



## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                                              |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------|
| <b>(51) International Patent Classification <sup>6</sup>:</b><br><b>C07C 9/00, 259/04, 259/06, 259/08,</b><br><b>A61K 31/28</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | <b>A1</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | <b>(11) International Publication Number:</b> <b>WO 99/12875</b><br><br><b>(43) International Publication Date:</b> 18 March 1999 (18.03.99) |
| <b>(21) International Application Number:</b> PCT/IL98/00441<br><b>(22) International Filing Date:</b> 10 September 1998 (10.09.98)<br><br><b>(30) Priority Data:</b><br>121748 11 September 1997 (11.09.97) IL<br><br><b>(71) Applicant (for all designated States except US):</b> YEDA RESEARCH AND DEVELOPMENT CO. LTD. [IL/IL]; P.O. Box 95, 76100 Rehovot (IL).<br><br><b>(72) Inventors; and</b><br><b>(75) Inventors/Applicants (for US only):</b> SHECHTER, Yoram [IL/IL]; Hanasi Harishon Street 51/5, 76303 Rehovot (IL). FRIDKIN, Matityahu [IL/IL]; Miller Street 23, 76284 Rehovot (IL). GOLDWASER, Itzhak [IL/IL]; Hagat Street 16, 75248 Rishon Le-Zion (IL). GERSHONOV, Bytan [IL/IL]; Bnei Brit Street 17, 45265 Hod Hasharon (IL).<br><br><b>(74) Agent:</b> BEN-AMI, Paulina; Yeda Research and Development Co. Ltd., The Weizmann Institute of Science, P.O. Box 95, 76100 Rehovot (IL). | <b>(81) Designated States:</b> AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).<br><br><b>Published</b><br><i>With international search report.</i> |                                                                                                                                              |
| <b>(54) Title:</b> VANADIUM COMPLEXES OF MONOHYDROXAMATES AND PHARMACEUTICAL COMPOSITIONS COMPRISING THEM                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                                              |
| <b>(57) Abstract</b><br><br>Monohydroxamate vanadium complexes of the formula (I) : R-CO-NHOH.X, wherein R is a residue selected from: (i) H <sub>2</sub> N-CH(COY)-(CH <sub>2</sub> ) <sub>n</sub> , wherein n is 1, 2 or 3, and Y is OH or NH <sub>2</sub> ; (ii) H <sub>2</sub> N-CH(COOH)-CH <sub>2</sub> -S-CH <sub>2</sub> -; and (iii) pyridyl, piperidyl or tetrahydroisoquinolyl; and X is a vanadium compound selected from a vanadyl (VO <sup>2+</sup> ), metavanadate (VO <sub>3</sub> <sup>-</sup> ) or vanadate (VO <sub>4</sub> <sup>3-</sup> ) salt, are useful for inducing normoglycemia and/or reducing blood glucose levels in diabetic patients.                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                                              |