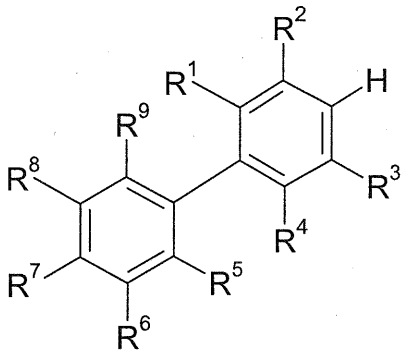
Claims

1. A compound of formula (I) or a pharmaceutically acceptable ~~ester, amide, carbamate or~~ salt thereof~~, including a salt of such an ester, amide or carbamate~~



(I)

in which

R^1 is selected from the group consisting of optionally substituted 5-10 membered heterocyclyl containing one or more oxygen, nitrogen and/or sulphur atoms, optionally substituted phenyl, optionally substituted naphthyl, optionally substituted C_{3-8}cycloalkyl, optionally substituted C_{5-6}cycloalkenyl, optionally substituted phenylC_{2-4}alkenyl, C_{2-8}alkenyl, haloC_{2-8}alkenyl, dihaloC_{2-8}alkenyl, trihaloC_{2-8}alkenyl, and C_{3-8}cycloalkylC_{2-4}alkenyl, wherein when said heterocyclyl, phenyl or naphthyl group or part of group is substituted, it is substituted with from 1 to 5 substituents, each substituent being independently selected from the group consisting of OR^A, $N(R^B)_2$, halogen, cyano, nitro, -C(O)C_{1-4}alkyl, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, haloC_{1-6} alkyl, dihaloC_{1-6}alkyl and trihaloC_{1-6}alkyl, and when said C_{3-8}cycloalkyl or C_{5-6}cycloalkenyl group is substituted, it is substituted with 1, 2 or 3 substituents selected from C_{1-5}alkyl, C_{1-5}alkenyl , C_{1-5}alkynyl, C_{1-5}alkyl substituted with up to 3 halogen atoms, -CO-C_{1-5}alkyl, and halogen;

R^2 is selected from the group consisting of -C(NH_2)=N-OH, -C(O)$N(R^C)_2$, cyano, -CHO, -CH=N-OH, -C(O)NH-OH, -C(CO_2H)=N-OH, -C(O-C_{1-4}alkyl)=NH, -C(NH_2)=N-NH_2, -C(O)-C(O)-NH_2, -C(O)CO_2H, -CO_2H, -CH_2-CO_2H, -CH(OH)CO_2H, -CH_2NH-$CONH_2$, -C_{1-6}alkyl-NH_2, -CH_2SO_3H, -NH-C(NH_2)=NH, -NH-C(O)NH_2, -N=C(-NH-CH_2CH_2-NH-), $NHSO_2R^D$, -S-CN, -S-C(NH_2)=NH, -S-C(NH_2)=N-OH, $SO_2N(R^E)_2$, SO_3H, cyanoC_{1-6}alkyl-, and optionally substituted 5-10 membered heterocyclyl containing from one to three nitrogen atoms, wherein when said heterocyclyl group is substituted, it is substituted with from 1 to 3 substituents, each substituent being independently selected from the group consisting of OR^A, $N(R^B)_2$, halogen, cyano, nitro, -C(O)C_{1-4}alkyl, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, haloC_{1-6} alkyl, dihaloC_{1-6}alkyl and trihaloC_{1-6}alkyl;

4-chloro-3',5'-difluoro-6-(1H-indazol-5-yl)-[1,1'-biphenyl]-2-carboxamide

6-(1H-benzo[d]imidazol-5-yl)-4-chloro-3',5'-difluoro-[1,1'-biphenyl]-2-carboxamide

3',5'-difluoro-N'-hydroxy-6-(1H-indol-5-yl)-4-methyl-[1,1'-biphenyl]-2-carboximidamide

