADHESIVE TAPE

(71) We, ELI LILLY AND COMPANY, a corporation of the state of Indiana, United States of America, of 740 South Alabama Street, Indianapolis, State of Indiana, United States of America, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed to be particularly described in and by the following statement:—

This invention concerns a pressure-sensitive medicated tape adapted for direct application to a skin lesion.

Occlusive dressings have been used in conjunction with anti-inflammatory steroids in the topical treatment of resistant, abnormal dermatological conditions such as psoriasis. With this technique, the anti-inflammatory steroid, in a cream or ointment base, is applied to the affected area and the entire area is covered with a plastic or other air-tight material to exclude both air and clothing from the area. The edges of the occlusive plastic material are then sealed to the adjacent normal skin with tape or held in place with a gauze wrapping.

With the existing occlusive dressing techniques, when the hands or fingers are involved, the patient must wear plastic gloves during treatment. Garment bags are presently used for covering lesions on the trunks or buttocks, and tight-fitting shower caps are utilized in treating lesions of the scalp. However, while the use of currently available occlusive dressings with anti-inflammatory steroids is preferable to mere application of the steroids to the surface, the present occlusive dressing techniques leave much to be desired. When plastic films, particularly garment bags, are used on infants and children, the danger of suffocation is ever-present, and the children must be closely watched throughout the treatment period. The ready flammability of some plastic films creates an additional hazard. Furthermore, when large areas of the body are covered, thermal homeostasis may be impaired.

A further undesirable feature of the con-

ventional occlusive dressings is their bulk and unsightliness, which often discourage patients from wearing occlusive dressings during their waking hours, and deprive them of their benefit for substantial periods of time during the day. Furthermore, it is not presently feasible to cover only the affected areas on a given part of the body. For example, if there are several affected areas on a hand or arm, the entire hand or arm must be covered by the occlusive dressing. Moreover, when large areas are involved, it is difficult to maintain intimate contact of the dressing over the entire affected area.

Still a further disadvantage of conventional treatment techniques is that the amount of medication applied to the affected areas cannot be accurately controlled, nor is there any assurance that the medication will remain in that area where it is most needed. In those instances in which occlusive dressings are not employed during the day, there is no assurance that the medication will not rub off onto clothing.

While ordinary porous bandages have been impregnated with various medicaments and then used to treat various skin conditions (see, for example Belgian patent 638,231), such bandages and dressings simply do not lend themselves to the treatment of psoriasis and other resistant abnormal skin diseases where a non-porous, non irritating dressing must be used.

An occlusive dressing which would overcome the above disadvantage would constitute a valuable contribution to the art. Ideally, such a dressing should be applied only to the affected areas, as ordinary adhesive bandages are applied to small wounds. The ideal dressing should also have a measured amount of the anti-inflammatory steroid thereon. With such a dressing, the patient would merely apply an adhesive medicated occlusive dressing directly to the lesion to be treated, thus avoiding the necessity of applying the steroid ointment or cream, wrapping the surrounding area with plastic and taping the plastic to normal skin.

Therefore, it is the object of the present invention to provide a novel occlusive dressing which overcomes the disadvantages of the conventional occlusive dressings.

- 5 In accordance with this invention there is provided a medicated adhesive tape adapted for direct application to a skin lesion, said tape having a flexible backing and a surface with a pressure-sensitive adhesive coating
10 based on an acrylate ester-acrylic acid copolymer and uniformly dispersed in the adhesive an anti-inflammatory steroid in a therapeutically effective concentration.

- 15 In a more specific, preferred embodiment of the invention there is provided a medicated adhesive tape adapted for direct application to a skin lesion, said tape having a surface with a pressure-sensitive adhesive coating comprising an acrylate ester-acrylic acid copolymer and flurandrenolone uniformly dispersed in a therapeutically effective concentration.

