3-Aminocyclopentane carboxamide derivatives

TECHNICAL FIELD OF THE INVENTION

The present invention relates to novel hydropyrrolopyrrole derivatives which inhibit the activity of fatty acid synthase (FASN; also abbreviated as FAS), to pharmaceutical compositions comprising them, to processes for their preparation, and to their use in therapy for the treatment of cancers.

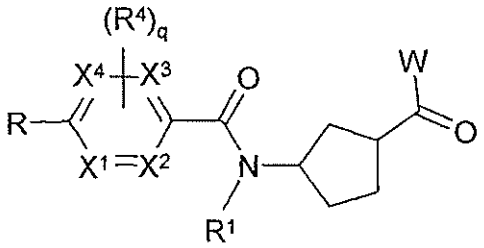
BACKGROUND OF THE INVENTION

Fatty Acid Synthase (FAS) is a critical enzyme for endogenous lipogenesis and plays an important role in the modulation of key intermediates of lipid and carbohydrate cellular metabolism. FAS is highly expressed in the tissues with high metabolic activity (for example liver, adipose tissue and brain) and there are good reasons to believe that a FAS inhibitor would cause beneficial metabolic effects in peripheral tissues. In addition, inhibition of FAS in the hypothalamus may result in reduced food intake. The non-specific irreversible FAS inhibitors cerulenin and C-75 have been reported in the literature to decrease brain levels of orexigenic neuropeptides and to decrease food intake.

FAS is also highly expressed in human sebocytes, the lipid producing cells of the sebaceous glands. Acne is the most common disorder involving the sebaceous gland. The pathogenesis of acne involves lipid (over)production by the sebaceous gland and it has been reported that inhibitors of mammalian FAS inhibit the production of sebum in sebocytes (US 2005/0053631). Acne cannot occur without sebum lipids. There is an unmet medical need in the treatment of acne for agents that reduce sebum production.

Patent Claims

1. Compounds of the formula I



I

in which

R denotes Ar, Het, -C≡C-Ar or -C≡C-Het,

W denotes $NR^2R^{2'}$ or Het^1,

R^1 denotes A, $[C(R^3)_2]_nAr^1$ or $[C(R^3)_2]_nCyc$,

R^2, $R^{2'}$ each, independently of one another, denote H, A or $[C(R^3)_2]_nCyc$,

R^4 denotes H, F, Cl, Br, OH, CN, NO_2, A', OA', SA', SO_2Me, COA', $CONH_2$, CONHA' or $CONA'_2$,

X^1, X^2, X^3, X^4 each, independently of one another, denote CH or N,

A denotes unbranched or branched alkyl with 1-10 C-atoms, wherein two adjacent carbon atoms may form a double bond and/or one or two non-adjacent CH- and/or CH_2-groups may be replaced by N-, O- and/or S-atoms and wherein 1-7 H-atoms may be replaced by R^5,

Cyc denotes cycloalkyl with 3-7 C-atoms, which is unsubstituted or monosubstituted by OH, Hal or A,

A' denotes unbranched or branched alkyl with 1-6 C-atoms, wherein 1-5 H-atoms may be replaced by F,

R^5 denotes F, Cl or OH,

Ar denotes phenyl, which is unsubstituted or mono-, di-, tri-, tetra- or pentasubstituted by Hal, A, $O[C(R^3)_2]_nHet^1$, Ar^1, $[C(R^3)_2]_pOR^3$,

$[C(R^3)_2]_pN(R^3)_2$, NO_2, CN, $[C(R^3)_2]_pCOOR^3$, $CON(R^3)_2$, $[C(R^3)_2]_pN(R^3)_2$, $N(R^3)_2COA$, NR^3SO_2A, $[C(R^3)_2]_pSO_2N(R^3)_2$, $S(O)_nA$, $O[C(R^3)_2]_mN(R^3)_2$, NHCOOA, $NHCON(R^3)_2$ and/or COA,

Ar^1 denotes phenyl or naphthyl, which is unsubstituted or mono-, di-, tri-, tetra- or pentasubstituted by Hal, A, $[C(R^3)_2]_pOR^3$, $[C(R^3)_2]_pN(R^3)_2$, NO_2, CN, $[C(R^3)_2]_pCOOR^3$, $[C(R^3)_2]_pN(R^3)_2$, $N(R^3)_2COA$, NR^3SO_2A, $[C(R^3)_2]_pSO_2N(R^3)_2$, $S(O)_nA$, $O[C(R^3)_2]_mN(R^3)_2$, NHCOOA, $NHCON(R^3)_2$ and/or COA,

R^3 denotes H or unbranched or branched alkyl with 1-6 C-atoms,

Het denotes a mono- or bicyclic saturated, unsaturated or aromatic heterocycle having 1 to 4 N, O and/or S atoms, which is unsubstituted or mono-, di-, tri-, tetra- or pentasubstituted by Hal, A, $[C(R^3)_2]_nOA'$, $[C(R^3)_2]_nN(R^3)_2$, SR^3, NO_2, CN, $COOR^3$, $CON(R^3)_2$, $COHet^1$, NR^3COA, NR^3SO_2A, $SO_2N(R^3)_2$, $S(O)_nA$, $O[C(R^3)_2]_mN(R^3)_2$, NHCOOA, $NHCON(R^3)_2$, CHO, COA, =S, =NH, =NA and/or =O (carbonyl oxygen),

Het^1 denotes a mono- or bicyclic saturated, unsaturated or aromatic heterocycle having 1 to 4 N, O and/or S atoms, which is unsubstituted or mono-, di-, tri-, tetra- or pentasubstituted by Hal, A, $[C(R^3)_2]_nOR^3$, $[C(R^3)_2]_nN(R^3)_2$, SR^3, NO_2, CN, $COOR^3$, $CON(R^3)_2$, NR^3COA, NR^3SO_2A, $SO_2N(R^3)_2$, $S(O)_nA$, $O[C(R^3)_2]_mN(R^3)_2$, NHCOOA, $NHCON(R^3)_2$, CHO, COA, =S, =NH, =NA and/or =O (carbonyl oxygen),

Hal denotes F, Cl, Br or I,

m denotes 1, 2 or 3,

n denotes 0, 1 or 2,

p denotes 0, 1, 2, 3 or 4,

q 0, 1, 2 or 3,

with the proviso that only one or two of X^1, X^2, X^3, X^4 denote N,

and pharmaceutically acceptable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios.

2. Compounds according to Claim 1 in which

R^4 denotes H, F, Cl, OA' or A',

and pharmaceutically acceptable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios.

3. Compounds according to Claim 1 or 2, in which

A denotes unbranched or branched alkyl with 1-10 C-atoms, wherein one or two non-adjacent CH- and/or CH_2-groups may be replaced by N- and/or O-atoms and 1-7 H-atoms may be replaced by R^5,

and pharmaceutically acceptable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios.

4. Compounds according to one or more of Claims 1-3, in which

Ar denotes phenyl, which is unsubstituted or mono-, di-, tri-, tetra- or pentasubstituted by $O[C(R^3)_2]_nHet^1$, Ar^1, A, CN and/or $[C(R^3)_2]_pOR^3$,

and pharmaceutically acceptable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios.

5. Compounds according to one or more of Claims 1-4, in which

Ar^1 denotes phenyl or naphthyl,

and pharmaceutically acceptable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios.

