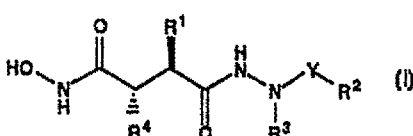




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(21) International Application Number: PCT/EP98/03683 (22) International Filing Date: 18 June 1998 (18.06.98) (30) Priority Data: 9713833.3 30 June 1997 (30.06.97) GB 9803335.0 17 February 1998 (17.02.98) GB (71) Applicant: F. HOFFMANN-LA ROCHE AG [CH/CH]; 124 Grenzacherstrasse, CH-4070 Basle (CH). (72) Inventors: BROADHURST, Michael, John; Ivy Cottage, High Street, Barley, Royston, Hertfordshire SG8 8HT (GB). JOHNSON, William, Henry; 87 West Hill, Hitchin, Hertfordshire SG5 3HX (GB). WALTER, Daryl, Simon; 149 Wadnall Way, Knebworth, Hertfordshire SG3 6DT (GB).	(74) Agent: LÖSCHNER, Thomas; 124 Grenzacherstrasse, CH-4070 Basle (CH). (81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, 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, 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, ML, MR, NE, SN, TD, TG). Published With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.	
(54) Title: HYDRAZINE DERIVATIVES		
(57) Abstract Hydrazine derivatives of formula (I) wherein Y signifies CO or SO₂; R¹ signifies lower alkyl, lower alkenyl, lower cycloalkyl, lower cycloalkyl-lower alkyl, aryl or aryl-lower alkyl; R² signifies lower alkyl, halo-lower alkyl, aryl-lower alkyl, aryl-lower alkenyl or aryl when Y signifies SO₂ and signifies lower alkyl, halo-lower alkyl, lower alkoxy, lower alkoxycarbonyl, acyl, lower cycloalkyl, aryl, aryl-lower alkyl, aryl-lower alkoxy or NR⁵R⁶ when Y signifies CO; and R³ signifies hydrogen, lower alkyl optionally substituted by cyano, amino, hydroxy, lower alkoxy, lower alkoxycarbonyl, heterocyclyl or heterocyclylcarbonyl, lower alkenyl, lower alkynyl, lower cycloalkyl, lower cycloalkyl-lower alkyl, aryl-lower alkyl, aryl-lower alkenyl, aryl or heterocyclyl; or R² and R³ together form the residue of a 5-, 6- or 7- membered cyclic amide, cyclic imide, cyclic sulphonamide or cyclic urethane group; R⁴ signifies lower alkyl, hydroxy-lower alkyl, lower alkenyl, lower cycloalkyl, lower cycloalkyl-lower alkyl or a grouping of the formula X-aryl, X-heteroaryl or -(CH₂)₁₋₂-CH=CR⁷R⁸; X signifies a spacer group; R⁵ and R⁶ each individually signify hydrogen, lower alkyl or aryl-lower alkyl; and R⁷ and R⁸ together represent a lower alkylene group in which one methylene group is optionally replaced by a hetero atom; and their pharmaceutically acceptable salts inhibit not only the release of tumour necrosis factor (TNF-α) and transforming growth factor (TGF-α) from cells, but also keratinocyte proliferation. They are useful as medicaments, especially for the treatment of inflammation, fever, haemorrhage, sepsis, rheumatoid arthritis, osteoarthritis, multiple sclerosis or psoriasis.  (I)		