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(54) **Title:** USE OF SUBSTITUTED PYRAZOLE COMPOUNDS FOR THE TREATMENT OF CARDIOVASCULAR RISK FACTORS CAUSED BY METABOLIC/FOOD DISORDERS

(57) **Abstract:** The present invention relates to the use of substituted pyrazole compounds for the treatment of metabolic syndrome in humans and animals and to corresponding medicaments.

Use of substituted pyrazole compounds for the treatment of cardiovascular risk factors caused by metabolic/food disorders

The present invention relates to the use of substituted pyrazole compounds for the treatment of metabolic syndrome in humans and animals and corresponding medicaments.

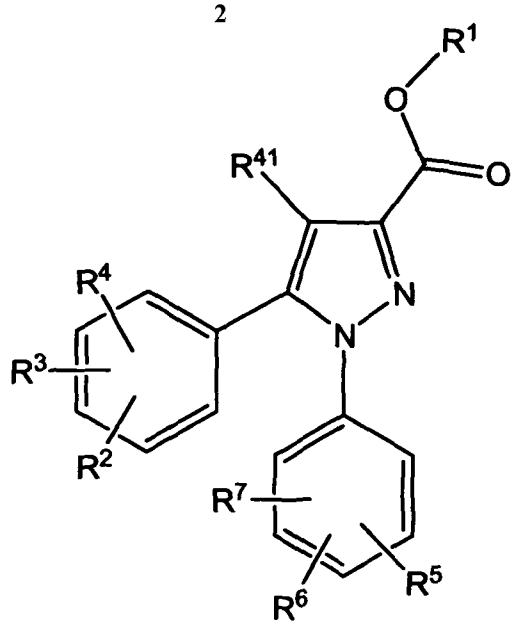
The metabolic syndrome is a widespread disease or health state involving high risks for a significant part of the population making it interesting to treat and to take precautions in way of a prophylaxis against or the avoid the metabolic syndrome.

Thus, it was an object of the present invention to provide compounds for use as active substances in medicaments, which are suitable for the treatment or prophylaxis of the metabolic syndrome.

Said object was achieved by using the substituted pyrazole compounds of general formula I and II given below and corresponding salts and solvates thereof.

It has been found that these compounds have a marked effect on the metabolic syndrome.

Thus, in one of its aspects the present invention relates to a medicament comprising at least one substituted pyrazole compounds of general formula I,



I

wherein

R^1 represents hydrogen or a linear or branched, substituted or unsubstituted, C_{1-4}-alkyl group,

R^2, R^3 and R^4 independently of each other represent hydrogen, a linear or branched C_{1-6}-alkyl group, a linear or branched C_{1-6}-alkoxy group, a halogen atom, CH_2F, CHF_2, CF_3, CN, OH, NO_2, -(C=O)-R^8, SH, SR^8, SOR^8, SO_2R^8, NH_2, NHR^8, NR^8R^9, -(C=O)-NH_2, -(C=O)-NHR^8 or -(C=O)-NR^8R^9 whereby R^8 and R^9 for each substituent independently represent linear or branched C_{1-6} alkyl,

R^5, R^6 and R^7 independently of each other represent hydrogen, a linear or branched C_{1-6}-alkyl group, a linear or branched C_{1-6}-alkoxy group, a halogen atom, CH_2F, CHF_2, CF_3, CN, OH, NO_2, -(C=O)-R^{10}, SH, SR^{10}, SOR^{10}, NH_2, NHR^{10}, $NR^{10}R^{11}$, -(C=O)-NH_2, -(C=O)-NHR^{10} and -(C=O)-$NR^{10}R^{11}$, whereby R^{10} and optionally R^{11} for each substituent independently represent linear or branched C_{1-6} alkyl;

R^{41} represents hydrogen, a linear or branched, substituted or unsubstituted, saturated or unsaturated C_{1-6}-alkyl group, a linear or branched, substituted or

unsubstituted, saturated or unsaturated C_{1-6}-alkoxy group, a halogen atom, CH_2F, CHF_2, CF_3, CN, OH, NO_2, -(C=O)-R^{10a}, SH, SR^{10a}, SOR^{10a}, NH_2, NHR^{10a}, $NR^{10a}R^{11a}$, -(C=O)-NH_2, -(C=O)-NHR^{10a} and -(C=O)-$NR^{10a}R^{11a}$, whereby R^{10a} and optionally R^{11a} for each substituent independently represent linear or branched C_{1-6} alkyl;

optionally in form of a corresponding N-oxide thereof, or a corresponding salt thereof, or a corresponding solvate thereof,

and optionally one or more pharmaceutically acceptable excipients.

These compounds have a surprising effect on the metabolic syndrome.

Preferred linear or branched, saturated or unsaturated aliphatic groups, which may be substituted by one or more substituents, may preferably be selected from the group consisting of methyl, ethyl, n-propyl, isopropyl, n-butyl, iso-butyl, sec-butyl, tert-butyl, n-pentyl, n-hexyl, n-heptyl, n-octyl, n-nonyl, n-decyl, vinyl, ethinyl, propenyl, propinyl, butenyl and butinyl.

In the context of this invention, alkyl and cycloalkyl radicals are understood as meaning saturated and unsaturated (but not aromatic), branched, unbranched and cyclic hydrocarbons, which can be unsubstituted or mono- or polysubstituted. In these radicals, C_{1-2}-alkyl represents C1- or C2-alkyl, C_{1-3}-alkyl represents C1-, C2- or C3-alkyl, C_{1-4}-alkyl represents C1-, C2-, C3- or C4-alkyl, C_{1-5}-alkyl represents C1-, C2-, C3-, C4-, or C5-alkyl, C_{1-6}-alkyl represents C1-, C2-, C3-, C4-, C5- or C6-alkyl, C_{1-7}-alkyl represents C1-, C2-, C3-, C4-, C5-, C6- or C7-alkyl, C_{1-8}-alkyl represents C1-, C2-, C3-, C4-, C5-, C6-, C7- or C8-alkyl, C_{1-10}-alkyl represents C1-, C2-, C3-, C4-, C5-, C6-, C7-, C8-, C9- or C10-alkyl and C_{1-18}-alkyl represents C1-, C2-, C3-, C4-, C5-, C6-, C7-, C8-, C9-, C10-, C11-, C12-, C13-, C14-, C15-, C16-, C17- or C18-alkyl. Furthermore, C_{3-4}-cycloalkyl represents C3- or C4-cycloalkyl, C_{3-5}-cycloalkyl represents C3-, C4- or C5-cycloalkyl, C_{3-6}-cycloalkyl represents C3-, C4-, C5- or C6-cycloalkyl, C_{3-7}-cycloalkyl represents C3-, C4-, C5-, C6- or C7-cycloalkyl, C_{3-8}-cycloalkyl represents C3-, C4-, C5-, C6-, C7- or C8-cycloalkyl, C_{4-5}-cycloalkyl represents C4- or C5-cycloalkyl, C_{4-6}-cycloalkyl represents C4-, C5- or C6-cycloalkyl,

C_{4-7}-cycloalkyl represents C4-, C5-, C6- or C7-cycloalkyl, C_{5-6}-cycloalkyl represents C5- or C6-cycloalkyl and C_{5-7}-cycloalkyl represents C5-, C6- or C7-cycloalkyl. In respect of cycloalkyl, the term also includes saturated cycloalkyls in which one or 2 carbon atoms are replaced by a heteroatom, S, N or O. However, mono- or polyunsaturated, preferably monounsaturated, cycloalkyls without a heteroatom in the ring also in particular fall under the term cycloalkyl as long as the cycloalkyl is not an aromatic system. The alkyl and cycloalkyl radicals are preferably methyl, ethyl, vinyl (ethenyl), propyl, allyl (2-propenyl), 1-propinyl, methylethyl, butyl, 1-methylpropyl, 2-methylpropyl, 1,1-dimethylethyl, pentyl, 1,1-dimethylpropyl, 1,2-dimethylpropyl, 2,2-dimethylpropyl, hexyl, 1-methylpentyl, cyclopropyl, 2-methylcyclopropyl, cyclopropylmethyl, cyclobutyl, cyclopentyl, cyclopentylmethyl, cyclohexyl, cycloheptyl, cyclooctyl, and also adamantyl, (if substituted also CHF_2, CF_3 or CH_2OH) as well as pyrazolinone, oxopyrazolinone, [1,4]-dioxane or dioxolane.

Here, in connection with alkyl and cycloalkyl - unless expressly defined otherwise - the term substituted in the context of this invention is understood as meaning replacement of at least one hydrogen radical by F, Cl, Br, I, NH_2, SH or OH, "polysubstituted" radicals being understood as meaning that the replacement takes effect both on different and on the same atoms several times with the same or different substituents, for example three times on the same C atom, as in the case of CF_3, or at different places, as in the case of -CH(OH)-CH=CH-$CHCl_2$. Particularly preferred substituents here are F, Cl and OH. In respect of cycloalkyl, the hydrogen radical can also be replaced by OC_{1-3}-alkyl or C_{1-3}-alkyl (in each case mono- or polysubstituted or unsubstituted), in particular methyl, ethyl, n-propyl, i-propyl, CF_3, methoxy or ethoxy.

The term $(CH_2)_{3-6}$ is to be understood as meaning -CH_2-CH_2-CH_2-, -CH_2-CH_2-CH_2-CH_2-, -CH_2-CH_2-CH_2-CH_2-CH_2- and -CH_2-CH_2-CH_2-CH_2-CH_2-CH_2-, $(CH_2)_{1-4}$ is to be understood as meaning -CH_2-, -CH_2-CH_2-, -CH_2-CH_2-CH_2- and -CH_2-CH_2-CH_2-CH_2-, $(CH_2)_{4-5}$ is to be understood as meaning -CH_2-CH_2-CH_2-CH_2- and -CH_2-CH_2-CH_2-CH_2-CH_2-, etc.

An aryl radical is understood as meaning ring systems with at least one aromatic ring but without heteroatoms even in only one of the rings. Examples are phenyl,

naphthyl, fluoranthenyl, fluorenyl, tetralinyl or indanyl, in particular 9H-fluorenyl or anthracenyl radicals, which can be unsubstituted or monosubstituted or polysubstituted.

