Title: ANTI-HERPES VIRUS PROPERTIES OF VARIOUS FORMS OF SOPHOROLIPIDS

1. $R' = R'' = \text{Ac or H}$
2. $R' = \text{Ac}; R'' = \text{H}$
3. $R' = \text{H}; R'' = \text{Ac}$
4. $R' = R'' = \text{H}$

5. $R' = R'' = \text{Ac or H}$
6. $R' = \text{Ac}; R'' = \text{H}$
7. $R' = \text{H}; R'' = \text{Ac}$
8. $R' = R'' = \text{H}$

Abstract: A method for treating a herpes-related viral infection in a subject by administering an effective amount of at least one sophorolipid.
1

TITLE:

ANTI-HERPES VIRUS PROPERTIES OF VARIOUS FORMS OF SOPHOROLIPIDS

INVENTORS:

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STATEMENT OF RELATED APPLICATIONS:

This patent application is the Patent Cooperation Treaty international patent application based on and claiming priority on US Provisional Patent Application No. 60/780,770 having a filing date of 9 March 2006, which was filed with the United States Patent and Trademark Office and titled ANTI-HERPES VIRUS PROPERTIES OF VARIOUS FORMS OF SOPHOROLIPIDS, and which is incorporated herein in its entirety by this reference.

BACKGROUND OF THE INVENTION:

1. Technical Field.

The present invention generally relates to the technical field of compounds and methods for the treatment or prophylaxis of herpes-type virus infections. The present invention more specifically relates to the technical field of the use of sophorolipids as antiviral agents for the use in treating herpes-related viruses and virus infections.
2. Prior Art.

Members of the herpes family of viruses are known to cause a variety of disorders throughout the world. It has been shown that these viruses can create cellular disorders and are known to cause genetic and cellular anomalies. Although there are several methods and agents for treating herpes-related viruses, the inventors are not aware of any uses of sophorolipids for treating such viruses.


Existing data suggests that glycolipids may be useful in treating very severe immune disorders. For example, glycolipids have been reported to be of interest for in vivo cancer treatment/anti-tumor cell activity, treatment of autoimmune disorders, in vivo and in vitro anti-endotoxic (septic) shock activity, regulation of angiogenesis, and apoptosis induction, all by cytokine activity. See, e.g., U.S. Patent No. 5,597,573 to Massey; U.S. Patent No. 5,514,661 to Piljac; U.S. Patent No. 5,648,343 to Carlson; and the references cited in notes 9-13 of Bisht, K.S. et al., J. Org. Chem, vol. 64, pp. 780-789 (1999). However, the inventors are not aware of any work other than the inventors' work that has been carried out regarding using sophorolipids to treat herpes-related viruses.

Thus, there exists a need to develop new and improved treatments for various viral infections. It is to the development and use of sophorolipids for the
treatment of herpes-related viral infections in humans, and other similar and related purposes, that the present invention is directed.

BRIEF SUMMARY OF THE INVENTION

A crude mixture of sophorolipids was synthesized by fermentation of Candida bombicola. Lactonic sophorolipid was separated from the crude mixture and all other fractions were mixed together to form a non-lactonic sophorolipid mixture. Ethyl 17-L-[(2'-O-β-D-glucopyranosyl-β-D-glucopyranosyl)-oxy]-cis-9-octadecenoate then was synthesized and then further treated to obtain Ethyl 17-L-[(2'-O-β-D glucopyranosyl-β-D-glucopyranosyl)-oxy]-cis-9-octadecenoate 6',6''-diacetate. Methyl 17-L-[(2''-O-β-D-glucopyranosyl-β-D-glucopyranosyl)-oxy]-cis-9-octadecenoate-6''-acetate also was synthesized by adding Lipase to a solution of methyl ester, (325.4 mg) and vinyl acetate (230.9 µl) in dry THF (5 ml), and further treatment.

Epstein-Barr Virus (EBV) was used as a model organism to test the anti-herpes virus activity of sophorolipids. P3HR-1 EBV were adsorbed on Daudi lymphoid cell lines and sophorolipids added. After incubation the supernatant of the medium was assayed using ELISA method for viroid capsid antigen (VCA).