- 25 The medicated tape of this invention insures that the anti-inflammatory steroid is uniformly distributed throughout the adhesive area of the tape, thereby making available a precisely measured amount of the steroid when the tape is placed on the site to be treated. The preferred anti-inflammatory steroid is flurandrenolone (6 α - fluoro - 16 α - hydroxy - hydrocortisone - 16 α - 17 α - acetonide) and its concentration is preferably in the range of 4-16 mcg. per square cm. of tape (0.4-1.6 mg. per 100 square cm. of tape).
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- Other anti-inflammatory steroids which can be employed in preparing the medicated tape of this invention include the 16 - methyl steroids, such as flumethasone (6 α ,9 α - difluoro - 16 α - methyl - 1,4 - pregnadiene - 11 β ,17 α ,21 - triol - 3,20 - dione), β - methasone (9 α - fluoro - 16 β - methyl - 1,4 - pregnadiene - 11 β ,17 α ,21 - triol - 3,20 - dione), dexamethasone (9 α - fluoro - 16 α - methyl - 1,4 - pregnadiene - 11 β ,17 α ,21 - triol - 3,20 - dione), and their 17 α esters, particularly the valerate and caproate esters; other acetonides including triamcinolone (9 α - fluoro - 16 α - hydroxycortisone - 16 α ,17 α - acetonide), 9 α ,11 β - dichloro - 6 α - fluoro - 1,4 - pregnadiene - 16 α ,17 α ,21 - triol - 3,20 - dione - 16 α ,17 α - acetonide, 9 α ,11 β - dichloro - 6 α ,21 - difluoro - 1,4 - pregnadiene - 16 α ,17 α - diol - 3,20 - dione - 16 α ,17 α - acetonide, 9 α ,11 β - dichloro - 6 α - fluoro - 1,4,6 - pregnatriene - 16 α ,17 α ,21 - triol - 3,20 - dione - 16 α ,17 α - acetonide; and the standard corticosteroids, cortisone, hydrocortisone, prednisolone, and medrol (6 α - methylprednisolone). Also useful are the 21 esters of any of the above anti-inflammatory steroids, including the propionates, acetates, phosphates, pivalates, etc., thereof. These steroids are included at a concentration equivalent in activity to 4-16
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mcg. of flurandrenolone per square cm. of tape.

The novel occlusive dressing of this invention is prepared by spraying a solution of one of the above steroids onto the adhesive surface of a tape having a layer of a pressure-sensitive adhesive already present on one side thereof, or by mixing one of the above steroids with the adhesive prior to application of the latter to the tape backing.

The use of the medicated tape of the present invention in the therapy of skin lesions which respond to treatment with anti-inflammatory steroids affords a number of distinct advantages over conventional methods of therapy in use prior to this invention: (1) percutaneous penetration of the anti-inflammatory steroid is enhanced; (2) uniform concentrations of the active agent are present over the entire area of the lesion being treated; (3) only the affected area need be covered; (4) intimate contact of the drug with the lesion is assured at all times; and (5) needless waste of the frequently expensive steroidal agent is prevented, since only the areas to be treated need be covered and loss of the drug onto clothing and normal areas of the body does not occur.

In one of the embodiments of the present invention, the medicated tape is prepared by spraying a solution of an anti-inflammatory steroid onto the adhesive surface of a tape having a layer of pressure-sensitive adhesive already present on one side thereof.

In the preferred embodiment, flurandrenolone is incorporated into the adhesive mixture prior to its application to a non-porous, flexible backing in a concentration such that the flurandrenolone is present in a concentration of from 4-16 mcg. per square cm. of tape (0.4-1.6 mg. per 100 square cm. of tape).