6. Compounds according to one or more of Claims 1-5, in which

Het denotes a mono- or bicyclic aromatic heterocycle having 1 to 4 N, O and/or S atoms, which is unsubstituted or mono- or

disubstituted by Hal, A, $[C(R^3)_2]_nOA'$, $S(O)_nA$, CN, $SO_2N(R^3)_2$ and/or $COHet^1$,

and pharmaceutically acceptable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios.

7. Compounds according to one or more of Claims 1-6, in which

Het^1 denotes a monocyclic saturated heterocycle having 1 to 4 N, O and/or S atoms, which is unsubstituted or mono- or disubstituted by A,

and pharmaceutically acceptable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios.

8. Compounds according to one or more of Claims 1-7, in which

Het denotes furyl, thienyl, pyrrolyl, imidazolyl, pyrazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyridyl, pyrimidinyl, triazolyl, tetrazolyl, oxadiazolyl, thiadiazolyl, pyridazinyl, pyrazinyl, benzoxazolyl, benzothiazolyl, benzimidazolyl, benzotriazolyl, indolyl, benzo-1,3-dioxolyl, benzodioxanyl, benzothiadiazolyl, indazolyl, benzofuranyl, quinolyl, isoquinolyl, oxazolo[5,4-b]-pyridyl, imidazo[1,2-a]pyridinyl or oxazolo[5,4-c]pyridyl, each of which is unsubstituted or mono- or disubstituted by Hal, A, $[C(R^3)_2]_nOA'$, $S(O)_nA$, CN, $SO_2N(R^3)_2$ and/or $COHet^1$,

and pharmaceutically acceptable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios.

9. Compounds according to one or more of Claims 1-8, in which

Het^1 denotes pyrrolidinyl, azetidinyl, oxetanyl, tetrahydroimidazolyl, tetrahydropyrazolyl, tetrahydrofuranyl, piperidinyl, piperazinyl, morpholinyl, hexahydropyridazinyl, hexahydropyrimidinyl, [1,3]dioxolanyl or tetrahydropyranyl, each of which is unsubstituted or mono- or disubstituted by A,

and pharmaceutically acceptable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios.

10. Compounds according to one or more of Claims 1-9, in which

R denotes Ar, Het, -C≡C-Ar or -C≡C-Het,,

W denotes $NR^2R^{2'}$ or Het^1,

R^1 denotes A, $[C(R^3)_2]_nAr^1$ or $[C(R^3)_2]_nCyc$,

R^2, $R^{2'}$ each, independently of one another, denote H, A or $[C(R^3)_2]_nCyc$,

R^4 denotes H, F, Cl, OA' or A',

X^1, X^2, X^3, X^4 each, independently of one another, denote CH or N,

A denotes unbranched or branched alkyl with 1-10 C-atoms, wherein one or two non-adjacent CH- and/or CH_2-groups may be replaced by N- and/or O-atoms and 1-7 H-atoms may be replaced by R^5,

Cyc denotes cycloalkyl with 3-7 C-atoms, which is unsubstituted or monosubstituted by OH or A,

A' denotes unbranched or branched alkyl with 1-6 C-atoms, wherein 1-5 H-atoms may be replaced by F,

R^5 denotes F, Cl or OH,

Ar denotes phenyl, which is unsubstituted or mono-, di-, tri-, tetra- or pentasubstituted by $O[C(R^3)_2]_nHet^1$, Ar^1, A, CN and/or $[C(R^3)_2]_pOR^3$,

Ar^1 denotes phenyl or naphthyl,

R^3 denotes H or unbranched or branched alkyl with 1-6 C-atoms,

Het denotes furyl, thienyl, pyrrolyl, imidazolyl, pyrazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyridyl, pyrimidinyl, triazolyl, tetrazolyl, oxadiazolyl, thiadiazolyl, pyridazinyl, pyrazinyl,

benzoxazolyl, benzothiazolyl, benzimidazolyl, benzotriazolyl, indolyl, benzo-1,3-dioxolyl, benzodioxanyl, benzothiadiazolyl, indazolyl, benzofuranyl, quinolyl, isoquinolyl, oxazolo[5,4-b]-pyridyl, imidazo[1,2-a]pyridinyl or oxazolo[5,4-c]pyridyl, each of which is unsubstituted or mono- or disubstituted by Hal, A, $[C(R^3)_2]_nOA'$, $S(O)_nA$, CN, $SO_2N(R^3)_2$ and/or $COHet^1$,

Het^1 denotes pyrrolidinyl, azetidinyl, oxetanyl, tetrahydroimidazolyl, tetrahydropyrazolyl, tetrahydrofuranyl, piperidinyl, piperazinyl, morpholinyl, hexahydropyridazinyl, hexahydropyrimidinyl, [1,3]dioxolanyl or tetrahydropyranyl, each of which is unsubstituted or mono- or disubstituted by A,

Hal denotes F, Cl, Br or I,

n denotes 0, 1 or 2,

p denotes 0, 1, 2, 3 or 4,

q 0, 1, 2 or 3,

with the proviso that only one or two of X^1, X^2, X^3, X^4 denote N,

and pharmaceutically acceptable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios.

11. Compounds according to Claim 1, selected from the group

No.	Name
"A1"	4-(1,3-benzoxazol-2-yl)-N-[(1R,3S)-3-(ethylcarbamoyl)cyclopentyl]-N-methyl-benzamide
"A2"	N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-N-methyl-4-(1-methyl-1H-benzoimidazol-2-yl)-benzamide
"A3"	4-benzothiazol-2-yl-N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-N-methyl-benzamide
"A4"	4'-[(R)-(tetrahydro-furan-3-yl)oxy]-biphenyl-4-carboxylic acid ((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-methyl-amide

"A5"	4-benzoxazol-2-yl-N-((1R,3S)-3-isopropylcarbamoyl-cyclopentyl)-N-methyl-benzamide
"A6"	4-benzoxazol-2-yl-N-((1R,3S)-3-cyclopropylcarbamoyl-cyclopentyl)-N-methyl-benzamide
"A7"	4-benzoxazol-2-yl-N-((1R,3S)-3-cyclopentylcarbamoyl-cyclopentyl)-N-methyl-benzamide
"A8"	4-benzoxazol-2-yl-N-[(1R,3S)-3-(cyclohexylmethyl-carbamoyl)-cyclopentyl]-N-methyl-benzamide
"A9"	4-benzoxazol-2-yl-N-methyl-N-[(1R,3S)-3-(pyrrolidine-1-carbonyl)-cyclopentyl]-benzamide
"A10"	4-(1,3-benzoxazol-2-yl)-N-[(1S,3R)-3-(ethylcarbamoyl)cyclopentyl]-N-methyl-benzamide
"A11"	4-(1H-benzimidazol-2-yl)-N-[(1R,3S)-3-(ethylcarbamoyl)cyclopentyl]-N-methyl-benzamide
"A12"	4-benzoxazol-2-yl-N-ethyl-N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-benzamide
"A13"	4-benzoxazol-2-yl-N-benzyl-N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-benzamide
"A14"	N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-N-methyl-4-oxazolo[5,4-b]pyridin-2-yl-benzamide
"A15"	N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-N-methyl-4-oxazolo[5,4-c]pyridin-2-yl-benzamide
"A16"	4'-methoxy-biphenyl-4-carboxylic acid ((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-methyl-amide
"A17"	4'-[(S)-(tetrahydro-furan-3-yl)oxy]-biphenyl-4-carboxylic acid ((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-methyl-amide
"A18"	4-benzoxazol-2-yl-N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-2-fluoro-N-methyl-benzamide
"A19"	N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-4-(5-fluoro-benzoxazol-2-yl)-N-methyl-benzamide

