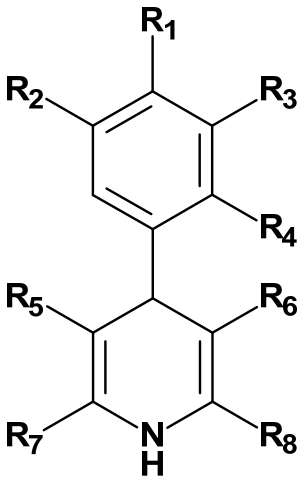
Claims

1. A compound of formula I:



I

where:

R_1 is selected from halo, CF_3, CN or NO_2;

R_2 is selected from halo, CH_3, CF_3, CN or NO_2;

R_3 is selected from H, halo, CH_3, CF_3, CN or NO_2;

R_4 is selected from H, halo, CN or CF_3;

R_5 and R_6 are independently selected from $R_{9a}C(O)O$-, $R_{9b}OC(O)$-, $R_{9c}C(O)NR_{9d}$-, $R_{9e}R_{9f}NC(O)$-, or an alkyl ketone having from 1 to 10 carbon atoms, which carbon atoms are branched or unbranched and are unsubstituted or substituted by one of more substituents selected from halo, and NO_2;

R_7 and R_8 are independently selected from H, $NR_{10a}R_{10b}$, OR_{10c} or C_1 to C_3 alkyl which is unsubstituted or substituted by one or more substituents selected from halo; and

R_{9a} to R_{9f} and R_{10a} to R_{10c} are independently selected from H and C_1 to C_6 alkyl which is unsubstituted or substituted by one or more substituents selected from halo,

or pharmaceutically acceptable salts and/or solvates thereof.

2. The compound according to Claim 1, wherein R_1 is selected from F, Cl, Br, CF_3 or NO_2.

3. The compound according to Claim 1 or Claim 2, wherein R_2 is selected from F, Cl, Br, CH_3, CF_3 or NO_2.

4. The compound according to any one of the preceding claims, wherein R_3 is selected from H, F, Cl, Br, CH_3, CF_3 or NO_2.

5. The compound according to any one of the preceding claims, wherein R_4 is selected from H, F, Cl, Br, or CF_3.

6. The compound according to any one of the preceding claims, wherein R_5 and R_6 are independently selected from $R_{9a}C(O)O$-, $R_{9b}OC(O)$-, or an alkyl ketone having from 1 to 10 carbon atoms, which carbon atoms are branched or unbranched and are unsubstituted or substituted by one of more substituents selected from Cl, F, and NO_2.

7. The compound according to any one of the preceding claims, wherein R_7 and R_8 are independently selected from H or C_1 to C_3 alkyl which is unsubstituted or substituted by one or more substituents selected from F and Cl.

8. The compound according to any one of the preceding claims, wherein R_{9a} to R_{9f} and R_{10a} to R_{10c} are independently selected from H and C_1 to C_3 alkyl which is unsubstituted or substituted by one or more substituents selected from F and Cl.

9. The compound according to any one of the preceding claims, wherein:
R_1 is selected from F, Cl, or CF_3; and/or
R_2 is selected from F, Cl, or CF_3; and/or
R_3 is selected from H, F, Cl, or CF_3; and/or
R_4 is selected from H, F, Cl, or CF_3; and/or
R_5 and R_6 are independently selected from $R_{9b}OC(O)$-, an alkyl ketone having from 1 to 3 carbon atoms, which carbon atoms are unsubstituted or substituted by one of more substituents selected from Cl and F; and/or
R_7 and R_8 are independently selected from H, or methyl which is unsubstituted or substituted by one or more substituents selected from F and Cl.

10. The compound according to any one of the preceding claims, wherein:
R_1 is selected from F or Cl; and/or
R_2 is selected from CF_3 or, more particularly, F; and/or
R_3 is selected from H or CF_3; and/or
R_4 is H; and/or
R_5 and R_6 are independently selected from $CH_3OC(O)$- or propan-2-onyl (e.g. R_5 and R_6 are both $CH_3OC(O)$-); and/or
R_7 and R_8 are independently selected from H and CH_3.

