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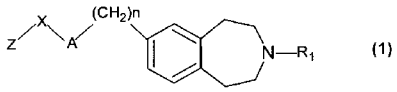
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(54) Title: BENZAZEPINE DERIVATIVES AND THEIR USE AS HSTAMINE H3 ANTAGONISTS



(1)

(57) Abstract: A compound having the formula (1) wherein: R1 is a group selected from C_{3-8} cycloalkyl, C_{1-6} alkyl, C_{1-6} alkylene-C_{3-8} cycloalkyl, each of which groups may optionally be substituted with C_{1-6} alkyl, halogen, haloC_{1-6} alkyl or OR15, or R1 is heterocyclyl, optionally substituted with C_{1-6} alkyl, haloC_{1-6} alkyl or OR15; n is 0, 1, 2, 3 or 4, the alkylene group -$(CH_2)_n$- formed thereby being optionally substituted with a group selected from C_{1-4} alkyl, C_{3-8} cycloalkyl and arylsulfonyl; A is a group selected from -N(R2)CO-, -CON(R2)-, -OC(O)-, -C(O)O-, -CO-, -C(R2)(OR3)-, -C(=N-O-R3)-, - C(=CR2R3)-, -C_{3-8} cycloalkylene-, -C(R2)(haloC_{1-6} alkyl)-, C_{1-4} alkylene and -C(OR3)(haloC_{1-6} alkyl)-; R2 and R3 are each independently selected from H, C_{1-6} alkyl, and C_{3-8} cycloalkyl, or, when A is -N(R2)CO- and X is absent, R2 may form, together with the adjacent nitrogen atom and Z, an N-containing heterocyclyl group, which may optionally be substituted; X is absent or is C_{1-4} alkylene or C_{2-4} alkenylene, each of which may optionally be substituted with one or more C_{1-4} alkyl groups, OR16, halogen or haloC_{1-6} alkyl; Z is selected from aryl, heteroaryl, C_{3-8} cycloalkyl, and heterocyclyl, each of which may optionally be substituted by a group selected from -Y-aryl, -Y-heteroaryl, -Y-C_{3-8} cycloalkyl and -Y-heterocyclyl, or, when X is present, Z may be H, or, when X is absent and A is -C(R2)(OR3)- or -N(R2)CO-, Z may be H, or, when A is -N(R2)CO- and X is absent, Z may form, together with the adjacent nitrogen atom and R2, an N-containing heterocyclyl group which may optionally be substituted, wherein, when A is -CO-, Z is linked to X or A via a carbon atom and wherein, when A is -N(R2)CO- and Z is H, R1 is C_{3-8} cycloalkyl; and Y represents a bond, C_{1-6} alkylene, CO, NR14, COC_{2-6} alkenylene, O, SO_2 or NHCOC_{1-6} alkylene; wherein said cycloalkyl, aryl, heteroaryl and heterocyclyl groups Z may be optionally substituted by one or more substituents which may be the same or different, and which are selected from halogen, haloC_{1-6} alkyl, hydroxy, cyano, nitro, =O, -R4, -CO_2R4, -COR4, -NR5R6, -C_{1-6} alkyl-NR5R6, -C_{3-8} cycloalkyl-NR5R6, - CONR12R13, -NR12COR13, -NR5SO_2R6, -OCONR5R6, -NR5CO_2R6, -NR4CONR5R6 or -SO_2NR5R6- SHR8, -alkyl-OR8, -SOR8, -OR9, -SO_2R9, -OSO_2R9, -alkyl-SO_2R9, -alkyl-CONHR9, -alkyl-SONHR9, -alkyl-COR10, -CO-alkyl-R10, -O-alkyl-R11 (wherein R4, R5 and R6 independently represent hydrogen, C_{1-6} alkyl, -C_{3-8} cycloalkyl, -C_{1-6} alkylene-C_{3-8} cycloalkyl, aryl, heterocyclyl or heteroaryl, wherein R8 represents C_{1-6} alkyl, wherein R9 represents C_{1-6} alkyl or aryl, wherein R10 represents aryl, wherein R11 represents C_{3-8} cycloalkyl or aryl, R12, R13, R14, R15 and R16 each independently represent H or C_{1-6} alkyl, and wherein -NR5R6 and -NR12R13 may represent a nitrogen containing heterocyclyl group); wherein said R4, R5, R6 R8, R9, R11 and R11 groups may be optionally substituted by one or more substituents which may be the same or different, and which are selected from the group consisting of halogen, hydroxy, C_{1-6} alkyl, C_{1-6} alkoxy, cyano, amino, =O or trifluoromethyl; and wherein substituents of Z selected from -Y-aryl, -Y-heteroaryl, -Y-C_{3-8}cycloalkyl and -Y-heterocyclyl may be optionally substituted by one or more substituents selected from =O, hydroxy, cyano, nitro, halogen, haloC_{1-6} alkyl and C_{1-6}alkyl; and wherein, when A is C_{1-4} alkylene, said

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cycloalkyl, aryl, heteroaryl or heterocyclyl group Z (such as a heterocyclyl group Z) is substituted at least with hydroxy, CF_3, or =0; and wherein, when A is CON(R2) n is 1; or a pharmaceutically acceptable salt or ester thereof, provided that: when A is -CO-, R1 is CH_3, C_{3-8} cycloalkyl-substituted C_{1-6} alkylene or n-butyl, n is 0 and X is $-CH_2CH_2-$, Z is not N-benzyl substituted 4-piperidinyl, N-(3-fluorobenzyl)-substituted 4-piperidinyl or N-acetyl substituted 4-piperidinyl; when A is -OC(O)-, R1 is cyclobutyl, n is 0 and X is $-CH_2CH_2-$, Z is not H; when A is -OC(O)-, R1 is n-propyl, n is 0 and X is $-CH_2-$, Z is not H; and when A is -CO-, R1 is CH_3, n is 0 and X is CH_2, Z is not H.