As shown in Table 1, five tested compounds displayed some degree of anti-herpes virus activity. The best activity was displayed by Ethyl 17-L-[(2'-O-β-D-glucopyranosyl-β-D-glucopyranosyl)-oxy]-cis-9-octadecenoate, which showed high activity. Accordingly, the results of the assay show that natural mixtures of lactonic, non-lactonic, ethyl, methyl esters of sophorolipids and 6',6''-diacetate ethyl sophorolipids can act as an anti-herpes virus agents.

Thus, the applications of sophorolipids in field of medicine would be tremendous to treat various infections, apart from other applications. Further, while sophorolipids can find applications in diversified fields, the present invention indicates that sophorolipids could be used as anti viral agents.
BRIEF DESCRIPTION OF THE FIGURE

FIG. 1 are representative structures of sophorolipids produced by Candida bombicola, with FIG. 1A showing lactonic sophorolipid and FIG. 1B showing open ring sophorolipid.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

General embodiments of the present invention are sophorolipids mixtures and methods of using such mixtures for the prophylaxis or treatment of humans and animals for herpes-related virus infections. One exemplary embodiment of this invention includes a method for treating a viral infection caused in a subject comprising the step of administering an effective amount of one or more sophorolipid. The term "effective amount", as used herein, includes a prophylactically effective amount and refers to an amount effective in treating or preventing a viral infection in a subject (e.g. human or animal) either as monotherapy or in combination with other agents. In one embodiment, the sophorolipid is Ethyl 17-L-[(2'-O-β-D-glucopyranosyl-β-D-glucopyranosyl)-oxy]-cis-9-octadecenoate.

1. Sophorolipid Fermentation

In one exemplary embodiment, the sophorolipids were synthesized by fermentation using Candida bombicola. The fermentation media was composed of glucose 100 g, yeast extract 10 g, urea 1 g and oleic acid 40 g in 1000 ml of water. After 7 days of fermentation, sophorolipids were extracted thrice using ethyl acetate. The extracts were pooled and the solvent therein removed. The obtained product was then washed with hexane to remove the residual fatty acids. In this embodiment, this product is considered a "crude mixture" of sophorolipid. The sophorolipid obtained then was dried in a vacuum desiccator.
2. Preparation of Lactonic sophorolipid

Column chromatographic separations were performed over silica gel 70 (Aldrich Chemical Co.) to separate lactonic sophorolipid from the crude mixture. 50 g of silica gel was used to pack a glass column (5 cm X 50 cm) in the eluent (CHCl₃/MeOH mixture, 9:1 v/v). 200 ml of eluent was run through the column before the crude mixture (dissolved in a minimal volume of eluent) was loaded onto the top of the column matrix. Different fractions were subsequently eluted (1 mL/min). Lactonic fraction was collected separately and all other fractions were mixed to form non-lactonic sophorolipid mixture.


A crude mixture of sophorolipids was synthesized by fermentation of Candida bombicola as disclosed above. Lactonic sophorolipid was separated from the crude mixture and all other fractions were mixed together to form a non-lactonic sophorolipid mixture. Ethyl 17-L-[(2'-O-β-D-glucopyranosyl-β-D-glucopyranosyl)-oxy]-cis-9-octadecenoate then was synthesized and then further treated to obtain Ethyl 17-L[(2'-O-β-D glucopyranosyl-β-D-glucopyranosyl)-oxy]-cis-9-octadecenoate 6',6''-diacetate. Methyl 17-L-[(2'-O-β-D-glucopyranosyl-β-D-glucopyranosyl)-oxy]-cis-9-octadecenoate-6''-acetate also was synthesized by adding Lipase to a solution of methyl ester, (325.4 mg) and vinyl acetate (230.9 μl) in dry THF (5 ml), and further treatment.

