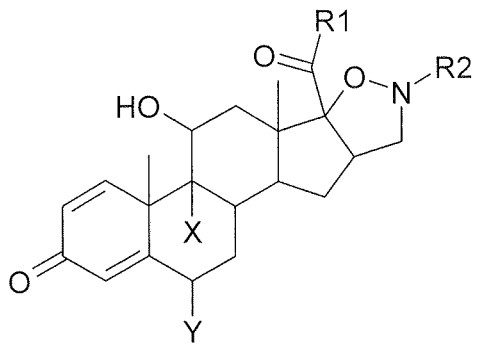
CLAIMS

1. A compound of general formula (I)



(I)

wherein

R1 is $(CH_2)_n$-Z-$(CH_2)_{n'}$-R4 wherein n and n' are each independently 0, 1 or 2;

Z is a single bond or is selected from the group consisting of S, O, CO and NR3, wherein R3 is selected from the group consisting of H, straight or branched $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$haloalkyl, $(C_3$-$C_8)$cycloalkyl, aryl, aryl$(C_1$-$C_6)$alkyl and heteroaryl, which are optionally substituted by CN;

R4 is selected from the group consisting of:

- H, halogen, OH, SH, CN, NH_2;
- aryl$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkylsulfonyl, $(C_1$-$C_6)$alkylcarbonyl, $(C_1$-$C_6)$alkylcarboxyl, O$(C_1$-$C_6)$alkylcarboxyl, $(C_1$-$C_6)$alkylamide and $(C_1$-$C_6)$alkoxy, which are optionally substituted by oxo groups;
- $(C_1$-$C_6)$alkyl which may be optionally substituted by one or more substituents selected from the group consisting of halogen atoms, CN, OH, NH_2, NO_2, CF_3 and SH;

- $(C_2$-$C_6)$alkynyl;
- a mono-, bi- or tricyclic saturated or partially saturated or unsaturated ring, such as $(C_3$-$C_8)$cycloalkyl, aryl, $(C_5$-$C_{10})$heterocycloalkyl or heteroaryl, optionally substituted by one or more halogen atoms or oxo groups;

R2 is ~~selected from the group consisting of~~

~~H;~~

~~straight or branched $(C_1$-$C_6)$alkyl;~~

~~$(CH_2)_m$R5, wherein R5 is heteroaryl optionally substituted with a substituent selected from the group consisting of oxo, OH, halogen, CN, NH_2, NO_2, aryl, $(C_1$-$C_6)$alkylsulfonyl, $(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$alkylthio, $(C_1$-$C_6)$alkylcarboxyl, $(C_1$-$C_6)$alkylamide, aryl$(C_1$-$C_6)$alkoxy and $(C_1$-$C_6)$alkyl, each of which is optionally substituted by one or more halogen atoms or COOH;~~

~~$(CH_2)_p$NR6R7;~~

~~$(CH_2)_p$NR6COR7;~~

~~$(CH_2)_p$NR6SO_2R7;~~

~~$(CH_2)_m$CONR6R7;~~

~~$(CH_2)_m$$SO_2$NR6R7;~~

~~$(CH_2)_m$COR7;~~

~~$(CH_2)_p$OR7;~~

~~$(CH_2)_m$$SO_q$R7;~~

~~wherein R6 and R7 are independently H or are selected from the group consisting of straight or branched $(C_1$-$C_6)$alkyl, $(C_3$-$C_8)$cycloalkyl, aryl$(C_1$-$C_6)$alkyl and a saturated, partially saturated or unsaturated, optionally fused ring~~

~~such as aryl, (C_5-C_{10})heterocycloalkyl or heteroaryl, which groups may be optionally substituted with one or more substituents selected from the group consisting of halogen, CN, oxo, NH_2, NO_2 and (C_1-C_6)alkyl;~~