"A20"	4-benzoxazol-2-yl-N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-2,6-difluoro-N-methyl-benzamide
"A21"	N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-N-methyl-4-(5-trifluoromethoxy-benzoxazol-2-yl)-benzamide
"A22"	4-benzoxazol-2-yl-N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-N-methyl-3-trifluoromethyl-benzamide
"A23"	4-(6-chloro-benzoxazol-2-yl)-N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-N-methyl-benzamide
"A24"	N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-N-methyl-4-naphthalen-2-yl-benzamide
"A25"	N-((1R,3S)-3-Ethylcarbamoyl-cyclopentyl)-4-isoquinolin-6-yl-N-methyl-benzamide
"A26"	4-benzofuran-5-yl-N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-N-methyl-benzamide
"A27"	N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-N-methyl-4-(1-methyl-1H-benzoimidazol-5-yl)-benzamide
"A28"	4-benzoxazol-2-yl-N-[(1R,3S)-3-(4-ethyl-piperazine-1-carbonyl)-cyclopentyl]-N-methyl-benzamide
"A29"	4-benzoxazol-2-yl-N-cyclopropylmethyl-N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-benzamide
"A30"	N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-4-(1H-indol-2-yl)-N-methyl-benzamide
"A31"	N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-N-methyl-4-[5-(pyrrolidine-1-carbonyl)-benzoxazol-2-yl]-benzamide
"A32"	4-benzoxazol-2-yl-N-[(1R,3S)-3-(cyclopentylmethyl-carbamoyl)-cyclopentyl]-N-methyl-benzamide
"A33"	4-benzoxazol-2-yl-N-methyl-N-[(1R,3S)-3-(oxetan-3-ylcarbamoyl)-cyclopentyl]-benzamide
"A34"	4-benzoxazol-2-yl-N-methyl-N-((1R,3S)-3-{[(S)-1-(tetrahydro-furan-2-yl)methyl]-carbamoyl}-cyclopentyl)-benzamide

"A35"	4-benzoxazol-2-yl-N-methyl-N-((1R,3S)-3-{[(R)-1-(tetrahydro-furan-2-yl)methyl]-carbamoyl}-cyclopentyl)-benzamide
"A36"	4-benzoxazol-2-yl-N-[(1R,3S)-3-(2-methoxy-ethylcarbamoyl)-cyclopentyl]-N-methyl-benzamide
"A37"	4-benzoxazol-2-yl-N-methyl-N-{(1R,3S)-3-[(R)-(tetrahydro-furan-3-yl)carbamoyl]-cyclopentyl}-benzamide
"A38"	4-benzoxazol-2-yl-N-methyl-N-{(1R,3S)-3-[(S)-(tetrahydro-furan-3-yl)carbamoyl]-cyclopentyl}-benzamide
"A39"	6-benzoxazol-2-yl-N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-N-methyl-nicotinamide
"A40"	5-benzoxazol-2-yl-pyridine-2-carboxylic acid ((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-methyl-amide
"A41"	N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-4-(5-methoxy-benzoxazol-2-yl)-N-methyl-benzamide
"A42"	4-(5-chloro-benzoxazol-2-yl)-N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-N-methyl-benzamide
"A43"	N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-N-methyl-4-(5-trifluoromethyl-benzoxazol-2-yl)-benzamide
"A44"	4-(1,3-benzoxazol-2-yl)-N-[(1R,3R)-3-(ethylcarbamoyl)cyclopentyl]-N-methyl-benzamide
"A45"	4-benzoxazol-2-yl-N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-3-methoxy-N-methyl-benzamide
"A46"	4-benzoxazol-2-yl-N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-2-methoxy-N-methyl-benzamide
"A47"	4-benzoxazol-2-yl-N-[(1R,3S)-3-(ethyl-methyl-carbamoyl)-cyclopentyl]-N-methyl-benzamide
"A48"	4-benzoxazol-2-yl-N-((1R,3S)-3-diethylcarbamoyl-cyclopentyl)-N-methyl-benzamide
"A49"	4'-methyl-biphenyl-4-carboxylic acid ((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-methyl-amide

"A50"	biphenyl-4-carboxylic acid ((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-methyl-amide
"A51"	3-chloro-biphenyl-4-carboxylic acid ((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-methyl-amide
"A52"	N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-4-(6-methoxy-4-methyl-pyridazin-3-yl)-N-methyl-benzamide
"A53"	5-phenyl-pyridine-2-carboxylic acid ((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-methyl-amide
"A54"	4-(4-chloro-phenylethynyl)-N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-N-methyl-benzamide
"A55"	N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-4-(4-fluoro-phenylethynyl)-N-methyl-benzamide
"A56"	N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-N-methyl-4-pyridin-4-yl-benzamide
"A57"	N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-2-fluoro-N-methyl-4-pyridin-4-yl-benzamide
"A58"	4'-ethyl-3,5-difluoro-biphenyl-4-carboxylic acid ((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-methyl-amide
"A59"	2'-methanesulfonyl-biphenyl-4-carboxylic acid ((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-methyl-amide
"A60"	2'-tert-butylsulfamoyl-biphenyl-4-carboxylic acid ((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-methyl-amide
"A61"	2'-sulfamoyl-biphenyl-4-carboxylic acid ((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-methyl-amide
"A62"	4'-chloro-biphenyl-4-carboxylic acid ((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-methyl-amide
"A63"	2',4'-difluoro-biphenyl-4-carboxylic acid ((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-methyl-amide
"A64"	2'-trifluoromethyl-biphenyl-4-carboxylic acid ((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-methyl-amide

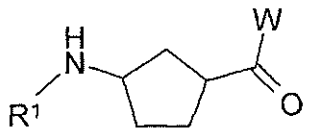
"A65"	2,2'-dimethyl-biphenyl-4-carboxylic acid ((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-methyl-amide
"A66"	4'-(bis-trifluoromethyl-amino)-biphenyl-4-carboxylic acid ((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-methyl-amide
"A67"	biphenyl-4-carboxylic acid methyl-[(1R,3S)-3-(1-methyl-cyclopropylcarbamoyl)-cyclopentyl]-amide
"A68"	4-benzoxazol-2-yl-N-methyl-N-[(1R,3S)-3-(1-methyl-cyclopropylcarbamoyl)-cyclopentyl]-benzamide
"A69"	N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-4-(4-methoxy-phenylethynyl)-N-methyl-benzamide
"A70"	N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-N-methyl-4-pyridin-4-ylethynyl-benzamide
"A71"	4-benzothiazol-2-yl-N-methyl-N-[(1R,3S)-3-(1-methyl-cyclopropylcarbamoyl)-cyclopentyl]-benzamide
"A72"	4-(4-fluoro-phenylethynyl)-N-methyl-N-[(1R,3S)-3-(1-methyl-cyclopropylcarbamoyl)-cyclopentyl]-benzamide
"A73"	4-benzoxazol-2-yl-N-methyl-N-[(1R,3S)-3-(1-propyl-cyclopropylcarbamoyl)-cyclopentyl]-benzamide
"A74"	4-(1,3-benzoxazol-2-yl)-N-methyl-N-[(1R,3S)-3-[[(1S)-1-methylpropyl]carbamoyl]cyclopentyl]benzamide
"A75"	4-(1,3-benzoxazol-2-yl)-N-methyl-N-[(1R,3S)-3-[[(1R)-1-methylpropyl]carbamoyl]cyclopentyl]benzamide
"A76"	4-(1,3-benzoxazol-2-yl)-N-[(1R,3S)-3-(cyclobutylcarbamoyl)cyclopentyl]-N-methyl-benzamide
"A77"	4-(1,3-benzoxazol-2-yl)-N-[(1R,3S)-3-[(trans-3-hydroxycyclobutyl)carbamoyl]cyclopentyl]-N-methyl-benzamide
"A78"	4-(1,3-benzoxazol-2-yl)-N-[(1R,3S)-3-[(cis-3-hydroxycyclobutyl)carbamoyl]cyclopentyl]-N-methyl-benzamide