11. The compound according to any one of the preceding claims, wherein at least one of R_7 and R_8 is H.

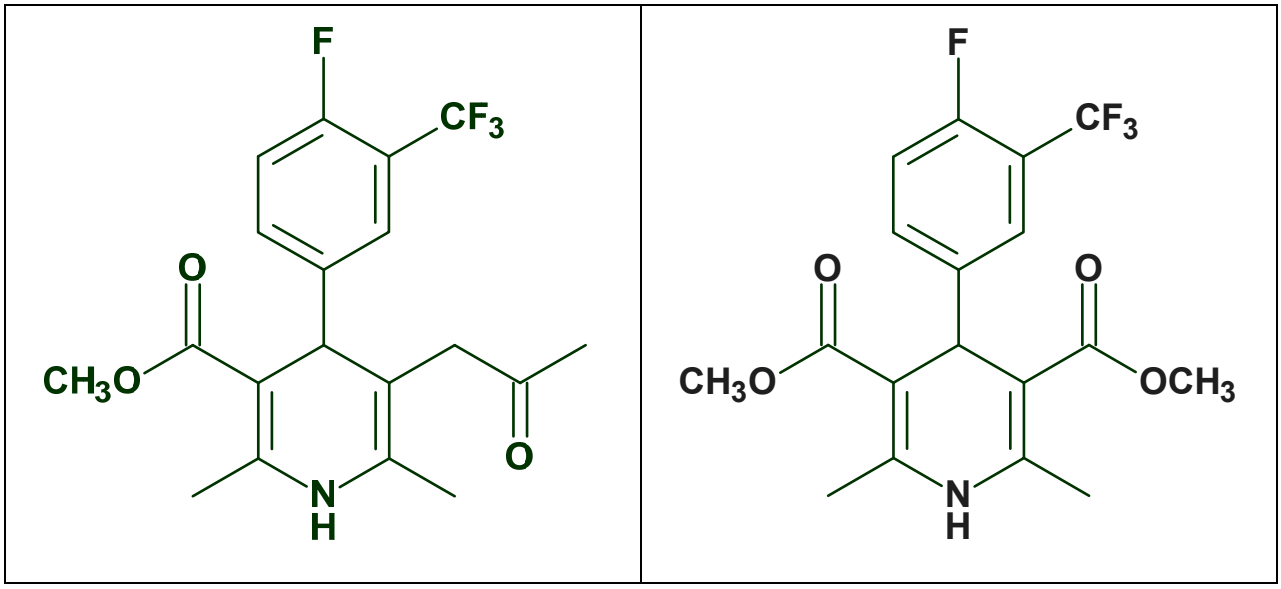
12. The compound according to any one of the preceding claims, wherein both of R_7 and R_8 is H.

