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(21) International Application Number: PCT/US98/27282 (22) International Filing Date: 22 December 1998 (22.12.98) (30) Priority Data: 08/997,208 23 December 1997 (23.12.97) US (71) Applicant (for all designated States except US): FERRING B.V. [NL/NL]; Marsstraat 9, P.O. Box 3129, NL-2130 KC Hoofddorp (NL). (72) Inventors; and (75) Inventors/Applicants (for US only): JUNIEN, Jean, Louis [FR/FR]; 36, avenue Eiffel, F-92310 Sevres (FR). RIVIERE, Pierre, J., M. [FR/US]; 4345 Nobel Drive #131, San Diego, CA 92122 (US). SCHTEINGART, Claudio, D. [AR/US]; 2655 Ellentown Road, La Jolla, CA 92037 (US). DIAZ, Javier, Sueiras [ES/US]; 8526 Villa La Jolla Drive #138, La Jolla, CA 92037 (US). TROJNAR, Jerzy, A. [SE/US]; 132 N. Sierra Avenue, Solana Beach, CA 92075 (US). VANDERAH, Todd, W. [US/US]; 1352 W. Cactus Bloom Way, Tucson, AZ 85737 (US). (74) Agents: SAMPLES, Kenneth, H. et al.; Fitch, Even, Tabin & Flannery, Room 1600, 120 South LaSalle Street, Chicago, IL 60603 (US).		(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, 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). Published <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>
(54) Title: KAPPA RECEPTOR OPIOID PEPTIDES		
(57) Abstract Peptides which exhibit high selectivity for the kappa opioid receptor (KOR) and long duration of peripheral action without significant entry into the brain are created which are sequences of four D-isomer amino acid residues having a C-terminus which is a mono- or di-substituted amide. Representative compounds, which have an affinity for the KOR at least 1,000 times their affinity for the mu opioid receptor and an ED₅₀ of not greater than about 0.5 mg/kg, include H-D-Phe-D-Phe-D-Nle-D-Arg-NHEt, H-D-Phe-D-Phe-D-Nle-D-Arg-morpholinyl, H-D-Phe-D-Phe-D-Nle-D-Arg-NH-4-picolyl, H-D-Phe-D-Phe-D-Nle-D-Arg-NHP, H-D-Phe-D-Phe-D-Nle-D-Arg-NHEt, H-D-Phe-D-Phe-D-Nle-D-Arg-NHMe, H-D-Phe-D-Phe-D-Leu-D-Orn-morpholinyl, H-D-4Fpa-D-Phe-D-Nle-D-Arg-NH-4-picolyl, H-D-Phe-D-Phe-D-Nle-D-Arg-NH-cyclopropyl, H-D-Ala-(2Thi)-D-3, 4Cpa-D-Leu-D-Arg-morpholinyl, H-D-Phe-D-Phe-D-Nle-D-Gmf-morpholinyl, H-D-Phe-D-Phe-D-Leu-D-Orn-NH(Aeb), H-D-Phe-D-Phe-D-Leu-D-Lys-morpholinyl, H-D-Phe-D-Phe-D-Nle-D-Arg-piperazinyl, and H-D-Phe-D-Phe-D-Nle-D-Arg-NH(Hoh).		