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Warner et al.

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(54) **TOPICAL DAPSONE AND DAPSONE/ADAPLENE COMPOSITIONS AND METHODS FOR USE THEREOF**

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(65) **Prior Publication Data**

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Related U.S. Application Data

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(51) **Int. Cl.**

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A61K 31/192	(2006.01)
A61K 9/00	(2006.01)

(52) **U.S. Cl.**

CPC ***A61K 31/192*** (2013.01); ***A61K 9/0014*** (2013.01); ***A61K 31/136*** (2013.01)

(58) **Field of Classification Search**

CPC A61K 31/136; A61K 9/0014
USPC 514/646
See application file for complete search history.

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(57) **ABSTRACT**

Dapsone and dapsone/adapalene compositions can be useful for treating a variety of dermatological conditions. The compositions of this disclosure include dapsone and/or adapalene in a polymeric viscosity builder. Subject compositions can be adjusted to optimize the dermal delivery profile of dapsone to effectively treat dermatological conditions and improve the efficiency of pharmaceutical products applied to the skin. Use of the polymeric viscosity builder provides compositions with increased concentrations of diethylene glycol monoethyl ether relative to compositions without the polymeric viscosity builder.

6 Claims, 3 Drawing Sheets

Figure 1. Appearance of formulations following 4 weeks of storage

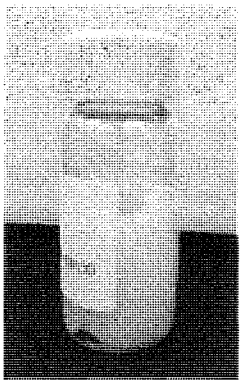
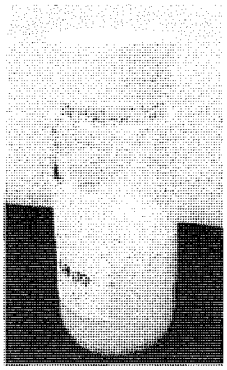
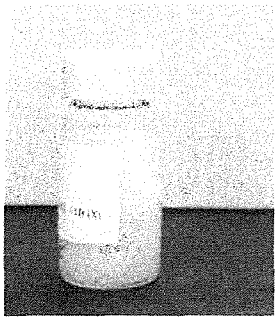
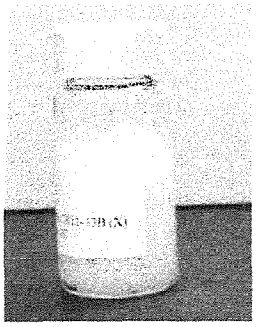
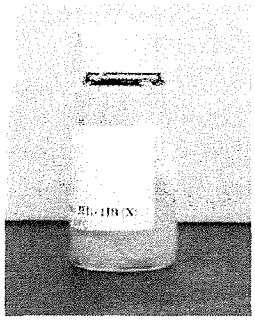
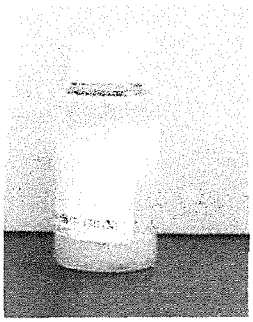
A1 at initial timepoint 	A2 at initial timepoint 
A1 after 4 weeks storage at 25^0C 	A2 after 4 weeks storage at 25^0C 
A1 after 4 weeks storage at 40^0C 	A2 after 4 weeks storage at 40^0C 

