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(54) **Title:** ARTIFICIAL TEAR, CONTACT LENS AND DRUG VEHICLE COMPOSITIONS AND METHODS OF USE THEREOF

(57) **Abstract:** The invention provides artificial tear compositions, artificial tear-gel compositions, contact lens storage compositions, contact lens treatment compositions, ophthalmological drug vehicle compositions and topical drug vehicle compositions comprising one or more nonionic surfactants with one or more non-Newtonian viscosity enhancing excipients and one or more of a polyol and or an electrolyte and methods of their use.

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 19/51825

A. CLASSIFICATION OF SUBJECT MATTER

IPC - C09K 3/00 (2019.01)

CPC - A61K 2300/00, A61K 9/08, A61K 9/0048, A61K 31/724, A61K 47/02, A61K 31/765, A61K 31/715, A61K 47/10, A61K 47/26, A61K 47/38, A61K 47/40, C11D 1/825, C11D 3/222, A61K 47/183

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)
See Search History document

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

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2018/0098937 A1 (PS THERAPIES LTD) 12 April 2018 (12.04.2018) the entire document, and more specifically: para [0001]-[0002], [0006], [0009], [0024], [0036], [0089], [0019], [0096], [0115], [0130]-[0131], [0141], [0150], [0161], [0165]-[0191], [0489]; claims 21 and 31	1-14, 19 and 26, 27a, 27b and 28-36
A	US 2014/0377210 A1 (GNT, LLC) 25 December 2014 (25.12.2014); the entire document	1-14, 19 and 26, 27a, 27b and 28-36
A	US 8,597,629 B1 (GNT, LLC) 03 December 2013 (03.12.2013); the entire document	1-14, 19 and 26, 27a, 27b and 28-36
A	US 2004/0097592 A1 (MORISHIMA et al.) 20 May 2004 (20.05.2004); the entire document	1-14, 19 and 26, 27a, 27b and 28-36
A	US 2016/0213609 A1 (BAUSCH & LOMB INCORPORATED) 28 July 2016 (28.07.2016); the entire document	1-14, 19 and 26, 27a, 27b and 28-36

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"D" document cited by the applicant in the international application
"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	Date of mailing of the international search report
17 December 2019	27 JAN 2020
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-8300	Authorized officer Lee Young Telephone No. PCT Helpdesk: 571-272-4300

Form PCT/ISA/210 (second sheet) (July 2019)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 19/51825

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.:
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:
his 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 searched, the appropriate additional search fees must be paid.

Group I: Claims 1-14, 19 and 26-36, directed to an artificial tear composition.

Group II: Claims 15-18 and 20-25, directed to an ophthalmological drug composition

Group III: Claims 37-38, directed to a method of reducing biofilm formation.

The inventions listed as Groups I-III 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:

please see the continuation at the end of this form

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.:
1-14, 19 and 26, 27a, 27b and 28-36

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.

continuation of Box III (lack of unity))

Special Technical Features:

Group I requires an artificial tear composition, not required by groups II-III.

Group II requires an ophthalmological drug, not required by groups I and III.

Group III requires a method of reducing biofilm formation comprising applying a composition comprising one or more nonionic surfactants and one or more viscosity enhancers, not required by groups I-II.

Common Technical Features:

Groups I and II share the technical feature of a composition comprising: polysorbate 80; poloxamer 407; poloxamer 188; polyoxyl castor oil; hydroxypropyl gamma cyclodextrin; carboxymethyl cellulose; polyethylene glycol 400; mannitol; magnesium chloride; sodium chloride; menthol; phosphate buffer and citrate buffer; sorbate; the composition has a pH; and wherein w/v denotes weight by volume of the total composition.