A heteroaryl radical is understood as meaning heterocyclic ring systems which have at least one unsaturated ring and can contain one or more heteroatoms from the group consisting of nitrogen, oxygen and/or sulfur and can also be mono- or polysubstituted. Examples which may be mentioned from the group of heteroaryls are furan, benzofuran, thiophene, benzothiophene, pyrrole, pyridine, pyrimidine, pyrazine, quinoline, isoquinoline, phthalazine, benzo-1,2,5-thiadiazole, benzothiazole, indole, benzotriazole, benzodioxolane, benzodioxane, carbazole and quinazoline.

Here, in connection with aryl and heteroaryl, substituted is understood as meaning substitution of the aryl or heteroaryl by R, OR, a halogen, preferably F and/or Cl, a CF_3, a CN, an NO_2, an NRR, a C_{1-6}-alkyl (saturated), a C_{1-6}-alkoxy, a C_{3-8}-cycloalkoxy, a C_{3-8}-cycloalkyl or a C_{2-6}-alkylene, with R meaning hydrogen or C_{1-6}-alkyl.

The term "salt" is to be understood as meaning any form of the active compound used according to the invention in which it assumes an ionic form or is charged and is coupled with a counter-ion (a cation or anion) or is in solution. By this are also to be understood complexes of the active compound with other molecules and ions, in particular complexes which are complexed via ionic interactions. It especially includes physiologically acceptable salts, which is to be used equivalently to pharmacologically acceptable salts.

The term "physiologically acceptable salt" means in the context of this invention any salt that is physiologically tolerated (most of the time meaning not being toxic- especially not caused by the counter-ion) if used appropriately for a treatment especially if used on or applied to humans and/or mammals.

These physiologically acceptable salts can be formed with cations or bases and in the context of this invention is understood as meaning salts of at least one of the

compounds used according to the invention - usually a (deprotonated) acid - as an anion with at least one, preferably inorganic, cation which is physiologically tolerated - especially if used on humans and/or mammals. The salts of the alkali metals and alkaline earth metals are particularly preferred, and also those with NH4, but in particular (mono)- or (di)sodium, (mono)- or (di)potassium, magnesium or calcium salts.

These physiologically acceptable salts can also be formed with anions or acids in the context of this invention is understood as meaning salts of at least one of the compounds used according to the invention - usually protonated, for example on the nitrogen - as the cation with at least one anion which are physiologically tolerated - especially if used on humans and/or mammals. By this is understood in particular, in the context of this invention, the salt formed with a physiologically tolerated acid, that is to say salts of the particular active compound with inorganic or organic acids which are physiologically tolerated - especially if used on humans and/or mammals. Examples of physiologically tolerated salts of particular acids are salts of: hydrochloric acid, hydrobromic acid, sulfuric acid, methanesulfonic acid, formic acid, acetic acid, oxalic acid, succinic acid, malic acid, tartaric acid, mandelic acid, fumaric acid, lactic acid or citric acid.

The term "solvate" according to this invention is to be understood as meaning any form of the active compound according to the invention in which this compound has attached to it via non-covalent binding another molecule (most likely a polar solvent) especially alcoholates, e.g. methanolate.

Unless otherwise stated, the compounds of the invention are also meant to include compounds which differ only in the presence of one or more isotopically enriched atoms. For example, compounds having the present structures except for the replacement of a hydrogen by a deuterium or tritium, or the replacement of a carbon by ^{13}C- or ^{14}C-enriched carbon or ^{15}N-enriched nitrogen are within the scope of this invention.

The invention also covers the use of any prodrug of the compounds described for the invention. Examples of well known methods of producing a prodrug of a given acting

compound are known to those skilled in the art and can be found e.g. in Krogsgaard-Larsen et al., Textbook of Drugdesign and Discovery, Taylor & Francis (April 2002).

The process to acquire the compounds according to the general formula I, II, and X as well as suitable dose ranges for the compound according to general formula X are described in or can easily be derived from EP 576 357 A1, EP 656 354 A1 and US 5,624,941 as well as EP969832 A1 and US 6,893,659 B2. All of these patents and applications are included here by reference.

As an addition to that substituted pyrazole compounds of general formula I or II, which comprise nitrogen-atom containing saturated, unsaturated or aromatic rings may be obtained in the form of their N-oxides by methods well known to those skilled in the art.

The medicament according to the present invention may be in any form suitable for the application to humans and/or animals, preferably humans including infants, children and adults and can be produced by standard procedures known to those skilled in the art. The composition of the medicament may vary depending on the route of administration.

The medicament of the present invention may for example be administered parentally in combination with conventional injectable liquid carriers, such as water or suitable alcohols. Conventional pharmaceutical excipients for injection, such as stabilizing agents, solubilizing agents, and buffers, may be included in such injectable compositions. These medicaments may for example be injected intramuscularly, intraperitoneally, or intravenously.

Solid oral compositions (which are preferred as are liquid ones) may be prepared by conventional methods of blending, filling or tabletting. Repeated blending operations may be used to distribute the active agent throughout those compositions employing large quantities of fillers. Such operations are conventional in the art. The tablets may for example be prepared by wet or dry granulation and optionally coated according to the methods well known in normal pharmaceutical practice., in particular with an enteric coating.

The mentioned formulations will be prepared using standard methods such as those described or referred to in the Spanish and US Pharmacopeias and similar reference texts.

Medicaments according to the present invention may also be formulated into orally administrable compositions containing one or more physiologically compatible carriers or excipients, in solid or liquid form. These compositions may contain conventional ingredients such as binding agents, fillers, lubricants, and acceptable wetting agents. The compositions may take any convenient form, such as tablets, pellets, capsules, lozenges, aqueous or oily solutions, suspensions, emulsions, or dry powdered forms suitable for reconstitution with water or other suitable liquid medium before use, for immediate or retarded release.

The liquid oral forms for administration may also contain certain additives such as sweeteners, flavoring, preservatives, and emulsifying agents. Non-aqueous liquid compositions for oral administration may also be formulated, containing edible oils. Such liquid compositions may be conveniently encapsulated in e.g., gelatin capsules in a unit dosage amount.

The compositions of the present invention may also be administered topically or via a suppository.

The daily dosage for humans and animals may vary depending on factors that have their basis in the respective species or other factors, such as age, sex, weight or degree of illness and so forth. The daily dosage for humans may preferably be in the range from1 to 2000, preferably 1 to 1500, more preferably 1 to 1000 milligrams of active substance to be administered during one or several intakes per day.

In a preferred embodiment of the medicament according to the invention for the compound comprised according to general formula I R^{41} represents hydrogen or a linear or branched, substituted or unsubstituted, saturated or unsaturated C_{1-6}-alkyl group; preferably hydrogen or C_{1-3}-alkyl; most preferably hydrogen, methyl or ethyl.

In a preferred embodiment of the medicament according to the invention for the compound comprised according to general formula I at least one of R^2, R^3 or R^4 represents hydrogen, while at least one of R^2, R^3 or R^4 is different from hydrogen.

In a preferred embodiment of the medicament according to the invention for the compound comprised according to general formula I R^2, R^3 and R^4 independently of each other represent hydrogen, a linear or branched C_{1-6}-alkyl group, a linear or branched C_{1-6}-alkoxy group, a halogen atom, or CF_3; preferably hydrogen, chlorine, bromine, C_{1-3}-alkyl, C_{1-3}-alkoxy, CF_3 or NO_2; most preferably R^2, R^3 and R^4 independently of each other represent hydrogen, methyl, ethyl, F, Cl, Br and CF_3.

In a preferred embodiment of the medicament according to the invention for the compound comprised according to general formula I R^5, R^6 and R^7 independently of each other represent hydrogen, a linear or branched C_{1-6}-alkyl group, a linear or branched C_{1-6}-alkoxy group, a halogen atom, or CF_3; preferably hydrogen, chlorine, bromine, C_{1-3}-alkyl, C_{1-3}-alkoxy, CF_3 or NO_2.

In a preferred embodiment of the medicament according to the invention for the compound comprised according to general formula I R^7 represents hydrogen.

In a preferred embodiment of the medicament according to the invention for the compound comprised according to general formula I R^5 and R^6 independently of each other represent a linear or branched C_{1-6}-alkyl group, a halogen atom, or CF_3, preferably R^5 and R^6 independently of each other represent methyl, ethyl, F, Cl, Br and CF_3.

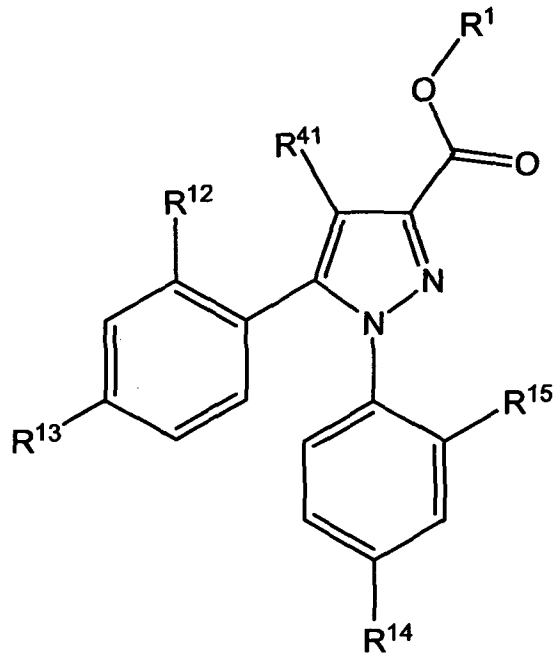
In a preferred embodiment of the medicament according to the invention for the compound comprised according to general formula I R^2 represents a chlorine or a bromine atom in the 4-position of the phenyl ring, while R^3 and R^4 represent hydrogen.

In a preferred embodiment of the medicament according to the invention for the compound comprised according to general formula I R^5 and R^6 each represent a

chlorine atoms in the 2- and 4-position of the phenyl ring, while R^7 represents hydrogen.

In a preferred embodiment of the medicament according to the invention for the compound comprised according to general formula I R^1 represents hydrogen, methyl or ethyl, preferably hydrogen.

