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25 June 2009

(54) Title: STABILIZING PROTEINS USING IONIC LIQUIDS

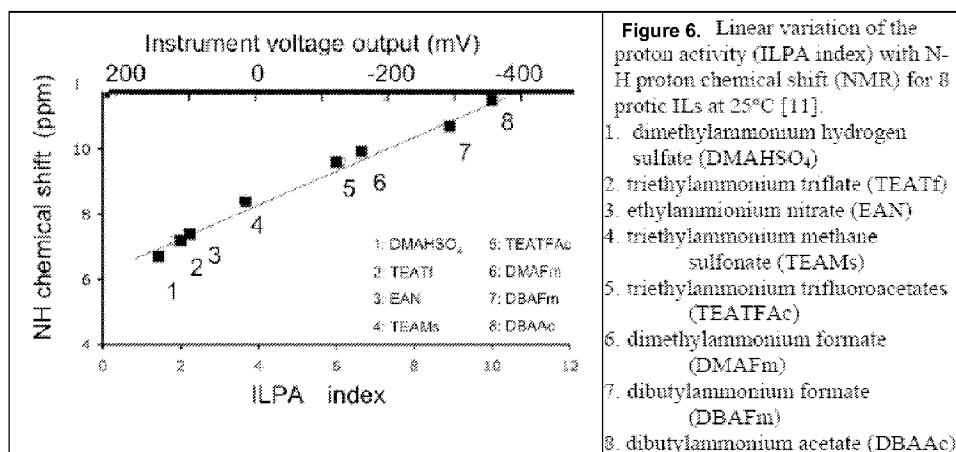


FIG. 6

(57) Abstract: Among other things, techniques and compositions for stabilizing proteins are disclosed. To stabilizing a protein, lyophilized protein is dissolved in a low-viscous solvent that includes water and ionic liquid. Compositions and techniques relate to reversible folding-unfolding, aggregation protection and multi-year stabilization in high protein concentration solutions of protic and/or aprotic ionic liquids.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2008/071254**A. CLASSIFICATION OF SUBJECT MATTER***C07K 1/00(2006.01)i, C07K 1/13(2006.01)i*

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)

IPC C07K 1/00

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

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

eKIPASS, NCBI PubMed database, Delphion Research Intellectual Property Network database, google scholar
"protein", "ionic", "stabilize", "ethylammonium nitrate", "NMR", "protic"**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	BYRNE N. et al. 'Reversible Folding-unfolding, Aggregation Protection, and Multi-year Stabilization, in High Concentration Protein Solutions, Using Ionic Liquids', Chemical Communications. Epub 19 April 2007, Vol 26, pages 2714-6. See the page 2714, column 1, line 26-39, column2, line 7-23, page 2715, column 1, line 10-18, page 1716, colimn 1, line 8-19.	1-16
P,X	BYRNE N. et al. 'Protein Unfolding, and the "Tuning In" of Reversible Intermediate States, in Protic Ionic Liquid Media', Journal of Molecular Biology. May 2008, Vol. 378, No. 3, pages 707-714. See the abstract, page 707, column2, page 711, column 2, Materials and Methods.	1-16
X	TAMAR L. et al. 'Many Protic Ionic Liquids Mediate Hydrocarbon-Solvent Interactions and Promote Amphiphile Self-Assembly', Langmuir. 2007(Epub 13 December 2006), Vol. 23, No. 2, pages 402-404. See the abstract, page 402, column 2.	1-16
P,A	ANGELL C. et al. 'Parallel Developments in Aprotic and Protic Ionic Liquids: Physical Chemistry and Applications', Acc. Chem. Res., 2007 (Epub 03 November 2007), Vol 40, No 11, pages 1228-1236. See the abstract.	1-16

☐ 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

"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 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

20 APRIL 2009 (20.04.2009)

Date of mailing of the international search report

21 APRIL 2009 (21.04.2009)

Name and mailing address of the ISA/KR

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2008/071254**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:

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

- I. Claims 1-16 directed to methods for stabilizing the lyophilized protein in ionic liquid and stabilizing solutions.
- II. Claims 17-19 directed to the method of measuring stability of a protein concerning denaturing enthalpy.

The inventions listed as Groups I, 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; they are separate inventions with distinct fields of search.

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 an additional fee, this Authority did not invite payment of any additional fee.
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.: 1-16

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.