"A79"	4-(1,3-benzoxazol-2-yl)-2-methoxy-N-methyl-N-[(1R,3S)-3-[(1-methylcyclopropyl)carbamoyl]cyclopentyl]benzamide
"A80"	N-methyl-N-[(1R,3S)-3-[(1-methylcyclopropyl)-carbamoyl]cyclopentyl]-4-(4-pyridyl)benzamide
"A81"	4-(4-cyanophenyl)-N-methyl-N-[(1R,3S)-3-[(1-methylcyclopropyl)carbamoyl]cyclopentyl]benzamide
"A82"	4-benzoxazol-2-yl-N-((1R,3S)-3-dimethylcarbamoyl-cyclopentyl)-N-methyl-benzamide
"A83"	N-methyl-N-[(1R,3S)-3-(1-methyl-cyclopropylcarbamoyl)-cyclopentyl]-4-pyridin-3-yl-benzamide
"A84"	4-benzoxazol-2-yl-N-methyl-N-[(1R,3S)-3-(1-methyl-cyclobutylcarbamoyl)-cyclopentyl]-benzamide
"A85"	4-benzoxazol-2-yl-3-methoxy-N-methyl-N-[(1R,3S)-3-(1-methyl-cyclopropylcarbamoyl)-cyclopentyl]-benzamide
"A86"	4-benzoxazol-2-yl-N-((1R,3S)-3-carbamoyl-cyclopentyl)-N-methyl-benzamide
"A87"	4-(7-cyano-imidazo[1,2-a]pyridin-2-yl)-N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-N-methyl-benzamide
"A88"	N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-N-methyl-4-(5-methyl-[1,2,4]oxadiazol-3-yl)-benzamide
"A89"	4-benzoxazol-2-yl-N-[(1R,3S)-3-(2-dimethylamino-1-methyl-ethylcarbamoyl)-cyclopentyl]-N-methyl-benzamide
"A90"	4-benzoxazol-2-yl-N-[(1R,3S)-3-((S)-2-hydroxy-1-methyl-ethylcarbamoyl)-cyclopentyl]-N-methyl-benzamide
"A91"	4-benzoxazol-2-yl-N-[(1R,3S)-3-((R)-2-hydroxy-1-methyl-ethylcarbamoyl)-cyclopentyl]-N-methyl-benzamide
"A92"	4-benzoxazol-2-yl-N-[(1R,3S)-3-((S)-2-methoxy-1-methyl-ethylcarbamoyl)-cyclopentyl]-N-methyl-benzamide
"A93"	N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-N-methyl-4-(5-sulfamoyl-benzooxazol-2-yl)-benzamide

"A94"	4-(5-ethanesulfonyl-benzooxazol-2-yl)-N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-N-methyl-benzamide
"A95"	N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-4-(1H-imidazol-2-yl)-N-methyl-benzamide
"A96"	4-(5,7-difluoro-benzoxazol-2-yl)-N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-N-methyl-benzamide
"A97"	4-benzoxazol-2-yl-N-[(1R,3S)-3-(2-hydroxy-ethylcarbamoyl)-cyclopentyl]-N-methyl-benzamide
"A98"	N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-4-(6-fluoro-benzooxazol-2-yl)-N-methyl-benzamide
"A99"	4-benzoxazol-2-yl-N-[(1R,3S)-3-(2-hydroxy-1,1-dimethyl-ethylcarbamoyl)-cyclopentyl]-N-methyl-benzamide
"A100"	N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-4-(7-fluoro-benzooxazol-2-yl)-N-methyl-benzamide
"A101"	4-(5,6-difluoro-benzoxazol-2-yl)-N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-N-methyl-benzamide
"A102"	N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-N-methyl-4-pyridin-3-yl-benzamide
"A103"	4'-cyano-biphenyl-4-carboxylic acid ((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-methyl-amide
"A104"	4'-fluoro-biphenyl-4-carboxylic acid ((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-methyl-amide
"A105"	N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-N-methyl-4-pyrimidin-5-yl-benzamide
"A106"	4-benzoxazol-2-yl-N-[(1R,3S)-3-(2-hydroxy-ethylcarbamoyl)-cyclopentyl]-N-methyl-benzamide
"A107"	N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-4-(1H-indazol-4-yl)-N-methyl-benzamide
"A108"	4-benzoxazol-2-yl-N-[(1R,3S)-3-(1-hydroxymethyl-cyclopropylcarbamoyl)-cyclopentyl]-N-methyl-benzamide

and pharmaceutically acceptable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios.

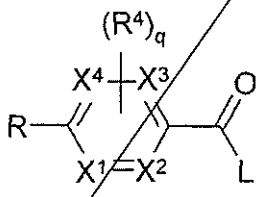
12. Process for the preparation of compounds of the formula I according to Claims 1-11 and pharmaceutically acceptable salts, tautomers and stereoisomers thereof, characterised in that
a compound of the formula II



II

in which R^1 and W have the meanings indicated in Claim 1,

is reacted with a compound of the formula III



III

in which R, R^4, X^1, X^2, X^3, X^4 and q have the meanings indicated in Claim 1,
and L denotes Cl, Br, I or a free or reactively functionally modified OH group,

and/or
a base or acid of the formula I is converted into one of its salts.

13. Medicaments comprising at least one compound of the formula I and/or pharmaceutically acceptable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios, and

optionally an pharmaceutically acceptable carrier, excipient or vehicle.

14. Compounds of the formula I and pharmaceutically acceptable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios, for the use for the treatment and/or prevention of cancer, multiple sclerosis, cardiovascular diseases, central nervous system injury and different forms of inflammation.

15. Compounds according to claim 14 for the use for the treatment and/or prevention of diseases selected from the group cancer of head, neck, eye, mouth, throat, esophagus, bronchus, larynx, pharynx, chest, bone, lung, colon, rectum, stomach, prostate, urinary bladder, uterine, cervix, breast, ovaries, testicles or other reproductive organs, skin, thyroid, blood, lymph nodes, kidney, liver, pancreas, brain, central nervous system, solid tumors and blood-borne tumors.

16. Medicaments comprising at least one compound of the formula I and/or pharmaceutically acceptable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios, and at least one further medicament active ingredient.

17. Set (kit) consisting of separate packs of

(a) an effective amount of a compound of the formula I and/or pharmaceutically acceptable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios,

and

(b) an effective amount of a further medicament active ingredient.

