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[54] POLYVINYLPYRROLIDONE-IODINE COMPOUNDS

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[52] **U.S. Cl.** ....**260/326.5 FL**, 260/295 Q, 260/613 B, 252/106 R, 252/107, 424/80
[51] **Int. Cl.** **C07d 27/08**
[58] **Field of Search** ....260/326.5 FL; 424/80

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[57] **ABSTRACT**

Hydrogen-bonded complexed compounds formed from an iodophor and a polyhydroxylated compound containing at least two hydroxyl groups which are useful in the preparation of iodophor-containing, abrasive, detergent compositions comprising said hydrogen-bonded complexed compound, a detergent, an abrasive substance and a pharmaceutically acceptable carrier therefor, said compositions being suitable to the abrasive germicidal cleansing of the skin and in the treatment of acne.

11 Claims, No Drawings

POLYVINYLPYRROLIDONE-IODINE COMPOUNDS

This invention relates to new and novel iodophor-containing abrasive detergent compositions which are useful for the cleansing of the skin by providing an abrasive and germicidal action concurrent with detergency. In particular it is concerned with a complexed compound comprising an iodophor and a polyhydroxy substance, a detergent and a skin-abrading substance in a pharmaceutically acceptable carrier therefor; the method for preparing the same and the method for its use in cleansing the skin as well as the method for its use in the therapy of the infected acne lesion.

Cleansing preparations, which are also intended to degerm the skin, have generally excluded elemental iodine as an antiseptic agent because of the well-known and inherent limitations of elemental iodine. Not only is iodine a toxic and corrosive substance, but it is also a highly reactive halogen capable of readily forming organic iodide salts and thereby destroying its germicidal properties as well as to render unstable the overall composition. This has been a particular problem in the preparation of cleansing compositions since the commonly utilized detergent compounds are generally alkaline metallic substances or metallic soaps and, therefore, are incompatible with elemental iodine. Although the availability of iodophor compounds has avoided some of the noxious, toxic properties of iodine, the basic chemical reaction between the elemental iodine and the alkaline ions of the organic detergents and soaps remains an incompatibility. Thus, even when an iodophor is utilized, we find that the available iodine will react with metallic ions to form iodide salts which not only lowers the germicidal potency of the respective iodophor compound but interferes with the detergency of the surface-active compound used.

When we approach the therapy of the acne patient, we find that iodine is contraindicated for use in the presence of acne. The usual iodine-containing preparations are such as to facilitate the penetration of the skin by significant quantities of iodine and thereby eliminates the use of iodine for such degerming purposes. Furthermore, since the acne lesion is most commonly manifested on the face, the known staining effects of preparations containing elemental iodine are such as to discourage its use by the patient. Another aspect to the use of cleansing preparation on the skin of the acne patient is the need to provide an abrasive action in order to facilitate the elimination of the comedone and the pustule. It is when such abrasive action is provided that the resultant denuded skin is particularly vulnerable to microbial invasion requiring the full protection of a broad spectrum germicidal agent. Moreover, the abraded skin is more readily penetrated by elemental iodine to result in a systemic absorption which disturbs the thyroid endocrine system.

The abrasive substances used for these purposes are all alkaline in reaction and therefore present still another limitation to the manufacture of such cleansing compositions. The alkaline abrasive substances are all basically incompatible with the iodine intended for use as a germicide and the overall results of this incompatibility is to restrict the selection of the germicidal agent to only those compounds which are capable of an inhibitory or microbistatic action, said compounds being compatible with the alkaline abrasive substances. This presents serious problems in the use of such germicidal agents as the tendency for mutating microbial strains to arise during an inhibitory stage not only complicates therapy but presents a new hazard to the patient through the development of widespread infection by resistant organisms.