17-L-[(2'-O-β-D-glucopyranosyl-β-D-glucopyranosyl)-oxy]-cis-9-octadecenoate was synthesized by adding 2 g of dry crude sophorolipid and 2.5 mL of 0.021 N sodium ethoxide in ethanol solution to a 100 mL round-bottomed flask equipped with a reflux condensor. The reaction assembly was protected from atmospheric moisture by a CaCl₂ guard tube, and the mixture was refluxed for 3 hr, and cooled to room temperature (30°C). The reaction mixture was then acidified using glacial acetic acid, concentrated by rotoevaporation and poured with stirring into 100 mL of ice-cold water that resulted in the precipitation of the sophorolipid ethylester as a white solid. The precipitate was filtered, washed with ice-water, and lyophilized.
The synthesized ethyl 17-L-[(2'-O-β-D-glucopyranosyl-β-D-glucopyranosyl)-oxy]-cis-9-octadecenoate (500 mg) was dissolved in 20 mL of dry tetrahydrofuran (THF). To this solution vinyl acetate (2 mL) and Novozym 435 (1 g) were added, and the suspension was stirred magnetically at 35°C for 96 hr. The enzyme was filtered off, the solvent was evaporated, and the product was purified by column chromatography (eluent CHCl₃/MeOH, 9:1) to give 490 mg of ethyl 17-L[(2'-O-β-D glucopyranosyl-β-D-glucopyranosyl)-oxy]-cis-9-octadecenoate 6',6''-diacetate.

The synthesis of other related compounds, such as methyl- and butyl-based compounds, can be accomplished by substituting sodium methoxide or sodium butoxide, respectively, for the sodium ethoxide, resulting in sophorolipid methylester and sophorolipid butylester, respectively. The amount of dry crude sophorolipid and the amount and normality of the sodium (CH₂)₃oxide can be varied appropriately by those of ordinary skill in the art without undue experimentation. Other types of suitable sophorolipids also can be synthesized by those of ordinary skill in the art without undue experimentation.

4. Viruses

Sophorolipids appear to exhibit superior antiviral activity and acceptable cytotoxicity for use as therapeutic agents for preventing or treating viral infections. In one embodiment of the present invention, the sophorolipids can be effective against viruses of the herpes family, which includes herpes simplex virus types 1 and 2 among other viruses.

A partial list of viruses contemplated to be treatable with the compounds of the present invention includes human cytomegalovirus; human herpesvirus 6; varicella-zoster virus; Epstein-Barr virus; herpesvirus simiae; equine herpesvirus-1, 2 and 3; neurolymphomatosis (Marek's disease); influenza viruses A, B and C; parainfluenza viruses-1,2,3 and 4; adenovirus; reovirus; respiratory syncytial virus; rhinovirus; coxsackie virus; echo virus; rubeola virus; hepatitis viruses of the types B and C; papovavirus; and others.

It is contemplated that the sophorolipids also may used to treat animal viruses. Animal viruses contemplated to be treatable include bovine...
rhinotracheitis virus, bovine mammillitis virus, and cercopithecine herpesvirus 1 (B-virus), which are all simplex viruses; pseudorabies virus (PRV, of swine); equine rhinopneumonitis; coital exanthema viruses (varicellaviruses); baboon herpesvirus; pongine (chimpanzee) herpesvirus (lymphocryptovirus); Marek's disease virus (of fowl); turkey herpesvirus; herpesvirus ateles; and herpesvirus saimiri (rhadinovirus); among others.

5. **Pharmaceutical Compositions and Administration**

A preferred embodiment of this invention can be used in the pharmaceutical industries as a therapeutic agent for the treatment or prophylaxis for diseases caused by herpes-related viruses. It is appreciated that sophorolipids may exhibit antiviral activity and, in some cases, can exhibit cytotoxicity. The sophorolipids that exhibit a relatively high antiviral activity and a relatively low cytotoxicity can be optimal for such treatment or prophylaxis options. Further, it is understood that a treatment with sophorolipids can include both a prophylactic treatment and/or a disease treatment.

Preferred embodiments of the compounds and compositions of the present invention can be used in the manufacture of medicaments and in antiviral treatment of humans and other animals by administration in accordance with conventional procedures, such as an active ingredient in pharmaceutical compositions. Preferred compounds of the present invention can be provided as pharmaceutically acceptable formulations and/or "prodrugs," and pharmaceutical salts.