3-Aminocyclopentane carboxamide derivatives

TECHNICAL FIELD OF THE INVENTION

The present invention relates to novel 3-aminocyclopentane carboxamide derivatives which inhibit the activity of fatty acid synthase (FASN; also abbreviated as FAS), to pharmaceutical compositions comprising them, to processes for their preparation, and to their use in therapy for the treatment of cancers.

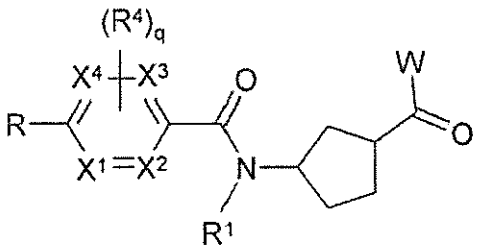
BACKGROUND OF THE INVENTION

Fatty Acid Synthase (FAS) is a critical enzyme for endogenous lipogenesis and plays an important role in the modulation of key intermediates of lipid and carbohydrate cellular metabolism. FAS is highly expressed in the tissues with high metabolic activity (for example liver, adipose tissue and brain) and there are good reasons to believe that a FAS inhibitor would cause beneficial metabolic effects in peripheral tissues. In addition, inhibition of FAS in the hypothalamus may result in reduced food intake. The non-specific irreversible FAS inhibitors cerulenin and C-75 have been reported in the literature to decrease brain levels of orexigenic neuropeptides and to decrease food intake.

FAS is also highly expressed in human sebocytes, the lipid producing cells of the sebaceous glands. Acne is the most common disorder involving the sebaceous gland. The pathogenesis of acne involves lipid (over)production by the sebaceous gland and it has been reported that inhibitors of mammalian FAS inhibit the production of sebum in sebocytes (US 2005/0053631). Acne cannot occur without sebum lipids. There is an unmet medical need in the treatment of acne for agents that reduce sebum production.

Patent Claims

1. Compounds of the formula I



I

in which

R denotes Ar, Het, -C≡C-Ar or -C≡C-Het,

W denotes $NR^2R^{2'}$ or Het^1,

R^1 denotes A, $[C(R^3)_2]_nAr^1$ or $[C(R^3)_2]_nCyc$,

R^2, $R^{2'}$ each, independently of one another, denote H, A or $[C(R^3)_2]_nCyc$,

R^4 denotes H, F, Cl, Br, OH, CN, NO_2, A', OA', SA', SO_2Me, COA', $CONH_2$, CONHA' or $CONA'_2$,

X^1, X^2, X^3, X^4 each, independently of one another, denote CH or N,

A denotes unbranched or branched alkyl with 1-10 C-atoms, wherein two adjacent carbon atoms may form a double bond and/or one or two non-adjacent CH- and/or CH_2-groups may be replaced by N-, O- and/or S-atoms and wherein 1-7 H-atoms may be replaced by R^5,

Cyc denotes cycloalkyl with 3-7 C-atoms, which is unsubstituted or monosubstituted by OH, Hal or A,

A' denotes unbranched or branched alkyl with 1-6 C-atoms, wherein 1-5 H-atoms may be replaced by F,

R^5 denotes F, Cl or OH,

Ar denotes phenyl, which is unsubstituted or mono-, di-, tri-, tetra- or pentasubstituted by Hal, A, $O[C(R^3)_2]_nHet^1$, Ar^1, $[C(R^3)_2]_pOR^3$,

$[C(R^3)_2]_pN(R^3)_2$, NO_2, CN, $[C(R^3)_2]_pCOOR^3$, $CON(R^3)_2$, $[C(R^3)_2]_pN(R^3)_2$, $N(R^3)_2COA$, NR^3SO_2A, $[C(R^3)_2]_pSO_2N(R^3)_2$, $S(O)_nA$, $O[C(R^3)_2]_mN(R^3)_2$, NHCOOA, $NHCON(R^3)_2$ and/or COA,

Ar^1 denotes phenyl or naphthyl, which is unsubstituted or mono-, di-, tri-, tetra- or pentasubstituted by Hal, A, $[C(R^3)_2]_pOR^3$, $[C(R^3)_2]_pN(R^3)_2$, NO_2, CN, $[C(R^3)_2]_pCOOR^3$, $[C(R^3)_2]_pN(R^3)_2$, $N(R^3)_2COA$, NR^3SO_2A, $[C(R^3)_2]_pSO_2N(R^3)_2$, $S(O)_nA$, $O[C(R^3)_2]_mN(R^3)_2$, NHCOOA, $NHCON(R^3)_2$ and/or COA,

R^3 denotes H or unbranched or branched alkyl with 1-6 C-atoms,

Het denotes a mono- or bicyclic saturated, unsaturated or aromatic heterocycle having 1 to 4 N, O and/or S atoms, which is unsubstituted or mono-, di-, tri-, tetra- or pentasubstituted by Hal, A, $[C(R^3)_2]_nOA'$, $[C(R^3)_2]_nN(R^3)_2$, SR^3, NO_2, CN, $COOR^3$, $CON(R^3)_2$, $COHet^1$, NR^3COA, NR^3SO_2A, $SO_2N(R^3)_2$, $S(O)_nA$, $O[C(R^3)_2]_mN(R^3)_2$, NHCOOA, $NHCON(R^3)_2$, CHO, COA, =S, =NH, =NA and/or =O (carbonyl oxygen),

Het^1 denotes a mono- or bicyclic saturated, unsaturated or aromatic heterocycle having 1 to 4 N, O and/or S atoms, which is unsubstituted or mono-, di-, tri-, tetra- or pentasubstituted by Hal, A, $[C(R^3)_2]_nOR^3$, $[C(R^3)_2]_nN(R^3)_2$, SR^3, NO_2, CN, $COOR^3$, $CON(R^3)_2$, NR^3COA, NR^3SO_2A, $SO_2N(R^3)_2$, $S(O)_nA$, $O[C(R^3)_2]_mN(R^3)_2$, NHCOOA, $NHCON(R^3)_2$, CHO, COA, =S, =NH, =NA and/or =O (carbonyl oxygen),

Hal denotes F, Cl, Br or I,

m denotes 1, 2 or 3,

n denotes 0, 1 or 2,

p denotes 0, 1, 2, 3 or 4,

q 0, 1, 2 or 3,

with the proviso that only one or two of X^1, X^2, X^3, X^4 denote N,

and pharmaceutically acceptable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios.

2. Compounds according to Claim 1 in which

R^4 denotes H, F, Cl, OA' or A',

and pharmaceutically acceptable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios.

3. Compounds according to Claim 1 or 2, in which

A denotes unbranched or branched alkyl with 1-10 C-atoms, wherein one or two non-adjacent CH- and/or CH_2-groups may be replaced by N- and/or O-atoms and 1-7 H-atoms may be replaced by R^5,

and pharmaceutically acceptable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios.

4. Compounds according to one or more of Claims 1-3, in which

Ar denotes phenyl, which is unsubstituted or mono-, di-, tri-, tetra- or pentasubstituted by $O[C(R^3)_2]_nHet^1$, Ar^1, A, CN and/or $[C(R^3)_2]_pOR^3$,

and pharmaceutically acceptable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios.

5. Compounds according to one or more of Claims 1-4, in which

Ar^1 denotes phenyl or naphthyl,

and pharmaceutically acceptable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios.

