

[54] INSULINOTROPIC HORMONE

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[21] Appl. No.: 532,111

[22] Filed: Jun. 1, 1990

Related U.S. Application Data

[63] Continuation of Ser. No. 148,517, Jan. 26, 1988, abandoned, which is a continuation-in-part of Ser. No. 859,928, May 5, 1986, abandoned.

[51] Int. Cl.<sup>5</sup> ..... A61K 37/02; A61K 37/28; C07K 7/10; C07K 7/34

[52] U.S. Cl. .... 514/12; 514/866; 530/308; 530/324

[58] Field of Search ..... 530/324, 303, 308; 514/12, 866

[56] References Cited

FOREIGN PATENT DOCUMENTS

0044168 1/1982 European Pat. Off. .

OTHER PUBLICATIONS

Uttenthal et al., J. Clin. End. Metab. 61=472-479 (1985).

Ghiglione et al., Diabetologia, 27=599-600 (1984).

Rudinger, Peptide Hormones, Parsons (Ed.) U. Park Press, Baltimore, pp. 1-7 (1976).

Schmidt et al., Diabetologia 28=704-707 (1985).

Bell et al., Nature, 302=716-718 (1983).

Andrews et al., J. Biol. Chem. 260=3910-3914.

Houghten, R. A. et al., Biotechniques 4:522-524, 526, 528 (Jul. 1986).

Meienhofer, J., In: Peptides 1984, Ragnarsson, U. (ed.) Almquist & Wiksell International, Stockholm (1984).

Sarson, D. L. et al., Diabetologia 22:33 (1982).

Hauner, H. et al., Ann. Nutr. Metab. 32:282-288 (1989).

Ganong, W., Review of Medical Physiology, 9th Ed., Lange Medical Publications, Los Altos, CA (1979) pp. 257-276.

Drucker, D. J. et al., Proc. Natl. Acad. Sci. USA 84:3434-3438 (1987).

Mojsov, S. et al., J. Clin. Invest. 79:616-619 (1987).

Holst, J. J. et al., FEBS Lett. 211:169-174 (1987).

Kreymann, B. et al., The Lancet, Dec. 5, 1987, pp. 1300-1304.

Weir, G. et al., Diabetes 38(3):338-342 (Mar. 1989).

Gefel, D. et al., Endocrinology 126 (4):2164-2168 (1990).

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[57] ABSTRACT

Derivatives of glucagon-like peptide I (GLP-1) have been found to have insulinotropic activity. The invention pertains to such derivatives, and to the use of such derivatives as a potential therapy for Diabetes Mellitus.

21 Claims, 6 Drawing Sheets



135 GLP II 145  
 His Ala Asp Gly Ser Phe Ser Asp Glu Met Asn Thr Ile Leu Asp Asn Leu Ala Thr Arg  
 CAT GCT GAT GGA TCC TTC TCT GAT GAG ATG AAC ACG ATT CTC GAT AAC CTT GCC ACC AGA 555  
 E-5  
 Asp Phe Ile Asn Trp Leu Ile Gln Thr Lys Ile Thr Asp Lys Lys End  
 GAC TTC ATC AAC TGG CTG ATT CAA ACC AAG ATC ACT GAC AAG AAA TAG gaatatttcaccatt 618  
 cacaaaccatcttcacaacatctcctgcccagtcactgggatgtacatttgaggcgcataatccgaagctatactgcttgc 697  
 E-6  
 atgcggaacgaatacatttcccttttagcgttgtgtaacccaaaggtgtaaatggaataaagttttccagggtgtgat 776  
 aaagtaacaactttacagtatgaaaaatgctggattctcaaatgtctcctcgttttgaagttaccgccctgagattact 855  
 tttctgtgtataaattgtaaattatcgcagtcacgacacacctggattacaacaacagaagacatggtaacctggtaac 933  
 gtagtggagaacctggaaaagagaacttctccttgaacctttgtcataaatgcgctcagcttcaatgtatcaagaat 1012  
 agattaaataaataatctcat 1024  
 3'

FIG. 1 CONT.