Figure 2. Polarized light images of dapsone in suspension formulations

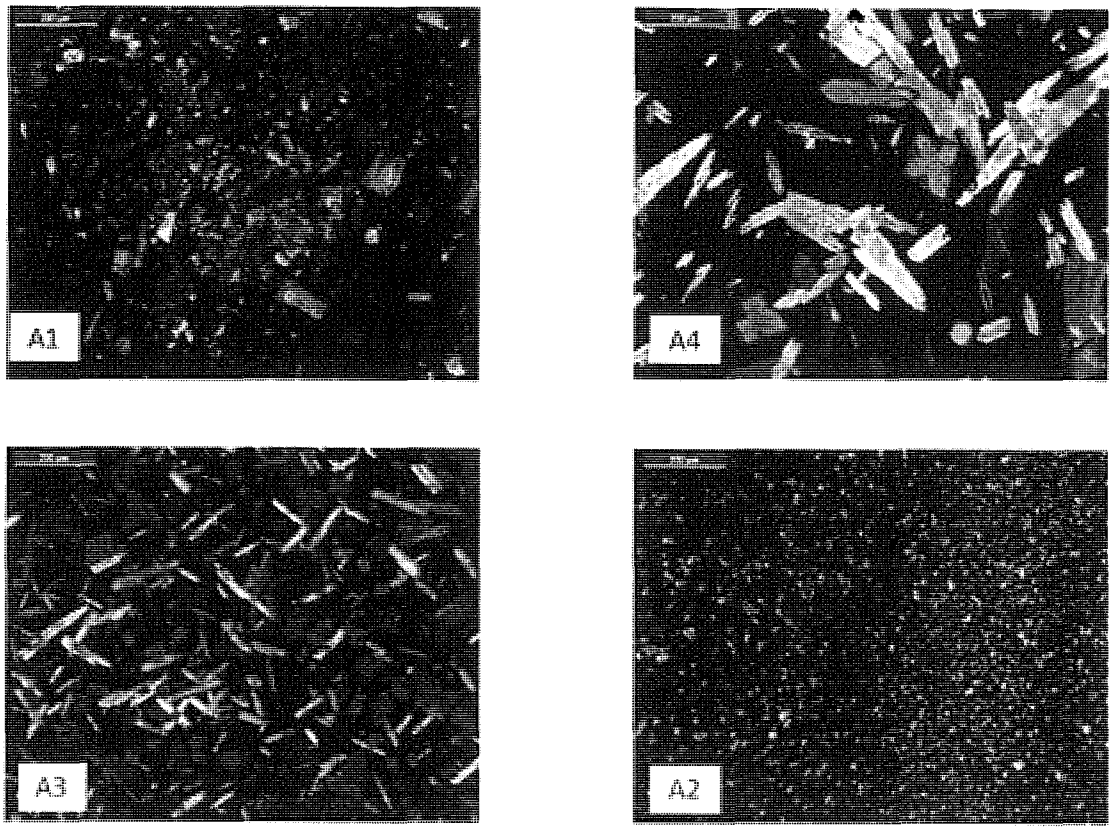
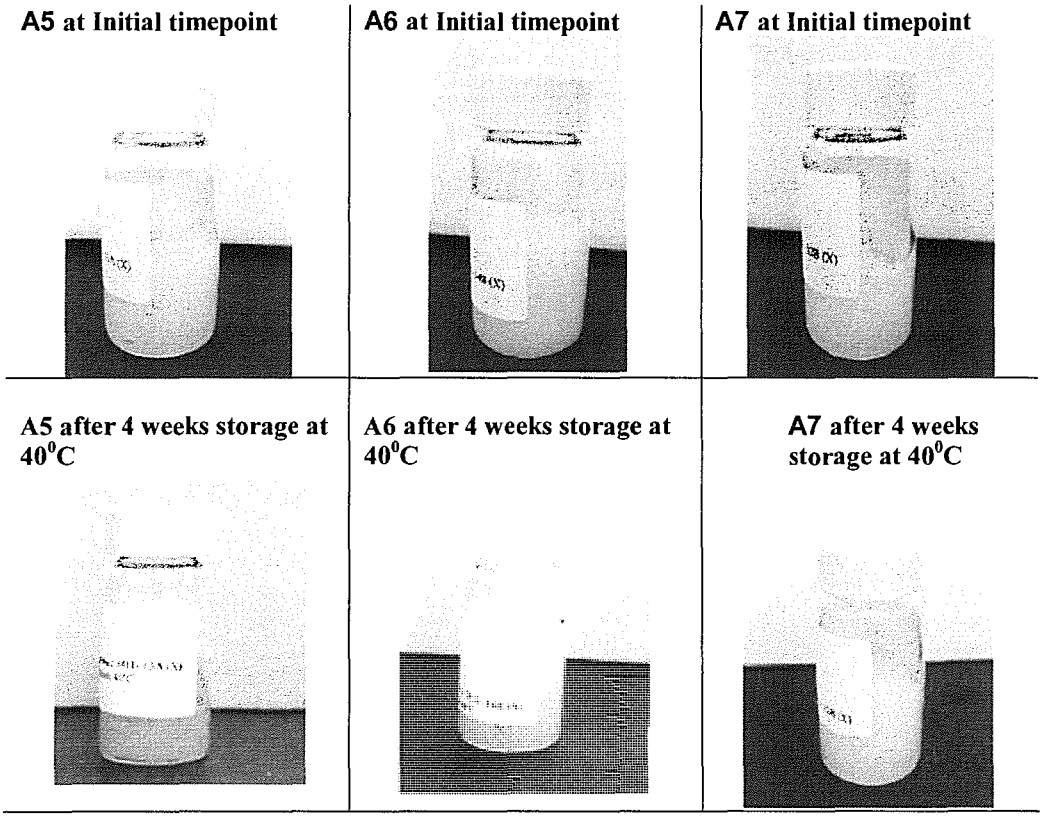


Figure 3. Appearance of formulations with antioxidants or chelating agents over 4 weeks



TOPICAL DAPSONE AND DAPSONE/ADAPLENE COMPOSITIONS AND METHODS FOR USE THEREOF

CROSS REFERENCE TO RELATED APPLICATIONS

This application claims the benefit of U.S. Provisional Application Ser. No. 61/728,403 filed on Nov. 20, 2012 and U.S. Provisional Application Ser. No. 61/770,768 filed on Feb. 28, 2013, both of which are incorporated by reference herein in their entirety.

