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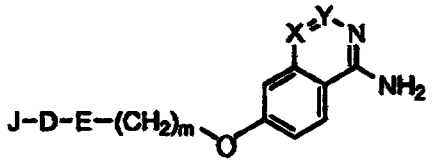
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(54) Title: SERINE PROTEASE INHIBITOR

(57) Abstract

The invention relates to a serine protease inhibitor having formula (I), in which J is H, R^1, R^1–O–C(O)–, R^1–C(O)–, R^1–SO_2–, R^3OOC–$(CHR^2)_p$–, $(R^{2a}, R^{2b})N$–CO–$(CHR^2)_p$– or Het–CO–$(CHR^2)_p$–; D is an amino–acid of the formula –NH–CHR^1–C(O)–, –NR^4–CH[$(CH_2)_qC(O)OR^1$]–C(O)–, –NR^4–CH[$(CH_2)_qC(O)N(R^{2a},R^{2b})$]–C(O)–, –$NR^4$–CH[$(CH_2)_qC(O)$Het]–C(O)–, D–1–Tiq, D–3–Tiq, D–Atc, Aic, D–1–Piq or D 3–Piq; E is –NR^2–CH_2 or the fragment (a), optionally substituted with (1–6C)alkyl, (1–6C)alkoxy or benzyloxy; R^1 is selected from (1–12C)alkyl, (2–12C)alkenyl, (2–12C)alkynyl, (3–12C)cycloalkyl and (3–12C)cycloalkyl(1–6C)alkylene, which groups may optionally be substituted with (3–12C)cycloalkyl, (1–6C)alkoxy, oxo, OH, CF_3 or halogen, and from (6–14C)aryl, (7–15C)aralkyl, (8–16C)aralkenyl and (14–20C)(bisaryl)alkyl, whereby the aryl groups may optionally be substituted with (1–6C)alkyl, (3–12C)cycloalkyl, (1–6C)alkoxy, OH, CF_3 or halogen; R^2, R^{2a} and R^{2b} are each independently selected from H, (1–8C)alkyl, (3–8C)alkenyl, (3–8C)alkynyl, (3–8C)cycloalkyl and (3–6C)cycloalkyl(1–4C)alkylene, which can each be optionally substituted with (3–6C)cycloalkyl, (1–6C)alkoxy, CF_3 or halogen, and from (6–14C)aryl and (7–15C)aralkyl whereby the aryl groups may optionally be substituted with (1–6C)alkyl, (3–6C)cycloalkyl, (1–6C)alkoxy, CF_3 or halogen; R^3 is defined for R^2 or Het–(1–6C)alkyl; R^4 is H or (1–3C)alkyl; X and Y are CH or N with the proviso that they are not both N; Het is a 4–, 5– or 6–membered heterocycle containing one or more heteroatoms selected from O, N and S; m is 1 or 2; p is 1, 2 or 3; q is 1, 2 or 3; t is 2, 3 or 4; or a prodrug; or a pharmaceutically acceptable addition salt and/or solvate thereof and its use in therapy and manufacture of a medicament for treating or preventing thrombin–mediated and thrombin–associated diseases.



(I)



(a)