It is contemplated that such pharmaceutical compositions can be administered topically, orally, or parentally and may take the form of tablets, lozenges, granules, capsules, pills, ampoules or suppositories. They may also take the form of ointments, gels, pastes, creams, sprays, lotions, suspensions, solutions and emulsions of the active ingredient in aqueous or non-aqueous diluents, syrups, granulates or powders. In addition to a compound of the present invention, the pharmaceutical compositions can also contain other pharmaceutically active compounds or a plurality of compounds of the invention.
Results

Treatment of Epstein-Bar Virus (EBV) by various sophorolipids demonstrated that sophorolipids can be used to treat subjects. As EBV is a model organism, tests on EBV demonstrate the anti-herpes virus activity of sophorolipids.

The efficacy of 17-L-[(2'-O-β-D-glucopyranosyl-β-D-glucopyranosyl)-oxy]-cis-9-octadecenoate was tested in an antiviral assay conducted in Daudi cell lines (P3HR-1 EBV) derived from Burkitt’s lymphoma. More particularly, the P3HR-1 EBV were adsorbed on Daudi lymphoid cell lines and sophorolipids were added subsequently thereafter. After incubation, the supernatant of the medium was assayed using ELISA method for viroid capsid antigen (VCA). The cells were maintained at 37°C in a humidified atmosphere with 5% CO₂ in culture with RPMI-1640 medium. The cells were transferred twice weekly and cell concentration adjusted to 2 X 10⁶/ml for use.

The P3HR-1 strain of EBV was used in the screening assays. The viruses were cultured at concentration of 2 x 10⁵/ml for two weeks in medium containing 2% FCS at 34°C in a humidified atmosphere with 5% CO₂. Concentrated virus then was prepared from the supernatant of the culture by centrifugation at 12,000 g for 90 min in a sorvall centrifuge. The pellets were resuspended in RPMI-1640 medium at 1/100 of the original volume and stored at -70°C. Murine monoclonal antibody to EBV viral capsid antigen (VCA), (Chemicon International, Inc., Temecula, California) was used for ELISA assay.

The assay to be used to determine antiviral activity against EBV was through the VCA production in Daudi cells using an ELISA assay. Superinfection was initiated by the incubation of 0.5 ml of an appropriate concentration of EBV with 10⁶ cells/tube in a total of 1 ml/tube. In most cases this amounts to a multiplicity of infection (MOI) of 0.1-0.2 based on VCA induction in Daudi cells. After adsorption at 37°C for 1 hr, 3 ml of RPMI-1640 medium was added. The cells were pelleted by centrifugation and supernatants discarded.

Sophorolipids in varying concentration in 4 ml of RPMI-1640 was added to the appropriate tubes. RPMI-1640 was added to positive and negative control tubes. Daudi cells infected with P3HR-1 virus and treated with the drug were
harvested by centrifugation and washed three times with PBS. The cells were pelleted and suspended to a concentration of $4 \times 10^6$ cells/ml in PBS. 100 µl of each suspension was dispensed in triplicate into a 96-well plate, air-dried and fixed with 95% Ethanol and 5% Acetic Acid. Uninfected cells were prepared in the same manner and used as controls. After washing the plate, primary and secondary antibodies diluted in 1% bovine serum albumin containing 0.05% Tween-20 were added sequentially to each well and incubated at room temperature. Antibody additions were separated by 3 washes with PBS containing 0.005% Tween-20. O-phenyldiamine (OPD) substrate was added and the reaction stopped with 3N H$_2$SO$_4$ after ~10 min. The optical density was measured at 492 nm and the EC$_{50}$ extrapolated using a computer software program.