FIELD

The present embodiments relate generally to compositions useful for treating a variety of dermatological conditions. In particular, some embodiments relate to dapsone and dapsone/adapalene compositions and methods for use thereof.

BACKGROUND

Acne is a group of common skin conditions characterized by the so-called "acneiform" or acne-like skin eruptions, which can be contaminated with bacteria, such as Propionibacterium acnes, and can also be marked by inflammation. Acne tends to occur in the areas of skin where the sebaceous glands are most active, such as the face. Acne is associated with psychological trauma, and, if left untreated, can lead to scar formation and disfigurement.

Classification and the diagnosis of various acne conditions can be complex, and even contradictory. Given this complexity and unpredictability, medication and other therapies, are often developed on a trial-and-error basis in order to determine the most effective course of treatment for a particular patient. The outcome of any particular acne treatment regimen greatly varies from patient to patient, as well as throughout treatment of a particular patient. In addition to the complexity and variability of acne conditions, treatment efficacy can be greatly affected by a patient's compliance with the treatment regimen. Patient compliance during acne treatment may be influenced by side effects, which, for topical medications, commonly include redness, itching, and skin peeling. The complexity of the drug regimen can also negatively affect patient compliance, particularly where two or more different topical medications are prescribed simultaneously. Another factor that negatively affects patient compliance is the cost of a drug regiment, which is considerably higher when multiple medications are prescribed. In some countries, acne is considered a cosmetic problem, and acne treatments are not covered by insurance plans, thus further increasing patient's treatment costs. Certain compositions for treatment of acne are available. Many of the available compositions include one active agent known to have anti-acne activity. Stability of compositions with multiple anti-acne agents can be problematic. Also, these compositions can be difficult to manufacture.

The problems described above are not confined to the treatment or acne, but are also applicable to a variety of other skin conditions, including, but not limited, to conditions or classes of conditions with complex or unknown etiology and that are difficult to classify or diagnose, in which, nevertheless, topical application of agents are known to be effective at least in some cases. Examples of such conditions or classes of conditions include psoriasis, rosacea and ichthyosis.

Accordingly, there is a continuing need for compositions

effective. The compositions and methods provided herein address these and other needs in the art.

SUMMARY

Dapsone, (4,4'-diaminodiphenyl sulfone) is a medicament possessing several beneficial medicinal activities. Dapsone is typically administered as one of the medicinal agents used in the treatment of leprosy. Dapsone and its derivatives are also effective for treatment of bacterial infections, protozoal infections such as malaria, pneumocystis carinii, and plasmonic infections such as toxoplasmosis.

Dapsone is also useful as an anti-inflammatory agent. It has been used to treat skin diseases characterized by the abnormal infiltration of neutrophils, such as Dermatitis herpetiformis, linear IgA dermatosis, pustular psoriasis, pyoderma gangrenosum, *acne vulgaris*, and Sweet's Syndrome.

Use of topical compositions of dapsone can be problematic. Topical compositions may act as drying agents for the skin. They remove essential oils and natural skin softeners from the skin thus causing it to be dry, itch and crack. Inclusion of exogeneous skin emollients, oils and the like, however, causes phase separation and precipitation of dapsone. Use of typical emulsifiers does not solve the dapsone precipitation owing to the lowered dapsone solubility and conflicting physical characteristics of the phases of the resulting composition. In particular, topical compositions including dapsone and methods are needed that would, for example, exhibit improved effectiveness, reduced side effects, or both, when used in a particular patient with a skin condition. Such improved topical compositions including dapsone and methods of their uses are also needed to improve treatment of patients with acne or suspected acne. The present dapsone and dapsone/adapalene compositions can be useful for treating a variety of dermatological conditions. Some useful compositions include dapsone and/or adapalene in a polymeric viscosity builder. Some compositions can be adjusted to optimize the dermal delivery profile of dapsone to effectively treat dermatological conditions and improve the efficiency of pharmaceutical products applied to the skin. Diethylene glycol monoethyl ether is a solubilizer for dapsone, thereby allowing compositions to be prepared with increased solubilized concentrations of dapsone. As a result, the compositions described herein are effective in treating dermatological conditions in a subject in need thereof.

Moreover, it has been found that use of a polymeric viscosity builder minimizes the intensity of yellowing of the composition caused by the increased solubility of dapsone in diethylene glycol monoethyl ether. In addition, the polymeric viscosity builder influences dapsone crystallization. This, in turn, results in compositions with improved aesthetics (i.e., reduction in particle size which minimizes "gritty" feeling upon application).

In one embodiment, there are provided compositions including dapsone, a first solubilizing agent which is diethylene glycol monoethyl ether, optionally at least one second solubilizing agent, a polymeric viscosity builder, and water, wherein the dapsone is present at a concentration of about 5% w/w to about 10% w/w.

In one embodiment, there are provided compositions including dapsone, a first solubilizing agent which is diethylene glycol monoethyl ether, optionally at least one second solubilizing agent, a polymeric viscosity builder, and water, wherein the dapsone is present at a concentration of about 3% w/w to 8% w/w.

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