- $(CH_2)_pR8$ wherein R8 is selected from the group consisting of halogen, oxo, CN, OH, NH_2, NO_2; (C_3-C_8)cycloalkyl, aryl and a saturated, partially saturated or unsaturated optionally fused ring such as (C_5-C_{10})heterocycloalkyl, which are optionally substituted by one or more substituents selected from the group consisting of halogen, CO, CN, (C_1-C_6)alkyl, (C_1-C_6)haloalkyl, (C_1-C_6)carboxyalkyl, (C_1-C_6)alkoxy, (C_1-C_6)haloalkoxy and (C_1-C_6)alkylsulfonyl;

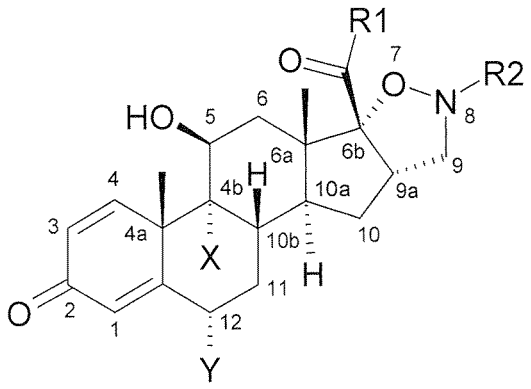
wherein ~~m and~~ p is~~are, each independently,~~ 0 or an integer from 1 to 6 ~~and q is 0, 1 or 2~~ and

X and Y are both fluorine~~independently selected from the group consisting of H and halogen~~ atoms

and pharmaceutically acceptable salts thereof~~,~~

~~with the proviso that when R2 is (C_1-C_6)alkyl, X and Y are not simultaneously H~~.

2. A compound according to claim 1 represented by general formula (I')



(I')

wherein 4a is (R), 4b is (R), 5 is (S), 6a is (S), 6b is (R), 9a is (S), 10a is (S), 10b is (S) and 12 is (S).

3. A compound according to claims 1 or 2, wherein

R1 is $(CH_2)_n$-Z-$(CH_2)_{n'}$-R4 wherein n and n' are each independently 0, 1 or 2;

Z is a single bond or is selected from the group consisting of S, O, CO and NR3, wherein R3 is selected from the group consisting of H, straight or branched $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$haloalkyl, $(C_3$-$C_8)$cycloalkyl, aryl, aryl$(C_1$-$C_6)$alkyl and heteroaryl, which are optionally substituted by CN;

R4 is selected from the group consisting of:

- H, halogen, OH, SH, CN, NH_2;
- aryl$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkylsulfonyl, $(C_1$-$C_6)$alkylcarbonyl, $(C_1$-$C_6)$alkylcarboxyl, O$(C_1$-$C_6)$alkylcarboxyl, $(C_1$-$C_6)$alkylamide and $(C_1$-$C_6)$alkoxy, which are optionally substituted by oxo groups;
- $(C_1$-$C_6)$alkyl which may be optionally substituted by one or more substituents selected from the group consisting of halogen atoms, CN, OH, NH_2, NO_2, CF_3 and SH;
- $(C_2$-$C_6)$alkynyl;
- a mono-, bi- or tricyclic saturated or partially saturated or unsaturated ring, such as $(C_3$-$C_8)$cycloalkyl, aryl, $(C_5$-$C_{10})$heterocycloalkyl or heteroaryl, optionally substituted by one or more halogen atoms or oxo groups;

R2 is ~~selected from the group consisting of~~

~~H;~~

~~$(CH_2)_mR5$, wherein R5 is heteroaryl optionally substituted with a substituent selected from the group consisting of oxo, OH, halogen, CN, NH_2, NO_2, aryl, $(C_1$-$C_6)$alkylsulfonyl, $(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$alkylthio, $(C_1$-$C_6)$alkylcarboxyl, $(C_1$-$C_6)$alkylamide, aryl$(C_1$-$C_6)$alkoxy and $(C_1$-$C_6)$alkyl, each of which is optionally substituted by one or more halogen atoms or COOH;~~