<table>
<thead>
<tr>
<th>Compound Name</th>
<th>Drug Unit</th>
<th>EC$_{50}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethyl ester di acetate</td>
<td>µM</td>
<td>&gt;100</td>
</tr>
<tr>
<td>Ethyl ester</td>
<td>µM</td>
<td>&lt;0.03</td>
</tr>
<tr>
<td>Di-acetate lactonic</td>
<td>µM</td>
<td>25.8</td>
</tr>
<tr>
<td>SL acid</td>
<td>µM</td>
<td>49.2</td>
</tr>
<tr>
<td>Methyl ester</td>
<td>µM</td>
<td>18.4</td>
</tr>
</tbody>
</table>

As shown in Table 1, in which the anti-herpes virus activity of various forms of sophorolipids (with results expressed as EC$_{50}$), all five tested compounds displayed some degree of anti-herpes virus activity. The best activity was displayed by Ethyl 17-L-[(2'-O-β-D-glucopyranosyl-β-D-glucopyranosyl)-oxy]-cis-9-octadecenoate, which showed high activity. Accordingly, the results of the assay show that natural mixtures of lactonic, non-lactonic, ethyl, methyl esters of sophorolipids and 6',6''-diacetate ethyl sophorolipids can act as an anti-herpes virus agents.

Thus, the invention is a method for treating a herpes-related viral infection in a subject comprising the step of administering an effective amount of at least
one sophorolipid to the subject. Preferably, the sophorolipid is 17-L-[(2'-O-β-D-glucopyranosyl- β-D-glucopyranosyl)-oxy]-cis-9-octadecenoate based and is produced by *Candida bombicola*.

In use, the at least one sophorolipid is administered to the subject in a pharmaceutically acceptable carrier. Preferably, the administration is by a method selected from the group consisting of intraperitoneal administration, intraarterial administration, and intravenous administration. Further, the sophorolipid is administered in a dose of between about 2 mg of the mixture per kilogram of the human or animal and about 30 mg of the mixture per kilogram of the human or animal.

The invention also is method for treating a herpes-related viral infection in a subject comprising the step of administering an effective amount of at least one sophorolipid to the subject, wherein the sophorolipid is produced by a process comprising the step of synthesizing the sophorolipid by fermentation of *Candida bombicola* in a fermentation media to form a natural mixture of lactonic sophorolipids and non-lactonic sophorolipids, and then utilizing the natural mixture for treatment of sepsis and septic shock in a human or animal.

Alternatively, the invention also is method for treating a herpes-related viral infection in a subject comprising the step of administering an effective amount of at least one sophorolipid to the subject, wherein the sophorolipid is produced by a process comprising the steps of:

a. synthesizing the sophorolipid by fermentation of *Candida bombicola* in a fermentation media to form a natural mixture of lactonic sophorolipids and non-lactonic sophorolipids;

b. separating the lactonic sophorolipids from the natural mixture to form a lactonic fraction and mixing all remaining fractions to form a non-lactonic fraction; and

c. utilizing the lactonic fraction for treatment of sepsis and septic shock in a human or animal.

Alternatively, the invention also is method for treating a herpes-related viral infection in a subject comprising the step of administering an effective amount of
at least one sophorolipid to the subject, wherein the sophorolipid is produced by a
process comprising the steps of:
a. synthesizing the sophorolipid by fermentation of Candida bombicola
in a fermentation media to form a natural mixture of lactonic sophorolipids and
non-lactonic sophorolipids;
b. separating the lactonic sophorolipids from the natural mixture to form
a lactonic fraction and mixing all remaining fractions to form a non-lactonic
fraction; and
c. utilizing the non-lactonic fraction for treatment of sepsis and septic
shock in a human or animal.

Preferably, the 17-L-[(2'-O-β-D-glucopyranosyl-β-D-glucopyranosyl)-oxy]-
cis-9-octadecenoate is selected from the group consisting of 17-L-[(2'-O-β-D-
glucopyranosyl-β-D-glucopyranosyl)-oxy]-cis-9-octadecenoate-6',6''-diacetate,
Hexyl 17-L[(2'-O-β-D glucopyranosyl-β-D-glucopyranosyl)-oxy]-cis-9-
octadecenoate, Ethyl 17-L[(2'-O-β-D glucopyranosyl-β-D-glucopyranosyl)-oxy]-
cis-9-octadecenoate, Butyl 17-L[(2'-O-β-D glucopyranosyl-β-D-glucopyranosyl)-oxy]-
cis-9-octadecenoate, and Methyl 17-L[(2'-O-β-D glucopyranosyl-β-D-
glucopyranosyl)-oxy]-cis-9-octadecenoate.