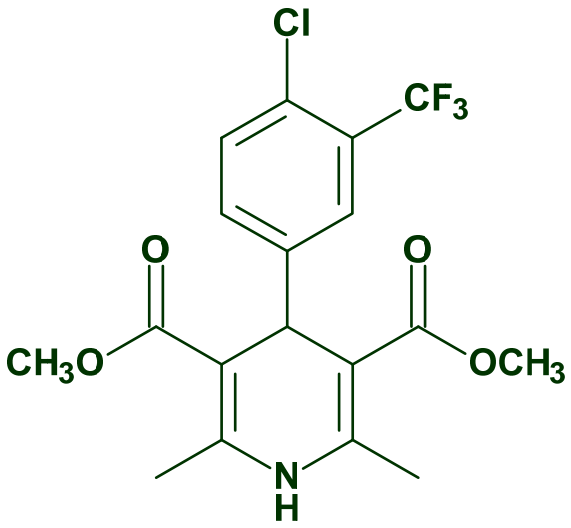
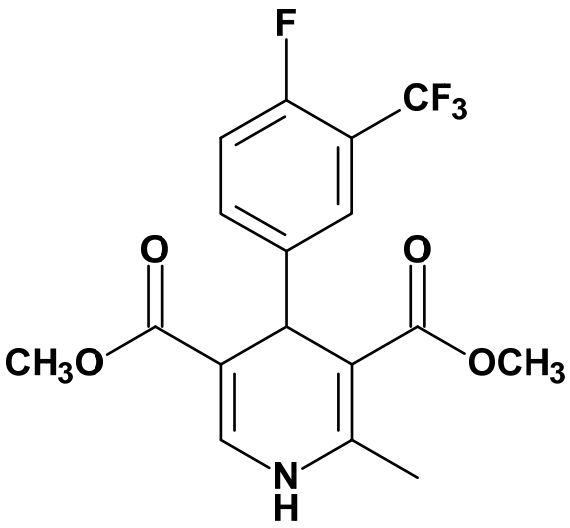
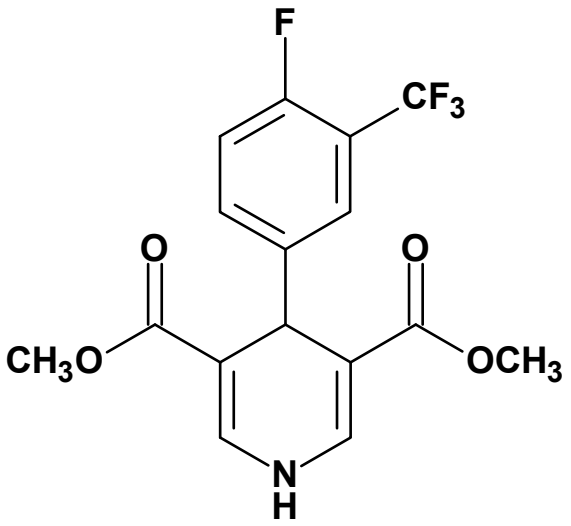
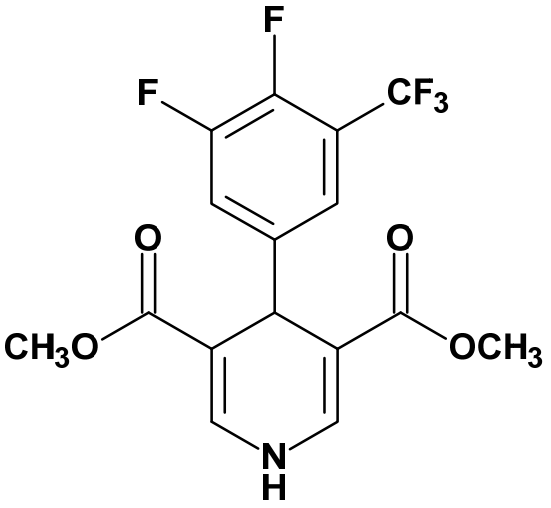
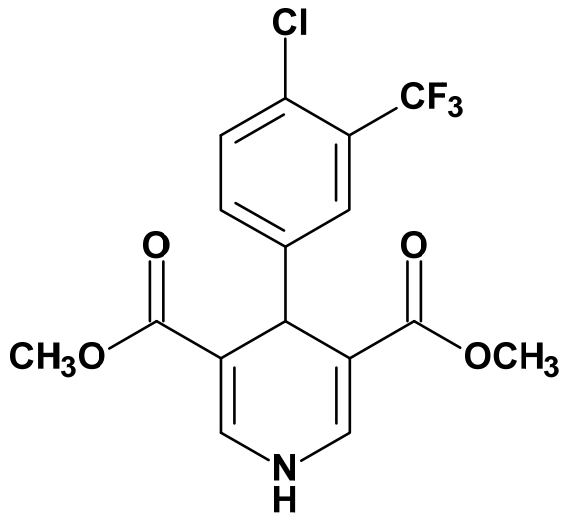
13. The compound according to any one of Claims 1 to 11, wherein R_7 is H and R_8 is CH_3.