In a preferred embodiment of the medicament according to the invention for the compound comprised according to general formula I is selected from a compound of general formula II



II

wherein

R^1 represents hydrogen or a linear or branched, substituted or unsubstituted, saturated or unsaturated C_{1-4}-alkyl group,

R^{12} in a compound according to general formula II represents hydrogen, a linear or branched, substituted or unsubstituted, saturated or unsaturated C_{1-6}-

alkyl group; a linear or branched, substituted or unsubstituted, saturated or unsaturated C_{1-6}-alkoxy group; a halogen atom, CN, OH, NO_2, SH, NH_2,

R^{13} represents a linear or branched, substituted or unsubstituted, saturated or unsaturated C_{1-6}-alkyl group; a linear or branched, substituted or unsubstituted, saturated or unsaturated C_{1-6}-alkoxy group; a halogen atom, CN, OH, NO_2, SH, NH_2,

R^{14} or R^{15} independently of each other represent a linear or branched, substituted or unsubstituted, saturated or unsaturated C_{1-6}-alkyl group; a linear or branched, substituted or unsubstituted, saturated or unsaturated C_{1-6}-alkoxy group; a halogen atom, CN, OH, NO_2, SH, NH_2,

R^{41} represents hydrogen, a linear or branched, substituted or unsubstituted, saturated or unsaturated C_{1-6}-alkyl group; a linear or branched, substituted or unsubstituted, saturated or unsaturated C_{1-6}-alkoxy group; a halogen atom, CN, OH, NO_2, SH, NH_2;

optionally in form of a corresponding N-oxide thereof, or a corresponding salt thereof, or a corresponding solvate thereof.

In a preferred embodiment of the medicament according to the invention for the compound comprised according to general formula II R^{41} represents hydrogen or a linear or branched C_{1-6}-alkyl group, preferably hydrogen, methyl or ethyl.

In a preferred embodiment of the medicament according to the invention for the compound comprised according to general formula II R^{12} represent hydrogen, a linear or branched C_{1-6}-alkyl group, a halogen atom, CH_2F, CHF_2, CF_3, CN, OH, NO_2, SH, or NH_2, preferably R^{12} represents hydrogen, methyl, ethyl, F, Cl, Br and CF_3.

In a preferred embodiment of the medicament according to the invention for the compound comprised according to general formula II R^{13} represents hydrogen, a linear or branched C_{1-6}-alkyl group, a halogen atom, CH_2F, CHF_2, CF_3, CN, OH, NO_2, SH, or NH_2, preferably R^{13} represents hydrogen, methyl, ethyl, F, Cl, Br and CF_3.

In a preferred embodiment of the medicament according to the invention for the compound comprised according to general formula II R^{14}, and R^{15} independently of each other represent a linear or branched C_{1-6}-alkyl group, a halogen atom, or CF_3, preferably R^{14} and R^{15} independently of each other represent methyl, ethyl, F, Cl, Br and CF_3.

In a preferred embodiment of the medicament according to the invention for the compound comprised according to general formula II R^{12} represents hydrogen.

In a preferred embodiment of the medicament according to the invention for the compound comprised according to general formula II R^{13} represents Cl or Br.

In a preferred embodiment of the medicament according to the invention for the compound comprised according to general formula II R^{14} and R^{15} each represent Cl.

In a preferred embodiment of the medicament according to the invention for the compound comprised according to general formula II R^{1} represents hydrogen, methyl or ethyl, preferably hydrogen.

In a preferred embodiment of the medicament according to the invention the compound comprised according to general formula I or II is selected from the group consisting of:

- 1-(2,4-dichlorophenyl)-5-(4-chlorophenyl)-4-methyl-1H-pyrazole-3-carboxylic acid,
- 1-(2,4-dichlorophenyl)-5-(4-bromophenyl)-4-methyl-1H-pyrazole-3-carboxylic acid,
- 1-(2,4-dichlorophenyl)-5-(4-chlorophenyl)-4-ethyl-1H-pyrazole-3-carboxylic acid,

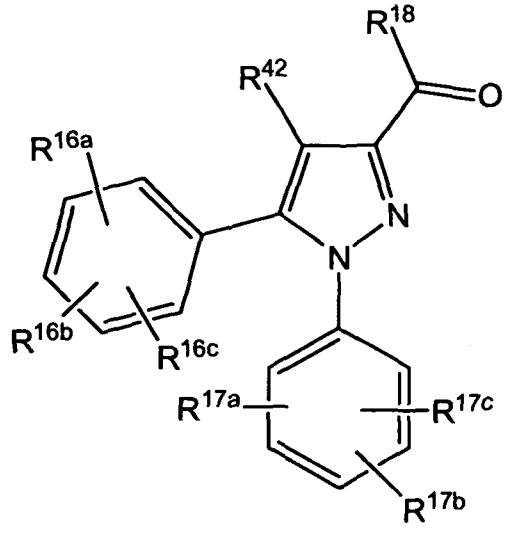
- 1-(2,4-dichlorophenyl)-5-(4-bromophenyl)-4-ethyl-1H-pyrazole-3-carboxylic acid

- 1-(2,4-dichlorophenyl)-5-(4-chlorophenyl)-1H-pyrazole-3-carboxylic acid, or

- 1-(2,4-dichlorophenyl)-5-(4-bromophenyl)-1H-pyrazole-3-carboxylic acid,

optionally in the form of a corresponding N-oxide, a corresponding salt or a corresponding solvate.

In another preferred embodiment of the medicament according to the invention the medicament comprises a combination consisting of at least one compound according to either of general formulas I or II and at least one substituted pyrazole compound according to general formula X,



X

wherein

R^{16a}, R^{16b} and R^{16c} independently of one another represent hydrogen, a linear or branched C_{1-6}-alkyl group, a linear or branched C_{1-6}-alkoxy group, a halogen atom, CH_2F, CHF_2, CF_3, CN, OH, NO_2, -(C=O)-R^{26}, SH, SR^{26}, SOR^{26}, SO_2R^{26}, NH_2, NHR^{26}, $NR^{26}R^{27}$, -(C=O)-NH_2, -(C=O)-NHR^{26} or -(C=O)-$NR^{26}R^{27}$ whereby R^{26} and R^{27} for each substituent independently represent linear or branched C_{1-6} alkyl,

R^{17a}, R^{17b} and R^{17c} independently of one another represent hydrogen, a linear or branched C_{1-6}-alkyl group, a linear or branched C_{1-6}-alkoxy group, a halogen atom, CH_2F, CHF_2, CF_3, CN, OH, NO_2, -(C=O)-R^{26}, SH, SR^{26}, SOR^{26}, SO_2R^{26}, NH_2, NHR^{26}, $NR^{26}R^{27}$, -(C=O)-NH_2, -(C=O)-NHR^{26} or -(C=O)-$NR^{26}R^{27}$ whereby R^{26} and R^{27} for each substituent independently represent linear or branched C_{1-6} alkyl,

R^{18} represents a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing cycloaliphatic group, which may be condensed with an optionally at least mono-substituted mono- or polycyclic ring system, or an optionally at least mono-substituted aryl or heteroaryl group, which may be condensed with an optionally at least mono-substituted mono- or polycyclic ring system, or an –$NR^{19}R^{20}$-moiety,

R^{19} and R^{20}, identical or different, represent a hydrogen atom, an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic radical, a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing cycloaliphatic group, which may be condensed with an optionally at least mono-substituted mono- or polycyclic ring system, or an optionally at least mono-substituted aryl or heteroaryl group, which may be condensed with an optionally at least mono-substituted mono- or polycyclic ring system and/or bonded via a linear or branched alkylene group, an –SO_2-R^{21}-moiety, or an –$NR^{22}R^{23}$-moiety, with the proviso that R^{19} and R^{20} do not identically represent hydrogen,

R^{21} represents a linear or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic group, a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing cycloaliphatic group, which may be condensed with a mono- or polycyclic ring-system, or an optionally at least mono-substituted aryl or heteroaryl group, which may be condensed with a mono- or polycyclic ring system and/or bonded via a linear or branched alkylene group,

R^{22} and R^{23}, identical or different, represent a hydrogen atom, an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic radical, a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing cycloaliphatic group, which may be condensed with an optionally at least mono-substituted mono- or polycyclic ring system, or an optionally at least mono-substituted aryl or heteroaryl group, which may be condensed with an optionally at least mono-substituted mono- or polycyclic ring system and/or bonded via a linear or branched alkylene group,

R^{42} in the compound according to general formula X represents hydrogen; a linear or branched, saturated or unsaturated, substituted or unsubstituted C_{1-6}-alkyl group; a linear or branched, saturated or unsaturated, substituted or unsubstituted C_{1-6}-alkoxy group, a halogen atom, CH_2F, CHF_2, CF_3, CN, OH, NO_2, -(C=O)-R^{24}, SH, SR^{24}, SOR^{24}, NH_2, NHR^{24}, $NR^{24}R^{25}$, -(C=O)-NH_2, -(C=O)-NHR^{24} and -(C=O)-$NR^{24}R^{25}$, whereby R^{24} and optionally R^{25} for each substituent independently represent linear or branched C_{1-6} alkyl;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding N-oxide thereof, or a corresponding salt thereof, or a corresponding solvate thereof.

In a preferred embodiment of the medicament according to the invention for the compound comprised according to general formula X R^{16a}, R^{16b} and R^{16c}

independently of one another represent a linear or branched C_{1-6}-alkyl group, a linear or branched C_{1-6}-alkoxy group, a halogen atom, CH_2F, CHF_2, CF_3, CN, OH, NO_2, -(C=O)-R', SH, SR', SOR', SO_2R', NH_2, NHR', NR'R'', -(C=O)-NH_2, -(C=O)-NHR' and -(C=O)-NR'R'' whereby R' and R'' for each substituent independently represent linear or branched C_{1-6} alkyl; preferably methyl, ethyl, F, Cl, Br and CF_3, more preferably R^{16a} represents a chlorine atom in the 4-position, whereas R^{16b}.and R^{16c} represent hydrogen.

In a preferred embodiment of the medicament according to the invention for the compound comprised according to general formula X R^{17a}, R^{17b} and R^{17c} independently of one another represent linear or branched C_{1-6}-alkyl group, a linear or branched C_{1-6}-alkoxy group, a halogen atom, CH_2F, CHF_2, CF_3, CN, OH, NO_2, -(C=O)-R', SH, SR', SOR', SO_2R', NH_2, NHR', NR'R'', -(C=O)-NH_2, -(C=O)-NHR' and -(C=O)-NR'R'', whereby R' and optionally R'' for each substituent independently represent linear or branched C_{1-6} alkyl, preferably R^{17a}, R^{17b} and R^{17c} represent methyl, ethyl, F, Cl, Br and CF3, more preferably R^{17a} and R^{17b} represent two chlorine atoms in 2- and 4-position and R^{17c} represents hydrogen.

