

sents lower alkyl, OH, NH₂, NHR⁴, or NR⁵R⁶ wherein R⁴, R⁵ and R⁶ independently are lower alkyl or cycloalkyl and n is an integer of from 2 to 4, with the provision that when X is CH₂, Y is OH or NH-(CH₂)_n-OH, and pharmacologically acceptable salts thereof. Said compounds are said to be useful for preventing and/or treating autoimmune diseases.

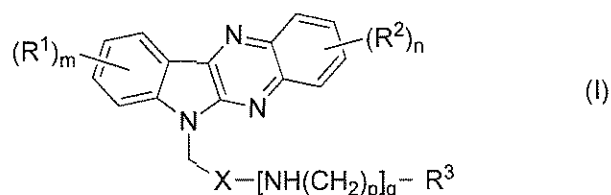
- 5 Some indoloquinolines also have been described for use as antiviral substances. Thus, in WO87/04436 the antiviral effect of a number of indoloquinolines, e.g. 2,3-dimethyl-6-(N,N-dimethylaminoethyl)-6H-indolo(2,3-b)quinoline (B-220), against herpes simplex virus of both type 1 and 2 is shown.

- 10 WO 2012/110631 discloses a pharmaceutical composition for topical administration comprising B-220 or a pharmaceutically acceptable salt thereof in a pharmaceutically acceptable carrier. The composition is useful for the treatment of herpes virus infections of the skin or mucous membranes in a mammal subject.

There however still remains a need for effective drugs and methods of treatment for primary as well as recurrent herpes infections.

15 SUMMARY OF THE INVENTION

According to a first aspect, a compound is provided according to formula (I)



wherein

m is an integer of from 0 to 4;

- 20 n is an integer of from 0 to 4;

p is an integer of from 1 to 4;

q is 0 or 1;

X is C=O, C=S or CH₂;

each R¹ is independently selected from halogen, C1-C6 alkyl, C2-C6 alkenyl, C2-C6 alkynyl, C3-C6 cycloalkyl, C1-C6 alkoxy, C2-C6 alkenyloxy, C2-C6 alkynyloxy, C3-C6 cycloalkyloxy, and OH, any alkyl, alkenyl, alkynyl or cycloalkyl optionally being substituted by at least one halogen;

each R² is independently selected from halogen, C1-C6 alkyl, C2-C6 alkenyl, C2-C6 alkynyl, C3-C6 cycloalkyl, C1-C6 alkoxy, C2-C6 alkenyloxy, C2-C6 alkynyloxy, C3-C6 cycloalkyloxy, and OH, any alkyl, alkenyl, alkynyl or cycloalkyl optionally being substituted by at least one halogen;

10 R³ is OH, NH₂, NHR⁴, NR⁴R⁵, or (NR⁴R⁵R⁶)⁺Y⁻;

R⁴ is selected from C1-C6 alkyl;

R⁵ is selected from C1-C6 alkyl;

R⁶ is selected from C1-C6 alkyl, optionally substituted with a halogen or OH; C2-C6 alkenyl; and C2-C6 alkynyl;

15 Y is a pharmaceutically acceptable anion;

and pharmaceutically acceptable salts thereof;

with the proviso that if X is CH₂ and q is 0, R³ is OH or (NR³R⁴R⁵)⁺Y⁻,

for use in the treatment of a herpes viral infection.

20 In one particular embodiment, a compound of formula (I) is provided for topical administration to a mammal subject suffering from a primary or recurrent herpes virus infection, especially of oral-facial type.

According to a further aspect, the use of a compound as defined herein above is provided, for the manufacture of a medicament for use in the treatment of a herpes viral infection.

In one embodiment, if X is CH₂ and q is 0, then R³ is (NR³R⁴R⁵)⁺Y⁻.

R^6 is selected from C1-C6 alkyl, optionally substituted with a halogen or OH; C2-C6 alkenyl; and C2-C6 alkynyl;

Y is a pharmaceutically acceptable anion;

and pharmaceutically acceptable salts thereof;

- 5 with the proviso if R^3 is different from $(NR^3R^4R^5)^+Y^-$, X is C=S.

According to a still further aspect a pharmaceutical composition is provided comprising a compound according to formula (I) as defined herein above, with the proviso if R^3 is different from $(NR^3R^4R^5)^+Y^-$, X is C=S, in association with at least one pharmaceutically acceptable excipient.

