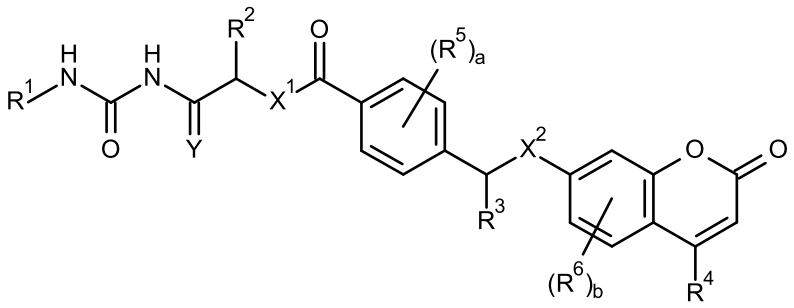
Claims

1. A compound of the general formula I



(I)

wherein

R^1 is hydrogen or a group $-CH_2R^{1a}$, where R^{1a} is selected from the group consisting of hydrogen, C_1-C_3-alkyl, phenyl, where phenyl is unsubstituted or may carry 1, 2 or 3 radicals independently selected from halogen, cyano, C_1-C_3-alkyl, C_1-C_3-haloalkyl and C_1-C_3-alkoxy; and a 5- to 10-membered heteroaromatic ring containing 1 to 4 heteroatoms or hetero-groups independently selected from the group consisting of N, NR^c, O and S as ring member, where the 5- to 10-membered heteroaromatic ring is unsubstituted or may carry 1, 2 or 3 radicals R^7;

R^2 is selected from the group consisting of hydrogen, methyl and fluorinated methyl;

R^3 is selected from the group consisting of hydrogen, methyl and fluorinated methyl;

R^4 is selected from the group consisting of hydrogen and C_1-C_4-alkyl;

each R^5 is independently selected from the group consisting of halogen, cyano, C_1-C_3-alkyl, C_1-C_3-haloalkyl, C_1-C_3-alkoxy and C_1-C_3-haloalkoxy;

each R^6 is independently selected from the group consisting of halogen, cyano, C_1-C_3-alkyl, C_1-C_3-haloalkyl, C_1-C_3-alkoxy and C_1-C_3-haloalkoxy;

each R^7 is independently selected from the group consisting of halogen, cyano, C_1-C_3-alkyl, C_1-C_3-haloalkyl, C_1-C_3-alkoxy and C_1-C_3-haloalkoxy;

X^1 is NR^a or O;

X^2 is NR^b, O or S;

Y represents an oxygen atom or two hydrogen atoms;

R^a, R^b, R^c are each independently selected from the group consisting of hydrogen and C_1-C_4-alkyl;

a is 0, 1, 2, 3 or 4; and

b is 0, 1, 2 or 3;

and the pharmaceutically acceptable salts thereof.

2. The compound as claimed in claim 1, wherein R^1 is selected from the group consisting of hydrogen and a group $-CH_2R^{1a}$, where R^{1a} is selected from the group consisting of hydrogen, methyl and a 5- to 6-membered monocyclic heteroaromatic ring containing 1 to 3 heteroatoms, in particular 1 heteroatom, independently selected from the group consisting of N, O and S, as ring member, where the 5- to 6-membered monocyclic heteroaromatic ring is unsubstituted or carries 1 radical R^7, where R^7 is selected from the group consisting of halogen, C_1-C_3-alkyl and C_1-C_2-alkoxy.

3. The compound as claimed in claim 2, wherein R^1 is selected from the group consisting of hydrogen and a group $-CH_2R^{1a}$, where R^{1a} is selected from the group consisting of hydrogen and an unsubstituted 5- to 6-membered monocyclic heteroaromatic ring containing 1 to 3 heteroatoms, in particular 1 heteroatom, independently selected from the group consisting of N, O and S, as ring member; where R^1 is in particular a group $-CH_2R^{1a}$, where R^{1a} is an unsubstituted 5- to 6-membered monocyclic heteroaromatic ring containing 1 to 3 heteroatoms, in particular 1 heteroatom, independently selected from the group consisting of N, O and S, as ring member.

4. The compound as claimed in any of claims 1 to 3, wherein

R^2 is hydrogen or methyl;

R^3 is hydrogen;

R^4 is methyl;

each R^5 is independently selected from the group consisting of halogen, C_1-C_3-alkyl and C_1-C_2-alkoxy;

each R^6 is independently selected from the group consisting of halogen, C_1-C_3-alkyl and C_1-C_2-alkoxy;

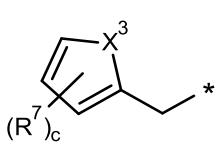
X^1 is NH or O;

X^2 is O;

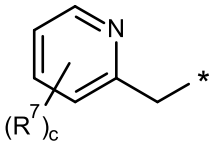
a is 0, 1 or 2; and

b is 0 or 1.

