(12) **United States Patent**   (10) **Patent No.:**   **US 7,056,886 B2**

Isaacs   (45) **Date of Patent:**   **Jun. 6, 2006**

(54) **GLP-2 FORMULATIONS**

(75) Inventor: **Indu J. Isaacs**, Andover, MA (US)

(73) Assignee: **NPS Allelix, Corp.**, Mississauga (CA)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 628 days.

(21) Appl. No.: **09/750,022**

(22) Filed: **Dec. 29, 2000**

(65) **Prior Publication Data**

US 2001/0027180 A1 Oct. 4, 2001

(30) **Foreign Application Priority Data**

Dec. 30, 1999 (GB) 9930882

(51) Int. Cl.
A61K 38/00 (2006.01)
A61K 38/26 (2006.01)
C07K 14/00 (2006.01)

(52) **U.S. Cl.** **514/12**; 530/308; 530/399; 530/324; 435/4; 435/287.1

(58) **Field of Classification Search** 514/12; 530/308, 399, 324; 435/4, 287.1
See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

4,985,244 A * 1/1991 Makino et al. 424/89

5,652,216 A * 7/1997 Kornfelt et al. 514/12
5,912,229 A * 6/1999 Thim et al. 514/12
5,952,301 A * 9/1999 Drucker 514/12
5,997,856 A * 12/1999 Hora et al. 424/85.2
6,120,761 A * 9/2000 Yamazaki et al. 424/85.1

FOREIGN PATENT DOCUMENTS

WO   97/39031   10/1997
WO   98/03547   1/1998
WO   99/43361   9/1999

OTHER PUBLICATIONS

Buhl et al., Naturally Occurring Products of Proglucagon 111–160 in the Porcine and Human Samll Intestine, J. Biol. Chem. 263, 8621–8624 (1988).*

Lund et al., Anglerfish Islet Pre–proglucagon II, Nucleotide and corresponding amino acid Sequenmce of the cDNA, J. Biol. Chem. 258, 3280–3284 (1983).*

* cited by examiner

Primary Examiner—Jon Weber
Assistant Examiner—Chih-Min Kam
(74) *Attorney, Agent, or Firm*—Foley & Lardner LLP

(57) **ABSTRACT**

The invention is directed to formulations of GLP-2 peptides and analogs thereof exhibiting superior stability following storage and/or exposure to elevated temperatures. The GLP-2 compositions comprise a GLP-2 peptide or an analog thereof, a phosphate buffer, L-histidine, and mannitol.
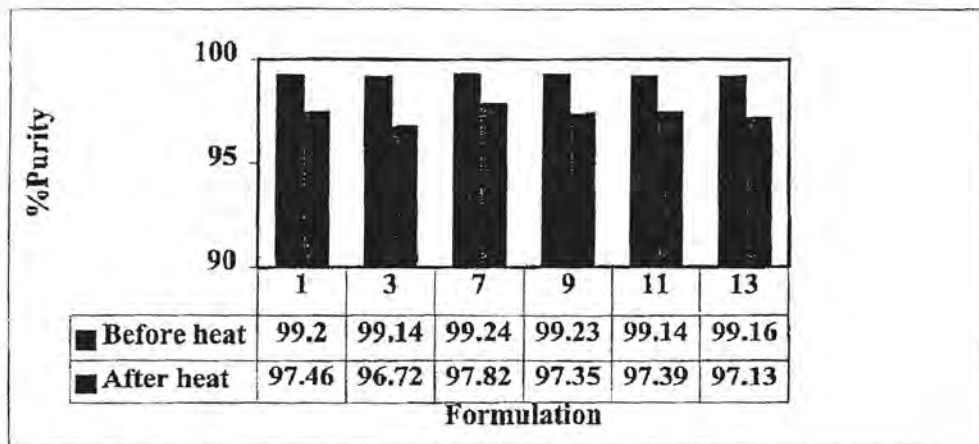
75 Claims, 6 Drawing Sheets

EXHIBIT 102
Carpenter
PENGAD 800-631-6989

Figure 1. Amino acids screening in buffers using heat stress.

