Aug. 7, 1945. F. C. SCHMELKES ET AL 2,381,621

COMPOSITE THERAPEUTIC FILM

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Fig. 1

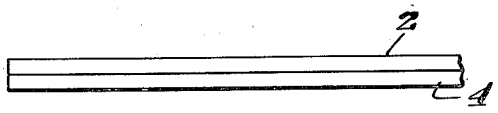


Fig. 2

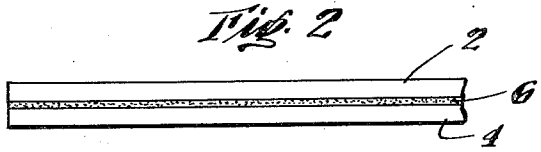


Fig. 3

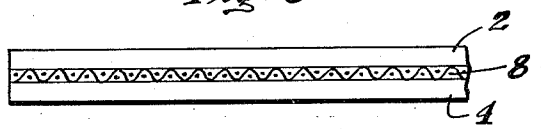
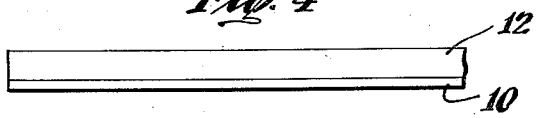


Fig. 4



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COMPOSITE THERAPEUTIC FILM

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Application August 22, 1942, Serial No. 455,975

1 Claim. (Cl. 167—84)

This invention relates to a therapeutic article in the form of a film and particularly to such an article adapted for applying to a moist lesion two or more medicinals which, while chemically incompatible, react with each other only relatively slowly.

Application of two or more therapeutic agents at the same time or in sequence is often desirable. Such instances are the use of two germicides, a germicide and a local anaesthetic, or an anti-bacterial substance and a tissue growth stimulant. Preparations such as solutions, jellies, and ointments containing two or more therapeutic agents are frequently impractical, particularly when chemical reaction between the various constituents reduces the shelf life of such multiple preparations.

The present invention provides a stable medicating article containing two or more therapeutic agents that may be chemically incompatible and permits their simultaneous application in an effective, convenient and simple manner.

The invention comprises a therapeutic article including a hydrophilic base material and a plurality of water soluble medicinal substances distributed in the base material. The major proportions and preferably practically all of the said substances are isolated from each other by the base material extending between the said substances, this arrangement being particularly advantageous in those cases where the medicinal substances are slowly interreactive and injurious to each other on relatively long contact. In the preferred embodiment, the invention comprises a plurality of pliable substantially dry films and incompatible medicinals disposed separately in the several films so that no one film will contain substances that are incompatible with each other. In another embodiment, the invention comprises such a therapeutic film containing a spacing layer, as of fabric or a thin non-medicated plastic or cementing layer that is readily penetrated by water, extending between adjacent ones of the plurality of plies and maintaining the plies out of contact with each other. Preferably the one of the plies that is to be next to the lesion when the composite is in use is relatively very thin, so as to offer a minimum of resistance to diffusion between the other ply and the lesion.

With a composite of the kind described, excellent results have been obtained in the application of two or more medicating materials that, when maintained in long contact with each other as in solution in the same film, undergo loss of activity but that are not so quickly reactive as to destroy each other to an objectionable extent in the relatively short period of time during which the incompatible substances are diffusing from the composite and into the body tissue when the composite is in use in a moist or weeping lesion.

The invention will be illustrated by description in connection with the drawing to which reference is made.

Figs. 1, 2, 3 and 4 show sectional views of the article of the present invention, the thickness being somewhat exaggerated in comparison with the other dimensions.

There are shown in Fig. 1 a plurality of films 2 and 4 and in Fig. 2 like films with a cementing material 6 adhering the films together. In the structure of Fig. 3, a spacing fabric 8 extends between two adjacent plies and is united to each of the plies which it serves to space from each other. In the structure of Fig. 4 there is shown a relatively thin film 10 joined to a much thicker film 12, the thinner film being the one that is in direct contact with the lesion when the article is in use. Because this film 10 is relatively very thin, it makes possible diffusion at a satisfactory rate of medicant from film 12 to the lesion. The cement 6 serves also as a spacing layer.

In the figures, the thicknesses are somewhat exaggerated in relation to other dimensions.

The various film members that have been described as well as the cementing layer 6 must be hydrophilic and, therefore, adapted to promote the diffusion of water and aqueous solutions of the medicants through the article. These films may be constituted largely or entirely of plastics that are hydrophilic and slowly softenable by and ultimately soluble in water as, for example, methyl cellulose (of which a suitable grade is Methocel), polymerized vinyl alcohol of plastic consistency, and a cellulose derivative such as an ether of cellulose and glycolic acid or a slowly soluble salt of it. The term "hydrophilic" as applied to the films or base materials is used to mean that the films permit the ready diffusion of aqueous liquid therein.

