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**Cypes et al.**

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(54) **PHOSPHORIC ACID SALT OF A  
DIPEPTIDYL PEPTIDASE-IV INHIBITOR**  
(75) Inventors: **Stephen Howard Cypes**, Santa Clara,  
CA (US); **Alex Minhua Chen**,  
Metuchen, NJ (US); **Russell R. Ferlita**,  
Westfield, NJ (US); **Karl Hansen**,  
Atlantic Highlands, NJ (US); **Ivan Lee**,  
Piscataway, NJ (US); **Vicky K. Vydra**,  
Fair Lawn, NJ (US); **Robert M.  
Wenslow, Jr.**, East Windsor, NJ (US)

(73) Assignee: **Merck & Co., Inc.**, Rahway, NJ (US)  
(\* ) Notice: Subject to any disclaimer, the term of this  
patent is extended or adjusted under 35  
U.S.C. 154(b) by 657 days.

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(65) **Prior Publication Data**  
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24, 2003.

(51) **Int. Cl.**  
**A61K 31/495** (2006.01)  
**C07D 471/04** (2006.01)  
(52) **U.S. Cl.** ..... **514/249; 544/350**  
(58) **Field of Classification Search** ..... **514/249;**  
**544/350**  
See application file for complete search history.

(56) **References Cited**  
U.S. PATENT DOCUMENTS  
6,479,692 B1 \* 11/2002 Ekwuribe et al. .... 558/413  
6,699,871 B2 3/2004 Edmondson et al.  
2003/0100563 A1 5/2003 Edmondson et al.  
2006/0287528 A1 \* 12/2006 Wenslow et al. .... 544/350  
2007/0021430 A1 \* 1/2007 Chen et al. .... 514/249

FOREIGN PATENT DOCUMENTS  
WO WO 2005/072530 A1 8/2005  
WO WO 2006/033848 A1 3/2006

OTHER PUBLICATIONS  
Edmondson, S.D., Drug Data Report, vol. 25, No. 3, pp. 245-246  
(2003).  
Database Prous DDR Online—Database Accession No. 2003: 3561.  
\* cited by examiner  
*Primary Examiner*—James O. Wilson  
*Assistant Examiner*—Ebenezer Sackey  
(74) *Attorney, Agent, or Firm*—Philippe L. Durette;  
Catherine D. Fitch

(57) **ABSTRACT**  
The dihydrogenphosphate salt of 4-oxo-4-[3-(trifluoromethyl)-5,6-dihydro [1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl]-1-(2,4,5-trifluorophenyl)butan-2-amine is a potent inhibitor of dipeptidyl peptidase-IV and is useful for the prevention and/or treatment of non-insulin dependent diabetes mellitus, also referred to as type 2 diabetes. The invention also relates to a crystalline monohydrate of the dihydrogenphosphate salt as well as a process for its preparation, pharmaceutical compositions containing this novel form and methods of use for the treatment of diabetes, obesity, and high blood pressure.