	1	3	7	9	11	13
▪ Before heat	99.2	99.14	99.24	99.23	99.14	99.16
▪ After heat	97.46	96.72	97.82	97.35	97.39	97.13

Formulation

Formulation

1. 10 mM Phosphate, 10 mM Glu
3. 10 mM Phosphate, 10 mM Citrate
7. 10 mM Phosphate, 10 mM Ser
9. 10 mM Phosphate, 10 mM Pro
11. 10 mM Phosphate, 10 mM His
13. 10 mM Phosphate, 10 mM Gly

Figure 2. Screening of buffers using heat stress.
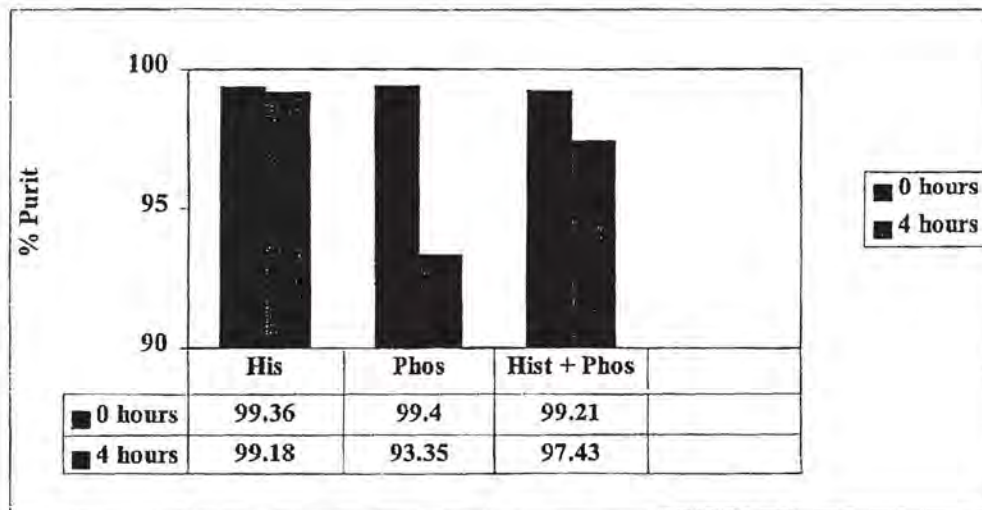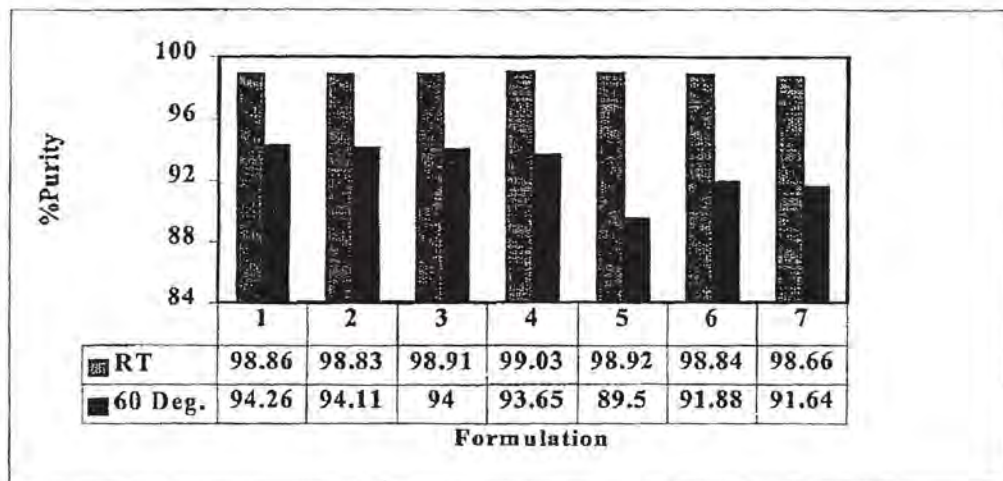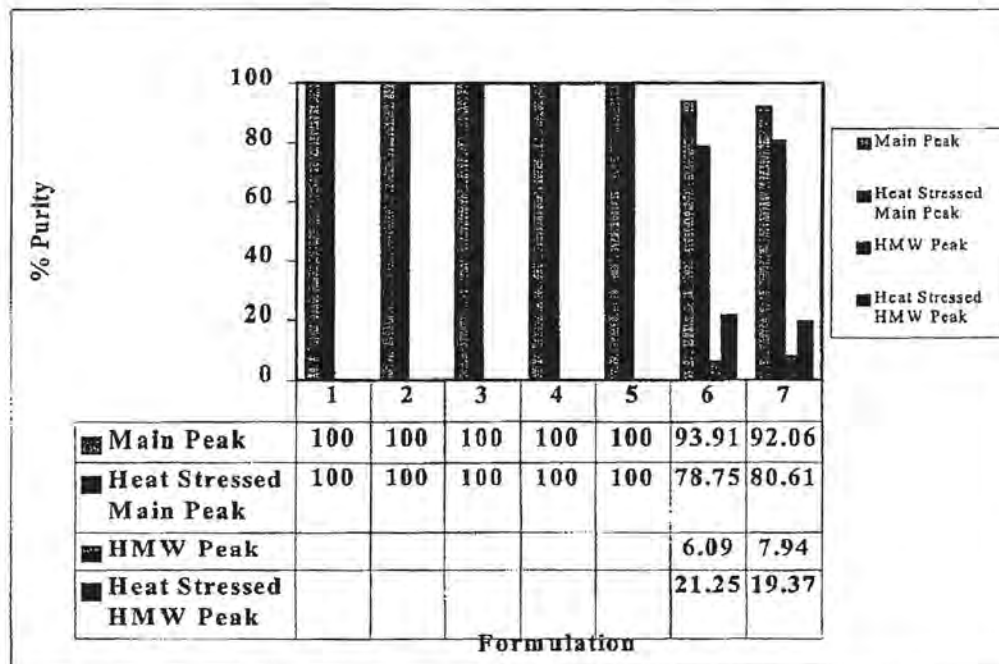

