STABLE BISMUTH TRIBROMOPHENATE OINTMENT AND PROCESS OF PREPARATION

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7 Claims

ABSTRACT OF THE DISCLOSURE

An effective ointment for the treatment of burns is bismuth tribromophenate in an oleaginous ointment base. However the composition has the disadvantage that it is unstable and the bismuth compound does not remain in suspension. A stable suspension of bismuth tribromophenate in an oleaginous ointment base is provided herein.

BACKGROUND OF THE INVENTION

This invention improves compositions in compositions for treating burns, that is, tissue injuries caused by thermal, electrical, radioactive, or chemical agents.

The common mechanism in burning is denaturation of protein, resulting in cell injury or cell death. Burns are always accompanied by edema, a collection of fluid or exudate beneath the traumatized skin area. The layers of the skin involved are destroyed by coagulation necrosis. During the second twenty-four hours after the burn the development of edema and exudate progressively lessens, and in two to three weeks dead skin is absorbed and liquefied, partially by enzymatic action and partially by leukocytic digestion. This action is also accompanied by the formation of serous exudate.

After the patient has been treated for shock and carefully planned fluid therapy has been instituted to replace lost fluid, consideration is given to treatment of local areas. Two general methods are usually employed: the closed method wherein mesh gauze bandages are applied; and the open method which involves local care followed by placing a cradle over the body so that sheets are not in contact with burned areas. In the open or exposure method wounds are allowed to dry to form eschars or scabs. Thus after surgical cleansing, the depth and distribution of burned areas determine whether the injury is best handled by exposure or by closed dressings. The determining factors for occlusive dressings are ease of achieving alleviation of burned areas during edema formation, need for immobilization to prevent cracking of eschar and the like. In either event topical application of one of several ointment bases, such as petrolatum, containing a broad range of antibiotics and/or chemicals suspended therein, for example, nitrofurans, sulfonamides, etc., is widely practiced.

SUMMARY OF THE INVENTION

A particularly effective ointment which has recently come into use for the treatment of burns is bismuth tribromophenate in a nonsaponifiable oleaginous ointment base. The bismuth tribromophenate ointment has been found to be particularly efficient in the treatment of burns, carbuncles, and similar skin problems because it is capable of adsorbing fluid exudate. However it has the disadvantage that even though it has been in use for several years a process still does not exist for producing a stable suspension of the bismuth tribromophenate in the ointment base. It has, therefore, been necessary to mix the bismuth tribromophenate in the oleaginous base locally in each hospital shortly prior to use. In accordance with the practice of this invention a stable suspension of bismuth tribromophenate in an oleaginous ointment base is provided.

DETAILED DESCRIPTION OF THE INVENTION

Since for this use the ointment base must be nonabsorbable and nonsaponifiable, oleaginous ointment bases are contemplated, such as white petrolatum, paraffin jelly, beeswax, and the like. A preferred base is paraffin jelly having a melting point of 43.5° C. The normal method of preparing ointments is to heat the oleaginous base, generally to its melting point, and then stir in the additional compounds, continuing to mix until the ointment has cooled. Bismuth tribromophenate however has a tendency to agglomerate during the cooling stage so that it is practically impossible to make a dependable suspension. Moreover the composition has no shelf life. The bismuth tribromophenate settles to the bottom of the ointment base in the first few months even under the best mixing procedures. Hence, if no burn case is admitted to a hospital for two or three months, the available ointment is not usable due to the settling of the bismuth tribromophenate.

Bismuth tribromophenate ointment is now the drug of choice for the treatment of burns and for skin grafting because it is a nontoxic, nonabsorbable and profoundly analgesic and dependable antiseptic. For this reason it is preferred by many physicians even though fresh batches may have to be prepared after a patient is admitted to a hospital. However prior mixing delays relief to the patient, and also is a source of potential infection. In accordance with the practice of this invention it has been found that if a carefully observed homogenization procedure is followed at an elevated temperature below the decomposition point of the bismuth tribromophenate a stable suspension of the bismuth tribromophenate in the oleaginous ointment base can be made.

The preparation of the stable suspension contemplated herein is accomplished by heating the oleaginous base to a temperature in the range of 40° C. to the decomposition temperature, usually about 65° C. Preferably at a temperature of 40° C. to 50° C. the bismuth tribromophenate is mixed with the ointment base by ordinary stirring means. At this elevated temperature the composition is then subjected to incomplete homogenization. It has been found that if, at this temperature, more than sixty percent by volume of the composition is homogenized, the ointment is not completely effective, and indeed, if less than twenty percent of the material is homogenized, a stable suspension does not result. The invention thus contemplates a stable suspension of two to ten weight percent based on the total composition of bismuth tribromophenate dispersed in an oleaginous ointment base. The suspension is rendered stable under incomplete homogenization conditions, at an elevated temperature below 65° C., such that only a quantity in the range of twenty to sixty percent of the composition is homogenized.

As is known in the art, the degree of homogenization is best controlled by the number of passes through a particular homogenizing device. Thus in a colloid mill requiring three passes for complete homogenization a stable composition does not result when the bismuth tribromophenate composition is passed through only once. In addition three passes has been found to result in an unsatisfactory product.

The preparation of the stable emulsion contemplated herein can best be illustrated by means of the following specific examples which are, of course, intended to be illustrative only since various modifications will occur to those skilled in the art. Thus several examples are given for the desired degree of homogenization are available. In the examples which follow five percent bismuth tribromophenate...
Phenate was incorporated in petroleum jelly based on the weight of the total composition.