**24 Claims, 5 Drawing Sheets**

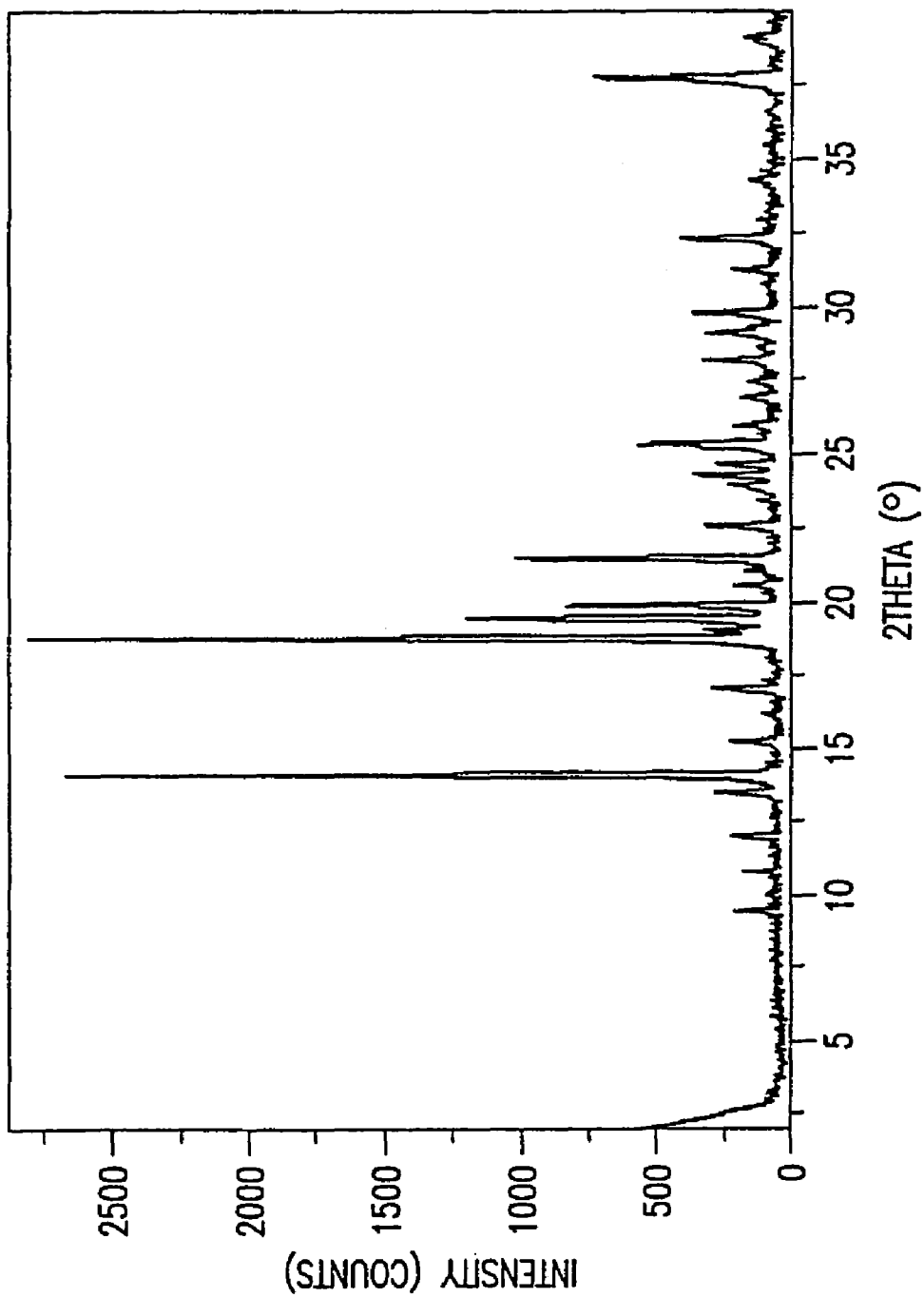


FIG.1

