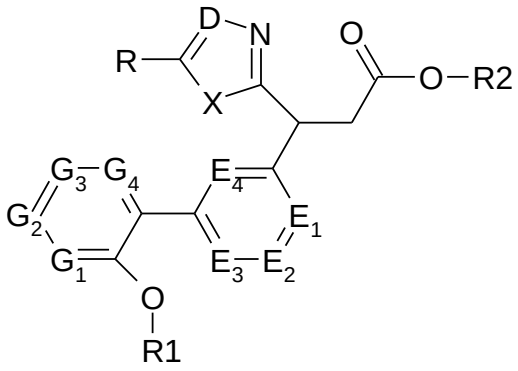
Claims

1. A compound of the formula I, in any of its stereoisomeric forms or a mixture of stereoisomeric forms in any ratio, or a physiologically acceptable salt thereof, or a physiologically acceptable solvate of any of them,



I,

wherein the meanings are:

X is S or O;
D is N or –C(R3)=;
R is H, (C_1-C_6)-alkyl, (C_3-C_8)-cycloalkyl;
R1 is H, (C_1-C_6)-alkyl, (C_3-C_8)-cycloalkyl, (C_1-C_6)-alkylen-(C_3-C_8)-cycloalkyl; wherein alkyl is optionally substituted by one ore more F-atoms;
R3 is H, methyl or ethyl;
R2 is Hydrogen or (C_1-C_6-)-alkyl;

E_1 is N or –C(R4)=;
E_2 is N or –C(R5)=;
E_3 is N or –C(R6)=;
E_4 is N or –C(R7)=; wherein none or one of E_1, E_2, E_3 or E_4 is N;

R4 is H or O-(C_1-C_6)-alkyl;
R5 is H F, Cl, CF_3, (C_1-C_6)-alkyl, (C_1-C_6)-cycloalkyl;

R6 is H or –O-CH_2-phenyl;
R7 is H;

G_1 is N or –C(R8)=;
G_2 is N or –C(R9)=;
G_3 is N or –C(R10)=;
G_4 is N or –C(R11)=; wherein none or one of G_1, G_2, G_3 or G_4 is N;
or G_3 and G_4 are –C(R10)= and –C(R11)=, wherein R10 and R11 form a 4 to 7 membered saturated carbocycle- or heterocycle with one or two oxygen atoms;
which is optionally mono- or disubstituted by (C_1-C_3)-alkyl;

R8 is H, F, Cl, (C_1-C_6)-alkyl, O-(C_1-C_6)-alkyl, CF_3 or OCF_3;
R9 is H, F, Cl, OH, O-(C_1-C_6)-alkyl, CH_2OH, CO-NH_2, (C_1-C_6)-alkyl, O-(C_1-C_6)-alkyl, CF_3 or OCF_3;
R10 is H, F, Cl, OH, (C_1-C_6)-alkyl, CH_2OH, CO-O-(C_1-C_6)-alkyl, SO_2-(C_1-C_6)-alkyl, CN, O-(C_1-C_6)-alkyl, CF_3 , CH_2-CN, $C(CH_3)_2$)-CN, (C_1-C_6)-alkyl-OH, -O-(C_1-C_6)-alkyl-OH, -O-CH_2-CO-(C_1-C_6)-alkyl or OCF_3;
R11 is H, F, Cl, OH, O-(C_1-C_6)-alkyl, CH_2OH, CO-methyl, CO-N(R20R21), CO-O-(C_1-C_6)-alkyl, CN, (C_1-C_6)-alkyl, O-(C_1-C_6)-alkyl or OCF_3; wherein R20 and R21 are independently from each other H or (C_1-C_3)-alkyl or form together with the nitrogen to which they are attached a 5 or 6 membered saturated ring.

2. A compound of the formula I, in any of its stereoisomeric forms or a mixture of stereoisomeric forms in any ratio, or a physiologically acceptable salt thereof, or a physiologically acceptable solvate of any of them, as claimed in claim 1, wherein R2 is Hydrogen.