However, these shared technical features do not represent a contribution over prior art, because the shared technical feature is being obvious over US 2010/0249062 A1 to Matsumura et al. (hereinafter Matsumura), in view of US 2016/0206599 A1 to PanOptica, Inc. (hereinafter PanOptica). Matsumura teaches a composition (abstract; The present invention provides an ophthalmic composition.) comprising: polysorbate 80 (para [0045]; The nonionic surfactant used in the present invention can include the surfactants which can be applied to an ophthalmic composition for contact lens by those skilled in the art, for example, polysorbate 80.); carboxymethyl cellulose (para [0031]-[0032]; The wetting solution-eye drops for contact lenses of the present invention comprises one or more compounds selected from the group consisting of a cellulose-based polymer. Typical examples of the cellulose-based polymer include hydroxypropylmethyl cellulose, carboxymethyl cellulose and salts thereof.); polyethylene glycol 400 (para [0031], [0038]; The wetting solution-eye drops for contact lenses of the present invention comprises one or more compounds selected from the group consisting of polyethylene glycol. The weight-average molecular weight of the polyethylene glycol may be about 100 to 50,000, and preferably about 400 to 20,000.); mannitol (para [0068], [0071]; Also, the wetting solution-eye drops for contact lenses of the present invention may contain one or more kinds of various components or additives appropriately selected according to a conventional method, depending on the use or the form so long as the effects of the present invention are not impaired. These components or additives include sugar alcohols, for example, xylitol, sorbitol, mannitol.); magnesium chloride (para [0068], [0076]; Also, the wetting solution-eye drops for contact lenses of the present invention may contain one or more kinds of various components or additives appropriately selected according to a conventional method, depending on the use or the form so long as the effects of the present invention are not impaired. These components or additives include tonicity agents, for example, magnesium chloride.); sodium chloride (para [0051]; Preferably, the wetting solution-eye drops for contact lenses of the present invention comprises an appropriate inorganic salt, if desired. The inorganic salts include sodium chloride.); menthol (para [0068], [0078]; Also, the wetting solution-eye drops for contact lenses of the present invention may contain one or more kinds of various components or additives appropriately selected according to a conventional method, depending on the use or the form so long as the effects of the present invention are not impaired. These components or additives include flavors, for example, menthol.); phosphate buffer and citrate buffer (para [0048]; Preferably, the wetting solution-eye drops for contact lenses of the present invention comprises appropriate buffering agents, if desired. The buffering agents used in the present invention include citrate buffering agent and phosphate buffering agent.); sorbate (para [0068], [0074]; Also, the wetting solution-eye drops for contact lenses of the present invention may contain one or more kinds of various components or additives appropriately selected according to a conventional method, depending on the use or the form so long as the effects of the present invention are not impaired. These components or additives include preservatives, disinfectants or antibacterial drugs, for example, potassium sorbate.); the composition has a pH (para [0082]; The pH of the wetting solution-eye drops for contact lenses of the present invention is adjusted to a value within the range to make the solution of the present invention applicable to human body, if desired. The pH is usually 4.0 to 9.0, preferably 5.0 to 8.5, particularly preferably 5.5 to 8.5.); and wherein w/v denotes weight by total volume of the composition (para [0024]; The term % as used herein represents w/v %, that is, the weight (g) of each component (solute) dissolved in 100 mL of solution unless otherwise indicated.).

Furthermore, Matsumura teaches that the present invention may comprise an appropriate nonionic surfactant, such as poloxamer 407, poloxamer 188, or polyoxyl castor oil. Matsumura though does not teach that the composition comprises poloxamer 407, poloxamer 188, and polyoxyl castor oil. However, it would have been obvious to one ordinary skilled in the art to utilize one or several of the non-ionic surfactants that Matsumura discloses, with routine experimentation; such as for example: the composition comprises poloxamer 407, poloxamer 188, and polyoxyl castor oil; in order to provide an ophthalmic composition which stabilizes the tear film during wearing contact lens, prevents eye dryness, imparts a favorable sensation in using, is highly convenient with no risk of misuse and shows a high efficiency in the course from manufacturing to sales (abstract). Furthermore, Matsumura does not teach hydroxypropyl gamma cyclodextrin. PanOptica, on the other hand, teaches hydroxypropyl gamma cyclodextrin (para [0048]; In some embodiments, the solubilizing agent in the formulation may be hydroxypropyl gamma cyclodextrin.). Therefore, it would have been obvious to one ordinary skilled in the art to utilize hydroxypropyl gamma cyclodextrin, as taught by PanOptica; with the composition that Matsumura teaches; because hydroxypropyl gamma cyclodextrin is a solubilizing agent (PanOptica; para [0048]); and because an ideal disclosed compound for use in ophthalmic solutions/suspensions should be soluble and/or miscible in aqueous media at normal ocular pH and tonicity (PanOptica; para [0259]).

Groups I, II and III share the technical feature of a composition comprising one or more nonionic surfactants and one or more viscosity enhancers. However, these shared technical features do not represent a contribution over prior art, because the shared technical feature is being anticipated by Matsumura. Matsumura teaches a composition comprising one nonionic surfactant (abstract; para [0044]-[0045]; The present invention provides an ophthalmic composition. In addition, the wetting solution-eye drops for contact lenses of the present invention may comprise an appropriate nonionic surfactant, such as polysorbate 80.); and one or more viscosity enhancers (para [0031]-[0032]; The wetting solution-eye drops for contact lenses of the present invention comprises one or more compounds selected from the group consisting of a cellulose-based polymer. Typical examples of the cellulose-based polymer include hydroxypropylmethyl cellulose, carboxymethyl cellulose and salts thereof.).

As the shared technical features were known in the art at the time of the invention, they cannot be considered common technical features that would otherwise unify the groups. Therefore, Groups I-III lack unity under PCT Rule 13.