It was unexpectedly found that liquid polyhydroxy compounds, such as glycerin, propylene glycol, polyoxyethylene glycols, having a molecular weight of from 200 to 1,000, and mixtures of the same, formed a new compound with an iodophor which resulted in a stabilizing action to the available iodine of the iodophor that would not only prevent the destruction of its germicidal potency in the presence of alkaline abrasive compounds and metallic surface-active substances, but would also assist the film-forming capacity of the iodophor to retain the iodine on the surface of the skin to permit virtually no penetration through the epidermal layers. It was found that a polyhydroxy compound containing at least two hydroxyl groups, as for example, propylene glycol, glycerin and a polyoxyethylene glycol, having a molecular weight of from 200 to 1,000, when present in a concentration of at least 1 per cent by weight, resulted in the formation of the new complexed compound with the iodophor substance to provide a substantivity to the surface film formed and to protect the available iodine against destruction. In this manner the iodine is prevented from combining with the skin proteins and thereby avoids staining the skin, at the same time that the full microbicidal properties of the iodine are preserved.

It was further found that this stabilizing action of the polyhydroxy compounds was limited to those liquid polyhydroxy compounds in which the iodophor is soluble. Thus, the higher polyoxyethylene glycols, as for example those members of this class of compounds having a molecular weight of 2,000 or greater, do not possess the property of combining with the iodophor nor of stabilizing the available iodine. The complexed compound of the polyhydroxy substance and the iodophor possesses new properties which are different from those of the respective moieties. Thus, the specific electrical conductivity of the new complexed compound differs from its individual components and is indicative of hydrogen-bond formation. There is a shift in the pH for the new complexed compound toward the neutral point and there is also an increased aqueous solubility for the complexed compound. The infra-red spectrum for the new compounds indicates a shift in the region of the hydroxyl group toward the hydrogen-bonded range.

The newly formed complex compounds of the iodophor and the polyhydroxy compound possess highly desirable physical, chemical and bacteriological properties permitting these to be utilized as antiseptic degerming compounds for the skin, apart from their use in the new compositions as described herein. These formed complexed compounds have advantages over their respective iodophor components in being stable and readily miscible with water and physiologic fluids. Thus it is known that, when an iodophor compound is heated at 40° C for varying periods of time, there will be a fall in its available iodine content. Furthermore, the iodophors are difficultly soluble in water and physiologic fluids. This fall is enhanced by the presence of water and further degradation occurs as is evidenced by a fall in pH of the solution and an increase in iodide concentration. In contrast to this, the newly formed complexed compound may be heated at 40° C, without a loss in available iodine content and is readily miscible with water. There is no increase in the iodide concentration and its pH remains unchanged. This improved stability is a marked advantage of the new complexed compound which is not observed in the presently available iodophor compounds. The full bacteriologic spectrum for these new compounds is preserved and they are active germicides in concentrations of 3 parts per million causing a germicidal effect within 15 seconds.

The new compositions are prepared by combining the selected polyhydroxy compound with an iodophor and mixing this with the detergent, the abrasive substance and the carrier therefor. Through the appropriate selection of the polyhydroxy compounds and the carrier, either semi-solid or liquid dosage forms may be obtained depending upon the patient's particular needs and preferences. The vehicle for the new compositions may be either a hydrophylic or a lipophilic carrier. When a hydrophilic carrier is preferred, then any of the pharmaceutically acceptable carriers, such as the polyoxyethylene glycols, having a molecular weight of from 1,500 to 6,000 and mixtures of the same, or Hydrophilic Ointment Base may be used, while such lipophilic vehicles as mineral oil, petrolatum and cocoa-butter will be found to be satisfactory carriers when this class is desired. Liquid dosage forms may be prepared through the use of either water, propylene glycol, alcohols, glycerin or the lower molecular weight polyoxyethylene glycol compounds or mixtures of these as the vehicle.

When a liquid hydrophilic preparation is preferred, a portion of the vehicle will serve as the stabilizing component to form the new compound, whereas the remainder serves as the principal vehicle for the liquid dosage form. This excess amount of vehicle may be replaced, wholly or in part, by water, a pharmaceutically acceptable alcohol, as for example, ethanol, propanol or isopropanol, or mixtures of the same, if desired. The lower viscosity mineral oils may also be utilized should a lipophilic liquid be desired. The particular selection of the vehicle to be used will depend upon the individual patient's requirements and the prescriber's preference.

