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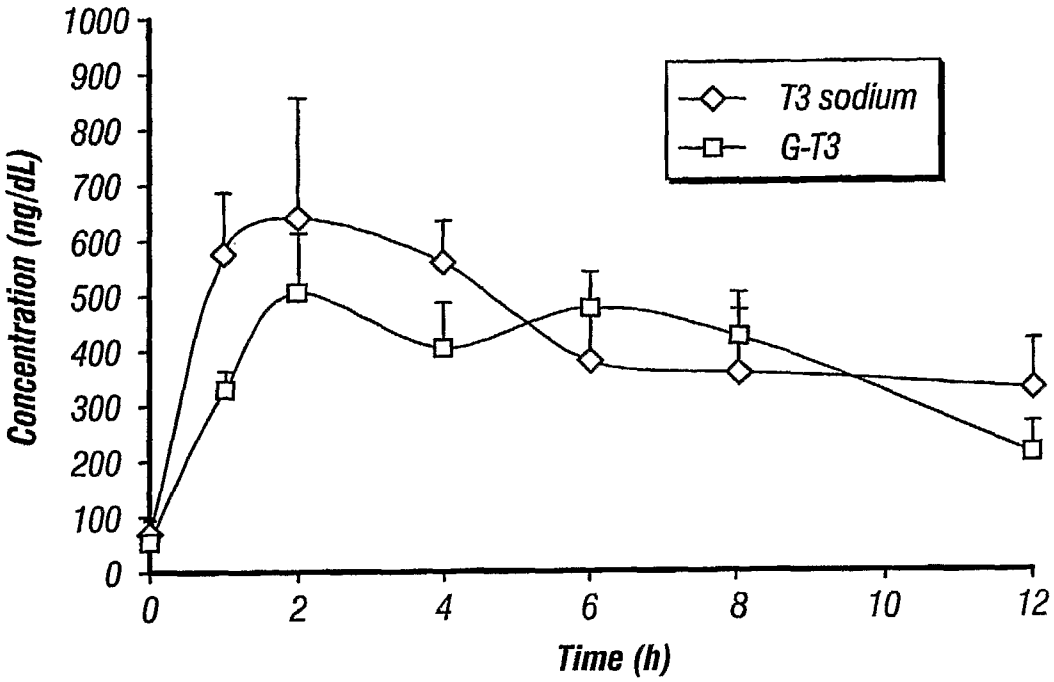
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[Continued on next page]

(54) Title: PRODRUGS OF T3 AND T4 WITH ENHANCED BIOAVAILABILITY



(57) Abstract: The invention relates to compositions of amino acid and peptide conjugates comprising T3 and/or T4. The T3 or T4 is covalently attached to at least one amino acid via the N-terminus, the C-terminus, a side chain of the peptide carrier, and/or interspersed within the peptide chain. Also discussed are methods for protecting and administering active agents and methods for treating thyroid disorders.

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Declarations under Rule 4.17:
— *as to the identity of the inventor (Rule 4.17(i))*
— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*
— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

Published:
— *with international search report*
— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

(88) Date of publication of the international search report:
25 October 2007

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 06/34790

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8): C12P 13/04; A01N 37/18, 38/00 (2007.01)
USPC: 930/120
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)
USPC: 930/120

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC: 930/180; 435/106; 514/2 (text search - see terms below)

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

PubWEST(USPT,PGPB,EPAB,JPAB); DialogPRO(MEDLINE); Google Scholar: peptide-iodothyronine, tetra-iodothyronine, tri-iodothyronine, thyroxine, glycine, Gly-T3, T4, Gly-T4, T3, Gly-T4, prodrug, covalent, C-terminus, oral, Lys, Glu, Ile, Tyr, Val, Ala-Ala, Pro-Pro, Glu-Glu, Phe-Phe, salt, HCL, acetate, sulfate, mesylate, etc.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2004/0087483 A1 (Piccariello et al.) 06 May 2004 (06.05.2004), entire document especially claims 1-5, 13, 20, and 25, and para [0011], [0019], [0029]-[0031], [0065]- [0066].	1-15
A	Kirkegaard et al. The Role of Thyroid Hormones in Depression. Eur J Endocrinol. January 1998, Vol. 138, No, 1, pages 1-9.	1-15

☐ Further documents are listed in the continuation of Box C. ☐

* 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	Date of mailing of the international search report
30 March 2007 (30.03.2007)	28 AUG 2007
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. 571-273-3201	Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 06/34790

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.: 16-35
because they relate to subject matter not required to be searched by this Authority, namely:

Claims 16-35 are unsearchable (not required to be searched by this ISA) based on Rule 39.1(v) as they are directed to mere presentations of information.

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:

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.:

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.