In a preferred embodiment of the medicament according to the invention for the compound comprised according to general formula X R^{18} represents a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing C_{3-8} cycloaliphatic group, which may be condensed with an optionally at least mono-substituted mono- or polycyclic ring system, or an optionally at least mono-substituted, 5- or 6-membered aryl or heteroaryl group, which may be condensed with an optionally at least mono-substituted mono- or polycyclic ring system, or an –$NR^{19}R^{20}$-moiety, preferably R^{18} represents a saturated, optionally at least mono-substituted, optionally one or more nitrogen-atoms as ring member containing C_{3-8} cycloaliphatic group, which may be condensed with an optionally at least mono-substituted mono- or polycyclic ring system, or an –$NR^{19}R^{20}$-moiety, more preferably R^{18} represents a pyrrolidinyl group, a piperidinyl group or a piperazinyl group, whereby each of these groups may be substituted with one or more C_{1-6}-alkyl groups, or an –$NR^{18}R^{19}$-moiety.

In a preferred embodiment of the medicament according to the invention for the compound comprised according to general formula X R^{19} and R^{20}, identical or different, represent a hydrogen atom, an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted C_{1-6}-aliphatic radical, a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing C_{3-8}-cycloaliphatic group, which may be condensed with an optionally at least mono-substituted mono- or polycyclic ring system, or an optionally at least mono-substituted, 5- or 6-membered aryl or heteroaryl group, which may be condensed with an optionally at least mono-substituted mono- or polycyclic ring system and/or bonded via a methylene (-CH_2-) or ethylene (-CH_2-CH_2)-group, an –SO_2-R^{21}-moiety, or an –$NR^{22}R^{23}$-moiety, preferably one of these residues R^{19} and R^{20} represents a hydrogen atom and the other one of these residues R^{19} and R^{20} represents a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing C_{3-8}-cycloaliphatic group, which may be condensed with an optionally at least mono-substituted mono- or polycyclic ring system, or an optionally at least mono-substituted, 5- or 6-membered aryl or heteroaryl group, which may be condensed with an optionally at least mono-substituted mono- or polycyclic ring system, an –SO_2-R^{21}-moiety, or an –$NR^{22}R^{23}$-moiety, or R^{19} and R^{20}, identical or different, each represent a C_{1-6} alkyl group, more preferably one of these residues R^{19} and R^{20} represents a hydrogen atom and the other one of these residues R^{19} and R^{20} represents an optionally at least mono-substituted pyrrolidinyl group, an optionally at least mono-substituted piperidinyl group, an optionally at least mono-substituted piperazinyl group, an optionally at least mono-substituted triazolyl group, an –SO_2-R^{21}-moiety, or an –$NR^{22}R^{23}$-moiety, or R^{19} and R^{20}, identical or different, represent a methyl group, an ethyl group, an n-propyl group, an isopropyl group, an n-butyl group, a sec-butyl group or a tert.-butyl group.

In a preferred embodiment of the medicament according to the invention for the compound comprised according to general formula X R^{21} represents a linear or branched, saturated or unsaturated, optionally at least mono-substituted C_{1-6} aliphatic group, a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing C_{3-8} cycloaliphatic group, which may be condensed with a mono- or polycyclic ring-system, or an optionally at least mono-

substituted, 5- or 6-membered aryl or heteroaryl group, which may be condensed with a mono- or polycyclic ring system and/or bonded via a methylene (-CH_2-) or ethylene (-CH_2-CH_2)-group, preferably R^{21} represents a C_{1-6}-alkyl group, a saturated, optionally at least mono-substituted cycloaliphatic group, which may be condensed with a mono- or polycyclic ring-system, or a phenyl group, which is optionally substituted with one or more C_{1-6} alkyl groups.

In a preferred embodiment of the medicament according to the invention for the compound comprised according to general formula X R^{22} and R^{23}, identical or different, represent a hydrogen atom, an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted C_{1-6} aliphatic radical, a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing C_{3-8} cycloaliphatic group, which may be condensed with an optionally at least mono-substituted mono- or polycyclic ring system, or an optionally at least mono-substituted, 5- or 6 membered aryl or heteroaryl group, which may be condensed with an optionally at least mono-substituted mono- or polycyclic ring system and/or bonded via a methylene (-CH_2-) or ethylene (-CH_2-CH_2)-group, preferably R^{22} and R^{23}, identical or different, represent a hydrogen atom or a C_{1-6} alkyl radical.

In a preferred embodiment of the medicament according to the invention for the compound comprised according to general formula X R^{42}, represents a hydrogen atom, an unbranched or branched, saturated or unsaturated, substituted or unsubstituted C_{1-6} alkyl group; preferably hydrogen, methyl or ethyl.

In a preferred embodiment of the medicament according to the invention for the compound comprised according to general formula X R^{16a}, R^{16b} and R^{16c} independently of each other represent hydrogen, a linear or branched C_{1-6}-alkyl group, a linear or branched C_{1-6}-alkoxy group, a halogen atom, or CF_3; preferably hydrogen, chlorine, bromine, C_{1-3}-alkyl, C_{1-3}-alkoxy, CF_3 or NO_2; most preferably R^{16a}, R^{16b} and R^{16c} independently of each other represent hydrogen, methyl, ethyl, F, Cl, Br and CF_3.

In a preferred embodiment of the medicament according to the invention for the compound comprised according to general formula X R^{17a}, R^{17b} and R^{17c} independently of each other represent hydrogen, a linear or branched C_{1-6}-alkyl group, a linear or branched C_{1-6}-alkoxy group, a halogen atom, or CF_3; preferably hydrogen, chlorine, bromine, C_{1-3}-alkyl, C_{1-3}-alkoxy, CF_3 or NO_2.

In a preferred embodiment of the medicament according to the invention for the compound comprised according to general formula X is represented by a structure wherein,

R^{16a} represents a halogen atom, preferably a chlorine or bromine atom, in its 4-position,

R^{16b} and R^{16c} represent hydrogen,

R^{17a} and R^{17b} represent halogen atoms, preferably chlorine atoms, in its 2- and 4-position,

R^{17c} represent hydrogen,

R^{18} represents a pyrrolidinyl group, a piperidinyl group, a piperazinyl group, a homo-piperazinyl group, a morpholinyl group, or an $-NR^{19}R^{20}$-moiety,

R^{19} represents a hydrogen atom or a linear or branched C_{1-6}-alkyl group,

R^{20} represents a linear or branched C_{1-6} alkyl group, an $-SO_2-R^{21}$-moiety, a pyrrolidinyl group, a piperidinyl group, a piperazinyl group, a homo-piperazinyl group, a morpholinyl group, a triazolyl group, whereby each of the heterocyclic rings may be substituted with one or more, identical or different, C_{1-6}-alkyl groups, and

R^{21} represents a phenyl group, which is optionally substituted with one or more C_{1-6} alkyl groups, which may be identical or different,

R^{42} in a compound according to general formula X represents a hydrogen atom, an unbranched or branched, saturated or unsaturated, substituted or unsubstituted C_{1-6} alkyl group, preferably hydrogen, methyl or ethyl,

optionally in form of a corresponding N-oxide thereof, or a corresponding salt thereof, or a corresponding solvate thereof.

In a preferred embodiment of the medicament according to the invention the compound comprised according to general formula X is selected from:

- 1-(2,4-dichlorophenyl)-5-(4-chlorophenyl)-4-methyl-N-(piperidin-1-yl)-1H-pyrazole-3-carboxamide;
- 1-(2,4-dichlorophenyl)-5-(4-bromophenyl)-4-methyl-N-(piperidin-1-yl)-1H-pyrazole-3-carboxamide;
- 1-(2,4-dichlorophenyl)-5-(4-chlorophenyl)-4-ethyl-N-(piperidin-1-yl)-1H-pyrazole-3-carboxamide,
- 1-(2,4-dichlorophenyl)-5-(4-bromophenyl)-4-ethyl-N-(piperidin-1-yl)-1H-pyrazole-3-carboxamide;
- 1-(2,4-dichlorophenyl)-5-(4-chlorophenyl)-N-(piperidin-1-yl)-1H-pyrazole-3-carboxamide or
- 1-(2,4-dichlorophenyl)-5-(4-bromophenyl)-N-(piperidin-1-yl)-1H-pyrazole-3-carboxamide

optionally in the form of a corresponding N-oxide, a corresponding salt or a corresponding solvate.

In a preferred embodiment of the medicament according to the invention at least one of the compound comprised is selected from:

- 1-(2,4-dichlorophenyl)-5-(4-chlorophenyl)-4-methyl-1H-pyrazole-3-carboxylic acid,

- 1-(2,4-dichlorophenyl)-5-(4-bromophenyl)-4-methyl-1H-pyrazole-3-carboxylic acid,

- 1-(2,4-dichlorophenyl)-5-(4-chlorophenyl)-4-ethyl-1H-pyrazole-3-carboxylic acid,
- 1-(2,4-dichlorophenyl)-5-(4-bromophenyl)-4-ethyl-1H-pyrazole-3-carboxylic acid,
- 1-(2,4-dichlorophenyl)-5-(4-chlorophenyl)-1H-pyrazole-3-carboxylic acid, or
- 1-(2,4-dichlorophenyl)-5-(4-bromophenyl)-1H-pyrazole-3-carboxylic acid

and

- 1-(2,4-dichlorophenyl)-5-(4-chlorophenyl)-4-methyl-N-(piperidin-1-yl)-1H-pyrazole-3-carboxamide;
- 1-(2,4-dichlorophenyl)-5-(4-bromophenyl)-4-methyl-N-(piperidin-1-yl)-1H-pyrazole-3-carboxamide;
- 1-(2,4-dichlorophenyl)-5-(4-chlorophenyl)-4-ethyl-N-(piperidin-1-yl)-1H-pyrazole-3-carboxamide;
- 1-(2,4-dichlorophenyl)-5-(4-bromophenyl)-4-ethyl-N-(piperidin-1-yl)-1H-pyrazole-3-carboxamide;
- 1-(2,4-dichlorophenyl)-5-(4-chlorophenyl)-N-(piperidin-1-yl)-1H-pyrazole-3-carboxamide or
- 1-(2,4-dichlorophenyl)-5-(4-bromophenyl)-N-(piperidin-1-yl)-1H-pyrazole-3-carboxamide

each optionally in the form of a corresponding N-oxide, a corresponding salt or a corresponding solvate.