6. Compounds according to one or more of Claims 1-5, in which

Het denotes a mono- or bicyclic aromatic heterocycle having 1 to 4 N, O and/or S atoms, which is unsubstituted or mono- or

disubstituted by Hal, A, $[C(R^3)_2]_nOA'$, $S(O)_nA$, CN, $SO_2N(R^3)_2$ and/or $COHet^1$,

and pharmaceutically acceptable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios.

7. Compounds according to one or more of Claims 1-6, in which

Het^1 denotes a monocyclic saturated heterocycle having 1 to 4 N, O and/or S atoms, which is unsubstituted or mono- or disubstituted by A,

and pharmaceutically acceptable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios.

8. Compounds according to one or more of Claims 1-7, in which

Het denotes furyl, thienyl, pyrrolyl, imidazolyl, pyrazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyridyl, pyrimidinyl, triazolyl, tetrazolyl, oxadiazolyl, thiadiazolyl, pyridazinyl, pyrazinyl, benzoxazolyl, benzothiazolyl, benzimidazolyl, benzotriazolyl, indolyl, benzo-1,3-dioxolyl, benzodioxanyl, benzothiadiazolyl, indazolyl, benzofuranyl, quinolyl, isoquinolyl, oxazolo[5,4-b]-pyridyl, imidazo[1,2-a]pyridinyl or oxazolo[5,4-c]pyridyl, each of which is unsubstituted or mono- or disubstituted by Hal, A, $[C(R^3)_2]_nOA'$, $S(O)_nA$, CN, $SO_2N(R^3)_2$ and/or $COHet^1$,

and pharmaceutically acceptable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios.

9. Compounds according to one or more of Claims 1-8, in which

Het^1 denotes pyrrolidinyl, azetidinyl, oxetanyl, tetrahydroimidazolyl, tetrahydropyrazolyl, tetrahydrofuranyl, piperidinyl, piperazinyl, morpholinyl, hexahydropyridazinyl, hexahydropyrimidinyl, [1,3]dioxolanyl or tetrahydropyranyl, each of which is unsubstituted or mono- or disubstituted by A,

and pharmaceutically acceptable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios.

10. Compounds according to one or more of Claims 1-9, in which

R denotes Ar, Het, -C≡C-Ar or -C≡C-Het,,

W denotes $NR^2R^{2'}$ or Het^1,

R^1 denotes A, $[C(R^3)_2]_nAr^1$ or $[C(R^3)_2]_nCyc$,

R^2, $R^{2'}$ each, independently of one another, denote H, A or $[C(R^3)_2]_nCyc$,

R^4 denotes H, F, Cl, OA' or A',

X^1, X^2, X^3, X^4 each, independently of one another, denote CH or N,

A denotes unbranched or branched alkyl with 1-10 C-atoms, wherein one or two non-adjacent CH- and/or CH_2-groups may be replaced by N- and/or O-atoms and 1-7 H-atoms may be replaced by R^5,

Cyc denotes cycloalkyl with 3-7 C-atoms, which is unsubstituted or monosubstituted by OH or A,

A' denotes unbranched or branched alkyl with 1-6 C-atoms, wherein 1-5 H-atoms may be replaced by F,

R^5 denotes F, Cl or OH,

Ar denotes phenyl, which is unsubstituted or mono-, di-, tri-, tetra- or pentasubstituted by $O[C(R^3)_2]_nHet^1$, Ar^1, A, CN and/or $[C(R^3)_2]_pOR^3$,

Ar^1 denotes phenyl or naphthyl,

R^3 denotes H or unbranched or branched alkyl with 1-6 C-atoms,

Het denotes furyl, thienyl, pyrrolyl, imidazolyl, pyrazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyridyl, pyrimidinyl, triazolyl, tetrazolyl, oxadiazolyl, thiadiazolyl, pyridazinyl, pyrazinyl,

benzoxazolyl, benzothiazolyl, benzimidazolyl, benzotriazolyl, indolyl, benzo-1,3-dioxolyl, benzodioxanyl, benzothiadiazolyl, indazolyl, benzofuranyl, quinolyl, isoquinolyl, oxazolo[5,4-b]-pyridyl, imidazo[1,2-a]pyridinyl or oxazolo[5,4-c]pyridyl, each of which is unsubstituted or mono- or disubstituted by Hal, A, $[C(R^3)_2]_nOA'$, $S(O)_nA$, CN, $SO_2N(R^3)_2$ and/or $COHet^1$,

Het^1 denotes pyrrolidinyl, azetidinyl, oxetanyl, tetrahydroimidazolyl, tetrahydropyrazolyl, tetrahydrofuranyl, piperidinyl, piperazinyl, morpholinyl, hexahydropyridazinyl, hexahydropyrimidinyl, [1,3]dioxolanyl or tetrahydropyranyl, each of which is unsubstituted or mono- or disubstituted by A,

Hal denotes F, Cl, Br or I,

n denotes 0, 1 or 2,

p denotes 0, 1, 2, 3 or 4,

q 0, 1, 2 or 3,

with the proviso that only one or two of X^1, X^2, X^3, X^4 denote N,

and pharmaceutically acceptable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios.

11. Compounds according to Claim 1, selected from the group

No.	Name
"A1"	4-(1,3-benzoxazol-2-yl)-N-[(1R,3S)-3-(ethylcarbamoyl)cyclopentyl]-N-methyl-benzamide
"A2"	N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-N-methyl-4-(1-methyl-1H-benzoimidazol-2-yl)-benzamide
"A3"	4-benzothiazol-2-yl-N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-N-methyl-benzamide
"A4"	4'-[(R)-(tetrahydro-furan-3-yl)oxy]-biphenyl-4-carboxylic acid ((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-methyl-amide

"A5"	4-benzoxazol-2-yl-N-((1R,3S)-3-isopropylcarbamoyl-cyclopentyl)-N-methyl-benzamide
"A6"	4-benzoxazol-2-yl-N-((1R,3S)-3-cyclopropylcarbamoyl-cyclopentyl)-N-methyl-benzamide
"A7"	4-benzoxazol-2-yl-N-((1R,3S)-3-cyclopentylcarbamoyl-cyclopentyl)-N-methyl-benzamide
"A8"	4-benzoxazol-2-yl-N-[(1R,3S)-3-(cyclohexylmethyl-carbamoyl)-cyclopentyl]-N-methyl-benzamide
"A9"	4-benzoxazol-2-yl-N-methyl-N-[(1R,3S)-3-(pyrrolidine-1-carbonyl)-cyclopentyl]-benzamide
"A10"	4-(1,3-benzoxazol-2-yl)-N-[(1S,3R)-3-(ethylcarbamoyl)cyclopentyl]-N-methyl-benzamide
"A11"	4-(1H-benzimidazol-2-yl)-N-[(1R,3S)-3-(ethylcarbamoyl)cyclopentyl]-N-methyl-benzamide
"A12"	4-benzoxazol-2-yl-N-ethyl-N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-benzamide
"A13"	4-benzoxazol-2-yl-N-benzyl-N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-benzamide
"A14"	N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-N-methyl-4-oxazolo[5,4-b]pyridin-2-yl-benzamide
"A15"	N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-N-methyl-4-oxazolo[5,4-c]pyridin-2-yl-benzamide
"A16"	4'-methoxy-biphenyl-4-carboxylic acid ((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-methyl-amide
"A17"	4'-[(S)-(tetrahydro-furan-3-yl)oxy]-biphenyl-4-carboxylic acid ((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-methyl-amide
"A18"	4-benzoxazol-2-yl-N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-2-fluoro-N-methyl-benzamide
"A19"	N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-4-(5-fluoro-benzoxazol-2-yl)-N-methyl-benzamide