3',5'-difluoro-N'-hydroxy-6-(1H-indol-6-yl)-4-methyl-[1,1'-biphenyl]-2-carboximidamide

3',5'-difluoro-N'-hydroxy-6-(1H-indazol-5-yl)-4-methyl-[1,1'-biphenyl]-2-carboximidamide

3',5'-difluoro-N'-hydroxy-6-(1H-indazol-5-yl)-4-propyl-[1,1'-biphenyl]-2-carboximidamide

3',5'-difluoro-N'-hydroxy-6-(1H-indol-5-yl)-4-propyl-[1,1'-biphenyl]-2-carboximidamide

3',5'-difluoro-N'-hydroxy-6-(1H-indazol-5-yl)-4-(trifluoromethyl)-[1,1'-biphenyl]-2-carboximidamide

3',5'-difluoro-N'-hydroxy-6-(1H-indol-6-yl)-4-(trifluoromethyl)-[1,1'-biphenyl]-2-carboximidamide

3',5'-difluoro-N'-hydroxy-6-(1H-indazol-6-yl)-4-(trifluoromethyl)-[1,1'-biphenyl]-2-carboximidamide

3',5'-difluoro-N'-hydroxy-6-(1H-indol-5-yl)-4-(trifluoromethyl)-[1,1'-biphenyl]-2-carboximidamide

3',5'-difluoro-6-(1H-indol-5-yl)-4-(trifluoromethyl)-[1,1'-biphenyl]-2-carboxamide

3',5'-difluoro-N'-hydroxy-6-(1H-indazol-6-yl)-4-propyl-[1,1'-biphenyl]-2-carboximidamide

N'-hydroxy-6-(1H-indazol-5-yl)-2'-methoxy-5'-methyl-4-(trifluoromethyl)-[1,1'-biphenyl]-2-carboximidamide

5'-chloro-N'-hydroxy-6-(1H-indol-5-yl)-2'-methoxy-4-(trifluoromethyl)-[1,1'-biphenyl]-2-carboximidamide

5'-chloro-N'-hydroxy-6-(1H-indazol-5-yl)-2'-methoxy-4-(trifluoromethyl)-[1,1'-biphenyl]-2-carboximidamide

2',5'-difluoro-N'-hydroxy-6-(1H-indazol-5-yl)-4-(trifluoromethyl)-[1,1'-biphenyl]-2-carboximidamide

3',5'-difluoro-6-(6-fluoro-1H-indol-5-yl)-N'-hydroxy-4-(trifluoromethyl)-[1,1'-biphenyl]-2-carboximidamide

N'-hydroxy-3-(1H-indazol-5-yl)-2-(naphthalen-1-yl)-5-(trifluoromethyl)benzimidamide

2-(benzo[d][1,3]dioxol-4-yl)-N'-hydroxy-3-(1H-indazol-5-yl)-5-(trifluoromethyl)benzimidamide

4'-fluoro-N'-hydroxy-6-(1H-indazol-5-yl)-2'-methoxy-4-(trifluoromethyl)-[1,1'-biphenyl]-2-carboximidamide

N'-hydroxy-6-(1H-indazol-5-yl)-3'-methyl-4-(trifluoromethyl)-[1,1'-biphenyl]-2-carboximidamide

3',4',5'-trifluoro-N'-hydroxy-6-(1H-indazol-5-yl)-4-(trifluoromethyl)-[1,1'-biphenyl]-2-carboximidamide

3',4'-difluoro-N'-hydroxy-6-(1H-indazol-5-yl)-4-(trifluoromethyl)-[1,1'-biphenyl]-2-carboximidamide

N'-hydroxy-3-(1H-indazol-5-yl)-2-(2-methoxypyridin-3-yl)-5-(trifluoromethyl)benzimidamide

2-(cyclopent-1-en-1-yl)-N'-hydroxy-3-(1H-indazol-5-yl)-5-(trifluoromethyl)benzimidamide

2-(3,5-dimethylisoxazol-4-yl)-N'-hydroxy-3-(1H-indazol-5-yl)-5-(trifluoromethyl)benzimidamide

2',4'-difluoro-N'-hydroxy-6-(1H-indazol-5-yl)-4-(trifluoromethyl)-[1,1'-biphenyl]-2-carboximidamide

or a pharmaceutically acceptable ~~ester, amide, carbamate or~~ salt thereof~~, including a salt of such an ester, amide or carbamate~~.