14. The compound according to any one of Claims 1 to 10, wherein R_7 and R_8 are both CH_3.

15. The compound according to any one of Claims 1 to 11, wherein R_7 is CH_3 and R_8 is H.

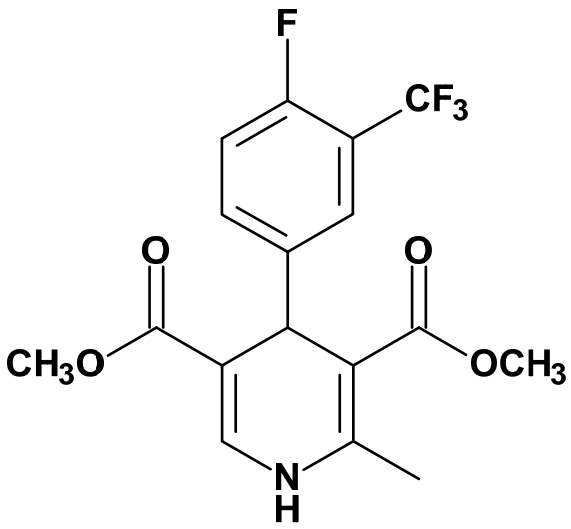
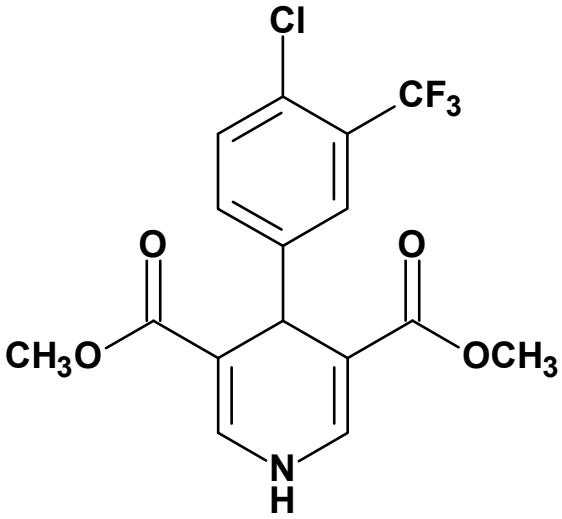
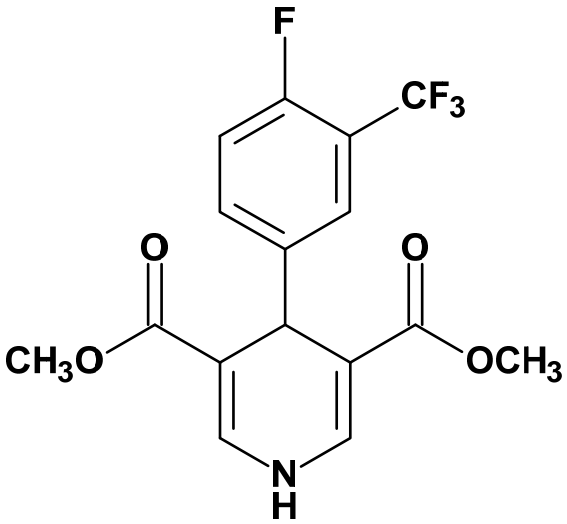
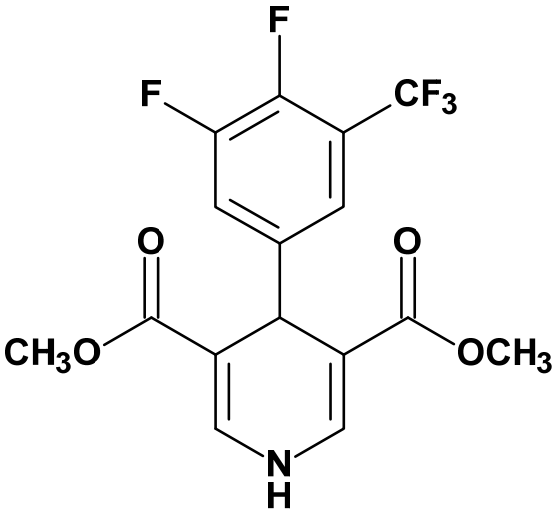
16. The compound according to any one of the preceding claims selected from the list,