The new compounds are formed from an iodophor which is a compound comprising elemental iodine and a carrier therefor. The iodophor is characterized by the formation of an iodine complex with the organic carrier to alter the physical, chemical and biologic properties of elemental iodine vehicle maintaining its antiseptic germicidal spectrum. Thus, a wide range of organic compounds have been shown to possess the necessary properties to form iodophors and these iodophors are suitable for the preparation of the new complexed compound of the iodophor and the polyhydroxy compound. Such compounds as polyvinylpyrrolidone-iodine, nonylphenoxypoly-(ethyleneoxy)-ethanol-iodine and undecoyliniumchloride-iodine are examples of different types of iodophors which may be used to prepare the new complexed compounds, although polyvinylpyrrolidone-iodine is a preferred iodophor compound for this purpose. When polyvinylpyrrolidone-iodine is used, the iodophor complex containing from 1 to 20 parts of active iodine per 100 parts of dry compound is preferred. Chemically it has been shown that the polymer, polyvinylpyrriolidone assumes a helical shape with the iodine molecules stored inside the helix. This structure indicates that the polyvinyl pyrrolidone combines with 1 mole of iodine per mole of monomer and also that it involved an ionic bond.

The polyhydroxy compounds capable of forming the new complexed compound with the aforesaid iodophors comprise the group consisting of glycerin, propylene glycol and the polyoxethylene glycols with a molecular weight of from 200 to 1,000 and mixtures of the same. A concentration of at least 1 per cent of the aforesaid polyhydroxy compounds is required for the formation of the complexed compound although amounts up to 50 per cent by weight may be utilized in certain instances, with a preferred or optimal concentration being at least 10 per cent by weight. When the newly formed complexed compounds are used in the present detergent compositions, their range in concentration will be from 1 to 30 per cent by weight.

The surface active agents useful to supply detergency to the present compositions may be either ionic or non-ionic compounds. When the non-ionic detergents are utilized, it is preferred that these be saturated compounds. The concentration of non-ionic detergents used for the new compositions will range from 5 to 35 per cent by weight, with a preferred concentration of 15 per cent by weight. When ionic detergents are preferred, then such compounds as the alkyl sulfo-esters of the formula $R—COO—CH_2CH_2—Na$, wherein R is a higher alkyl group having from 10 to 18 carbon atoms in chain length, sodium N-cyclohexyl-N-palmitoyltaurate, sodium N-fatty adid-N-methyltaurate, sodium N-methyl-N-palmitoyltaurate, and sodium lauryl sulfate may be used.

The abrasive properties of the new compositions are contributed by pumice, kaolin, sand, or mixtures of the same. The particle size of the abrasive substances may range from 100 to 1,000 microns, depending on the degree of abrasiveness desired. The amount of abrasive compound to be incorporated in the new composition will depend upon the degree of abrasive action desired and may range from 5 to 50 per cent by weight, with a preferred concentration being 25 per cent by weight. Pumice, N.F., is a preferred abrading agent and either the fine, medium, or coarse (N.F.) grades of this material may be used according to the needs of the patient. Those patients with thinner epithelial layers and who have a mild form of acne disease will require a lesser degree of abrasion than will those patients exhibiting thicker keratinized epithelial layers or in those instances where pustule formation is pronounced. In the former instance the abrasive compound with a particle size range of from 100 to 300 microns will be ordinarily preferred, whereas in the latter instance the preferred particle size range will be from 700 to 1,000 microns, and for those patients presenting an intermediate form of the disease, a particle size range of abrasive substance of between 300 to 700 microns is utilized. The concentration of abrasive material will also depend upon the particular characteristics of the patient's skin and a range of concentration of from 10 to 25 per cent by weight will generally be found satisfactory for the thinner skin of the younger patient, whereas a concentration of from 25 to 50 per cent of the abrasive substance will be most often employed for the patient with the thicker keratinized skin.