"A20"	4-benzoxazol-2-yl-N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-2,6-difluoro-N-methyl-benzamide
"A21"	N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-N-methyl-4-(5-trifluoromethoxy-benzoxazol-2-yl)-benzamide
"A22"	4-benzoxazol-2-yl-N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-N-methyl-3-trifluoromethyl-benzamide
"A23"	4-(6-chloro-benzoxazol-2-yl)-N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-N-methyl-benzamide
"A24"	N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-N-methyl-4-naphthalen-2-yl-benzamide
"A25"	N-((1R,3S)-3-Ethylcarbamoyl-cyclopentyl)-4-isoquinolin-6-yl-N-methyl-benzamide
"A26"	4-benzofuran-5-yl-N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-N-methyl-benzamide
"A27"	N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-N-methyl-4-(1-methyl-1H-benzoimidazol-5-yl)-benzamide
"A28"	4-benzoxazol-2-yl-N-[(1R,3S)-3-(4-ethyl-piperazine-1-carbonyl)-cyclopentyl]-N-methyl-benzamide
"A29"	4-benzoxazol-2-yl-N-cyclopropylmethyl-N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-benzamide
"A30"	N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-4-(1H-indol-2-yl)-N-methyl-benzamide
"A31"	N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-N-methyl-4-[5-(pyrrolidine-1-carbonyl)-benzoxazol-2-yl]-benzamide
"A32"	4-benzoxazol-2-yl-N-[(1R,3S)-3-(cyclopentylmethyl-carbamoyl)-cyclopentyl]-N-methyl-benzamide
"A33"	4-benzoxazol-2-yl-N-methyl-N-[(1R,3S)-3-(oxetan-3-ylcarbamoyl)-cyclopentyl]-benzamide
"A34"	4-benzoxazol-2-yl-N-methyl-N-((1R,3S)-3-{[(S)-1-(tetrahydro-furan-2-yl)methyl]-carbamoyl}-cyclopentyl)-benzamide

"A35"	4-benzoxazol-2-yl-N-methyl-N-((1R,3S)-3-{[(R)-1-(tetrahydro-furan-2-yl)methyl]-carbamoyl}-cyclopentyl)-benzamide
"A36"	4-benzoxazol-2-yl-N-[(1R,3S)-3-(2-methoxy-ethylcarbamoyl)-cyclopentyl]-N-methyl-benzamide
"A37"	4-benzoxazol-2-yl-N-methyl-N-{(1R,3S)-3-[(R)-(tetrahydro-furan-3-yl)carbamoyl]-cyclopentyl}-benzamide
"A38"	4-benzoxazol-2-yl-N-methyl-N-{(1R,3S)-3-[(S)-(tetrahydro-furan-3-yl)carbamoyl]-cyclopentyl}-benzamide
"A39"	6-benzoxazol-2-yl-N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-N-methyl-nicotinamide
"A40"	5-benzoxazol-2-yl-pyridine-2-carboxylic acid ((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-methyl-amide
"A41"	N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-4-(5-methoxy-benzoxazol-2-yl)-N-methyl-benzamide
"A42"	4-(5-chloro-benzoxazol-2-yl)-N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-N-methyl-benzamide
"A43"	N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-N-methyl-4-(5-trifluoromethyl-benzoxazol-2-yl)-benzamide
"A44"	4-(1,3-benzoxazol-2-yl)-N-[(1R,3R)-3-(ethylcarbamoyl)cyclopentyl]-N-methyl-benzamide
"A45"	4-benzoxazol-2-yl-N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-3-methoxy-N-methyl-benzamide
"A46"	4-benzoxazol-2-yl-N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-2-methoxy-N-methyl-benzamide
"A47"	4-benzoxazol-2-yl-N-[(1R,3S)-3-(ethyl-methyl-carbamoyl)-cyclopentyl]-N-methyl-benzamide
"A48"	4-benzoxazol-2-yl-N-((1R,3S)-3-diethylcarbamoyl-cyclopentyl)-N-methyl-benzamide
"A49"	4'-methyl-biphenyl-4-carboxylic acid ((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-methyl-amide

"A50"	biphenyl-4-carboxylic acid ((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-methyl-amide
"A51"	3-chloro-biphenyl-4-carboxylic acid ((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-methyl-amide
"A52"	N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-4-(6-methoxy-4-methyl-pyridazin-3-yl)-N-methyl-benzamide
"A53"	5-phenyl-pyridine-2-carboxylic acid ((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-methyl-amide
"A54"	4-(4-chloro-phenylethynyl)-N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-N-methyl-benzamide
"A55"	N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-4-(4-fluoro-phenylethynyl)-N-methyl-benzamide
"A56"	N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-N-methyl-4-pyridin-4-yl-benzamide
"A57"	N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-2-fluoro-N-methyl-4-pyridin-4-yl-benzamide
"A58"	4'-ethyl-3,5-difluoro-biphenyl-4-carboxylic acid ((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-methyl-amide
"A59"	2'-methanesulfonyl-biphenyl-4-carboxylic acid ((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-methyl-amide
"A60"	2'-tert-butylsulfamoyl-biphenyl-4-carboxylic acid ((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-methyl-amide
"A61"	2'-sulfamoyl-biphenyl-4-carboxylic acid ((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-methyl-amide
"A62"	4'-chloro-biphenyl-4-carboxylic acid ((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-methyl-amide
"A63"	2',4'-difluoro-biphenyl-4-carboxylic acid ((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-methyl-amide
"A64"	2'-trifluoromethyl-biphenyl-4-carboxylic acid ((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-methyl-amide

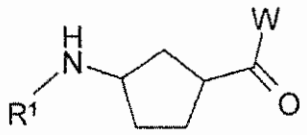
"A65"	2,2'-dimethyl-biphenyl-4-carboxylic acid ((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-methyl-amide
"A66"	4'-(bis-trifluoromethyl-amino)-biphenyl-4-carboxylic acid ((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-methyl-amide
"A67"	biphenyl-4-carboxylic acid methyl-[(1R,3S)-3-(1-methyl-cyclopropylcarbamoyl)-cyclopentyl]-amide
"A68"	4-benzoxazol-2-yl-N-methyl-N-[(1R,3S)-3-(1-methyl-cyclopropylcarbamoyl)-cyclopentyl]-benzamide
"A69"	N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-4-(4-methoxy-phenylethynyl)-N-methyl-benzamide
"A70"	N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-N-methyl-4-pyridin-4-ylethynyl-benzamide
"A71"	4-benzothiazol-2-yl-N-methyl-N-[(1R,3S)-3-(1-methyl-cyclopropylcarbamoyl)-cyclopentyl]-benzamide
"A72"	4-(4-fluoro-phenylethynyl)-N-methyl-N-[(1R,3S)-3-(1-methyl-cyclopropylcarbamoyl)-cyclopentyl]-benzamide
"A73"	4-benzoxazol-2-yl-N-methyl-N-[(1R,3S)-3-(1-propyl-cyclopropylcarbamoyl)-cyclopentyl]-benzamide
"A74"	4-(1,3-benzoxazol-2-yl)-N-methyl-N-[(1R,3S)-3-[[(1S)-1-methylpropyl]carbamoyl]cyclopentyl]benzamide
"A75"	4-(1,3-benzoxazol-2-yl)-N-methyl-N-[(1R,3S)-3-[[(1R)-1-methylpropyl]carbamoyl]cyclopentyl]benzamide
"A76"	4-(1,3-benzoxazol-2-yl)-N-[(1R,3S)-3-(cyclobutylcarbamoyl)cyclopentyl]-N-methyl-benzamide
"A77"	4-(1,3-benzoxazol-2-yl)-N-[(1R,3S)-3-[(trans-3-hydroxycyclobutyl)carbamoyl]cyclopentyl]-N-methyl-benzamide
"A78"	4-(1,3-benzoxazol-2-yl)-N-[(1R,3S)-3-[(cis-3-hydroxycyclobutyl)carbamoyl]cyclopentyl]-N-methyl-benzamide