The invention also is a composition for prophylaxis or treatment of herpes-
related viral infection in a human or animal comprising a mixture of sophorolipids.
Preferably, the composition has the formula Ethyl 17-L-[(2'-O-β-D-
glucopyranosyl-β-D-glucopyranosyl)-oxy]-cis-9-octadecenoate.

In use, the composition preferably is mixed with a pharmaceutically
acceptable carrier. A preferred pharmaceutically acceptable carrier is selected
from the group consisting of physiologically compatible buffers, physiological
saline, a mixture consisting of saline and glucose, and heparinized sodium-citrate-
citric acid-dextrose solution. Similarly, the composition is a pharmaceutically
acceptable salt of the mixture of sophorolipids.

The foregoing detailed description of the preferred embodiments and
the appended figure has been presented only for illustrative and descriptive purposes
and are not intended to be exhaustive or to limit the scope and spirit of the invention. The embodiments were selected and described to best explain the principles of the invention and its practical applications. One skilled in the art will recognize that many variations can be made to the invention disclosed in this specification without departing from the scope and spirit of the invention.
What is claimed is:

1. A method for treating a herpes-related viral infection in a subject comprising the step of administering an effective amount of at least one sophorolipid.

2. The method as claimed in Claim 1, wherein the sophorolipid is 17-L-[(2'-O-β-D-glucopyranosyl-β-D-glucopyranosyl)-oxy]-cis-9-octadecenoate based.

3. The method as claimed in Claim 1, wherein the sophorolipid is produced by Candida bombicola.

4. The method as claimed in Claim 1, wherein the at least one sophorolipid is administered in a pharmaceutically acceptable carrier.

5. The method as claimed in Claim 1, wherein the sophorolipid is administered by a method selected from the group consisting of intraperitoneal administration, intraarterial administration, and intravenous administration.

6. The method as claimed in Claim 5, wherein the sophorolipid is administered in a dose of between about 2 mg of the mixture per kilogram of the human or animal and about 30 mg of the mixture per kilogram of the human or animal.

7. The method as claimed in Claim 1, wherein the sophorolipid is produced by a process comprising the step of synthesizing the sophorolipid by fermentation of Candida bombicola in a fermentation media to form a natural mixture of lactonic sophorolipids and non-lactonic sophorolipids, and then utilizing the natural mixture for treatment of sepsis and septic shock in a human or animal.

8. A method for treating a herpes-related viral infection in a subject comprising the step of administering an effective amount of at least one sophorolipid, wherein:

   the sophorolipid is 17-L-[(2'-O-β-D-glucopyranosyl-β-D-glucopyranosyl)-oxy]-cis-9-octadecenoate based; and

   the sophorolipid is produced by Candida bombicola.
9. The method as claimed in Claim 8, wherein the at least one
sophorolipid is administered:
in a pharmaceutically acceptable carrier; and
by a method selected from the group consisting of intraperitoneal
administration, intraarterial administration, and intravenous administration.

10. The method as claimed in Claim 8, wherein the at least one
sophorolipid is administered:
in a pharmaceutically acceptable carrier;
by a method selected from the group consisting of intraperitoneal
administration, intraarterial administration, and intravenous administration; and
in a dose of between about 2 mg of the mixture per kilogram of the human
or animal and about 30 mg of the mixture per kilogram of the human or animal.

11. The method as claimed in Claim 1, wherein the sophorolipid is
produced by a process comprising the steps of:
a. synthesizing the sophorolipid by fermentation of Candida bombicola
in a fermentation media to form a natural mixture of lactonic sophorolipids and
non-lactonic sophorolipids; and
b. separating the lactonic sophorolipids from the natural mixture to form
a lactonic fraction and mixing all remaining fractions to form a non-lactonic
fraction,
and then utilizing the lactonic fraction for treatment of sepsis and septic shock in a
human or animal.