Another highly preferred aspect of the invention is the use of a compound of general formula I or II described above or of a combination of compounds described above with at least one compound according to formulas I or II and at least one compound

according to general formula X for the manufacture of a Medicament for the treatment of the metabolic syndrome.

As defined here treatment does also include prophylaxis.

The Metabolic syndrome is described in detail by Eckel et al., The Lancet, Vol. 365 (2005), 1415-1428, included here by reference. Even though according to Eckel et al. there is no homogemeous definition of definition of the metabolic syndrome it can clearly be derived from the article and the statements of the WHO that metabolic syndrome is to be considered as a disease which can and has to be treated. Especially it involves inter alia (pathophysiological) changes in the blood parameter, especially lipid parameters. Even though obesity plays an important role in the metabolic syndrome some aspects of the syndrome are weight independent, especially some lipid parameters. Especially the positive influence on the weight independent aspects of the metabolic syndrome (see e.g. Pagotto and Pasquali, The Lancet, Vol. 365 (2005), 1363, 1364, included by reference) like some blood parameters, especially lipid parameters, including influence on Triglyceride levels, is one of the major and surprising advantages of the compounds according to general formula I or II, and their combination with compounds according to general formula X. On the other hand given the interrelation between metabolic syndrome and diabetes, especially diabetes type II, glucose intolerance and insulin resistance the compounds do have an influence here. Given the very nature of the metabolic syndrome treatment of it seems also to be beneficial for the treatment of cardiovascular diseases especially cardiovascular risk factors, including prophylaxis. As a last point it thus might also be that the compounds act also in food disorders, including obesity.

Independently of that and as a major point in a preferred embodiment of the use according to the invention the metabolic syndrome is weight independent.

Thus in a preferred embodiment of the use according to the invention the medicament is influencing/treating the blood parameters, especially the lipid parameters. It seems that the compounds advantageously lower the proportion of LDL bodies//proteins and raise thye proportion of HDL bodies/proteins.

Thus in a preferred embodiment of the use according to the invention the medicament is for the treatment of diabetes, especially type II, glucose intolerance and insulin resistance.

A preferred aspect of the invention is the use of a compound of general formula I or II described above or of a combination of compounds described above of at least one compound according to formulas I or II and at least one compound according to general formula X for the manufacture of a medicament for the treatment of diabetes, especially type II, glucose intolerance and insulin resistance.

Another preferred aspect of the invention is also a method of treatment encompassing abovementioned uses, wherein a compound of general formula I or II, and a combination of these with a compound of general formula X is applied to a person in need thereof, treating metabolic syndrome, especially weight independent, cardiovascular diseases especially fighting cardiovascular risk factors, influencing the blood parameters, especially the lipid parameters, diabetes, especially type II, glucose intolerance and insulin resistance.

A highly preferred embodiment of the invention is drawn to N-Oxides of the compounds according to general formula X as described above, which showed improved attributes when used as pharmaceutically active compounds in the body of a mammal.

Especially preferred are thus the following compounds:

- 1-(2,4-dichlorophenyl)-5-(4-chlorophenyl)-4-methyl-N-(piperidin-1-yl)-1H-pyrazole-3-carboxamide, N-oxide;
- 1-(2,4-dichlorophenyl)-5-(4-bromophenyl)-4-methyl-N-(piperidin-1-yl)-1H-pyrazole-3-carboxamide, N-oxide;
- 1-(2,4-dichlorophenyl)-5-(4-chlorophenyl)-4-ethyl-N-(piperidin-1-yl)-1H-pyrazole-3-carboxamide, N-oxide;
- 1-(2,4-dichlorophenyl)-5-(4-bromophenyl)-4-ethyl-N-(piperidin-1-yl)-1H-pyrazole-3-carboxamide, N-oxide;

- 1-(2,4-dichlorophenyl)-5-(4-chlorophenyl)-N-(piperidin-1-yl)-1H-pyrazole-3-carboxamide, N-oxide or
- 1-(2,4-dichlorophenyl)-5-(4-bromophenyl)-N-(piperidin-1-yl)-1H-pyrazole-3-carboxamide, N-oxide.

A thus preferred embodiment encompasses also a medicament comprising at least one of the N-oxide compounds of general formula X or especially at least one of the preferred 6 N-oxides listed above as well as optionally one or more pharmaceutically acceptable excipients.

In a further preferred embodiment at least one of the N-oxide compounds of general formula X or especially at least one of the preferred 6 N-oxides listed above is used for the manufacture of a medicament for the prophylaxis and/or treatment of disorders of the central nervous system, disorders of the immune system, disorders of the cardiovascular system, disorders of the endocrinous system, disorders of the respiratory system, disorders of the gastrointestinal tract or reproductive disorders; for the prophylaxis and/or treatment of food intake disorders, preferably bulimia, anorexia, cachexia, obesity, type II diabetus mellitus (non-insuline dependent diabetes mellitus), more preferably obesity; for the prophylaxis and/or treatment of psychosis; for the prophylaxis and/or treatment of alcohol abuse and/or alcohol addiction, nicotine abuse and/or nicotine addiction, drug abuse and/or drug addiction and/or medicament abuse and/or medicament addiction, preferably drug abuse and/or drug addiction and/or nicotine abuse and/or nicotine addiction; for the prophylaxis and/or treatment of cancer, preferably for the prophylaxis and/or treatment of one or more types of cancer selected from the group consisting of brain cancer, bone cancer, lip cancer, mouth cancer, esophageal cancer, stomach cancer, liver cancer, bladder cancer, pancreas cancer, ovary cancer, cervical cancer, lung cancer, breast cancer, skin cancer, colon cancer, bowel cancer and prostate cancer, more preferably for the prophylaxis and/or treatment of one or more types of cancer selected from the group consisting of colon cancer, bowel cancer and prostate cancer; metabolic syndrome, especially weight independent, cardiovascular diseases, cardiovascular risk factors, glucose intolerance and insulin resistance; for the prophylaxis and/or treatment of one or more disorders selected from the group consisting of bone disorders, preferably osteoporosis (e.g. osteoporosis associated

with a genetic predisposition, sex hormone deficiency, or ageing), cancer-associated bone disease or Paget`s disease of bone; schizophrenia, anxiety, depression, epilepsy, neurodegenerative disorders, cerebellar disorders, spinocerebellar disorders, cognitive disorders, cranial trauma, head trauma, stroke, panic attacks, peripheric neuropathy, glaucoma, migraine, Morbus Parkinson, Morbus Huntington, Morbus Alzheimer, Raynaud's disease, tremblement disorders, compulsive disorders, senile dementia, thymic disorders, tardive dyskinesia, bipolar disorders, medicament-induced movement disorders, dystonia, endotoxemic shock, hemorragic shock, hypotension, insomnia, immunologic disorders, sclerotic plaques, vomiting, diarrhea, asthma, memory disorders, pruritus, pain, or for potentiation of the analgesic effect of narcotic and non-narcotic analgesics, or for influencing intestinal transit.

Medicaments/drugs, which are frequently the subject of misuse include opioids, barbiturates, cannabis, cocaine, amphetamines, phencyclidine, hallucinogens and benzodiazepines.

Another highly preferred aspect of the invention is the use of the N-Oxides of the compounds according to general formula I or II, the N-oxides X of the compounds according to general formula X as well as the combinations tereof as active principle bound to and/or eluting from a medicinal implant especially a cardiovascular implant, most preferably a stent, especially for the prophylaxis or treatment of restenosis. As - as described above - it seems that the compounds advantageously lower the proportion of LDL bodies//proteins and raise the proportion of HDL bodies/proteins the drug eluting from the stent, bound thereto physically or chemically (covalently or non-covalently), will be positively influencing the effectivity of a cardiovascular stent allowing it a longer time of implantation.

For this embodiment the following compounds - as well as combinations between the respective compounds of dormula I or II and X - are especially preferred:

(formula I or II:)

- 1-(2,4-dichlorophenyl)-5-(4-chlorophenyl)-4-methyl-1H-pyrazole-3-carboxylic acid,

- 1-(2,4-dichlorophenyl)-5-(4-bromophenyl)-4-methyl-1H-pyrazole-3-carboxylic acid,
- 1-(2,4-dichlorophenyl)-5-(4-chlorophenyl)-4-ethyl-1H-pyrazole-3-carboxylic acid,
- 1-(2,4-dichlorophenyl)-5-(4-bromophenyl)-4-ethyl-1H-pyrazole-3-carboxylic acid,
- 1-(2,4-dichlorophenyl)-5-(4-chlorophenyl)-1H-pyrazole-3-carboxylic acid, or
- 1-(2,4-dichlorophenyl)-5-(4-bromophenyl)-1H-pyrazole-3-carboxylic acid

and

(formula X:)

- 1-(2,4-dichlorophenyl)-5-(4-chlorophenyl)-4-methyl-N-(piperidin-1-yl)-1H-pyrazole-3-carboxamide;
- 1-(2,4-dichlorophenyl)-5-(4-bromophenyl)-4-methyl-N-(piperidin-1-yl)-1H-pyrazole-3-carboxamide;
- 1-(2,4-dichlorophenyl)-5-(4-chlorophenyl)-4-ethyl-N-(piperidin-1-yl)-1H-pyrazole-3-carboxamide;
- 1-(2,4-dichlorophenyl)-5-(4-bromophenyl)-4-ethyl-N-(piperidin-1-yl)-1H-pyrazole-3-carboxamide;
- 1-(2,4-dichlorophenyl)-5-(4-chlorophenyl)-N-(piperidin-1-yl)-1H-pyrazole-3-carboxamide or
- 1-(2,4-dichlorophenyl)-5-(4-bromophenyl)-N-(piperidin-1-yl)-1H-pyrazole-3-carboxamide

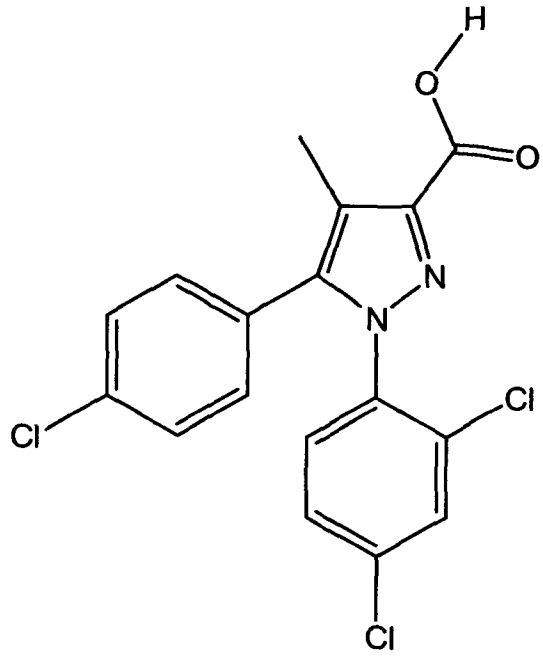
each optionally in the form of a corresponding N-oxide, a corresponding salt or a corresponding solvate.