3. A compound of the formula I, in any of its stereoisomeric forms or a mixture of stereoisomeric forms in any ratio, or a physiologically acceptable salt thereof, or a

physiologically acceptable solvate of any of them, as claimed in any one or more of claims 1 and 2, wherein

R is Hydrogen, methyl or ethyl;

R1 is H, methyl, ethyl, CF_3, -CH_2-cyclopropyl or -CH_2-$C(CH_3)_3$;

R2 is Hydrogen;

R4 is H or O-methyl;

R5 is H F, Cl, CF_3, (C_1-C_6)-alkyl, cyclopropyl;

R8 is H, F, Cl, methyl, O-methyl, CF3 or OCF_3;

R9 is H, F, Cl, OH, O-propyl, CH_2OH, CO-NH_2, methyl, O-methyl, CF_3 or OCF_3;

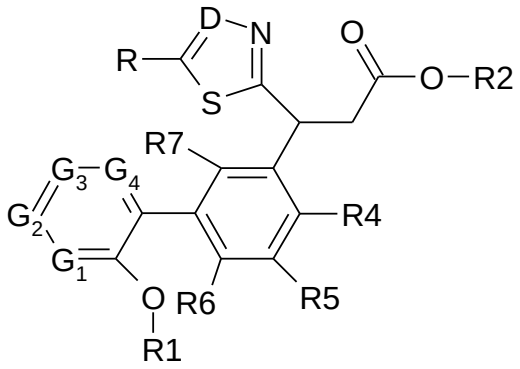
R10 is H, F, Cl, OH, i-propyl, t-butyl, CH_2OH, CO-O-methyl, SO_2-methyl, CN, methyl, O-methyl, CF_3 or OCF_3;

R11 is H, F, Cl, OH, O-methyl, O-i-propyl, CH_2OH, CO-methyl, CO-N(methyl)$_2$, CO-pyrrolidin, CO-O-methyl, CN, methyl or OCF_3.

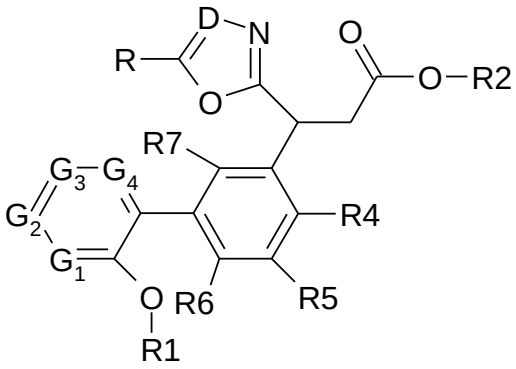
4. A compound of the formula I, in any of its stereoisomeric forms or a mixture of stereoisomeric forms in any ratio, or a physiologically acceptable salt thereof, or a physiologically acceptable solvate of any of them, as claimed in any one or more of claims 1 to 3, wherein

G_3 and G_4 are –C(R10)= and –C(R11)=, wherein R10 and R11 form a 5 or 6 membered saturated carbocycle or heterocycle with one or two oxygen atoms; which is optionally mono- or disubstituted by halogen and or (C_1-C_3)-alkyl.

5. A compound of the formula I-1 or I-11, in any of its stereoisomeric forms or a mixture of stereoisomeric forms in any ratio, or a physiologically acceptable salt thereof, or a physiologically acceptable solvate of any of them, wherein



I-1,



I-11

wherein the groups D, R, R1, R2, R4, R5, R6, R7, R8, R9, R10, R11 are defined as in the compounds of formula I in claims 1 to 4, wherein

G_1 is–C(R8)=;

G_2 is–C(R9)=;

G_3 is–C(R10)=;

G_4 –C(R11)=.

6. A compound of the formula I, in any of its stereoisomeric forms or a mixture of stereoisomeric forms in any ratio, or a physiologically acceptable salt thereof, or a physiologically acceptable solvate of any of them, as claimed in any one or more of claims 1 to 5, wherein the compound is chosen from

(S)-3-(5'-tert-Butyl-2'-methoxy-biphenyl-3-yl)-3-thiazol-2-yl-propionic acid

3-(5-Fluoro-2',6'-dimethoxy-biphenyl-3-yl)-3-(5-methyl-thiazol-2-yl)-propionic acid

3-(5-Chloro-2',6'-dimethoxy-biphenyl-3-yl)-3-(5-methyl-thiazol-2-yl)-propionic acid

3-(2',6'-Dimethoxy-biphenyl-3-yl)-3-(5-methyl-thiazol-2-yl)-propionic acid

3-(5-Chloro-2'-fluoro-6'-methoxy-biphenyl-3-yl)-3-(5-methyl-thiazol-2-yl)-propionic acid