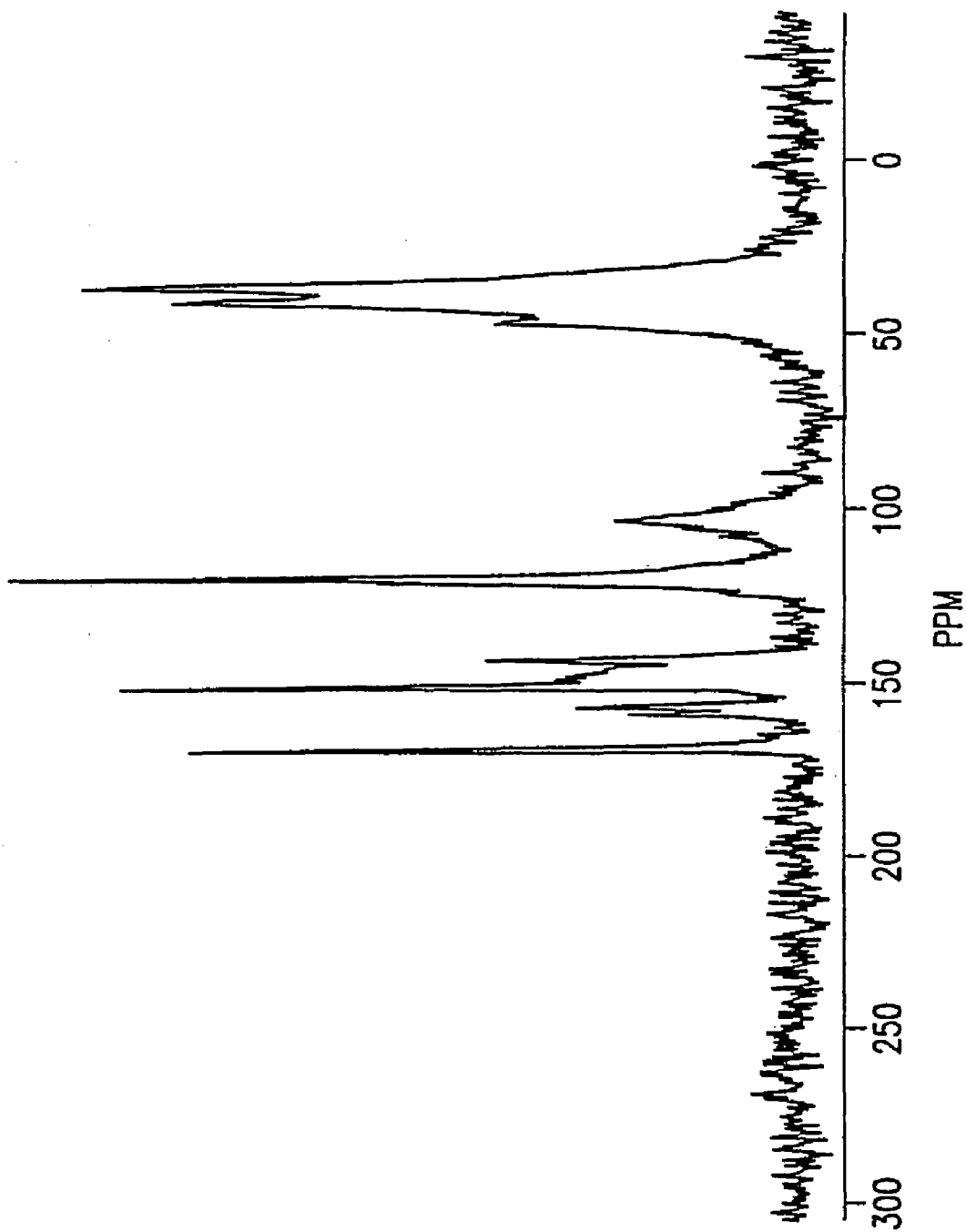


FIG. 2

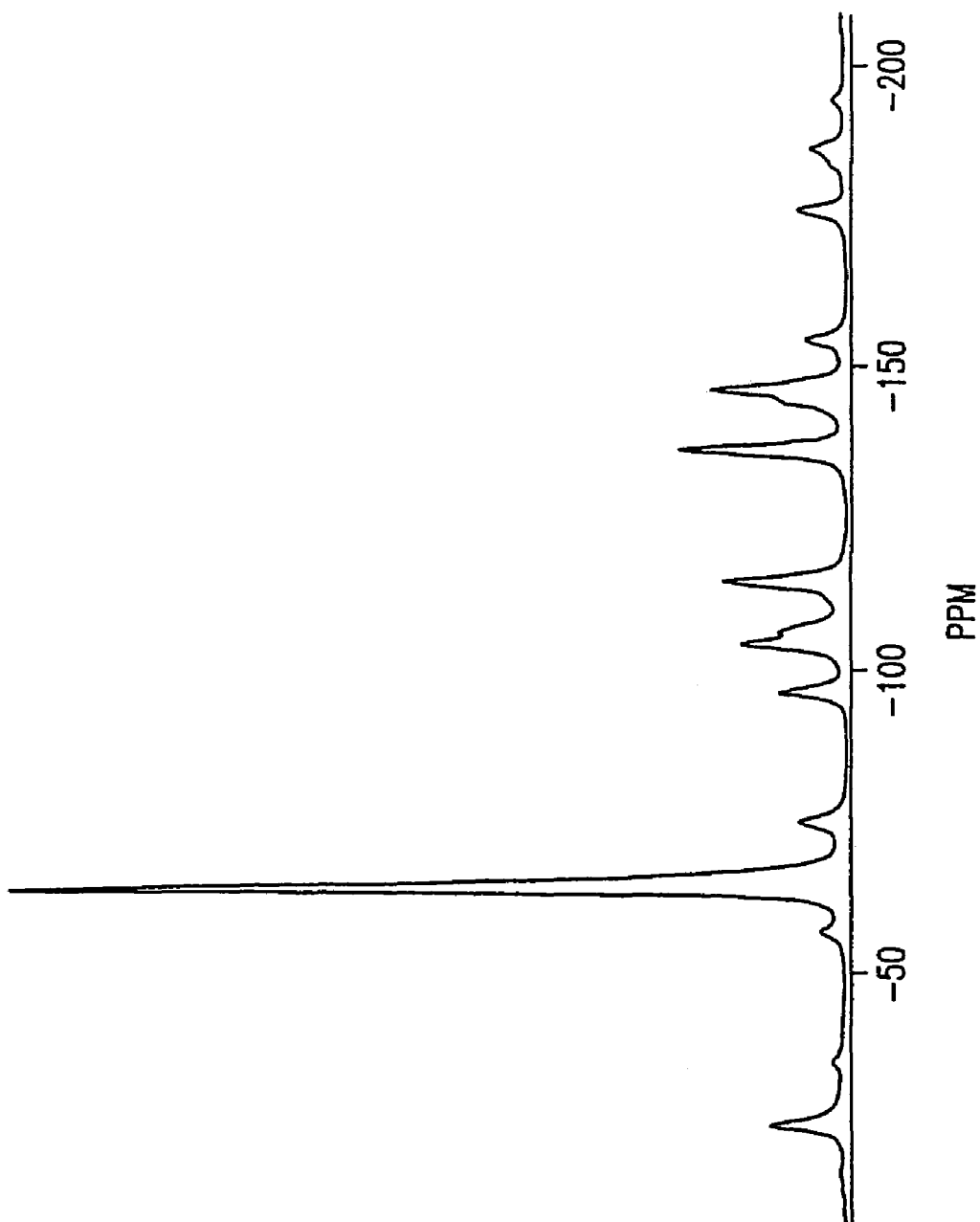


FIG.3