STIMULATION OF cAMP IN RIN 1046-38

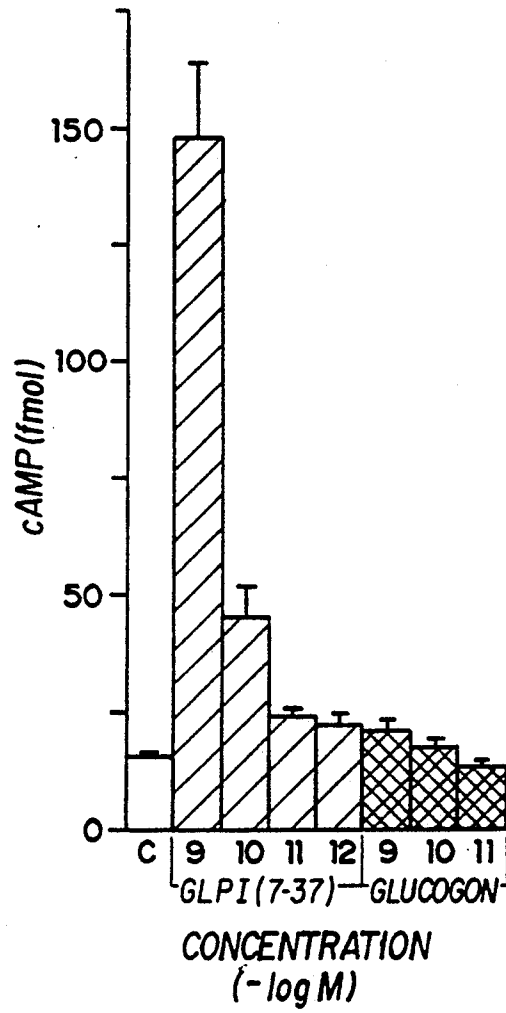


FIG. 2

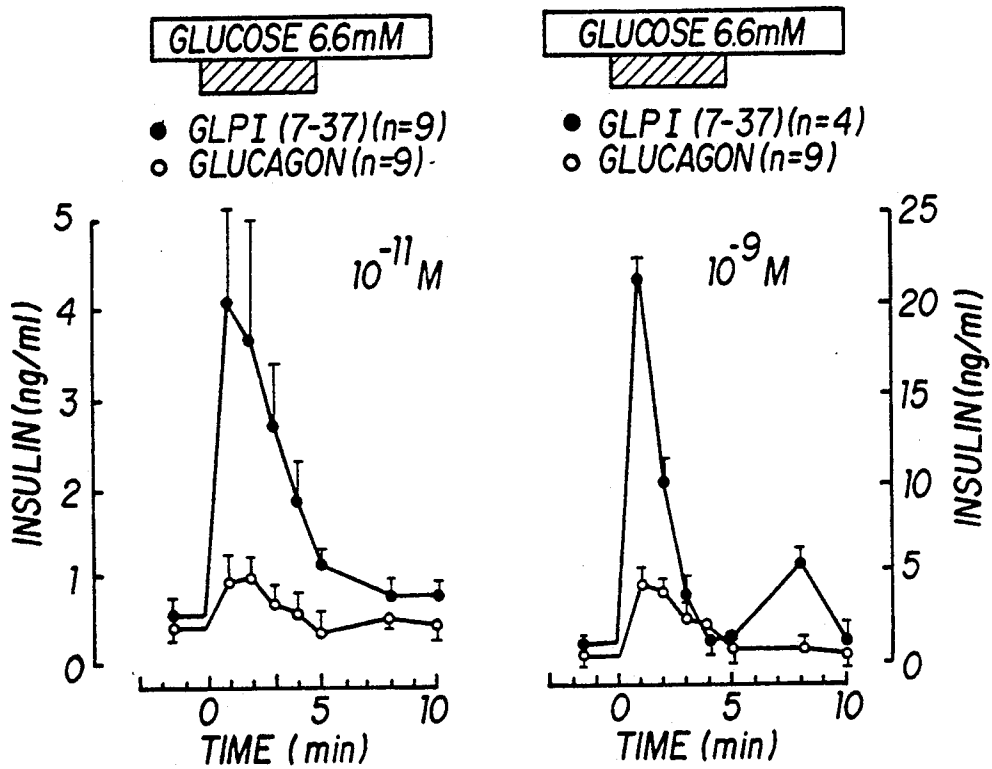


FIG. 3

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