The tape backing must, quite obviously, be flexible, in order to conform to the curvature of the body surface to which it is applied and should preferably, further, be made of non-porous material in order that the final product may serve as an occlusive dressing. The nature of the adhesive must be such as to permit diffusion of the steroid through the adhesive layer and must itself, of course, be non-irritating to the skin. Its adhesive strength should be sufficiently great to permit adherent bonding of the resulting tape to skin surfaces under light pressure and to remain firmly adherently bonded to the skin during normal activity. The adhesive bond, however, must not be so great as to pull off layers of skin when the tape is removed from the area being treated. Tape backings and adhesives fulfilling the foregoing requirements are described in U.S. Patent No. RE 24,906.

The following examples set forth illustrative procedures by which the application of

flurandrenolone to the tape can be accomplished.

EXAMPLE 1

- 5 A tape 1.5 inches in width was prepared by laminating an isoamyl acrylate-acrylic acid co-polymer onto a cellophane sheet in accordance with Example 1 of U.S. Patent RE 24,906. (The word "cellophane" is a registered Trade Mark). The tape was spirally wrapped, adhesive side out, around a cylinder 38 inches in circumference so that there was neither overlapping nor exposed cylinder surface. The cylinder was 9 inches high and easily accommodated a 180-inch roll of tape. While the cylinder was revolved at 24 r.p.m., 100 cc. of an acetone solution containing 10.0 mg. flurandrenolone was sprayed at 15 psi (pounds per square inch) using an air brush with a medium needle along the center of the tape as the cylinder revolved. Next the spray was directed to the edges where the wrappings meet. The spraying of the center and edges was alternated until all of the solution had been applied. The tape was dried for about 20 minutes and then rerolled onto a spool. Analysis showed that flurandrenolone was present on the adhesive layer at a concentration of 0.402 mg. per 100 square cm. of tape. Assay of the tape 21 days after application showed that there had been no loss in flurandrenolone activity during storage.

EXAMPLE 2

- 35 A polymer, prepared by co-polymerizing the acrylate ester of commercial fusel oil and acrylic acid in 19:1 ratio in ethyl acetate solvent using benzoylperoxide as a catalyst, was dissolved in a 70:30 ethyl acetate-isopropanol solvent mixture so as to give a 20 percent concentration. Flurandrenolone was dissolved in this solution in an amount equivalent to 0.1 percent of the amount of polymer present. The resulting solution was coated onto a silicone release paper in a uniform layer of sufficient thickness to provide 418 mg. of adhesive per 100 square cm. of release paper, and the solvent removed by drying. Next, a polyethylene film was laminated onto the adhesive using heat, and the silicone release paper was removed. Analysis indicated that flurandrenolone was present in the adhesive layer in an amount equivalent to about 0.4 mg. per 100 square cm. of tape.

- 55 For the above specifically described tapes, the adhesive is prepared by co-polymerizing a major amount of an acrylate ester and a minor amount of acrylic acid. Suitable acrylate esters, in addition to those mentioned above, include 2-ethylbutyl acrylate, ethyl acrylate, iso-octyl acrylate and the like, as set forth in the U.S. Patent RE 24,906. As also taught in that patent, acrylic acid, methacrylic acid, itaconic acid, acrylamide and methacryl-

amide can be used as co-monomers with the acrylate ester. The ratio of acrylate ester to acrylic acid, or its equivalent, can be in the range 88—97:12—3, e.g. 92—96:8.4. If desired, a thinner layer of adhesive can be laminated onto the tape and then a second layer containing both adhesive and flurandrenolone can be laminated on top of the first layer so as to give a higher concentration of flurandrenolone in that adhesive layer which will be immediately adjacent to the skin on application of the tape to the affected area.

Tapes containing 0.8 and 1.6 mg. of flurandrenolone per 100 square cm. of tape are prepared in exactly analogous fashion by adjusting the amount of the steroid added to the solutions of Examples 1 and 2.