17. The compound as claimed in any one of claims 1 to 16 together with a further therapeutic agent, for simultaneous, sequential or separate administration.

18. A pharmaceutical composition which comprises a compound as claimed in any one of claims 1 to 16, together with a pharmaceutically acceptable carrier.

19. The compound as claimed in any one of claims 1 to 17, or the composition as claimed in claim 18, for use as a medicament.

20. The compound as claimed in any one of claims 1 to 17, or the composition as claimed in claim 18, for use in the treatment or prophylaxis of a condition associated with a disease or disorder associated with estrogen receptor activity.

21. Use of a compound as claimed in any one of claims 1 to 17, for the manufacture of a medicament for the treatment or prophylaxis of a condition associated with a disease or disorder associated with estrogen receptor activity, wherein the condition associated with a disease or disorder associated with estrogen receptor activity is selected from the group consisting of ~~bone loss,~~ bone fractures, osteoporosis, cartilage degeneration, endometriosis, uterine fibroid disease, hot flushes, ~~increased levels of LDL cholesterol,~~ cardiovascular disease, impairment of cognitive functioning, age-related mild cognitive impairment, cerebral degenerative disorders, restenosis, gynecomastia, vascular smooth muscle cell proliferation, obesity, incontinence, anxiety, depression, perimenopausal depression, post-partum depression, premenstrual syndrome, manic depression, dementia, obsessive compulsive behavior, attention deficit disorder, attention deficit hyperactivity disorder, sleep disorders, irritability, impulsivity, anger management, hearing disorders, multiple sclerosis, Parkinson's disease, Alzheimer's disease, Huntington's disease, amyotrophic lateral sclerosis, spinal cord injury, stroke, autoimmune disease, inflammation, IBD, IBS, sexual dysfunction, hypertension, retinal degeneration, lung cancer, colon cancer, breast cancer, uterus cancer, prostate cancer, the bile duct cancer form named cholangiocarcinoma, benign prostatic hyperplasia, lower urinary tract symptoms, overactive bladder, interstitial cystitis, painful bladder symptoms, vaginal atrophy, wound healing, chronic pain, sepsis, inflammatory and neuropathic pain, ovarian cancer, melanoma, lymphoma, atherosclerosis, left ventricular hypertrophy, congestive heart failure, mesothelioma, gallbladder cancer and extra-hepatic cholangiocarcinoma.

22. Use of a compound as claimed in any one of claims 1 to 17, for the manufacture of a medicament for the treatment or prophylaxis of a condition associated with a disease or disorder associated with estrogen receptor activity, wherein the condition associated with a disease or disorder associated with estrogen receptor activity is selected from the group consisting of ~~bone loss,~~ bone fractures, osteoporosis, cartilage

degeneration, endometriosis, uterine fibroid disease, hot flushes, ~~increased levels of LDL cholesterol,~~ cardiovascular disease, restenosis, gynecomastia, vascular smooth muscle cell proliferation, obesity, incontinence, anxiety, depression, perimenopausal depression, post-partum depression, premenstrual syndrome, manic depression, dementia, obsessive compulsive behavior, attention deficit disorder, attention deficit hyperactivity disorder, sleep disorders, irritability, impulsivity, anger management, hearing disorders, spinal cord injury, stroke, autoimmune disease, inflammation, IBD, IBS, sexual dysfunction, hypertension, retinal degeneration, lung cancer, colon cancer, breast cancer, uterus cancer, prostate cancer, the bile duct cancer form named cholangiocarcinoma, benign prostatic hyperplasia, lower urinary tract symptoms, overactive bladder, interstitial cystitis, painful bladder symptoms, vaginal atrophy, wound healing, chronic pain, sepsis, inflammatory and neuropathic pain, ovarian cancer, melanoma, lymphoma, atherosclerosis, left ventricular hypertrophy, congestive heart failure, mesothelioma, gallbladder cancer and extra-hepatic cholangiocarcinoma.