12. The method as claimed in Claim 1, wherein the sophorolipid is
produced by a process comprising the steps of:
a. synthesizing the sophorolipid by fermentation of Candida bombicola
in a fermentation media to form a natural mixture of lactonic sophorolipids and
non-lactonic sophorolipids; and
b. separating the lactonic sophorolipids from the natural mixture to form
a lactonic fraction and mixing all remaining fractions to form a non-lactonic
fraction,
and then utilizing the non-lactonic fraction for treatment of sepsis and septic shock in a
human or animal.
13. The method as claimed in Claim 2, wherein the 17-L-[(2'-O-β-D-
  glucopyranosyl-β-D-glucopyranosyl)-oxy]-cis-9-octadecenoate is selected from
  the group consisting of 17-L-[(2'-O-β-D-glucopyranosyl-β-D-glucopyranosyl)-oxy]-
  cis-9-octadecenoate-6',6''-diacetate, Hexyl 17-L[(2'-O-β-D glucopyranosyl-β-D-
  glucopyranosyl)-oxy]-cis-9-octadecenoate, Ethyl 17-L[(2'-O-β-D glucopyranosyl-β-
  D-glucopyranosyl)-oxy]-cis-9-octadecenoate, Butyl 17-L[(2'-O-β-D glucopyranosyl-
  β-D-glucopyranosyl)-oxy]-cis-9-octadecenoate, and Methyl 17-L[(2'-O-β-D
  glucopyranosyl-β-D-glucopyranosyl)-oxy]-cis-9-octadecenoate.

14. A composition for prophylaxis or treatment of herpes-related viral
  infection in a human or animal comprising a mixture of sophorolipids.

15. The composition as claimed in Claim 14 having the formula Ethyl 17-
  L-[(2'-O-β-D-glucopyranosyl-β-D-glucopyranosyl)-oxy]-cis-9-octadecenoate.

16. The composition as claimed in Claim 14 mixed with a
  pharmaceutically acceptable carrier.

17. The composition as claimed in Claim 16, wherein the
  pharmaceutically acceptable carrier is selected from the group consisting of
  physiologically compatible buffers, physiological saline, a mixture consisting of
  saline and glucose, and heparinized sodium-citrate-citric acid-dextrose solution.

18. The composition as claimed in Claim 14, wherein composition is a
  pharmaceutically acceptable salt of the mixture of sophorolipids.
FIG. 1

A

1. \( R' = R'' = \text{Ac} \text{ or H} \\
2. \( R' = \text{Ac}; R'' = \text{H} \\
3. \( R' = \text{H}; R'' = \text{Ac} \\
4. \( R' = R'' = \text{H} \\

B

5. \( R' = R'' = \text{Ac} \text{ or H} \\
6. \( R' = \text{Ac}; R'' = \text{H} \\
7. \( R' = \text{H}; R'' = \text{Ac} \\
8. \( R' = R'' = \text{H} \\

\text{SUBSTITUTE SHEET (RULE 26)}
INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER
   IPC(8) - A61K 31/70, A61K 31/715 (2007.01)
   USPC - 514/25, 53
   According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED
   Minimum documentation searched (classification system followed by classification symbols)
   USPC: 514/25, 53

   Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
   USPC: 514/25, 53
   (text search)

   Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
   PubWEST(PGPL,USPT,USOC,EPAB,JPA); Google; PubMed
   Search terms: sophorolipid, herpes, virus, bombicola, sophorose lipid

C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<th>Category*</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
</tr>
</thead>
</table>

* Special categories of cited documents:
   "A" document defining the general state of the art which is not considered to be of particular relevance
   "E" earlier application or patent but published on or after the international filing date
   "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
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   "P" document published prior to the international filing date but later than the priority date claimed
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   "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
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   "Z" document member of the same patent family

Date of the actual completion of the international search
26 August 2007 (26.08.2007)

Date of mailing of the international search report
18 OCT 2007

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Authorized officer: Lee W. Young
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PCT OSP: 571-272-7774

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