"A79"	4-(1,3-benzoxazol-2-yl)-2-methoxy-N-methyl-N-[(1R,3S)-3-[(1-methylcyclopropyl)carbamoyl]cyclopentyl]benzamide
"A80"	N-methyl-N-[(1R,3S)-3-[(1-methylcyclopropyl)-carbamoyl]cyclopentyl]-4-(4-pyridyl)benzamide
"A81"	4-(4-cyanophenyl)-N-methyl-N-[(1R,3S)-3-[(1-methylcyclopropyl)carbamoyl]cyclopentyl]benzamide
"A82"	4-benzoxazol-2-yl-N-((1R,3S)-3-dimethylcarbamoyl-cyclopentyl)-N-methyl-benzamide
"A83"	N-methyl-N-[(1R,3S)-3-(1-methyl-cyclopropylcarbamoyl)-cyclopentyl]-4-pyridin-3-yl-benzamide
"A84"	4-benzoxazol-2-yl-N-methyl-N-[(1R,3S)-3-(1-methyl-cyclobutylcarbamoyl)-cyclopentyl]-benzamide
"A85"	4-benzoxazol-2-yl-3-methoxy-N-methyl-N-[(1R,3S)-3-(1-methyl-cyclopropylcarbamoyl)-cyclopentyl]-benzamide
"A86"	4-benzoxazol-2-yl-N-((1R,3S)-3-carbamoyl-cyclopentyl)-N-methyl-benzamide
"A87"	4-(7-cyano-imidazo[1,2-a]pyridin-2-yl)-N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-N-methyl-benzamide
"A88"	N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-N-methyl-4-(5-methyl-[1,2,4]oxadiazol-3-yl)-benzamide
"A89"	4-benzoxazol-2-yl-N-[(1R,3S)-3-(2-dimethylamino-1-methyl-ethylcarbamoyl)-cyclopentyl]-N-methyl-benzamide
"A90"	4-benzoxazol-2-yl-N-[(1R,3S)-3-((S)-2-hydroxy-1-methyl-ethylcarbamoyl)-cyclopentyl]-N-methyl-benzamide
"A91"	4-benzoxazol-2-yl-N-[(1R,3S)-3-((R)-2-hydroxy-1-methyl-ethylcarbamoyl)-cyclopentyl]-N-methyl-benzamide
"A92"	4-benzoxazol-2-yl-N-[(1R,3S)-3-((S)-2-methoxy-1-methyl-ethylcarbamoyl)-cyclopentyl]-N-methyl-benzamide
"A93"	N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-N-methyl-4-(5-sulfamoyl-benzooxazol-2-yl)-benzamide

"A94"	4-(5-ethanesulfonyl-benzooxazol-2-yl)-N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-N-methyl-benzamide
"A95"	N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-4-(1H-imidazol-2-yl)-N-methyl-benzamide
"A96"	4-(5,7-difluoro-benzoxazol-2-yl)-N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-N-methyl-benzamide
"A97"	4-benzoxazol-2-yl-N-[(1R,3S)-3-(2-hydroxy-ethylcarbamoyl)-cyclopentyl]-N-methyl-benzamide
"A98"	N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-4-(6-fluoro-benzooxazol-2-yl)-N-methyl-benzamide
"A99"	4-benzoxazol-2-yl-N-[(1R,3S)-3-(2-hydroxy-1,1-dimethyl-ethylcarbamoyl)-cyclopentyl]-N-methyl-benzamide
"A100"	N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-4-(7-fluoro-benzooxazol-2-yl)-N-methyl-benzamide
"A101"	4-(5,6-difluoro-benzoxazol-2-yl)-N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-N-methyl-benzamide
"A102"	N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-N-methyl-4-pyridin-3-yl-benzamide
"A103"	4'-cyano-biphenyl-4-carboxylic acid ((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-methyl-amide
"A104"	4'-fluoro-biphenyl-4-carboxylic acid ((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-methyl-amide
"A105"	N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-N-methyl-4-pyrimidin-5-yl-benzamide
"A106"	4-benzoxazol-2-yl-N-[(1R,3S)-3-(2-hydroxy-ethylcarbamoyl)-cyclopentyl]-N-methyl-benzamide
"A107"	N-((1R,3S)-3-ethylcarbamoyl-cyclopentyl)-4-(1H-indazol-4-yl)-N-methyl-benzamide
"A108"	4-benzoxazol-2-yl-N-[(1R,3S)-3-(1-hydroxymethyl-cyclopropylcarbamoyl)-cyclopentyl]-N-methyl-benzamide

and pharmaceutically acceptable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios.

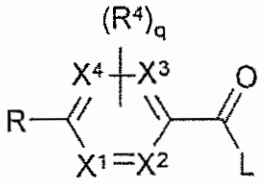
12. Process for the preparation of compounds of the formula I according to Claims 1-11 and pharmaceutically acceptable salts, tautomers and stereoisomers thereof, characterised in that
a compound of the formula II



II

in which R^1 and W have the meanings indicated in Claim 1,

is reacted with a compound of the formula III



III

in which R, R^4, X^1, X^2, X^3, X^4 and q have the meanings indicated in Claim 1,
and L denotes Cl, Br, I or a free or reactively functionally modified OH group,

and/or
a base or acid of the formula I is converted into one of its salts.

13. Medicaments comprising at least one compound of the formula I according to claim 1 and/or pharmaceutically acceptable salts, tautomers and stereoisomers thereof, including mixtures thereof in all

ratios, and optionally an pharmaceutically acceptable carrier, excipient or vehicle.

14. Compounds of the formula I according to claim 1 and pharmaceutically acceptable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios, for the use for the treatment and/or prevention of cancer, multiple sclerosis, cardiovascular diseases, central nervous system injury and different forms of inflammation.

15. Compounds according to claim 14 for the use for the treatment and/or prevention of diseases selected from the group cancer of head, neck, eye, mouth, throat, esophagus, bronchus, larynx, pharynx, chest, bone, lung, colon, rectum, stomach, prostate, urinary bladder, uterine, cervix, breast, ovaries, testicles or other reproductive organs, skin, thyroid, blood, lymph nodes, kidney, liver, pancreas, brain, central nervous system, solid tumors and blood-borne tumors.

16. Medicaments comprising at least one compound of the formula I according to claim 1 and/or pharmaceutically acceptable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios, and at least one further medicament active ingredient.

17. Set (kit) consisting of separate packs of

(a) an effective amount of a compound of the formula I according to claim 1 and/or pharmaceutically acceptable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios, and

(b) an effective amount of a further medicament active ingredient.