23. Use of a compound as claimed in any one of claims 1 to 16 in labelled form as a diagnostic agent for the diagnosis of conditions associated with a disease or disorder associated with estrogen receptor activity.

24. The use of claim 23 for *in vitro* use.

~~24~~25. Use of a compound as claimed in any one of claims 1 to 16 or a labelled form of such a compound as a reference compound in a method of identifying ligands for the estrogen receptor.

~~25~~26. A compound or composition as claimed in claim 20, or a use as claimed in claim 23, wherein the condition associated with a disease or disorder associated with estrogen receptor activity is selected from the group consisting of ~~bone loss,~~ bone fractures, osteoporosis, cartilage degeneration, endometriosis, uterine fibroid disease, hot flushes, ~~increased levels of LDL cholesterol,~~ cardiovascular disease, impairment of cognitive functioning, age-related mild cognitive impairment, cerebral degenerative disorders, restenosis, gynecomastia, vascular smooth muscle cell proliferation, obesity, incontinence, anxiety, depression, perimenopausal depression, post-partum depression, premenstrual syndrome, manic depression, dementia, obsessive compulsive behavior, attention deficit disorder, attention deficit hyperactivity disorder, sleep disorders, irritability, impulsivity, anger management, hearing disorders, multiple sclerosis, Parkinson's disease, Alzheimer's disease, Huntington's disease, amyotrophic lateral sclerosis, spinal cord injury, stroke, autoimmune disease, inflammation, IBD, IBS, sexual dysfunction, hypertension, retinal degeneration, lung cancer, colon cancer, breast cancer, uterus cancer, prostate cancer, the bile duct cancer form named cholangiocarcinoma, benign prostatic hyperplasia, lower urinary tract symptoms, overactive bladder, interstitial cystitis, painful bladder symptoms, vaginal atrophy, wound healing, chronic pain, sepsis, inflammatory and neuropathic pain, ovarian cancer, melanoma, lymphoma, atherosclerosis, left ventricular hypertrophy, congestive heart failure, mesothelioma, gallbladder cancer and extra-hepatic cholangiocarcinoma.

~~26~~27. A compound or composition as claimed in claim 20, or a use as claimed in claim 23, wherein the condition associated with a disease or disorder associated with estrogen receptor activity is selected from the group consisting of ~~bone loss,~~ bone fractures, osteoporosis, cartilage degeneration, endometriosis, uterine fibroid disease, hot flushes, ~~increased levels of LDL cholesterol,~~ cardiovascular disease, restenosis, gynecomastia, vascular smooth muscle cell proliferation, obesity, incontinence, anxiety, depression, perimenopausal depression, post-partum depression, premenstrual syndrome, manic depression, dementia, obsessive compulsive behavior, attention deficit disorder, attention deficit hyperactivity disorder, sleep disorders, irritability, impulsivity, anger management, hearing disorders, spinal cord injury, stroke, autoimmune disease, inflammation, IBD, IBS, sexual dysfunction, hypertension, retinal degeneration, lung cancer, colon cancer, breast cancer, uterus cancer, prostate cancer, the bile duct cancer form named cholangiocarcinoma, benign prostatic hyperplasia, lower urinary tract symptoms, overactive bladder, interstitial cystitis, painful bladder symptoms, vaginal atrophy, wound healing, chronic pain, sepsis, inflammatory and neuropathic pain, ovarian cancer, melanoma, lymphoma, atherosclerosis, left ventricular hypertrophy, congestive heart failure, mesothelioma, gallbladder cancer and extra-hepatic cholangiocarcinoma.