~~$(CH_2)_pNR6R7$;~~

~~$(CH_2)_pNR6COR7$;~~

~~$(CH_2)_pNR6SO_2R7$;~~

~~$(CH_2)_mCONR6R7$;~~

~~$(CH_2)_mSO_2NR6R7$;~~

~~$(CH_2)_mCOR7$;~~

~~$(CH_2)_pOR7$;~~

~~$(CH_2)_mSO_qR7$;~~

~~wherein R6 and R7 are independently H or are selected from the group consisting of straight or branched $(C_1$-$C_6)$alkyl, $(C_3$-$C_8)$cycloalkyl, aryl$(C_1$-$C_6)$alkyl and a saturated, partially saturated or unsaturated, optionally fused ring such as aryl, $(C_5$-$C_{10})$heterocycloalkyl or heteroaryl, which groups may be optionally substituted with one or more substituents selected from the group consisting of halogen, CN, oxo, NH_2, NO_2 and $(C_1$-$C_6)$alkyl;~~

- $(CH_2)_pR8$ wherein R8 is selected from the group consisting of halogen, oxo, CN, OH, NH_2, NO_2; $(C_3$-$C_8)$cycloalkyl, aryl and a saturated, partially saturated or unsaturated optionally fused ring such as $(C_5$-$C_{10})$heterocycloalkyl, which are optionally substituted by one or more substituents selected from the group consisting of halogen, CO, CN, $(C_1$-

C_6)alkyl, (C_1-C_6)haloalkyl, (C_1-C_6)carboxyalkyl, (C_1-C_6)alkoxy, (C_1-C_6)haloalkoxy and (C_1-C_6)alkylsulfonyl;

wherein ~~m and~~ p is~~are, each independently,~~ 0 or an integer from 1 to 6 ~~and q is 0, 1 or 2~~ and

X and Y are both fluorine~~independently selected from the group consisting of H and halogen~~ atoms

and pharmaceutically acceptable salts thereof.

4. A compound according to anyone of claims 1 to 3, wherein R1 is $(CH_2)_n$-Z-$(CH_2)_{n'}$-R4, wherein n is 0 or 1; Z is a single bond or is selected from the group consisting of S, O and NR3, wherein R3 is H or (C_1-C_6)alkyl; n' is 0, 1 or 2; R4 is selected from the group consisting of H, halogen, CN, OH; (C_1-C_6)alkyl, optionally substituted by one or more substituents selected from the group consisting of halogen atoms, CN, OH, NH_2, NO_2, CF_3 and SH; aryl(C_1-C_6)alkyl, (C_1-C_6)alkynyl, (C_1-C_6)alkylsulfonyl, (C_1-C_6)alkylcarbonyl, O(C_1-$_6$)alkylcarbonyl, (C_1-C_6)alkylamide, (C_1-C_6)alkylcarboxyl, (C_5-C_{10})heterocycloalkyl and heteroaryl, which are optionally substituted by oxo groups.

5. A compound according to claim 4, wherein R4 is selected from the group consisting of methyl, ethyl, benzothiazole, benzooxazole, tetrahydrofuran, tetrahydropyran, methylsulfonyl, methylcarbonyl, chlorine, fluorine, trifluoromethyl, methylcarboxyl, ethylcarboxyl, methoxy, ethoxy, trifluoromethyl and butynyl.

6. A compound according to claim 4, wherein R3 is H or methyl.

7. A compound according to anyone of claims 1 to 3, wherein R2 is ~~H or is selected from the group consisting of $(CH_2)_m$R5 wherein m is 1 or 2, R5 is~~

~~heteroaryl optionally substituted by a group selected from halogen, CN, OH, CF3, $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$haloalkyl, $(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$alkylsulfonyl and aryl; $(CH_2)_m$CONR6R7 wherein m is 0, R6 is $(C_1$-$C_6)$alkyl and R7 is aryl; $(CH_2)_m$COR7, wherein m is 1, R7 is aryl, heteroaryl or $(C_5$-$C_{10})$heterocycloalkyl; $(CH_2)_p$OR7, wherein p is 2 and R7 is aryl or aryl$(C_1$-$C_6)$alkyl; $(CH_2)_m SO_q$R7 wherein m is 0 or 2, q is 0 or 2 and R7 is $(C_1$-$C_6)$alkyl or aryl; and~~ $(CH_2)_p$R8 wherein p is 1, 2 or 3 and R8 is selected from the group consisting of aryl and $(C_5$-$C_{10})$heterocycloalkyl, optionally substituted by one or more substituents selected from the group consisting of halogen, oxo, CN, OH, CF_3, $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$haloalkyl, $(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$haloalkoxy, $(C_1$-$C_6)$alkylcarboxyl and $(C_1$-$C_6)$alkylsulfonyl.