In practice it will be found desirable to first form the complexed compound between the polyhydroxy compound and the iodophor prior to its incorporation with the remainder of the ingredients. This may be accomplished by adding the selected iodophor compound to the appropriate polyhydroxy compound and stirring until complete solution is achieved. Gentle heating may be employed if desired. The complexed iodophor compound is then incorporated with the remainder of the ingredients by levigation or other suitable mixing method. The order of mixing for the particular ingredients is not critical since the essential step of the stabilizing process is the formation of the newly formed complexed compound described above.

The new compositions are light-brown in color and exhibit excellent cleansing properties. The new compositions are stable, with the full range of germicidal activity of the iodophor preserved and are safe for use on human skin as well as being non-sensitizing nor primary irritants.

When it is desired to cleanse the skin, employing the new composition, then an appropriate quantity of the new composition is applied directly to the moistened skin; a thick lather developed by brisk rubbing and the suds removed by rinsing with water. When it is desired to treat the acne lesions, the abrasive action of the present compositions serves to remove the covering of the comedone to permit a direct contact of the germicidal agent with the infecting organism so that the full microbicidal action may be obtained at the same time that the skin is cleansed. The same procedure is used to cleanse the skin of the acne patient as is used in the method of cleansing described above. The frequency of use for the acne patient will depend upon the severity of the disease and the degree of response obtained, but generally twice daily will be sufficient. With more frequent usage, the surface layers of the skin will be abraded and this may require an interruption of treatment until a remission occurs, but this abrasion is a desired object of therapy since it permits the formation of new skin with consequent healing of the acne.

The following examples illustrate the present invention, but it is not intended that these be limited thereby:

EXAMPLE 1

In a suitable container is placed 10 grams of propylene glycol and 10 grams of polyvinylpyrrolidone-iodine. The mixture is stirred until complete solution is achieved and gentle heating may be utilized if desired. The new complexed compound is formed between the propylene glycol and the polyvinylpyrrolidone-iodine. The new compound thus formed is readily miscible with water in all proportions in contrast to the slow, more difficult solubility of polyvinylpyrrolidone-iodine. The pH of the new compound is approximately neutral, being between pH 6 and pH 7. The new compound formation is established by the increase observed in the boiling point of propylene glycol, which now begins to distill at 80° C at a pressure of 0.1 mm Hg., in contrast to the boiling point for propylene glycol at this same pressure being 45.5° C. The infra-red spectrum for the mixture indicates a shift in the region of 3,650 cm^{-1} to below 3,550 cm^{-1} which establishes hydrogen bond complex compound formation. Moreover, the specific electrical conductance for the new compound is greater than the sum of its individual components and is confirmatory hydrogen bond complexing. The new complex thus formed is stable and there is no loss in available iodine under the ordinary conditions of storage. The full spectrum of microbicidal activity is preserved for the iodophor component of the new complex.

EXAMPLE 2

in a suitable container is placed 5 grams of glycerin and 99 grs. of nonylphenoxypoly-(ethyleneoxy)-ethanol-iodine. The mixture is stirred until complese solution is achieved to form the complexed compound between the glycerin and the nonylphenoxypoly-(ethyleneoxy)-ethanol-iodine. Upon prolonged cooling at temperatures below 0°, a brown, amorphous solid is obtained which decomposes at temperatures of about 24° C, in contrast to the melting point of glycerin obtained in this matter of 17.8. This confirmatory of new compound formation since the melting point of the glycerin would have been lowered had a simple mixture remained. The infra-red spectrum indicates a shift in the region of 3,650 cm^{-1} to below 3,550 cm^{-1} to establish hydrogen bond complex compound formation.

EXAMPLE 3

In a suitable container is placed 100 grams of polyvinylpyrrolidone-iodine and to this is added 20 grams of polyoxyethylene glycol, having a molecular weight of 200. The mixture is stirred until solution is achieved, employing gentle heating if necessary. The new complex thus formed indicates an increased specific electrical conductance which is greater than the sum of the individual components to establish hydrogen-bonded complex compound formation. The infrared spectrum of the new compound thus formed indicates a shift in the range of 3,650 cm^{-1} to below 3,550 cm^{-1} to confirm hydrogen-bonding.