3-(5-Chloro-2',3',6'-trimethoxy-biphenyl-3-yl)-3-(5-methyl-thiazol-2-yl)-propionic acid

3-(5-Chloro-5'-hydroxy-2'-methoxy-biphenyl-3-yl)-3-(5-methyl-thiazol-2-yl)-propionic acid

3-(5-Fluoro-4'-hydroxymethyl-2',6'-dimethoxy-biphenyl-3-yl)-3-oxazol-2-yl-propionic acid

3-(5-Chloro-2',6'-dimethoxy-biphenyl-3-yl)-3-(5-methyl-[1,3,4]oxadiazol-2-yl)-propionic acid

3-(5-Chloro-2',6'-dimethoxy-4'-methyl-biphenyl-3-yl)-3-(5-methyl-[1,3,4]oxadiazol-2-yl)-propionic acid

3-[3-Chloro-5-(6-methoxy-2,2-dimethyl-2,3-dihydro-benzofuran-7-yl)-phenyl]-3-(5-methyl-[1,3,4]oxadiazol-2-yl)-propionic acid

(R)-3-(5'-Isopropyl-2'-methoxy-biphenyl-3-yl)-3-(5-methyl-[1,3,4]oxadiazol-2-yl)-propionic acid

3-(2'-Methoxy-5'-methyl-5-trifluoromethyl-biphenyl-3-yl)-3-(5-methyl-[1,3,4]oxadiazol-2-yl)-propionic acid

3-(5'-tert-Butyl-2'-methoxy-5-trifluoromethyl-biphenyl-3-yl)-3-(5-methyl-[1,3,4]oxadiazol-2-yl)-propionic acid

3-(2',6'-Dimethoxy-5-trifluoromethyl-biphenyl-3-yl)-3-(5-methyl-[1,3,4]oxadiazol-2-yl)-propionic acid

3-(2',6'-Dimethoxy-4'-methyl-5-trifluoromethyl-biphenyl-3-yl)-3-(5-methyl-[1,3,4]oxadiazol-2-yl)-propionic acid

3-[3-(6-Methoxy-2,2-dimethyl-2,3-dihydro-benzofuran-7-yl)-5-trifluoromethyl-phenyl]-3-(5-methyl-[1,3,4]oxadiazol-2-yl)-propionic acid

3-(2'-Fluoro-6'-methoxy-5-trifluoromethyl-biphenyl-3-yl)-3-(5-methyl-[1,3,4]oxadiazol-2-yl)-propionic acid

3-(5'-Fluoro-2'-methoxy-5-trifluoromethyl-biphenyl-3-yl)-3-(5-methyl-[1,3,4]oxadiazol-2-yl)-propionic acid

3-[5'-(Cyano-dimethyl-methyl)-5-fluoro-2'-methoxy-biphenyl-3-yl]-3-(5-methyl-[1,3,4]oxadiazol-2-yl)-propionic acid.

7. A compound of the formula I as claimed in any one or more of claims 1 to 6 or a physiologically acceptable salt thereof or a physiologically acceptable solvate of any of them for use as a pharmaceutical.

8. A pharmaceutical composition, which comprises at least one compound of the formula I as claimed in any one or more of claims 1 to 6 or a physiologically

acceptable salt thereof or a physiologically acceptable solvate of any of them and a pharmaceutically acceptable carrier.

9. Use of a compound of the formula I as claimed in any one or more of claims 1 to 6 or a physiologically acceptable salt thereof or a physiologically acceptable solvate of any of them for the manufacture of a medicament for the treatment of heart failure, congestive heart failure, cardiomyopathy, myocardial infarction, left ventricular dysfunction, cardiac hypertrophy, valvular heart diseases, hypertension, atherosclerosis, peripheral arterial occlusive disease, restenosis, vascular permeability disorders, treatment of edema, thrombosis, rheumatoid arthritis, osteoarthritis, renal failure, cystic fibrosis, chronic bronchitis, chronic obstructive pulmonary disease, asthma, immunological diseases, diabetic complications, fibrotic diseases, pain, ischemia and/or reperfusion damage, and neurodegenerative diseases, or for the manufacture of a medicament for cardioprotection or renoprotection or for the manufacture of a medicament as a diuretic.

10. Use of a compound of the formula I as claimed in any one or more of claims 1 to 6 or a physiologically acceptable salt thereof or a physiologically acceptable solvate of any of them for the manufacture of a medicament for the treatment of atrial fibrillation.