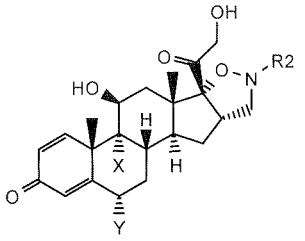
8. A compound according to claim 7, wherein R2 is selected from the group consisting of phenyl, thiophenyl, pyridyl, imidazolyl, thiazolyl, benzyloxyethyl, phenylsulfanyl, phenylpropyl, phenoxyethyl, isoxazolyl, benzoyl, furancarbonyl, methanesulfonyl, dihydropyridinemethyl and methylphenylamide, cyclopentenone, benzofuran, furan, dihydrobenzodioxin radicals.

~~9. A compound according to anyone of claims 1 to 3, wherein X and Y are both H or fluorine atoms or X is chlorine and Y is H.~~

~~10. A compound according to anyone of claims 1 or 2, wherein R2 is a straight or branched $(C_1$-$C_6)$alkyl.~~

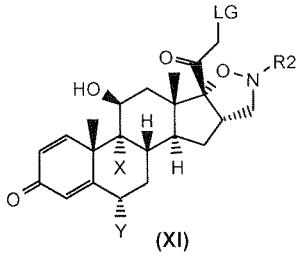
9~~11~~. A process for the preparation of compounds as defined in anyone of the previous claims, wherein R1=$(CH_2)_n$-Z-$(CH_2)_{n'}$-R4, wherein n=1, which comprises:

- the reaction of compounds of formula (VI)



(VI)

with methanesulfonyl chloride or p-toluenesulfonyl chloride to obtain compounds of general formula (XI)

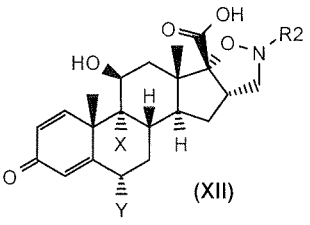


(XI)

wherein the leaving group (LG) may be displaced by nucleophiles.

10~~12~~. A process for the preparation of compounds as defined in anyone of the previous claims, wherein R1=$(CH_2)_n$-Z-$(CH_2)_{n'}$-R4 wherein n=0, which comprises:

- the reaction of compounds of formula (VI) under oxidizing conditions to obtain the intermediates of general formula (XII)



(XII)

- the treatment of compound of formula (XII) with one or more equivalents of an acid activating agent and then with a nucleophile.

11~~13~~. A pharmaceutical composition comprising a compound as defined in anyone of the claims 1 to 8~~10~~, together with one or more pharmaceutically acceptable carriers and/or excipients.

12~~14~~. A combination of a compound as defined in anyone of the claims 1 to 8~~10~~ with one or more active ingredients selected from the classes of beta2-agonists, antimuscarinic agents, corticosteroids, mitogen-activated protein kinases (P38 MAP kinase) inhibitors, nuclear factor kappa-B kinase subunit beta (IKK2) inhibitors, human neutrophil elastase (HNE) inhibitors, phosphodiesterase 4 (PDE4) inhibitors, leukotriene modulators, non-steroidal anti-inflammatory agents (NSAIDs) and mucus regulators.

13~~15~~. A compound as defined in anyone of the claims 1 to 8~~10~~, for use as a medicament.

14~~16~~. A compound as defined in anyone of the claims 1 to 8~~10~~, for use in the prevention and/or treatment of any disease wherein the decrease in the number, activity and movement of inflammatory cells is involved.

15~~17~~. Use of a compound as defined in any one of the claims 1 to 8~~10~~ for the preparation of a medicament for prevention and/or treatment of any disease wherein a decrease in the number, activity and movement of inflammatory cells is involved.