5. The compound as claimed in claim 1, wherein R^1 is selected from the group CH_2-I' or CH_2-II'



(CH_2-I')



(CH_2-II')

wherein * indicates the point of attachment to the urea nitrogen atom;

each R^7 is independently selected from the group consisting of halogen, cyano, C_1-C_3-alkyl, C_1-C_3-haloalkyl, C_1-C_3-alkoxy and C_1-C_3-haloalkoxy;

X^3 is NR^c, O or S;

R^c is selected from the group consisting of hydrogen and C_1-C_4-alkyl; and

c is 0, 1, 2 or 3.

6. The compound as claimed in claim 5, wherein

R^2 is hydrogen or methyl;

R^3 is hydrogen;

R^4 is methyl;

each R^5 is independently selected from the group consisting of halogen, C_1-C_3-alkyl and C_1-C_2-alkoxy;

each R^6 is independently selected from the group consisting of halogen, C_1-C_3-alkyl and C_1-C_2-alkoxy;

each R^7 is independently selected from the group consisting of halogen, C_1-C_3-alkyl and C_1-C_2-alkoxy;

X^1 is NH or O;

X^2 is O;

X^3 is O or S;

a is 0, 1 or 2;

b is 0 or 1; and

c is 0 or 1.

7. The compound as claimed in claim 6, wherein

R^2 is hydrogen;

R^3 is hydrogen;

R^4 is methyl;

X^1 is NH or O;

X^2 is O;

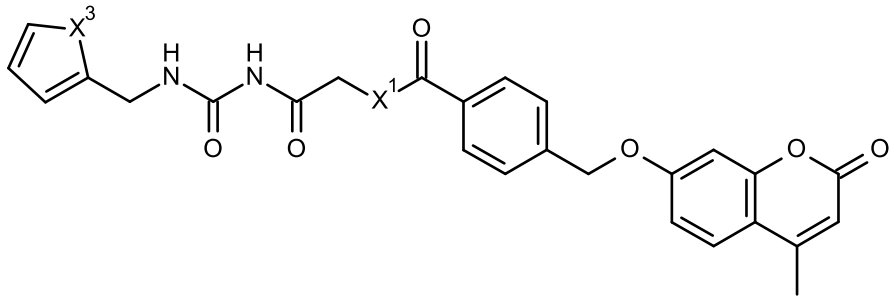
X^3 is O or S;

a is 0;

b is 0; and

c is 0.

8. A compound of formula I as defined in any of claims 1 to 7, which corresponds to the formula I-A,



(I-A)

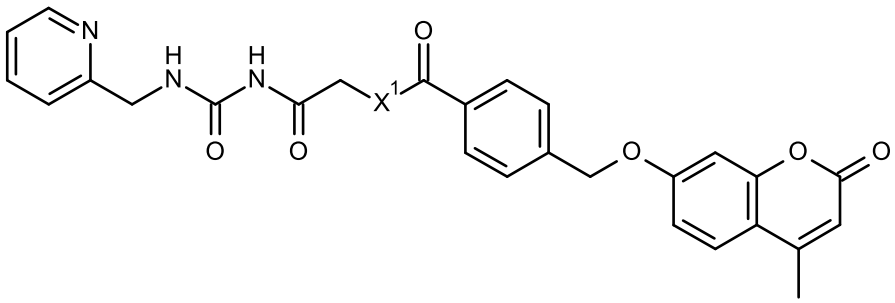
wherein

X^1 is NH or O; and

X^3 is O or S;

and the pharmaceutically acceptable salts thereof,

or to the formula I-B,



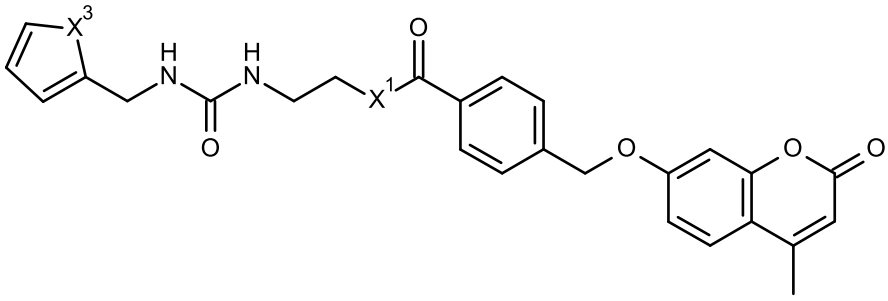
(I-B)

wherein

X^1 is NH or O;

and the pharmaceutically acceptable salts thereof,

or to the formula I-C,



(I-C)

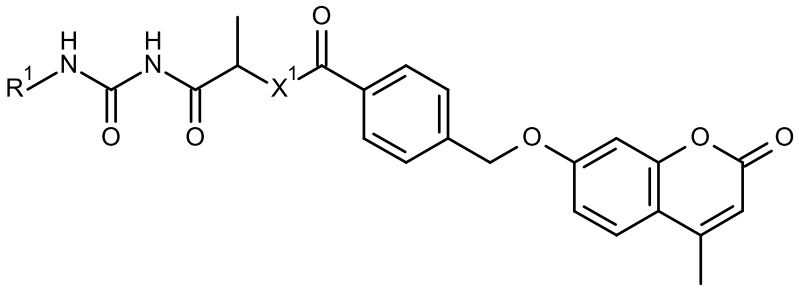
wherein

X^1 is NH or O; and

X^3 is O or S;

and the pharmaceutically acceptable salts thereof,

or to the formula I-D,



(I-D)

wherein

R^1 is hydrogen or methyl; and

X^1 is NH or O;

and the pharmaceutically acceptable salts thereof.

