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(54) Title: SYNTHETIC NEUROMODULATORY PEPTIDES

(57) Abstract: A pharmaceutical composition comprising a synthetic neuromodulatory peptide is described. The invention discloses neuromodulatory peptides as defined in the claims and methods of using such molecules for therapeutic application. The neuromodulatory peptides included in the composition have been found to be effective in treatment of depression and other mood disorders, including anxiety.



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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 20/22623

A. CLASSIFICATION OF SUBJECT MATTER

IPC - C07K 5/10, A61K 38/08, A61P 25/28, A61P 3/06, C07K 7/64 (2020.01)

CPC - C07K 5/0202, C07K 5/0205, C07K 5/1008, C07K 5/06156, C07K 5/0808, C07K 5/06043, A61K 38/00

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.
A	WO 2000/108285 A1 (SNOW BRAND MILK PROD CO LTD.[JP]) 12 September 2008 (12.09.2008) claims 1-4, SEQ ID NO: 22	1, 2, 5, 7-9, 12, 14, 16, 20, 22, 23, 26, 28-32, (41-43)/(1,2,5,7-9,12,14,16,20,22,23,26,28-32), 45, 46, 49, 52-54, 57, 59, 60, (63-65)/(45,46,49,52-54,57,59,60)
A	JPH 05194254 A (BANYU PHARMA CO LTD) 03 August 1993 (03.08.1993) Disclosure, Machine Translation, In 2 to In 3	1, 2, 5, 7-9, 12, 14, 16, 20, 22, 23, 26, 28-32, (41-43)/(1,2,5,7-9,12,14,16,20,22,23,26,28-32), 45, 46, 49, 52-54, 57, 59, 60, (63-65)/(45,46,49,52-54,57,59,60)

Further documents are listed in the continuation of Box C.

See patent family annex.

* Special categories of cited documents:	"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
"A" document defining the general state of the art which is not considered to be of particular relevance	"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
"D" document cited by the applicant in the international application	"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
"E" earlier application or patent but published on or after the international filing date	"&" document member of the same patent family
"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	

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 20/22623

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.: 44, 66-98  
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:

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.

\*\*\*\*\* See Supplemental Sheet to continue \*\*\*\*\*

- 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, 2, 5, 7-9, 12, 14, 16, 20, 22, 23,26, 28-32, (41-43)/(1,2,5,7-9,12,14,16,20,22,23,26,28-32), 45, 46, 49, 52-54, 57, 59, 60, (63-65)/(45,46,49,52-54,57,59,60), restricted to R1 is W, R2 is D, R3 is Q, R

- 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.

INTERNATIONAL SEARCH REPORT  
Information on patent family members

International application No.

PCT/US 20/22623

In Continuation of Box III. Observations where unity of invention is lacking:

Group I+, claims 1-43, 45-65, directed to a composition comprising a synthetic neuromodulatory tetrapeptide of formula (I) or formula (Ia). The composition will be searched to the extent that the tetrapeptide encompasses R1 is W, R2 is D, R3 is Q, R4 is V, i.e., SEQ ID NO: 14 (Trp-Asp-Gln-Val) (NOTE: the first claimed invention is the tetrapeptide wherein R1 is W, R2 is D, R3 is N, R4 is V. However, the amino acid sequence Trp-Asp-Asn-Val is not disclosed in either the Sequence Listing or instant specification, and therefore cannot be searched). It is believed that claims 1, 2, 5, 7-9, 12, 14, 16, 20, 22, 23, 26, 28-32, (41-43)/(1,2,5,7-9,12,14,16,20,22,23,26,28-32), 45, 46, 49, 52-54, 57, 59, 60, (63-65)/(45,46,49,52-54,57,59,60) encompass this first named invention, and thus these claims will be searched without fee to the extent that the tetrapeptide encompasses R1 is W, R2 is D, R3 is Q, R4 is V, i.e., SEQ ID NO: 14. Additional tetrapeptide(s) will be searched upon the payment of additional fees. Applicants must specify the claims that encompass any additionally elected tetrapeptide(s). Applicants must further indicate, if applicable, the claims which encompass 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. An exemplary election would be tetrapeptide wherein R1 is F, R2 is Q, R3 is S, R4 is E, SEQ ID NO: 10, i.e., claims 1, 3, 5, 6, 8, 10, 12, 14, 17, 22, 24, 27, 33-36, (41-43)/(1,3,5,6,8,10,12,14,17,22,24,27,33-36), 45, 47-50, 52, 53, 55, 58, 59, 61, (63-65)/(45,47-50,52,53,55,58,59,61).

The inventions listed as Group I+ do not relate to a single special technical feature 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 feature of some inventions of Group I+ is a specific tetrapeptide recited therein.

The inventions of Group I+ share the technical features of a composition comprising a synthetic neuromodulatory tetrapeptide of formula (I). Some inventions of Group I+ share the technical features of a composition comprising a synthetic neuromodulatory tetrapeptide of formula (Ia). However, these shared technical features do not represent an improvement over prior art as being obvious over WO 2008/108285 A1 to SNOW BRAND MILK PROD CO LTD.[JP] (12 September 2008) (hereinafter "SNOWBRAND").

SNOWBRAND discloses a synthetic tetrapeptide of formula (I) or formula (Ia) wherein R1 is F, R2 is Q, R3 is S, R4 is E (claim 1, SEQ ID NO: 22, Phe-Gln-Ser-Glu).

SNOWBRAND discloses "[a] food, beverage or feed for inhibiting hepatic dysfunction containing the peptide according to any one of Claims 1 to 3" (claim 4), but does not specifically disclose a composition comprising said peptide Phe-Gln-Ser-Glu (SEQ ID NO: 22). However, it would have been obvious to one of ordinary skill in the art how to select an optimal hepatic dysfunction inhibitor (claim 3) among the 28 peptidic inhibitors disclosed by SNOWBRAND.

SNOWBRAND does not specifically disclose that said peptide Phe-Gln-Ser-Glu (SEQ ID NO: 22) is a neuromodulatory tetrapeptide. However, said limitation is met by/inherently present in SNOWBRAND as follows:

Per Applicant, peptide Phe-Gln-Ser-Glu, i.e., the peptide disclosed by Applicant as SEQ ID NO: 10, is a neuromodulatory tetrapeptide (instant application, claims 33-36, 61). As SNOWBRAND discloses the tetrapeptide of the identical chemical structure, SNOWBRAND necessarily discloses the claimed characteristic or function.

As the technical features would have been obvious to one of ordinary skill in the art at the time of the invention, they cannot be considered special technical features that would otherwise unify the inventions.

Therefore, Groups I+ lack unity under PCT Rule 13 because they do not share a same or corresponding technical feature.