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(54) **PEPTIDE AGONISTS OF GLP-1 ACTIVITY**

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Related U.S. Application Data

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(51) **Int. Cl.⁷** **A61K 38/00**

(52) **U.S. Cl.** **514/12**; 514/2; 530/300;
530/303

(58) **Field of Search** 514/12, 2; 530/300,
530/303

(56) **References Cited**

U.S. PATENT DOCUMENTS

5,424,286 A 6/1995 Eng 514/2
5,545,618 A 8/1996 Buckley et al. 514/12

FOREIGN PATENT DOCUMENTS

WO WO 98/05351 2/1998
WO WO 98/08871 3/1998
WO WO 98/11126 * 3/1998 C07K1/107
WO WO 98/11126 A 3/1998
WO WO 98/22577 A 5/1998
WO WO 98/30231 A 7/1998
WO WO 99/07404 2/1999
WO WO 99/25727 5/1999
WO WO 99/25728 5/1999
WO WO 99/43707 9/1999
WO WO 99/43708 9/1999
WO WO 99/46283 9/1999

OTHER PUBLICATIONS

J. Eng et al. Isolation and characterization of Exendin-4, an Exendin-3 analogue, from *Heloderma suspectum* venom. 1992. *J. Biol. Chem.*, 267(11): 7402-05.*
C. Orskov, *Diabetologia*, 701 (1992).
M. Nauck et al., *Horm. Metab. Res.*, 411 (1997).
Jean-Pierre Raufman, *Reg. Peptides* 61: 1-18 (1996).
Janet A. Meurer, et al. "Properties of Native and In Vitro Glycosylated Forms Of The Glucagon-Like Peptide-1 Receptor Antagonist Exendin (9-39)", *Metabolism*, vol. 48, No. 6 (Jun.), 1999, pp 716-724.
M.M. Byrne et al., *European Journal of Clinical Investigation*, 72 (1998).
C.F. Deacon et al., *Diabetologia*, 271 (1998).
C. Deacon et al., *Diabetes*, 764 (1998).
U. Ritzel et al., *Journal of Endocrinology*, 93 (1998).
R. Pederson et al., *Diabetes*, 1253 (1998).
R. Goke et al., *European Journal of Neuroscience*, 2294 (1995).
R. Goke et al., *The Journal of Biological Chemistry*, 19650 (1993).
M. Pohl et al., *The Journal of Biological Chemistry*, 9778 (1998).
N.H. Greig et al., *Diabetologia*, 45 (1999).
Y. Chen et al., *The Journal of Biological Chemistry*, 4108 (1997).
J.J. Holst, *Annu. Rev. Physiol.*, 257 (1997).
D. A. D'Alessio et al., *J. Clin. Invest. (USA)* 93 (5):2263-6 (1994).

* cited by examiner

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(57) **ABSTRACT**

The present invention relates to novel peptide conjugates which have increased stability and are useful in the treatment of excess levels of blood glucose.