9. The compound [2-(2-furylmethylcarbamoylamino)-2-oxo-ethyl] 4-[(4-methyl-2-oxo-chromen-7-yl)oxymethyl]benzoate and its pharmaceutically acceptable salts.

10. The compound 4-[(4-methyl-2-oxo-chromen-7-yl)oxymethyl]-N-[2-(2-thienylmethylcarbamoylamino)ethyl]benzamide and its pharmaceutically acceptable salts.

11. The compound [2-oxo-2-(2-pyridylmethylcarbamoylamino)ethyl] 4-[(4-methyl-2-oxo-chromen-7-yl)oxymethyl]benzoate and its pharmaceutically acceptable salts.

12. A compound of formula I as defined in claim 1, which is selected from N-[2-(2-furylmethylcarbamoylamino)-2-oxo-ethyl]-4-[(4-methyl-2-oxo-chromen-7-yl)oxymethyl]benzamide, [2-oxo-2-(2-thienylmethylcarbamoylamino)ethyl] 4-[(4-methyl-2-oxo-chromen-7-yl)oxymethyl]-benzoate, and 4-[(4-methyl-2-oxo-chromen-7-yl)oxymethyl]-N-[2-oxo-2-(2-thienylmethylcarbamoylamino)ethyl]-benzamide, and the pharmaceutically acceptable salts thereof.

13. A compound of formula I as defined in claim 1, which is selected from (1-methyl-2-oxo-2-ureido-ethyl) 4-[(4-methyl-2-oxo-chromen-7-yl)oxymethyl]benzoate and [1-methyl-2-(methylcarbamoylamino)-2-oxo-ethyl] 4-[(4-methyl-2-oxo-chromen-7-yl)oxymethyl]benzoate, and the pharmaceutically acceptable salts thereof.

14. A pharmaceutical composition comprising at least one compound of the general formula I as defined in any of claims 1 to 13 or at least one pharmaceutically acceptable salt thereof and at least one pharmaceutically acceptable carrier.

15. The compound as claimed in any of claims 1 to 13 or a pharmaceutically acceptable salt thereof, for use as a medicament.

16. Use of a compound as claimed in any of claims 1 to 13 or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment or prophylaxis of muscle wasting conditions.

17. Use of a compound as claimed in any of claims 1 to 13 or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for the treatment or prophylaxis of skeletal or cardiac muscle atrophy resulting from one of the following diseases or conditions: congestive heart failure, chronic heart failure, cancer, cancer treatment with myotoxic and/or cardiotoxic substances such as doxorubicin, congenital myopathy, AIDS, chronic obstructive pulmonary disease (COPD), chronic renal diseases, renal failure, diabetes, severe burns, sarcopenia during aging, reduction in blood supply, temporary or long term immobilization, long term mechanical ventilation, denervation, prolonged weightlessness and malnutrition.

18. Use of a compound as claimed in any of claims 1 to 13 or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment or prophylaxis of conditions which are associated with an increased Muscle RING Finger 1 (MuRF1) expression, in particular of myopathies which are associated with an increased Muscle RING Finger 1 (MuRF1) expression.

19. The use as claimed in claim 18, where the myopathy is selected from critical illness myopathy, nemaline myopathy, inflammatory myopathy, myopathy from diabetes, myopathy from pulmonary hypertension, myopathy from chronic heart failure, myopathy from kidney failure and myopathy from tumor cachexia.

20. Use of a compound as claimed in any of claims 1 to 13 or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment or prophylaxis of cardiac conditions associated with systolic or diastolic dysfunction.

21. Use of a compound as claimed in any of claims 1 to 13 or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment or prophylaxis of diabetes.

22. Use of a compound as claimed in any of claims 1 to 13 or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment or prophylaxis of

- skeletal or cardiac muscle atrophy resulting from or associated with heart failure with reduced ejection fraction (HF-rEF), heart failure with preserved ejection fraction (HF-pEF), hypertension or tumor cachexia;
- muscle atrophy and/or cardiac toxicity induced by Doxorubicin;
- sarcopenia and/or cardiomyopathy due to aging;
- muscle atrophy due to chronic renal disease;
- diaphragm weakness due to mechanical ventilation or congestive heart failure;
- congenital myopathy, in particular congenetic muscle atrophy;
- diabetes-induced muscle atrophy; and/or
- diabetes.

23. Use of a compound selected from compounds of the general formula I, as defined in any of claims 1 to 13, or a pharmaceutically acceptable salts thereof, in the manufacture of a medicament for treating or preventing a condition, as defined in any of claims 16 to 22.