Example 1

Using a water bath, 9,500 grams of the petrolatum base were heated at a temperature of 45° C. to form a liquid melt. After the petrolatum was melted 500 grams of bismuth tribromophenate were added and the mixing was continued for five minutes. The product was kept at the constant temperature of 45° C. during the mixing period. After thorough mixing the product was placed in a colloid mill. After partial homogenization by virtue of one pass through the mill the product was collected in a vessel, placed in the water bath and reheated to 45° C. As soon as the composition reached this temperature, it was again run through the colloid mill. The second run through the colloid mill being completed, the product was allowed to cool to approximately 20° C. and then poured into suitably sized containers. This suspension of bismuth tribromophenate, known to be twenty to sixty percent homogenized, has been found to be stable even after six months. At the end of this period the ointment remained suspended and consistent in analysis.

Whereas the desired degree of homogenization is in the range of twenty to sixty percent by volume, it has been found that the ideal extent of homogenization is thirty-five percent by volume. Bismuth tribromophenate thus prepared is available to adsorb the serum exudate, with the base free to support rate of the serum. It is emphasized however that even with the proper degree of homogenization, if the homogenization is not conducted at the required elevated temperature a stable suspension still does not result. Thus, if petrolatum and bismuth tribromophenate are passed through a homogenizer under conditions resulting in twenty to sixty percent homogenization but at a temperature below 45° C., the resulting product is unsatisfactory. Without being bound by any theory of this invention, it appears that if a shearing of all the bismuth tribromophenate particles takes place they are no longer effective or available for medication and adsorption. The therapeutic and adsorbent properties are reduced. On the other hand if an insufficient quantity of the particles is subjected to the shearing action a stable composition does not result. Stated somewhat differently twenty to sixty percent of the particles in the bismuth tribromophenate ointment must be in the size range of less than two microns. The dispersion is then stable. This can be illustrated by the following examples using the same quantities of materials as in Example 1, but different degrees of homogenization.

Example 2

A mixture of bismuth tribromophenate prepared in accordance with Example 1 at a temperature of 45° C. was homogenized in a colloid mill, preparing an ultimate ointment resulting in a degree of homogenization of about fifteen percent. There was some agglomeration on standing after cooling, and within six months bismuth tribromophenate settled to the bottom of the container. The resulting product was better in appearance than one made by mere stirring, but the ointment was unstable.

Example 3

Following the procedure of Example 1 an ointment was prepared. However at 45° C. the composition was homogenized in a colloid mill under conditions producing a degree of homogenization of between sixty and eighty percent. It was found that the increased degree of homogenization did not improve the suspension. Rather the increased degree of shearing of bismuth tribromophenate particles reduced the therapeutic efficiency of the resulting ointment as an antiseptic and adsorbent, reducing its analgesic properties.

Example 4

Following the procedure of Example 1 but using 9,800 grams of petrolatum and 200 grams of bismuth tribromophenate a composition was made known to be thirty-five percent homogenized. The ointment was used at Vanderbilt University Hospital in the treatment of burns with excellent results.

It can thus be seen that by the practice of this invention an improved ointment containing bismuth tribromophenate can be rendered stable without losing its therapeutic values. The provision of this ointment in stable form makes it available at anytime, even after long standing, for the treatment of a variety of skin problems requiring an emollient containing a nonabsorbable antiseptic which is capable of adsorbing fluid exudate. It will be understood of course that minor quantities, say, one-half to five percent of other medicinals can be incorporated in the composition as is known in the art. In addition modifiers, for instance, mineral oil, can also be added to the ointment base. These and other variations will occur to those skilled in this field. Such ramifications are deemed to be within the scope of this invention.

What is claimed is:

1. A stable suspension for the treatment of burns, consisting of bismuth tribromophenate in a nonabsorbable, oleaginous ointment base not absorbed into the skin, said suspension containing two to ten weight percent based on the composition of bismuth tribromophenate dispersed therein, the suspension rendered stable by incomplete homogenization at a temperature in the range of 40° C. to 65° C. such that at said temperature only a quantity in the range of twenty to sixty volume percent of the bismuth tribromophenate particles in the ointment are homogenized to a size range of less than two microns.

2. The composition of claim 1 wherein the oleaginous ointment base is paraffin jelly having a melting point of 43.3° C. and wherein the bismuth tribromophenate is dispersed therein in an amount of five weight percent.

3. The composition of claim 1 having two weight percent of the bismuth tribromophenate dispersed therein.

4. The composition of claim 1, rendered stable by the homogenization of thirty to forty volume percent thereof.

5. A process for the preparation of a stable suspension for the treatment of burns, consisting of bismuth tribromophenate containing two to ten weight percent bismuth tribromophenate in a nonabsorbable, oleaginous ointment base which comprises heating the oleaginous ointment base to a temperature in the range of 40° C. to 65° C., mixing the bismuth tribromophenate in the oleaginous base, and said temperature homogenizing the mixture until at least twenty percent but not more than sixty percent by volume of the bismuth tribromophenate particles in the ointment are homogenized to a size range of less than two microns.

6. The process of claim 5 wherein the temperature of homogenization is 40° C. to 50° C.

7. The process of claim 5 wherein the degree of homogenization is thirty-five percent by volume.

References Cited


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