EXAMPLE 4

To 1 Kg. of undecoyliniumchloride-iodine iodophor is added 10 grams of polyoxyethylene glycol with a molecular weight of 1000 and the whole intimately mixed while warming at a temperature of between 40° C and 50° C. New compound formation is established by the increase of specific electrical conductivity as well as the shift in the infra-red spectrum 3,650 cm^{-1} to below 3,550 cm^{-1} to establish hydrogen-bond complexing.

EXAMPLE 5

In place of the respective use of propylene glycol, glycerin and polyoxyethylene glycols having a molecular weight of from 200 to 1,000, as is described in Examples 1 through 4 above, there may be substituted, wholly or in part, any other member of the group consisting of propylene glycol, glycerin and polyoxyethylene glycols having a molecular weight of from 200 to 1,000, in said respective processes described above and in equivalent weights. Complexed compound formation will result between the respective iodophor compound and said polyhydroxy compound. The range in concentration described for the amount of polyhydroxy compound utilized to form the new complexed compound is from 1 to 50 per cent by weight.

EXAMPLE 6

In place of the respective polyvinylpyrrolidone-iodine, nonylphenoxypoly-(ethyleneoxy)-ethanol-iodine and undecoyliniumchloride-iodine used as described in Examples 1 through 5 above, there may be substituted in place thereof, either wholly or in part, any member of the group of iodophors consisting of polyvinylpyrrolidone, nonylphenoxypoly-(ethyleneoxy)-ethanol-iodine and undecoyliniumchloride-iodine compound in the respective processes described. New complexed compound formation will occur between the respective iodophor and the appropriate polyhydroxy compound selected.

EXAMPLE 7

In a suitable container is placed 65 parts of polyoxyethylene glycol-6,000 and 35 parts of polyoxyethylene glycol-400. The mixture is melted and stirred to achieve a homogeneous mass and 20 parts of the complexed iodophor compound formed from the polyvinylpyrrolidone-iodine and propylene glycol, as described in Example 1 above, is added and to this is added 50 parts medium grade pumice, N.F. The mixture is stirred to achieve a homogeneous distribution, while 30 parts of coconut fatty acid ester of sodium isethionate are added and then the whole milled. The detergent iodophor composition thus formed is ready for unit packaging.

EXAMPLE 8

In place of the polyoxyethylene glycol-6,000 there may be substituted any polyoxyethylene glycol member of the group consisting of polyoxyethylene glycols with a molecular weight of from 1,500 to 4,000. When the compounds of this series are used, then lesser quantities of the polyoxyethylene glycol-400 as is described in Example 7 above, may be required and the range of concentration for the liquid polyoxyethylene glycol may be as low as 10 parts when polyoxyethylene glycol-1,500 is used, or as high as 35 parts when polyoxyethylene glycol-4,000 is used. Similarly, in place of the polyoxyethylene glycol-400, as described above, there may be substituted, wholly or in part, a liquid polyoxyethylene glycol with a molecular weight of from 200 to 800. The range in concentration for the respective liquid polyoxyethylene glycol compounds to be used will vary in relationship to the molecular weight of the higher members of the series used, to wit, the polyoxyethylene glycols of from 1,500 to 6,000 and may range from 10 to 35 per cent by weight.

In place of the complexed iodophor compound formed from polyvinylpyrrolidone-iodine and propylene glycol as is described in Example 7 above, there may be substituted, wholly or in part, the complexed compound formed from an iodophor and dihydroxy compound as described in Examples 1 through 6 above. The range in concentration for the respective complexed iodophor-dihydroxy compound present in said composition is from 1 to 30 per cent by weight.