	His	Phos	Hist + Phos
0 hours	99.36	99.4	99.21
4 hours	99.18	93.35	97.43

Figure 3. Screening of Bulking agents analyzed by RP-HPLC.

	1	2	3	4	5	6	7
RT	98.86	98.83	98.91	99.03	98.92	98.84	98.66
60 Deg.	94.26	94.11	94	93.65	89.5	91.88	91.64

Formulation

Formulation

1. 25 mM Histidine, 35 mM phosphate, 3% Mannitol

2. 50 mM Histidine, 35 mM phosphate, 3% Mannitol

3. 75 mM Histidine, 35 mM phosphate, 3% Mannitol

4. 25 mM Histidine, 25 mM phosphate, 3% sucrose

5. 25 mM Histidine, 25 mM phosphate, 3% trehalose

6. 25 mM Histidine, 25 mM phosphate, 3% maltose

7. 25 mM Histidine, 25 mM phosphate, 3% lactose

Figure 4. Bulking agents analyzed by SE-HPLC.

	1	2	3	4	5	6	7
Main Peak	100	100	100	100	100	93.91	92.06
Heat Stressed Main Peak	100	100	100	100	100	78.75	80.61
HMW Peak						6.09	7.94
Heat Stressed HMW Peak						21.25	19.37

Formulation

Formulation

1.   25 mM Histidine, 35 mM phosphate, 3% Mannitol

2.   50 mM Histidine, 35 mM phosphate, 3% Mannitol

3.   75 mM Histidine, 35 mM phosphate, 3% Mannitol

4.   25 mM Histidine, 25 mM phosphate, 3% sucrose

5.   25 mM Histidine, 25 mM phosphate, 3% trehalose

6.   25 mM Histidine, 25 mM phosphate, 3% maltose

7.   25 mM Histidine, 25 mM phosphate, 3% lactose

DOCKET ALARM

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts

Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research

With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips

Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.

fastcase®
Smarter legal research.