Anti-inflammatory steroids useful in preparing the occlusive dressings and medicated tapes of this invention are commercially available under various trademarks or can be prepared by the processes of the art. Methods for preparing specific compounds are described in U.S. Patents No. 3,126,375, flurandrenolone; No. 3,312,590, β -methasone - 17 α esters; Nos. 3,147,249 and 3,152,154, general preparation of 17 α esters; Nos. 3,291,815 and 3,264,332, flumethasone; No. 3,048,158, general method of preparing acetonides; and No. 3,201,391, methods of preparing 11 β -chloro steroids and general preparative methods for 21 esters. It will be understood by those skilled in the art that the methods of preparing any given derivatives of a basic steroid are well known and can be used interchangeably from one steroid to another.

The above steroids are incorporated into the adhesive layer of tape or sprayed onto the adhesive layer of tape in the same manner as described in Examples 1 and 2 for flurandrenolone. It will be understood by one skilled in the art that the amounts of the particular steroid to be used will vary according to the activity of the particular steroid.

WHAT WE CLAIM IS:—

1. A medicated adhesive tape adapted for direct application to a skin lesion, said tape having a flexible backing and a surface with a pressure-sensitive adhesive coating based on an acrylate ester-acrylic acid co-polymer and uniformly dispersed in the adhesive an anti-inflammatory steroid in a therapeutically effective concentration.

2. The tape of claim 1, in which said co-polymer is one which has been prepared by co-polymerizing an acrylate ester monomer with acrylic acid in a weight ratio of acrylate ester monomer to acrylic acid of from 88:12 to 97:3.

3. A tape according to claim 1 wherein the anti-inflammatory steroid is selected from flumethasone, β -methasone, dexamethasone,



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flurandrenolone to the tape can be accomplished.

EXAMPLE 1

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amide can be used as co-monomers with the acrylate ester. The ratio of acrylate ester to acrylic acid, or its equivalent, can be in the range 88-97:12-3, e.g. 92-96:8.4. If desired, a thinner layer of adhesive can be laminated onto the tape and then a second layer containing both adhesive and flurandrenolone can be laminated on top of the first layer so as to give a higher concentration of flurandrenolone in that adhesive layer which will be immediately adjacent to the skin on application of the tape to the affected area.

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2. The tape of claim 1, in which said co-polymer is one which has been prepared by co-polymerizing an acrylate ester monomer with acrylic acid in a weight ratio of acrylate ester monomer to acrylic acid of from 88:12 to 97:3.

3. A tape according to claim 1 wherein the anti-inflammatory steroid is selected from flumethasone, β -methasone, dexamethasone,



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- and the 17α esters thereof, triamcinolone, 9α , 11β - dichloro - 6α - fluoro - 1,4 - pregnadiene - 16α - 17α - 21 - triol - 3,20 - dione - 16α - 17α - acetonide, 9α - 11β -
- 5 dichloro - 6α - 21 - difluoro - 1,4 - pregnadiene - 16α - 17α - diol - 3,20 - dione - 16α - 17α - acetonide, 9α - 11β - dichloro - 6α - fluoro - 1,4,6 - pregnatriene - 16α - 17α -
- 10 21 - triol - 3,20 - dione - 16α - 17α - acetonide, cortisone, hydrocortisone, prednisolone, medrol, and the 21 esters of the above steroids.
4. A tape according to claims 1, 2 or 3, wherein the steroid is present at a concentration equivalent in activity to 4—16 mcg. of
- 15 flurandrenolone per square cm. of tape.
5. A tape according to claim 1 in which the anti-inflammatory steroid is flurandrenolone.
- 20 6. The tape of claim 5, in which the copolymer is one which has been prepared by

co-polymerizing an acrylate ester monomer with acrylic acid in a weight ratio of acrylate ester monomer to acrylic acid of from 92:8 to 96:4.

7. The tape of claim 5, in which the flurandrenolone is present in an amount equivalent from 0.4 to 1.6 mg. per 100 square cm. of tape.

8. The tape of any of claims 1 to 7, in which the adhesive coating is on a nonporous flexible backing.

9. A medicated adhesive tape, according to any preceding claim and substantially as herein described, with particular reference to any one of the specific examples.

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