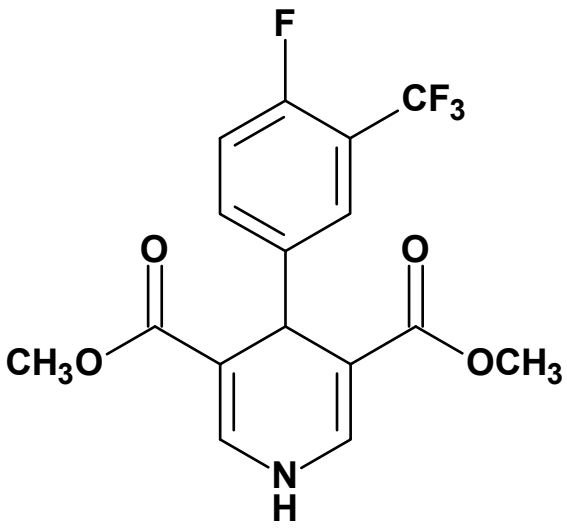
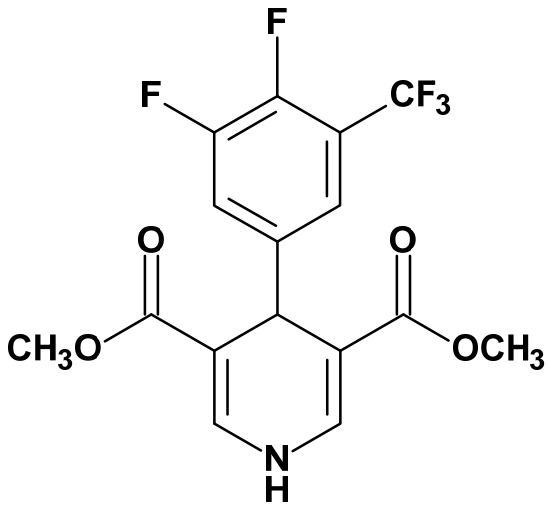
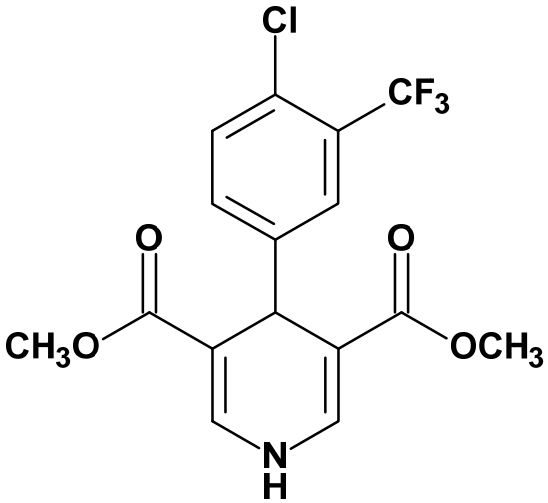
or salts and solvates thereof.

17. The compound according to any one of the preceding claims selected from the list,

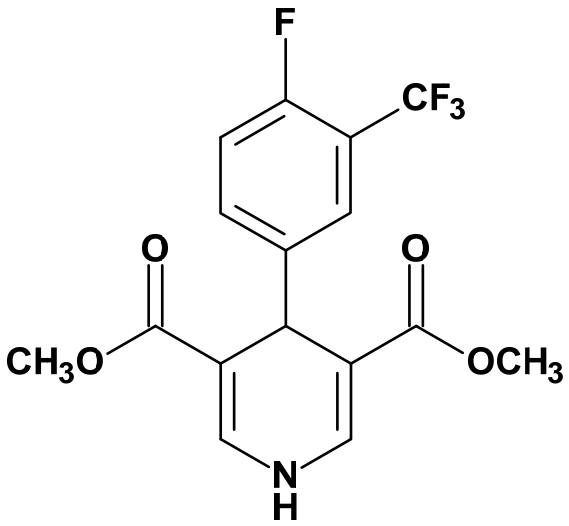
or salts and solvates thereof.

18. The compound according to any one of the preceding claims selected from the list,

or salts and solvates thereof.

19. The compound according to any one of the preceding claims wherein the compound is



or salts and solvates thereof.

20. A pharmaceutical composition comprising a compound of formula I, or salts and solvates thereof, as described in any one of Claims 1 to 19 in combination with one or more of a pharmaceutically acceptable carrier, adjuvant, or vehicle.

21. A compound of formula I, or salts and solvates thereof, as described in any one of Claims 1 to 19 for use in medicine.