In place of the coconut fatty acid ester of sodium isethionate, as used in Example 7 above, there may be substituted, wholly or in part, a detergent compound selected from the group consisting of an alkyl-sulfo ester of the formula $R—COO—CH_2—CH_2—Na$, wherein R is a higher alkyl group, sodium N-cyclohexyl-N-palmitoyltaurate, sodium N-fatty acid-N-methyltaurate, sodium N-methyl-B-palmitoyltaurate and sodium lauryl sulfate. The range in concentration for the aforesaid detergent compounds is from 5 to 35 per cent by weight.

In place of the pumice, as described in Example 7 above, there may be substituted, wholly or in part, kaolin or sand. The particle size of the kaolin or sand, which may be used to supply abrasiveness to the composition, may range in particle size of from 100 to 1,000 microns, depending upon the overall abrasion desired and the amount of the abrasive compound to be incorporated in the new compositions, may range from 5 to 50 per cent by weight.

EXAMPLE 9

In a suitable container is placed 100 grams of polyoxyethylene glycol-1,000 and to this is added 20 per cent by weight of nonylphenoxypoly-(ethyleneoxy)-ethanol-iodine. The mixture is stirred gently, warmed to achieve solution and then 5 per cent by weight of glycerin is added and stirred. To this mixture are then added, in sequence, 15 per cent by weight of sodium lauryl sulfate and 35 per cent by weight of finely divided sand, having a particle size of between 100 and 300 microns. The mixture is stirred while cooling to room temperature. The new composition is a semi-solid ointment-like material which lathers into a copious foam in the presence of water. The new composition may be packaged in tubes for convenient dispensing.

EXAMPLE 10

To 10 grams of USP Hydrophilic Petrolatum is added 1 gram of the complexed compound formed from polyvinylpyrrolidone and polyoxyethylene glycol-1,000 and 0.75 grams of sodium lauryl sulfate. The mixture is stirred and 3 grams of kaolin, having a particle size of between 700 and 1,000 microns is incorporated into the mixture and the whole milled.

The new composition is packaged into unit dosage containers and is ready for use.

EXAMPLE 11

To 100 ml. of polyoxyethylene glycol-200 is added 10 grams of polyvinylpyrrolidone-iodine and 20 grams of sodium-N-coconut fatty acide amide of methyltaurate. The mixture is stirred until complete solution is achieved and then 7.5 grams of pumice, with a particle size of between 300 to 700 microns, is suspended in the mixture and the whole milled. The new composition is now ready for use in cleansing the skin.

EXAMPLE 12

In a suitable container is placed 100 grams of polyoxyethylene glycol-800 and 30 grams of undecoyliniumchloride-iodine. The mixture is warmed to achieve solution and to this is added 25 grams of polyoxyethylene glycol-1,500 with stirring. When a homogeneous mixture is obtained, 15 grams of sodium N-cyclohexyl-N-palmitoyltaurate and 20 grams of pumice N.F., coarse grade, are incorporated. The entire mixture is then milled to achieve a uniform distribution and packaged in unit containers.

EXAMPLE 13

In place of the respective iodophor, as described in Examples 9 through 12 above, there may be substituted any other iodophor of the group consisting of polyvinylpyrrilidone-iodine, nonylphenoxypoly-(ethyleneoxy)-ethanol-iodine and undecoyliniumchloride-iodine and mixtures of the same.

In place of the complexed compound formed, as described in Examples 9 through 12 above, there may be substituted any one of the formed complexed compounds obtained as a result of Examples 1 through 6 above, and mixtures of the same.

In place of the respective solid polyoxyethylene glycols, having a molecular weight of from 1,500 to 6,000, used as described in Examples 9 through 12 above, there may be substituted any other polyoxyethylene glycol selected from the group consisting of polyoxyethylene glycols, having a molecular weight of from 1,500 to 6,000 and mixtures of the same.

In place of the respective liquid polyoxyethylene glycols with a molecular weight of from 200 to 800 there may be substituted any other member of the group of polyoxyethylene glycols with a molecular weight of from 200 to 800 and mixtures of the same.

