The present invention relates to methods and compositions for modifying mucous membranes. In particular, the present invention relates to treating diseases associated with mucous membranes by changing the intrinsic chemical composition and/or physical features of a target mucous membrane.
INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER

<table>
<thead>
<tr>
<th>IPC(8)</th>
<th>USPC</th>
<th>CPC</th>
</tr>
</thead>
<tbody>
<tr>
<td>A61 K 31/66 (2014.01)</td>
<td>514/121</td>
<td>A61K 31/66 (2014.1)</td>
</tr>
</tbody>
</table>

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)

<table>
<thead>
<tr>
<th>IPC(8)</th>
<th>USPC</th>
<th>CPC</th>
</tr>
</thead>
<tbody>
<tr>
<td>A61 K 31/66 (2014.01)</td>
<td>514/121</td>
<td>A61K 31/66 (2014.1)</td>
</tr>
</tbody>
</table>

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

USPC - 514/121 (keyword delimited)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

PatBase, Orbit, STN, Google Patents, PubChem Google Scholar

Search terms used: mucus*, mucous*, mucin*, mucin, reduc*, TCEP, carboxymethyl, phosphine, viscosity, rheology, tear, lacrima*

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>
<tbody>
<tr>
<td>Y</td>
<td>US 2009/0010914 A1 (TAYLOR et al) 08 January 2009 (08.01.2009) entire document</td>
<td>1-5, 7-9, 22, 23, 26, 27, 64</td>
</tr>
<tr>
<td>Y</td>
<td>WO 2008/067403 A2 (TILL et al) 05 June 2008 (05.06.2008) entire document</td>
<td>1-5, 7-9, 22, 23, 26, 27, 64</td>
</tr>
</tbody>
</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)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"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

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search: 29 December 2014

Date of mailing of the international search report: 14 JAN 2015

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US, Commissioner for Patents
PO. Box 1450, Alexandria, Virginia 22313-1450
Facsimile No. 571-273-3201

Authorized officer: Blaine R. Copenheaver

Form PCT/ISA/210 (second sheet) (July 2009)
INTERNATIONAL SEARCH REPORT

INTERNATIONAL application No.
PCT/US2014/048391

Box No. II  Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.: because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☑ Claims Nos.: 28-63 because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III  Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

See Extra Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☑ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-5, 7-8, 19-27, 64

Remark on Protest

☐ The additional search fees were accompanied by the applicant’s protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant’s protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

Form PCT/ISA/210 (continuation of first sheet (2)) (July 2009)
This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees need to be paid.

Group I: Claims 1-27 and 64 are drawn to a composition for modifying a mucous membrane.

Group II: Claims 65-69 are drawn to a method comprising applying a sensitizing agent to a mucous membrane and then irradiating said mucous membrane to activate said sensitizing agent.

The first invention of Group I is restricted to a composition for modifying a mucous membrane comprising a first agent that physically interacts or reacts with one or more components of said mucous membrane and/or its intimately associated adherent thin film and a physiologically acceptable carrier; wherein said component is an aqueous component; wherein said first agent is selected from the group consisting of reducing agents; and wherein said reducing agent is TCEP. It is believed that claims 1-5, 7-9, 19-27, and 64 read on this first named invention and thus these claims will be searched without fee to the extent that they read on the above embodiment.

Applicant is invited to elect additional formula(e) for each additional compound to be searched in a specific combination by paying an additional fee for each set of election. An exemplary election would be a composition for modifying a mucous membrane comprising a first agent that physically interacts or reacts with one or more components of said mucous membrane and/or its intimately associated adherent thin film and a physiologically acceptable carrier; wherein said component is a lipid component; wherein said first agent is selected from the group consisting of reducing agents; and wherein said reducing agent is TCEP. Additional formula(e) will be searched upon the payment of additional fees. Applicants must specify the claims which read on any additional elected inventions. Applicants must further indicate, if applicable, the claims which read on the first named invention if different than what was indicated above for this group. Failure to clearly identify how any paid additional invention fees are to be applied to the "+" group(s) will result in only the first claimed invention to be searched/examined.

The inventions listed in Groups I+ and II do not relate to a single general inventive concept under PCT Rule 13.1, because under PCT Rule 13.2 they lack the same or corresponding special technical features for the following reasons:

The special technical features of Group I+, compositions for modifying a mucous membrane, are not present in Group II; and the special technical features of Group II, methods comprising applying a sensitizing agent to a mucous membrane, are not present in Group I+.

The Groups I+ compositions do not share a significant structural element, requiring the selection of alternatives for the first agent that interacts or reacts with one or more components of said mucous membrane.

The Groups I+ and II share the technical features of a composition for modifying a mucous membrane comprising a first agent that physically interacts or reacts with one or more components of said mucous membrane and/or its intimately associated adherent thin film and a physiologically acceptable carrier; and a topical administration formulation comprising the composition thereof, wherein said composition is provided as a formulation selected from the group consisting of a dissolvable plug, drop, a spray, a solution, a suspension, a cream, a lotion and an ointment. However, these shared technical features do not represent a contribution over the prior art.

Specifically, US 2008/0317765 A1 to Izraeli et al. teach a composition for modifying a mucous membrane comprising a first agent that physically interacts or reacts with one or more components of said mucous membrane and/or its intimately associated adherent thin film (Para. [0006]; Para. [0078]; Para. [0023]) and a physiologically acceptable carrier (Para. [0050], ...the compositions of the present invention may further comprise one or more of a variety of agents such as for example pH adjusters, carriers, excipients, diluents, antibiotics, antioxidants, vehicles...); and a topical administration formulation comprising the composition thereof, wherein said composition is provided as a formulation selected from the group consisting of a dissolvable plug, drop, a spray, a solution, a suspension, a cream, a lotion and an ointment (Para. [0106], pharmaceutical composition of the present invention may be formulated in the form of suppositories, tablets, films, patches, and gels for oral, buccal, nasal, ocular, and topical routes; as well as spray formulations, drops, dry powder, suspensions and the like).

The inventions listed in Groups I+ and II therefore lack unity under Rule 13 because they do not share a same or corresponding special technical feature.