2 Claims, 8 Drawing Sheets

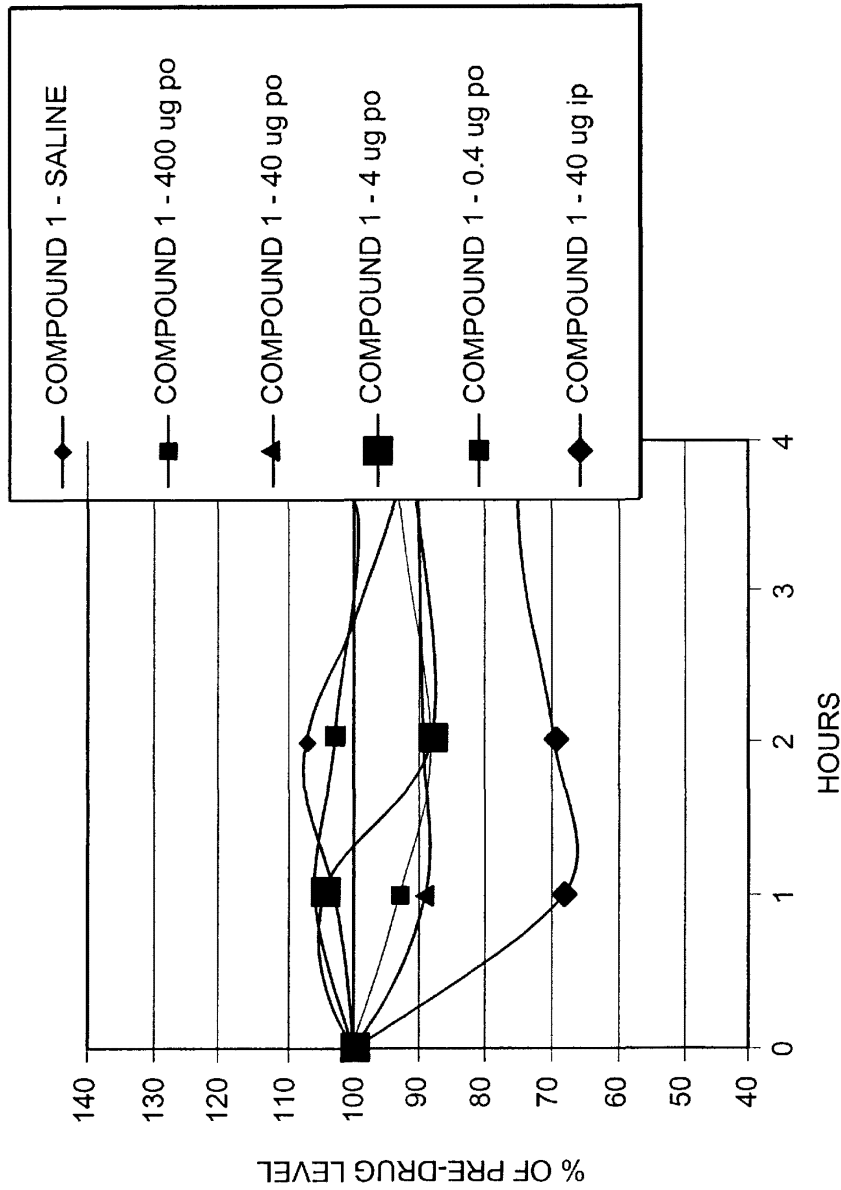


FIG. 1

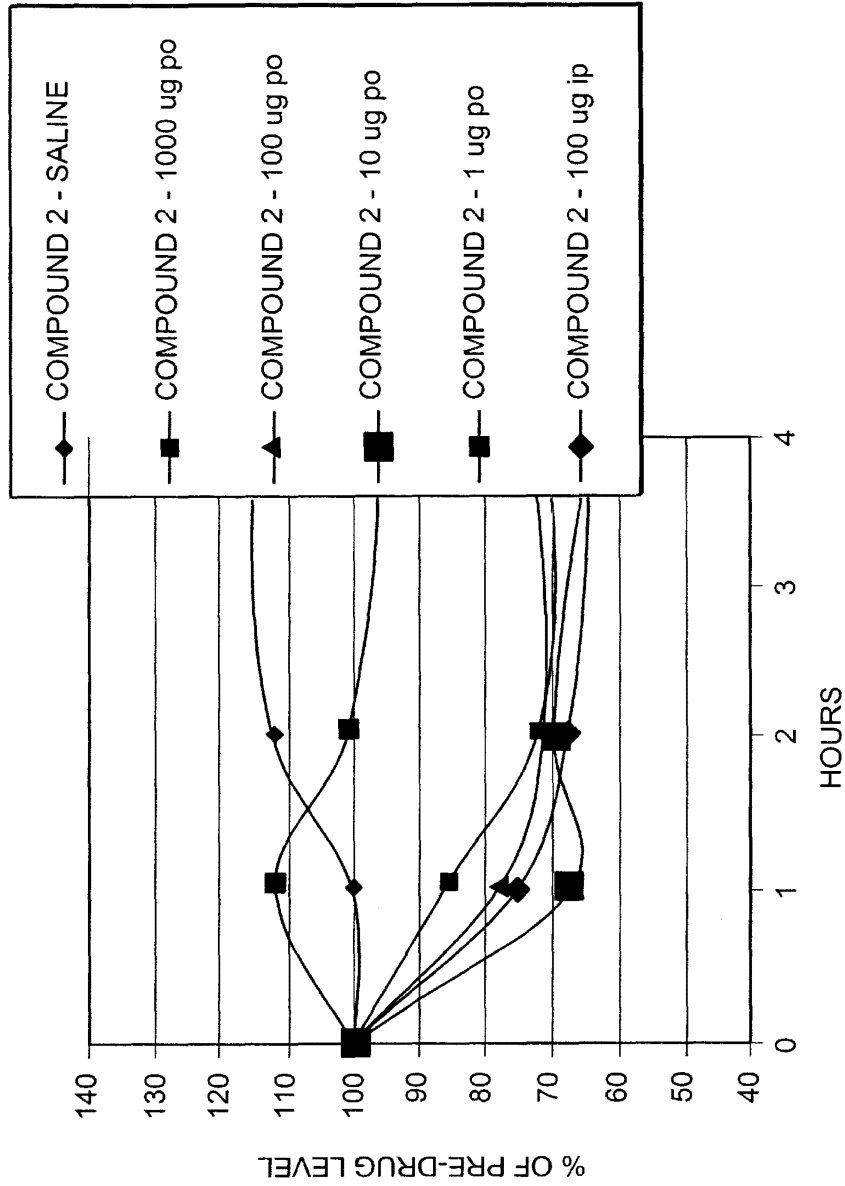


FIG. 2