The present invention is illustrated below with the aid of examples. These illustrations are given solely by way of example and are not intended to limit the present invention.

Examples:

Example 1:

1-(2,4-dichlorophenyl)-5-(4-chlorophenyl)-4-methyl-1H-pyrazole-3-carboxylic acid



Pharmacological Data/Testing:

The compound according to example 1 seems to be an inhibitor of high blood levels of triglicerides and other factors which contribute to the metabolic syndrome. This effect is probed in obese mice fed with high fat diet. In the following paragraphs the method of this study is described.

I. In-vivo testing for lipid parameters or other parameters important for metabolic syndrome (especially of triglycerides) in blood plasma

The study is done using male mice (e.g. B6 Lep ob/ob, obtained from Charles River (France)). Mice are divided in 3 groups: I (control), II (vehicle), III (example 0).

Group I:

The animals of the group I receive the standard diet (e.g. D-12450B, Research Diets, NJ, USA).

Group II:

The animals of the groups II and III are fed with a High Fat Diet (e.g. D-12492, Research Diets, NJ, USA), in both cases for 7 weeks (References 1 and 2).

Group III:

The animals of the groups III are fed with a High Fat Diet (e.g. D-12492, Research Diets, NJ, USA), in both cases for 7 weeks (References 1 and 2).

At the end of the feeding period of 7 weeks, the treatment period (14 days) is started: Group II mice receive the vehicle (10 ml/kg/day, po, of the aqueous solution of acacia gum, 5% W/V). Group III is administered with 30 mg/kg/day, p.o., of the compound according to Example 1. Group I does not receive any treatment. The three groups of mice have the same diet than in the previous period.

At the end of the 14 days period of treatment, the blood levels of lipid parameters or other parameters important for metabolic syndrome, especially of certain triglicerides in the plasma of the animals are determined.

The analysis of the whole blood samples is done according to the methods known in the art like for example using test strips "Lipid panel" and the photometric Analyzer Cardio-Check Test System, from PA Instruments Polymer Technology Systems Indianapolis, IN-46268, USA (Distributed in Spain by Novalab Iberica S.A.L, Madrid, Spain).

References

1.-Lambert P.D. et al.."Cyliary neurotrophic factor activates leptin-like pathways and reduces body fat"
P.N.A.S. 2001, 28 (8) : 4652-4657

2.- Grasa M.M. et al "Oleoyl-Estrone lowens the body weight of both ob/ob and db/db mice. Hozm. Metab. Res 2000, 32 : 246-250

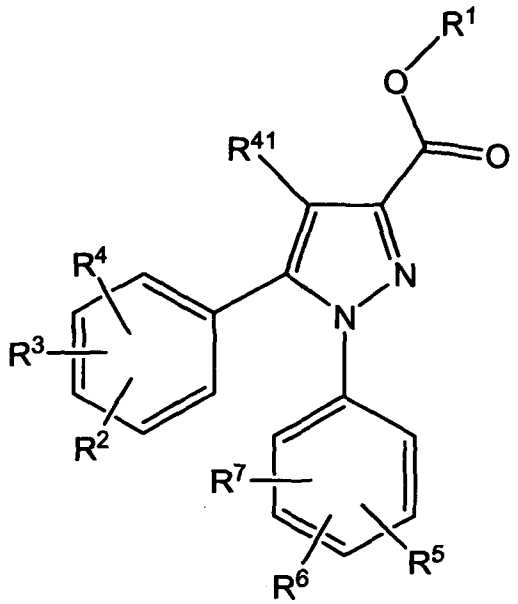
II. In-vivo testing for regulation of triglycerides in blood plasma

In a second set of experiments similar to the tests shown above the TG (triglyceride) levels of diet-induced obese mice in blood is determined.
Mice receiving a high fat diet are - after a feeding period of 6 days - either treated p.o. with vehicle (0,5 % HPMC) or with the compound according to example 1 (30 mg/kg/day p.o.).

TG levels in blood are determined on day 28 after beginning of the treatment.

Claims:

1. Medicament comprising at least one substituted pyrazole compounds of general formula I,



I

wherein

R^1 represents hydrogen or a linear or branched, substituted or unsubstituted, C_{1-4}-alkyl group,

R^2, R^3 and R^4 independently of each other represent hydrogen, a linear or branched C_{1-6}-alkyl group, a linear or branched C_{1-6}-alkoxy group, a halogen atom, CH_2F, CHF_2, CF_3, CN, OH, NO_2, -(C=O)-R^8, SH, SR^8, SOR^8, SO_2R^8, NH_2, NHR^8, NR^8R^9, -(C=O)-NH_2, -(C=O)-NHR^8 or -(C=O)-NR^8R^9 whereby R^8 and R^9 for each substituent independently represent linear or branched C_{1-6} alkyl,

R^5, R^6 and R^7independently of each other represent hydrogen, a linear or branched C_{1-6}-alkyl group, a linear or branched C_{1-6}-alkoxy group, a halogen atom, CH_2F, CHF_2, CF_3, CN, OH, NO_2, -(C=O)-R^{10}, SH, SR^{10}, SOR^{10}, NH_2, NHR^{10}, $NR^{10}R^{11}$, -(C=O)-NH_2, -(C=O)-NHR^{10} and -(C=O)-$NR^{10}R^{11}$, whereby

R^{10} and optionally R^{11} for each substituent independently represent linear or branched C_{1-6} alkyl;

R^{41} represents hydrogen, a linear or branched, substituted or unsubstituted, saturated or unsaturated C_{1-6}-alkyl group, a linear or branched, substituted or unsubstituted, saturated or unsaturated C_{1-6}-alkoxy group, a halogen atom, CH_2F, CHF_2, CF_3, CN, OH, NO_2, -(C=O)-R^{10a}, SH, SR^{10a}, SOR^{10a}, NH_2, NHR^{10a}, $NR^{10a}R^{11a}$, -(C=O)-NH_2, -(C=O)-NHR^{10a} and -(C=O)-$NR^{10a}R^{11a}$, whereby R^{10a} and optionally R^{11a} for each substituent independently represent linear or branched C_{1-6} alkyl;

optionally in form of a corresponding N-oxide thereof, or a corresponding salt thereof, or a corresponding solvate thereof,

and optionally one or more pharmaceutically acceptable excipients.

2. Medicament according to claim 1, characterized in that in the compound according to general formula I R^{41} represents hydrogen or a linear or branched, substituted or unsubstituted, saturated or unsaturated C_{1-6}-alkyl group; preferably hydrogen or C_{1-3}-alkyl; most preferably hydrogen, methyl or ethyl.

3. Medicament according to any of claims 1 or 2, characterized in that in the compound according to general formula I at least one of R^2, R^3 or R^4 represents hydrogen, while at least one of R^2, R^3 or R^4 is different from hydrogen.

4. Medicament according to any one of claims 1 to 3, characterized in that in the compound according to general formula I R^2, R^3 and R^4 independently of each other represent hydrogen, a linear or branched C_{1-6}-alkyl group, a linear or branched C_{1-6}-alkoxy group, a halogen atom, or CF_3; preferably hydrogen, chlorine, bromine, C_{1-3}-alkyl, C_{1-3}-alkoxy, CF_3 or NO_2; most preferably R^2, R^3 and R^4 independently of each other represent hydrogen, methyl, ethyl, F, Cl, Br and CF_3.

5. Medicament according to any one of claims 1 to 4, characterized in that in the compound according to general formula I R^5, R^6 and R^7 independently of each other represent hydrogen, a linear or branched C_{1-6}-alkyl group, a linear or branched C_{1-6}-alkoxy group, a halogen atom, or CF_3; preferably hydrogen, chlorine, bromine, C_{1-3}-alkyl, C_{1-3}-alkoxy, CF_3 or NO_2.

6. Medicament according to any one of claims 1 to 5, characterized in that in the compound according to general formula I R^7 represents hydrogen.

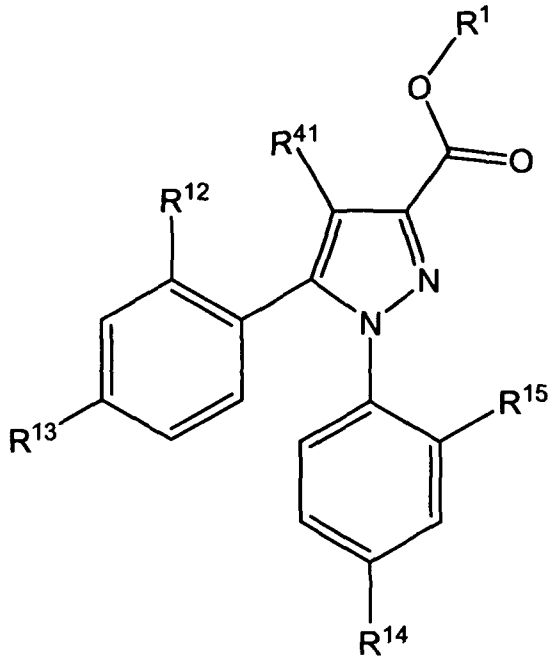
7. Medicament according to any one of claims 1 to 6, characterized in that in the compound according to general formula I R^5 and R^6 independently of each other represent a linear or branched C_{1-6}-alkyl group, a halogen atom, or CF_3, preferably R^5 and R^6 independently of each other represent methyl, ethyl, F, Cl, Br and CF_3.

8. Medicament according to any one of claims 1 to 7, characterized in that in the compound according to general formula I R^2 represents a chlorine or a bromine atom in the 4-position of the phenyl ring, while R^3 and R^4 represent hydrogen.

9. Medicament according to any one of claims 1 to 8, characterized in that in the compound according to general formula I R^5 and R^6 each represent a chlorine atoms in the 2- and 4-position of the phenyl ring, while R^7 represents hydrogen.

10. Medicament according to any one of claims 1 to 9, characterized in that in the compound according to general formula I R^1 represents hydrogen, methyl or ethyl, preferably hydrogen.