- 10 In another aspect, there is provided a compound according to formula (I) as defined herein above, with the proviso if R^3 is different from $(NR^3R^4R^5)^+Y^-$, X is C=S, for use in therapy.

In another aspect, there is provided a patch, stick, spray dispenser, tube, or pen containing a pharmaceutical composition comprising a compound according to formula (I) as defined herein above, with the proviso if R^3 is different from $(NR^3R^4R^5)^+Y^-$, X is C=S.

- 15 In one embodiment, the pharmaceutical composition is an antiviral composition suitable for the treatment of a viral infection, e.g. a herpes viral infection.

In one particular embodiment, the composition of the ~~invention~~disclosure is useful for topical administration to a mammal subject suffering from a primary or recurrent herpes virus infection, especially of oral-facial type.

- 20 In one embodiment, the pharmaceutical composition of the ~~invention~~disclosure additionally comprises at least one additional therapeutically active ingredient suitable for topical administration.

According to one ~~aspect~~embodiment, the ~~invention-disclosure~~ relates to a compound of formula (I) as defined herein, or a pharmaceutically acceptable salt thereof, for use in the treatment of herpes virus infections of the skin or mucous membranes in a mammal subject by
5 topical administration of a therapeutically effective dose thereof to the skin and/or mucous membrane of the mammal subject.

According to another ~~aspect~~embodiment, the ~~invention-disclosure~~ relates to a method of prophylactic and/or curative treatment of herpes virus infections of the skin or mucous membranes in a mammal subject comprising topical administration of a therapeutically effective
10 dose of a compound of formula (I) as defined herein or a pharmaceutically acceptable salt thereof.

In one embodiment, the method also comprises topical administration, in combination or in sequence, of at least one additional pharmaceutically active ingredient suitable for topical administration, e.g. selected from antiviral agents, antibiotics, anaesthetic agents, analgesic agents, antiphlogistic agents, and anti-inflammatory agents.

5 | ~~Further aspects-embodiments of the invention-disclosure as well as embodiments thereof~~ are described herein below and as defined in the claims.

BRIEF DESCRIPTION OF THE DRAWING

Figure 1 is a bar graph showing the viral titer as $\log_{10}$ PFU/ml in HSV-1 infected in THCEC cells treated with inventive compounds, and with Acyclovir, respectively.

10 DETAILED DESCRIPTION OF THE INVENTION

In the following the description, any reference to a compound of formula (I) also should be construed as a reference to a compound of any of the embodiments thereof, e.g. as represented by formulas (Ia)-(Is), unless otherwise indicated or apparent from the context.

15 Furthermore, unless otherwise indicated or apparent from the context, the following definitions shall apply throughout the specification and the appended claims.

“Pharmaceutically acceptable” means being useful in preparing a pharmaceutical composition that is generally safe, non-toxic and neither biologically nor otherwise undesirable and includes being useful for veterinary use as well as human pharmaceutical use.

20 “Treatment” as used herein includes prophylaxis of the named disorder or condition, or amelioration or elimination of the disorder once it has been established.

“An effective amount” refers to an amount of a compound that confers a therapeutic effect on the treated subject. The therapeutic effect may be objective (i.e., measurable by some test or marker) or subjective (i.e., subject gives an indication of or feels an effect).

25 Unless otherwise stated or indicated, the term “C₁₋₆ alkyl” denotes a straight or branched alkyl group having from 1 to 6 carbon atoms. Examples of such C₁₋₆ alkyl according to the

37. The pharmaceutical composition according to any one of the claims 33-36, wherein the additional therapeutically active agent is present in an amount of 0.005-5% (w/w).

5 38. The pharmaceutical composition according to any of claims 30-37, for use in the prophylaxis and/or treatment of a herpes virus infection in a mammal subject.

39. The pharmaceutical composition according to any one of the claims 30-38, for dermal or mucosal treatment.

10 40. The pharmaceutical composition according to any one of the claims 30-39, in the form of a cream, liquid, lotion, gel, spray, foam or ointment.

41. A patch, stick, spray dispenser, tube, or pen containing a pharmaceutical composition according to any one of the claims 30-40.

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42. ~~A method of treatment of a herpes virus infection by administration of a therapeutically effective amount of a compound according to any one of the claims 1 to 9 or 19 to 27, to a mammal in need of such treatment.~~ The use of a compound according to any one of the claims 1 to 9 or 19 to 27 in the manufacture of a medicament for treatment of a herpes virus
20 infection.