In place of the specified detergent compound utilized in Examples 9 through 12 above, there may be substituted any one of the detergents of the group consisting of the alkyl sulfoesters of the formula R—COO—CH_2—CH_2—Na, wherein R is a higher alkyl group, sodium N-cyclohexyl-N-palmitoyltaurate, sodium N-fatty acid-H-methyltaurate, sodium N-methyl-N-palmitoyltaurate, sodium lauryl sulfate and mixtures of the same.

In place of the respective abrasive compound designated for the composition described in Examples 9 through 12 above, there may be substituted any other abrasive compound selected from the group consisting of kaolin, pumice and sand, and mixtures of the same, the particle size of said abrasive substance ranging from 100 to 1,000 microns.

EXAMPLE 14

When it is desired to cleanse and degerm the skin, then a sufficient quantity of compositions described in Examples 7 through 13 above, are placed in contact with the moistened skin and a foam developed by brisk rubbing. The new composition is permitted to remain in contact with the skin surface for at least one minute and then rinsed with water.

For certain purposes, as for example, for cleansing of the hands and arms of surgeons and operating room personnel prior to a surgical procedure, the cleansing process described above is conducted for a period of at least 3 minutes, with 5 minutes being a preferred skin contact time. The presence of the abrasive together with the detergent avoids the need to use a scrubbing brush or sponge in the cleansing process. Moreover, the deeper pockets of microbes as are entrapped in the pores of the skin are emptied by the abrasive cleansing. This results in a superior cleansing action that is obtained by the older methods.

The use of the liquid and semi-solid detergent abrasive iodophor-containing cleansing compositions provide a new flexibility in the cleansing of the patient's skin. Unlike bar soaps, these preparations may be used for body areas which are not readily accessible to the bar soap and at the same time providing its own brush-like action.

EXAMPLE 15

When it is desired to treat the infected acne lesion, then a suitable quantity of the new compositions described in Examples 6 through 13 above is applied to the previously moistened affected area. A copious lather is developed by brisk rubbing for a period of at least 1 minute and the suds rinsed. The procedure may be repeated, if desired. The cleansing step is conducted at least twice daily and preferably three times a day. In this manner, the removal of the comedones will be facilitated at the same time that the skin is cleansed and degermed. The full microbicidal activity of elemental iodine is possessed by these new compositions and their germicidal activity is not inhibited by the presence of pus and blood. A microbicidal effect is generally obtained within a period of 1 minute, although some resistant forms of micro-organisms may require a longer time.

After several treatments, the superficial skin layers will be found to be replaced by a new growth of healthy skin, generally not involved with the acne process. The infection, which most often accompanies the acne lesion and is responsible for the pitting and pock-marked scars of the skin, is avoided by the consistent use of the new compositions. It may be necessary on occasion to interrupt the course of therapy because the abrading process is proceeding at a much faster rate than is desired by the clinician, and this may be conveniently accomplished without basically interfering with the progressive therapeutic response.

EXAMPLE 16

One gram of nonylphenoxypoly-(ethyleneoxy)-ethanol-iodine is placed in a beaker and heated in an oven at 40° C for 30 hours. At the end of this time the available iodine of the preparation is determined by titration with standardized sodium thiosulfate test solution. The amount of available iodine is found to fall to a value of 40 per cent of its original value.

In another beaker is placed an equivalent quantity of the complexed compound formed as a result of Example 2 above, and is subjected to the same treatment. There is a recovery of about 99 per cent of the original amount of available iodine. This establishes the stability of the newly formed complexed compound.

By a similar test it was found that polyvinylpyrrolidone-iodine lost approximately 15 per cent of its available iodine, whereas the composition of claim **1** remained stable with a loss of less than 2 per cent of its pre-treatment available iodine. When the higher polyoxyethylene glycols, having a molecular weight of from 1,500 to 6,000 are used in place of the propylene glycol, glycerin or the polyoxyethylene glycols, having a molecular weight of from 200 to 1,000, then no stabilizing action as was observed with the aforesaid liquid polyhydroxy compound occurred and the same rate of the fall in the iodine level was found for the mixture as was found for the component iodophor not complexed.