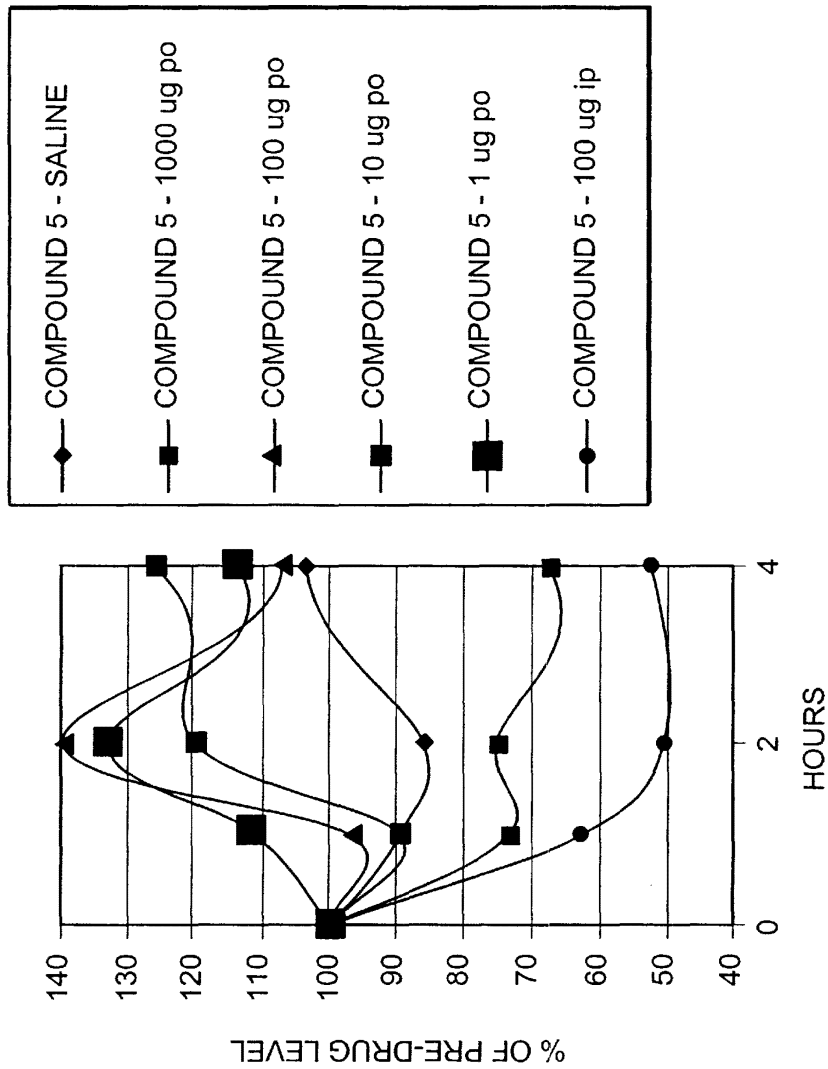


FIG. 3

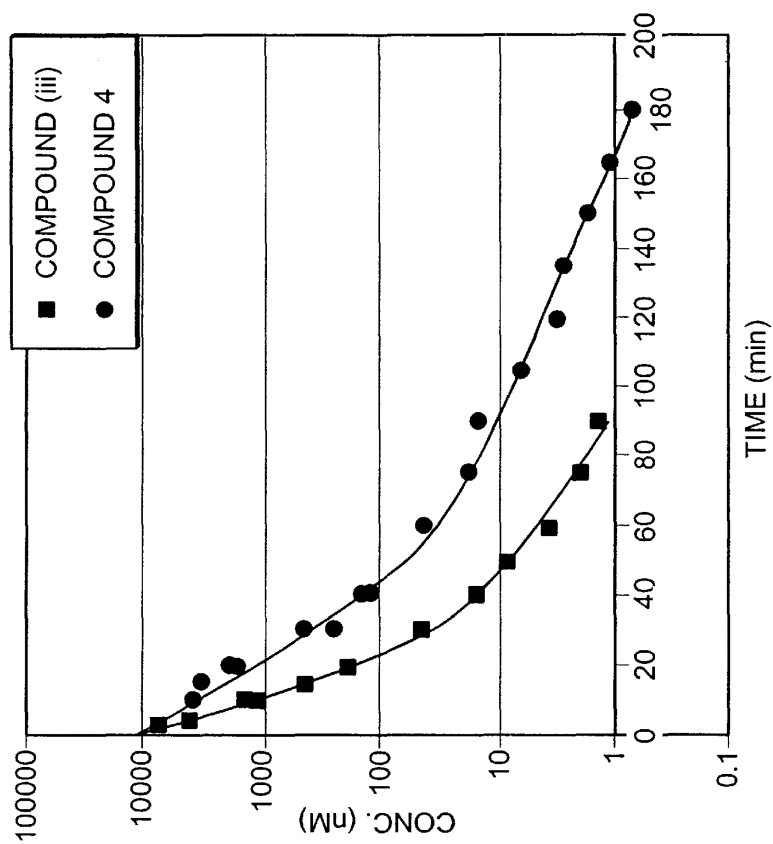


FIG. 4

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