22. A compound of formula I, or salts and solvates thereof, as described in any one of Claims 1 to 19 for use in the treatment or prevention of a disease condition that is associated with increased $K_{Ca}3.1$ or altered activity, wherein the disease condition that is associated with increased $K_{Ca}3.1$ or altered activity is selected from one or more of inflammatory bowel diseases (IBD), fibrotic diseases (lung, liver, renal, cardiac, conjunctival, corneal), non-alcoholic fatty liver disease (NAFLD), nonalcoholic steatohepatitis (NASH), gliomas (glioblastoma), lung cancer, pancreatic cancer, hepatocellular carcinoma, ovarian cancer, colorectal cancer, cystic fibrosis, diabetic renal disease, glomerulonephritis, bone resorption, inflammatory arthritis, multiple sclerosis, atherosclerosis, restenosis following angioplasty, in-stent neo-atherosclerosis, stroke, traumatic brain injury, Alzheimer's disease, hereditary xerocytosis, sickle cell anemia, leukaemia, asthma, allergic rhinitis, microglial activation, nitric oxide-dependent neurodegeneration, neuro-oncological diseases and orphan red blood cell disorders.

23. Use of a compound of formula I, or salts and solvates thereof, as described in any one of Claims 1 to 19 in the preparation of a medicament for the treatment or prevention of a disease condition that is associated with increased $K_{Ca}3.1$ or altered activity, wherein the disease condition that is associated with increased $K_{Ca}3.1$ or altered activity is selected from one or more of inflammatory bowel diseases (IBD), fibrotic diseases (lung, liver, renal, cardiac, conjunctival, corneal), non-alcoholic fatty liver disease (NAFLD), nonalcoholic steatohepatitis (NASH), gliomas (glioblastoma), lung cancer, pancreatic cancer, hepatocellular carcinoma, ovarian cancer, colorectal cancer, cystic fibrosis, diabetic renal disease, glomerulonephritis, bone resorption, inflammatory arthritis, multiple sclerosis, atherosclerosis, restenosis following angioplasty, in-stent neo-atherosclerosis, stroke, traumatic brain injury, Alzheimer's disease, hereditary xerocytosis, sickle cell anemia, leukaemia, asthma, allergic rhinitis, microglial activation, nitric oxide-dependent neurodegeneration, neuro-oncological diseases and orphan red blood cell disorders.

24. Use of an effective amount of a compound of formula, or salts and solvates thereof, as described in any one of Claims 1 to 19 in the manufacture of a medicament for the treatment or prevention of a disease condition that is associated with increased $K_{Ca}3.1$ or altered activity, wherein the disease condition that is associated with increased $K_{Ca}3.1$ or altered activity is selected from one or more of inflammatory bowel diseases (IBD), fibrotic diseases (lung, liver, renal, cardiac, conjunctival, corneal), non-alcoholic fatty liver disease (NAFLD), nonalcoholic steatohepatitis (NASH), gliomas (glioblastoma), lung cancer, pancreatic cancer, hepatocellular carcinoma, ovarian cancer, colorectal cancer, cystic fibrosis, diabetic renal disease, glomerulonephritis, bone resorption, inflammatory arthritis, multiple sclerosis, atherosclerosis, restenosis following angioplasty, in-stent neo-atherosclerosis, stroke, traumatic brain injury, Alzheimer's disease, hereditary xerocytosis, sickle cell anemia, leukaemia, asthma, allergic rhinitis, microglial activation, nitric oxide-dependent neurodegeneration, neuro-oncological diseases and orphan red blood cell disorders.

25. The compound for use of Claim 22, the use of Claim 23 or the use of Claim 24, wherein the disease condition that is associated with increased $K_{Ca}3.1$ or altered activity is selected from one or more of inflammatory bowel diseases (IBD), fibrotic diseases (lung, liver, renal, cardiac, conjunctival, corneal), non-alcoholic fatty liver disease (NAFLD), nonalcoholic steatohepatitis (NASH), gliomas (glioblastoma), lung cancer, pancreatic cancer, hepatocellular carcinoma, ovarian cancer, colorectal cancer, cystic fibrosis, diabetic renal disease, glomerulonephritis, bone resorption, inflammatory arthritis, multiple sclerosis, atherosclerosis, restenosis following angioplasty, in-stent neo-atherosclerosis, stroke, traumatic brain injury, Alzheimer's disease, hereditary xerocytosis, sickle cell anemia,

leukaemia, asthma, allergic rhinitis, microglial activation and nitric oxide-dependent neurodegeneration.

26. The compound for use, or the uses of Claim 25, wherein the disease condition is stroke.

27. The compound for use, or the uses of Claim 25, wherein the disease condition is one or both of lung fibrosis and hereditary xerocytosis.