When aqueous solutions containing 1 per cent of available iodine were prepared from an iodophor selected from the group consisting of polyvinylpyrrolidone-iodine, nonylphenoxylpoly-(ethyleneoxy)-ethanol-iodine and undecoyliniumchloride-iodine were stored at temperatures of 40° C for a period of one week, the pH of the solution was found to drop from approximately pH 5.5 at the start, to pH 2. In contrast to this, the heating of the new complexed liquid components prepared at the same concentration of available iodine described above, showed no fall from the original pH values which were maintained for the test period at the same temperature. When this test was repeated, utilizing a higher polyoxyethylene glycole, having a molecular weight of from 2,000 to 6,000, there was no stabilizing effect observed. In those preparations wherein the pH of the solution dropped after heating or wherein the available iodine content was lowered, a comparable increase in the iodide levels was found.

EXAMPLE 17

When it is desired to obtain a germicidal effect, then this may be accomplished by applying a formed complexed compound as described in claims **1** through **6**, directly to the surface to be degermed. The formed complexed compound exerts a germicidal action within 15 to 30 seconds on such organisms as *Staphylococcus aureus*, *Cornynebactereum diphteriae*, *Salmonella typhosa*, *Clostridium perfringens*, *Candida albicans*, *Saccharomyces carlsbergensis*, *Pseudomonas aeruginosa*, *Aerobacter aerogenes*, *Excherichia coli* at a concentration as low as 3 parts per million. Spore and other resistant forms may require a longer period of contact for germicidal action but in general these organisms will be killed within a practical time period.

What is claimed is:

1. The hydrogen-bonded compound of the formula X, wherein R is polyvinylpyrrolidone-iodine and X is a compound selected from the group consisting of propylene glycol, glycerin and polyoxyethylene glycol, having a molecular weight of from 200 to 1,000.

2. The compound of claim **1**, wherein R is a polyvinylpyrrolidone-iodine and X is propylene glycol.

3. The compound of claim **1**, wherein R is polyvinylpyrrolidone-iodine and X is glycerin.

4. The compound of claim **1**, wherein R is polyvinylpyrrolidone-iodine and X is polyoxyethylene glycol with a molecular weight of 200.

5. The compound of claim **1**, wherein R is polyvinylpyrrolidone-iodine and X is polyoxyethylene glycol with a molecular weight of 400.

6. The compound of claim **1**, wherein R is polyvinylpyrrolidone-iodine and X is polyoxyethylene glycol with a molecular weight of 600.

7. The compound of claim **1**, wherein R is polyvinylpyrrolidone-iodine and X is polyoxyethylene glycol with a molecular weight of 800.

8. The compound of claim **1**, wherein R is polyvinylpyrrolidone-iodine and X is polyoxyethylene glycol with a molecular weight of 1,000.

9. The method for preparing the composition of claim **1** comprising the steps of adding at least 1 per cent of a polyhydroxy compound containing at least two hydroxyl groups, selected from the group consisting of propylene glycol, glycerin and polyoxyethylene glycol having a molecular weight of from 200 to 1,000, to polyvinylpyrrolidone-iodine, and recovering the formed hydrogen-bonded complexed compound consisting of the polyhydroxy compound and the polyvinylpyrrolidone-iodine.

10. The process of claim **9**, said polyhydroxy compound being propylene glycol and said iodophor being polyvinylpyrrolidone-iodine.

11. The process of claim **9**, said iodophor being polyvinylpyrrolidone-iodine and said polyhydroxy compound being glycerin.

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UNITED STATES PATENT OFFICE
CERTIFICATE OF CORRECTION

Patent No. 3,671,545 Dated June 20, 1972

Inventor(s) ALFRED HALPERN

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

-- Assignee: Synergistics
Yonkers, New York 10701

Signed and sealed this 6th day of February 1973.

(SEAL)
Attest:

EDWARD M.FLETCHER,JR.
Attesting Officer

ROBERT GOTTSCHALK
Commissioner of Patents