In addition to the base materials of hydrophilic nature, the films include also the selected medicating material, chemically incompatible ones being separated from each other by the film forming material extending between the major proportions at least of such incompatible substances. Suitably the incompatible substances are disposed separately in the several films. Thus, a germicide containing available chlorine

is contained in one of the individual films shown in the drawing and a germicide or local anaesthetic subject to reaction with chlorine may be contained in another of the films.

Whereas the drawing shows two films plied together, the number is not limited to two and a plurality of more than two films may be used, the relationship of any two of the films to each other being as illustrated in the drawing.

The cementing material used may be simply portions of the film forming materials adhered to each other, say surface portions that have been initially softened by vaporized solvent and then pressed together. Or the cementing material may be some other hydrophilic, readily water penetrable cement such as a very thin film of any one of the film forming materials applied initially in a suitable volatile solvent for such material, solvents for the film forming base materials disclosed being water, alcohol, acetone, or methanol, the organic solvents used containing some water. A solution of 75 parts of water and 25 parts of alcohol is a particularly convenient solvent for the cellulose ether. We use the word solvent to include any volatile liquid which may serve as a true solvent or as a medium for a dispersion. Wherever we use the word solution, we include true solutions, colloidal solutions, and dispersions.

The films are cast in a manner suitable for the casting of films of plastic materials. Thus there is made a dope containing the desired film forming material, the selected medicating substance or compatible substances, and a solvent for the base material and preferably also for the medicating material present. Thus, there may be used a solvent of the kind mentioned above in connection with the formation of the cement. The dope so formed and of concentration to give to it a freely flowing to syrupy consistency is cast upon plate glass or other smooth surface, the solvent evaporated, and the remaining film stripped from the casting surface and dried. The film is then plied with another film similarly made, for instance, containing a different medicinal that is incompatible with that in the first film. Films made as described are non-porous but water penetrable.

When the spacing cloth is used, the preformed films may be pressed against the cloth sufficiently to adhere the cloth to the surfaces of the films, the surfaces of the films being suitably solvent softened before being impressed against the cloth. More conveniently, a solution of the film forming base material that is preferably rather thick and contains medicant, is spread upon one side of the cloth and a like solution of the incompatible medicant is coated upon the other side in manner that is usual in the coating of both sides of fabrics with such compositions as pyroxylin solutions.

When the films are preformed before assembly, they may be made of predetermined desired thickness. When they are formed by spreading upon the fabric member and then evaporating the volatile solvent present, the film first formed is suitably made relatively thick. After such impregnation then the second film is applied as a relatively thin layer over one side of the impregnated cloth, this thinner film being applied directly over a moist lesion when the article is in use.

The structure of the present invention is particularly useful in applying medication with azochloramide (N,N' - dichloroazodicarbonamidine) and a germicidal sulfanilamide compound examples of which are sulfanilamide itself, sulfathiazole, and sulfapyridine. The azochloramide destroys anti-sulfanilamide bodies known to be present in infected wounds. Before use, the azochloramide and the sulfanilamide compounds, known to be mutually destructive, are kept isolated in separate films of the composite article.

Preferably the azochloramide is contained in the one of the films that is applied directly over the lesion when the article is in use. The azochloramide so disposed reaches the tissue of the lesion first and prepares the site for the sulfa drug. In this way the full activity of the sulfanilamide compound is preserved. It will be noted that the chemicals are extracted in their original form, that is, without losing their chemical identities.

In general, the films are used in substantially dry condition, that is, of moisture content approximating that in equilibrium with the air or below that which causes development of objectionable tackiness of the films. Also, the base material of the films is preferably non-metabolizable by microorganisms.

The invention will be further illustrated by detailed description in connection with specific examples of the practice of the invention.

Example 1

A homogeneous paste is prepared from the following materials: 27 parts Methocel, of viscosity 100 centipoises (cps.), 5.6 parts glycerin, 3.75 parts sulfanilamide, 250 parts water and 250 parts ethyl alcohol. This paste is applied to gauze using standard fabric coating equipment and the solvents removed by evaporation. The paste is applied in amounts sufficient to result in a weight of film of 1.5 to 2.0 ounces per square yard exclusive of the weight of the fabric.

A second homogeneous paste is prepared from 40 parts of Methocel, 100 cps., 10 parts triacetin, 1 part Azochloramide (N,N'-dichloroazodicarbonamidine) and 500 parts of water. The above coated fabric is treated in a similar manner with the second paste at a rate sufficient to result in the film weighing 0.2 to 0.3 ounce per square yard exclusive of the weight of fabric and sulfanilamide containing coating. The finished material is cut into the desired widths and used as a therapeutic film.