11. Medicament according to one or more of claims 1 to 10, characterized in that the compound according to general formula I is selected from a compound of general formula II



II

wherein

R^1 represents hydrogen or a linear or branched, substituted or unsubstituted, saturated or unsaturated C_{1-4}-alkyl group,

R^{12} in a compound according to general formula II represents hydrogen, a linear or branched, substituted or unsubstituted, saturated or unsaturated C_{1-6}-alkyl group; a linear or branched, substituted or unsubstituted, saturated or unsaturated C_{1-6}-alkoxy group; a halogen atom, CN, OH, NO_2, SH, NH_2,

R^{13} represents a linear or branched, substituted or unsubstituted, saturated or unsaturated C_{1-6}-alkyl group; a linear or branched, substituted or unsubstituted, saturated or unsaturated C_{1-6}-alkoxy group; a halogen atom, CN, OH, NO_2, SH, NH_2,

R^{14} or R^{15} independently of each other represent a linear or branched, substituted or unsubstituted, saturated or unsaturated C_{1-6}-alkyl group; a linear or branched, substituted or unsubstituted, saturated or unsaturated C_{1-6}-alkoxy group; a halogen atom, CN, OH, NO_2, SH, NH_2,

R^{41} represents hydrogen, a linear or branched, substituted or unsubstituted, saturated or unsaturated C_{1-6}-alkyl group; a linear or branched, substituted or unsubstituted, saturated or unsaturated C_{1-6}-alkoxy group; a halogen atom, CN, OH, NO_2, SH, NH_2;

optionally in form of a corresponding N-oxide thereof, or a corresponding salt thereof, or a corresponding solvate thereof.

12. Medicament according to claim 11, characterized in that in a compound according to general formula II R^{41} represents hydrogen or a linear or branched C_{1-6}-alkyl group, preferably hydrogen, methyl or ethyl.

13. Medicament according to any of claims 11 or 12 characterized in that in a compound according to general formula II R^{12} represent hydrogen, a linear or branched C_{1-6}-alkyl group, a halogen atom, CH_2F, CHF_2, CF_3, CN, OH, NO_2, SH, or NH_2, preferably R^{12} represents hydrogen, methyl, ethyl, F, Cl, Br and CF_3.

14. Medicament according to any of claims 11 to 13 characterized in that in the compound according to general formula II R^{13} represents hydrogen, a linear or branched C_{1-6}-alkyl group, a halogen atom, CH_2F, CHF_2, CF_3, CN, OH, NO_2, SH, or NH_2, preferably R^{13} represents hydrogen, methyl, ethyl, F, Cl, Br and CF_3.

15. Medicament according to any one of claims 11 to 14, characterized in that in the compound according to general formula II R^{14}, and R^{15} independently of each other represent a linear or branched C_{1-6}-alkyl group, a halogen atom, or CF_3, preferably R^{14} and R^{15} independently of each other represent methyl, ethyl, F, Cl, Br and CF_3.

16. Medicament according to any one of claims11 to 15, characterized in that in a compound according to general formula II R^{12} represents hydrogen.

17. Medicament according to any one of claims11 to 16, characterized in that in the compound according to general formula II R^{13} represents Cl or Br.

18. Medicament according to any one of claims 11 to 17, characterized in that in the compound according to general formula II R^{14} and R^{15} each represent Cl.

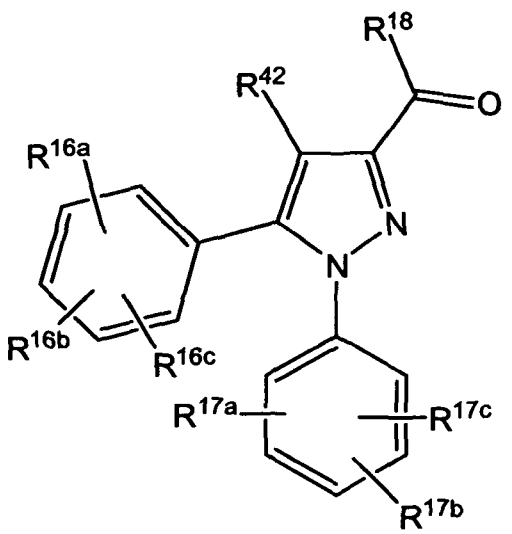
19. Medicament according to any one of claims 11 to 18, characterized in that in the compound according to general formula II R^{1} represents hydrogen, methyl or ethyl, preferably hydrogen.

20. Medicament according to one or more of claims 1 to 19, characterized in that the compound according to general formula I or II is selected from the group consisting of:

- 1-(2,4-dichlorophenyl)-5-(4-chlorophenyl)-4-methyl-1H-pyrazole-3-carboxylic acid,
- 1-(2,4-dichlorophenyl)-5-(4-bromophenyl)-4-methyl-1H-pyrazole-3-carboxylic acid,
- 1-(2,4-dichlorophenyl)-5-(4-chlorophenyl)-4-ethyl-1H-pyrazole-3-carboxylic acid,
- 1-(2,4-dichlorophenyl)-5-(4-bromophenyl)-4-ethyl-1H-pyrazole-3-carboxylic acid
- 1-(2,4-dichlorophenyl)-5-(4-chlorophenyl)-1H-pyrazole-3-carboxylic acid, or
- 1-(2,4-dichlorophenyl)-5-(4-bromophenyl)-1H-pyrazole-3-carboxylic acid,

optionally in the form of a corresponding N-oxide, a corresponding salt or a corresponding solvate.

21. Medicament according to any of claims 1 to 20, comprising at least one compound according to either of general formulas I or II and at least one substituted pyrazole compound according to general formula X,



X

wherein

R^{16a}, R^{16b} and R^{16c} independently of one another represent hydrogen, a linear or branched C_{1-6}-alkyl group, a linear or branched C_{1-6}-alkoxy group, a halogen atom, CH_2F, CHF_2, CF_3, CN, OH, NO_2, -(C=O)-R^{26}, SH, SR^{26}, SOR^{26}, SO_2R^{26}, NH_2, NHR^{26}, $NR^{26}R^{27}$, -(C=O)-NH_2, -(C=O)-NHR^{26} or -(C=O)-$NR^{26}R^{27}$ whereby R^{26} and R^{27} for each substituent independently represent linear or branched C_{1-6} alkyl,

R^{17a}, R^{17b} and R^{17c} independently of one another represent hydrogen, a linear or branched C_{1-6}-alkyl group, a linear or branched C_{1-6}-alkoxy group, a halogen atom, CH_2F, CHF_2, CF_3, CN, OH, NO_2, -(C=O)-R^{26}, SH, SR^{26}, SOR^{26}, SO_2R^{26}, NH_2, NHR^{26}, $NR^{26}R^{27}$, -(C=O)-NH_2, -(C=O)-NHR^{26} or -(C=O)-$NR^{26}R^{27}$ whereby R^{26} and R^{27} for each substituent independently represent linear or branched C_{1-6} alkyl,

R^{18} represents a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing cycloaliphatic group, which may be condensed with an optionally at least mono-substituted mono- or polycyclic ring system, or an optionally at least mono-substituted aryl or heteroaryl group, which may be condensed with an optionally at least mono-substituted mono- or polycyclic ring system, or an $-NR^{19}R^{20}$-moiety,

R^{19} and R^{20}, identical or different, represent a hydrogen atom, an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic radical, a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing cycloaliphatic group, which may be condensed with an optionally at least mono-substituted mono- or polycyclic ring system, or an optionally at least mono-substituted aryl or heteroaryl group, which may be condensed with an optionally at least mono-substituted mono- or polycyclic ring system and/or bonded via a linear or branched alkylene group, an $-SO_2-R^{21}$-moiety, or an $-NR^{22}R^{23}$-moiety, with the proviso that R^{19} and R^{20} do not identically represent hydrogen,

R^{21} represents a linear or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic group, a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing cycloaliphatic group, which may be condensed with a mono- or polycyclic ring-system, or an optionally at least mono-substituted aryl or heteroaryl group, which may be condensed with a mono- or polycyclic ring system and/or bonded via a linear or branched alkylene group,

R^{22} and R^{23}, identical or different, represent a hydrogen atom, an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted aliphatic radical, a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing cycloaliphatic group, which may be condensed with an optionally at least

mono-substituted mono- or polycyclic ring system, or an optionally at least mono-substituted aryl or heteroaryl group, which may be condensed with an optionally at least mono-substituted mono- or polycyclic ring system and/or bonded via a linear or branched alkylene group,

R^{42} in the compound according to general formula X represents hydrogen; a linear or branched, saturated or unsaturated, substituted or unsubstituted C_{1-6}-alkyl group; a linear or branched, saturated or unsaturated, substituted or unsubstituted C_{1-6}-alkoxy group, a halogen atom, CH_2F, CHF_2, CF_3, CN, OH, NO_2, -(C=O)-R^{24}, SH, SR^{24}, SOR^{24}, NH_2, NHR^{24}, $NR^{24}R^{25}$, -(C=O)-NH_2, -(C=O)-NHR^{24} and -(C=O)-$NR^{24}R^{25}$, whereby R^{24} and optionally R^{25} for each substituent independently represent linear or branched C_{1-6} alkyl;

optionally in form of one of the stereoisomers, preferably enantiomers or diastereomers, a racemate or in form of a mixture of at least two of the stereoisomers, preferably enantiomers and/or diastereomers, in any mixing ratio, or a corresponding N-oxide thereof, or a corresponding salt thereof, or a corresponding solvate thereof.

22. Medicament according to claim 21, characterized in that in the compound according to general formula X R^{16a}, R^{16b} and R^{16c} independently of one another represent a linear or branched C_{1-6}-alkyl group, a linear or branched C_{1-6}-alkoxy group, a halogen atom, CH_2F, CHF_2, CF_3, CN, OH, NO_2, -(C=O)-R', SH, SR', SOR', SO_2R', NH_2, NHR', NR'R", -(C=O)-NH_2, -(C=O)-NHR' and -(C=O)-NR'R" whereby R' and R" for each substituent independently represent linear or branched C_{1-6} alkyl; preferably methyl, ethyl, F, Cl, Br and CF_3, more preferably R^{16a} represents a chlorine atom in the 4-position, whereas R^{16b} and R^{16c} represent hydrogen.