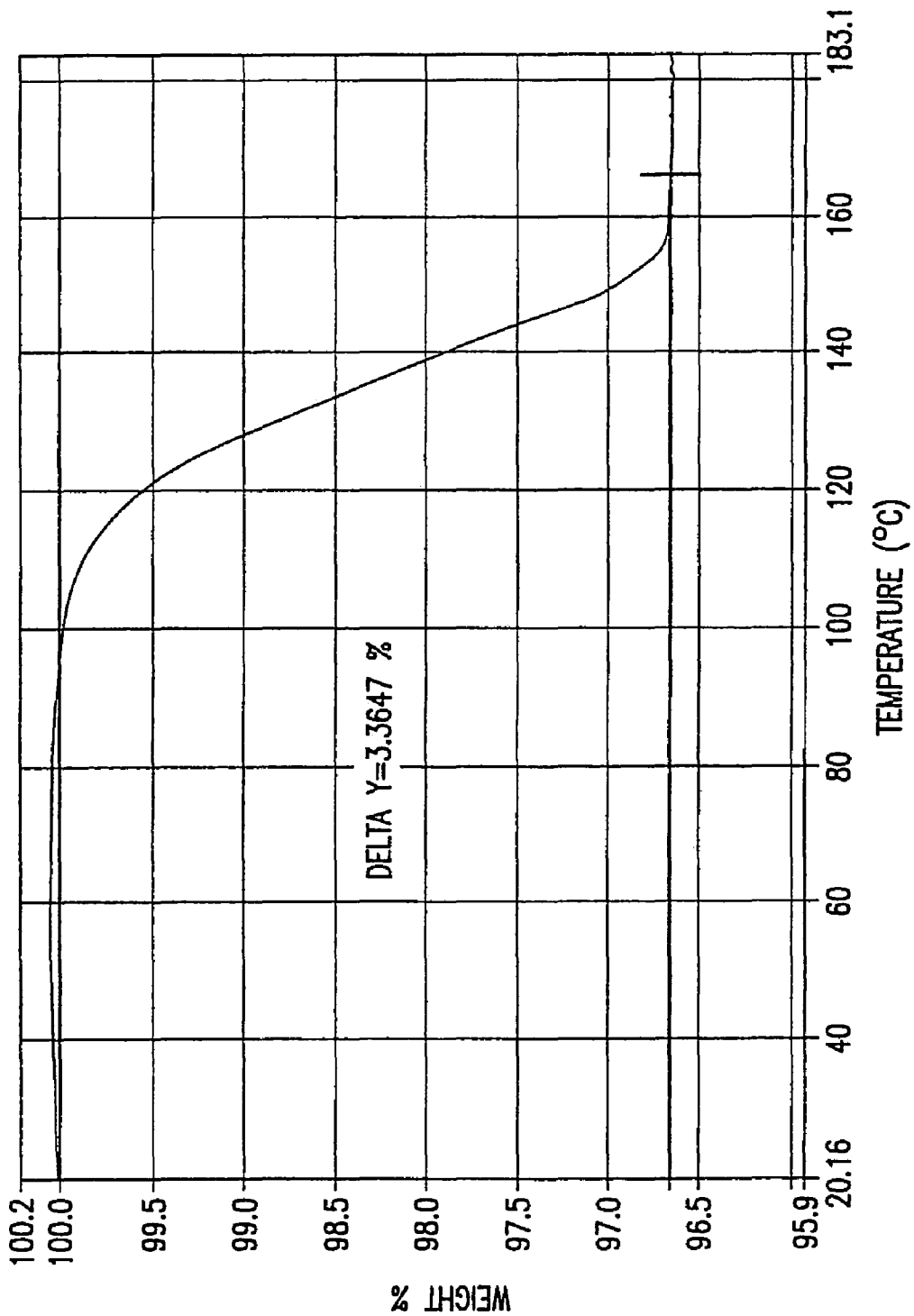


FIG.4

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