Example 2

Sixty parts of polyvinyl alcohol (type B, medium viscosity), 12 parts glycerin, 8 parts sulfanilamide, 300 parts water and 400 parts ethyl alcohol are mixed to a homogeneous solution. This solution is poured into drying trays in thin layers and the solvent caused to evaporate by the application of heat or exposure to dried air. To this dried film there is added a thin layer of a solution made from 30 parts Methocel, 4000 cps., 1 part Azochloramide, 10 parts triacetin, 300 parts water and 270 parts acetone. The solvents are removed by evaporation as before and the double layered film is stripped from the drying tray and cut into the desired size. Sufficient liquid is poured into the trays to give the sulfanilamide containing layer a weight of 2 ounces per square yard and the Azochloramide layer a weight of 0.2 to 0.3 ounce per square yard. This therapeutic film is normally used with the Azochloramide containing layer adjacent to the wound surface.

Example 3

A homogeneous paste made from 30 parts of

polyvinyl alcohol (type B medium viscosity), 6 parts glycerin, 4 parts sulfadiazine, 150 parts ethyl alcohol, and 200 parts water is applied to Cellophane in a manner described in Example 1, at such a rate that the dried film will have a weight of 1.5 to 1.8 ounce per square yard, exclusive of the weight of the Cellophane backer.

A second layer weighing 0.2 to 0.3 ounce per square yard after drying, is applied directly over the first layer. The paste used in the second layer is made from 25 parts of Methocel, 8 parts Azochloramide, 12 parts triacetin, 200 parts ethyl acetate and 250 parts acetone.

Example 4

20 parts of Methocel, 100 cps., 6 parts glycerine, 6 parts sulfathiazole, 200 parts methyl alcohol and 300 parts water are worked up into a homogeneous paste. This is applied to surgical gauze in a manner described in Example 1, at the rate of 2.0 ounces per square yard.

A thin coating amounting to approximately 0.1 ounce per square yard is applied over this first coating. This second layer consists of unplasticized Methocel and is obtained by coating the previous material with a thin solution of Methocel in methyl alcohol. It provides a neutral separating layer.

A third layer is applied at such a rate so as to result in a layer weighing 0.2 to 0.4 ounce per square yard. The material used in preparing this third layer consists of a homogeneous thin paste composed of 50 parts Methocel 15 cps., 5 parts triacetin, 1 part succinchloramide, and 300 parts water.

Example 5

Films weighing 1.5 to 2.5 ounces to the square yard may be made as described in any of the above numbered examples from a composition including an alkaline buffer in conjunction with a germicidal sulfanilamide compound, the buffer establishing the pH when the film is in use at a pH of about 8 to 10, at which pH the sulfanilamide composition is more effective as a germicide than at lower pH values. These mixtures all give films which are alkaline in nature.

The compositions applied are in solution in a mixture of alcohol and water, the non-volatile materials being as follows:

(1) 75 parts Methocel, 15 cps., 10 parts sulfanilamide, 10 parts glycerin, 1 part calcium carbonate, and 0.2 part sodium carbonate.

(2) 75 parts Methocel, 100 cps., 8 parts sulfathiazole, 10 parts glycerine, and 1.5 parts secondary sodium phosphate.

(3) 75 parts polyvinyl alcohol, 5 parts sulfadiazine, 15 parts glycerin, 0.2 part sodium carbonate, 1.0 part sodium bicarbonate and 1.0 part calcium carbonate.

(4) 60 parts Methocel, 4,000 cps., 10 parts sulfanilamide, 10 parts triacetin, 1 part calcium carbonate, 0.8 part borax, and 0.2 part boric acid.

It will be understood that films made as described are preferably sterilized before use, as, for example, by autoclaving with steam for a short period of time.

Certain subject matter herein disclosed but not claimed is covered in our copending application Ser. No. 456,458, filed on August 26, 1942, and entitled Sulfanilamide film.

It will be understood also that it is intended to cover all changes and modifications of the example of the invention herein chosen for the purpose of illustration, which do not constitute departures from the spirit and scope of the invention.

What we claim is:

A dressing for a liquid exuding lesion which comprises a plurality of plies, at least one of which is thin, of pliable, hydrophilic, non-porous but water penetrable material in film form, azochloramide distributed throughout the one of the said plies that is thin and that is to be in contact with the lesion when the dressing is in use, and a bacteriostatic sulfanilamide compound distributed throughout another of said plies, so that the azochloramide is extracted and reaches the lesion first after application of the dressing to the lesion and prepares the site for the sulfanilamide compound in advance of contact of the sulfanilamide compound with the lesion.

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