23. Medicament according to any of claims 21 or 22, characterized in that in the compound according to general formula X R^{17a}, R^{17b} and R^{17c} independently of one another represent linear or branched C_{1-6}-alkyl group, a linear or branched C_{1-6}-alkoxy group, a halogen atom, CH_2F, CHF_2, CF_3, CN, OH, NO_2, -(C=O)-R', SH, SR', SOR', SO_2R', NH_2, NHR', NR'R", -(C=O)-NH_2, -(C=O)-NHR' and -

(C=O)-NR'R", whereby R' and optionally R" for each substituent independently represent linear or branched C_{1-6} alkyl, preferably R^{17a}, R^{17b} and R^{17c} represent methyl, ethyl, F, Cl, Br and CF3, more preferably R^{17a} and R^{17b} represent two chlorine atoms in 2- and 4-position and R^{17c} represents hydrogen.

24. Medicament according to any of claims 21 to 23, characterized in that in the compound according to general formula X R^{18} represents a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing C_{3-8} cycloaliphatic group, which may be condensed with an optionally at least mono-substituted mono- or polycyclic ring system, or an optionally at least mono-substituted, 5- or 6-membered aryl or heteroaryl group, which may be condensed with an optionally at least mono-substituted mono- or polycyclic ring system, or an $-NR^{19}R^{20}$-moiety, preferably R^{18} represents a saturated, optionally at least mono-substituted, optionally one or more nitrogen-atoms as ring member containing C_{3-8} cycloaliphatic group, which may be condensed with an optionally at least mono-substituted mono- or polycyclic ring system, or an $-NR^{19}R^{20}$-moiety, more preferably R^{18} represents a pyrrolidinyl group, a piperidinyl group or a piperazinyl group, whereby each of these groups may be substituted with one or more C_{1-6}-alkyl groups, or an $-NR^{18}R^{19}$-moiety.

25. Medicament according to any of claims 21 to 24, characterized in that in the compound according to general formula X R^{19} and R^{20}, identical or different, represent a hydrogen atom, an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted C_{1-6}-aliphatic radical, a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing C_{3-8}-cycloaliphatic group, which may be condensed with an optionally at least mono-substituted mono- or polycyclic ring system, or an optionally at least mono-substituted, 5- or 6-membered aryl or heteroaryl group, which may be condensed with an optionally at least mono-substituted mono- or polycyclic ring system and/or bonded via a methylene ($-CH_2-$) or ethylene ($-CH_2-CH_2$)-group, an $-SO_2-R^{21}$-moiety, or an $-NR^{22}R^{23}$-moiety, preferably one of these residues R^{19} and R^{20}

represents a hydrogen atom and the other one of these residues R^{19} and R^{20} represents a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing C_{3-8}-cycloaliphatic group, which may be condensed with an optionally at least mono-substituted mono- or polycyclic ring system, or an optionally at least mono-substituted, 5- or 6-membered aryl or heteroaryl group, which may be condensed with an optionally at least mono-substituted mono- or polycyclic ring system, an $-SO_2-R^{21}$-moiety, or an $-NR^{22}R^{23}$-moiety, or R^{19} and R^{20}, identical or different, each represent a C_{1-6} alkyl group, more preferably one of these residues R^{19} and R^{20} represents a hydrogen atom and the other one of these residues R^{19} and R^{20} represents an optionally at least mono-substituted pyrrolidinyl group, an optionally at least mono-substituted piperidinyl group, an optionally at least mono-substituted piperazinyl group, an optionally at least mono-substituted triazolyl group, an $-SO_2-R^{21}$-moiety, or an $-NR^{22}R^{23}$-moiety, or R^{19} and R^{20}, identical or different, represent a methyl group, an ethyl group, an n-propyl group, an isopropyl group, an n-butyl group, a sec-butyl group or a tert.-butyl group.

26. Medicament according to any of claims 21 to 25, characterized in that in the compound according to general formula X R^{21} represents a linear or branched, saturated or unsaturated, optionally at least mono-substituted C_{1-6} aliphatic group, a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing C_{3-8} cycloaliphatic group, which may be condensed with a mono- or polycyclic ring-system, or an optionally at least mono-substituted, 5- or 6-membered aryl or heteroaryl group, which may be condensed with a mono- or polycyclic ring system and/or bonded via a methylene ($-CH_2-$) or ethylene ($-CH_2-CH_2$)-group, preferably R^{21} represents a C_{1-6}-alkyl group, a saturated, optionally at least mono-substituted cycloaliphatic group, which may be condensed with a mono- or polycyclic ring-system, or a phenyl group, which is optionally substituted with one or more C_{1-6} alkyl groups.

27. Medicament according to any of claims 21 to 26, characterized in that in the compound according to general formula X R^{22} and R^{23}, identical or different,

represent a hydrogen atom, an unbranched or branched, saturated or unsaturated, optionally at least mono-substituted C_{1-6} aliphatic radical, a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as ring member containing C_{3-8} cycloaliphatic group, which may be condensed with an optionally at least mono-substituted mono- or polycyclic ring system, or an optionally at least mono-substituted, 5- or 6 membered aryl or heteroaryl group, which may be condensed with an optionally at least mono-substituted mono- or polycyclic ring system and/or bonded via a methylene (-CH_2-) or ethylene (-CH_2-CH_2)-group, preferably R^{22} and R^{23}, identical or different, represent a hydrogen atom or a C_{1-6} alkyl radical.

28. Medicament according to any of claims 21 to 27, characterized in that in the compound according to general formula X R^{42}, represents a hydrogen atom, an unbranched or branched, saturated or unsaturated, substituted or unsubstituted C_{1-6} alkyl group; preferably hydrogen, methyl or ethyl.

29. Medicament according to any one of claims 21 to 28, characterized in that in the compound according to general formula X R^{16a}, R^{16b} and R^{16c} independently of each other represent hydrogen, a linear or branched C_{1-6}-alkyl group, a linear or branched C_{1-6}-alkoxy group, a halogen atom, or CF_3; preferably hydrogen, chlorine, bromine, C_{1-3}-alkyl, C_{1-3}-alkoxy, CF_3 or NO_2; most preferably R^{16a}, R^{16b} and R^{16c} independently of each other represent hydrogen, methyl, ethyl, F, Cl, Br and CF_3.

30. Medicament according to any one of claims 21 to 29, characterized in that in the compound according to general formula X R^{17a}, R^{17b} and R^{17c} independently of each other represent hydrogen, a linear or branched C_{1-6}-alkyl group, a linear or branched C_{1-6}-alkoxy group, a halogen atom, or CF_3; preferably hydrogen, chlorine, bromine, C_{1-3}-alkyl, C_{1-3}-alkoxy, CF_3 or NO_2.

31. Medicament according to any of claims 21 to 30, characterized in that the compound according to general formula X is represented by a structure wherein,

R^{16a} represents a halogen atom, preferably a chlorine or bromine atom, in its 4-position,

R^{16b} and R^{16c} represent hydrogen,

R^{17a} and R^{17b} represent halogen atoms, preferably chlorine atoms, in its 2- and 4-position,

R^{17c} represent hydrogen,

R^{18} represents a pyrrolidinyl group, a piperidinyl group, a piperazinyl group, a homo-piperazinyl group, a morpholinyl group, or an $-NR^{19}R^{20}$-moiety,

R^{19} represents a hydrogen atom or a linear or branched C_{1-6}-alkyl group,

R^{20} represents a linear or branched C_{1-6} alkyl group, an $-SO_2-R^{21}$-moiety, a pyrrolidinyl group, a piperidinyl group, a piperazinyl group, a homo-piperazinyl group, a morpholinyl group, a triazolyl group, whereby each of the heterocyclic rings may be substituted with one or more, identical or different, C_{1-6}-alkyl groups, and

R^{21} represents a phenyl group, which is optionally substituted with one or more C_{1-6} alkyl groups, which may be identical or different,

R^{42} in a compound according to general formula X represents a hydrogen atom, an unbranched or branched, saturated or unsaturated, substituted or unsubstituted C_{1-6} alkyl group, preferably hydrogen, methyl or ethyl,

optionally in form of a corresponding N-oxide thereof, or a corresponding salt thereof, or a corresponding solvate thereof.

32. Medicament according to any of claims 21 to 31, characterized in that the compound according to general formula X is selected from:

- 1-(2,4-dichlorophenyl)-5-(4-chlorophenyl)-4-methyl-N-(piperidin-1-yl)-1H-pyrazole-3-carboxamide;
- 1-(2,4-dichlorophenyl)-5-(4-bromophenyl)-4-methyl-N-(piperidin-1-yl)-1H-pyrazole-3-carboxamide;
- 1-(2,4-dichlorophenyl)-5-(4-chlorophenyl)-4-ethyl-N-(piperidin-1-yl)-1H-pyrazole-3-carboxamide,
- 1-(2,4-dichlorophenyl)-5-(4-bromophenyl)-4-ethyl-N-(piperidin-1-yl)-1H-pyrazole-3-carboxamide;
- 1-(2,4-dichlorophenyl)-5-(4-chlorophenyl)-N-(piperidin-1-yl)-1H-pyrazole-3-carboxamide or
- 1-(2,4-dichlorophenyl)-5-(4-bromophenyl)-N-(piperidin-1-yl)-1H-pyrazole-3-carboxamide

optionally in the form of a corresponding N-oxide, a corresponding salt or a corresponding solvate.

33. Medicament according to any of claims 21 to 32, characterized in that at least the following compounds are used:

- 1-(2,4-dichlorophenyl)-5-(4-chlorophenyl)-4-methyl-1H-pyrazole-3-carboxylic acid,
- 1-(2,4-dichlorophenyl)-5-(4-bromophenyl)-4-methyl-1H-pyrazole-3-carboxylic acid,
- 1-(2,4-dichlorophenyl)-5-(4-chlorophenyl)-4-ethyl-1H-pyrazole-3-carboxylic acid,
- 1-(2,4-dichlorophenyl)-5-(4-bromophenyl)-4-ethyl-1H-pyrazole-3-carboxylic acid,
- 1-(2,4-dichlorophenyl)-5-(4-chlorophenyl)-1H-pyrazole-3-carboxylic acid, or

- 1-(2,4-dichlorophenyl)-5-(4-bromophenyl)-1H-pyrazole-3-carboxylic acid

and

- 1-(2,4-dichlorophenyl)-5-(4-chlorophenyl)-4-methyl-N-(piperidin-1-yl)-1H-pyrazole-3-carboxamide;
- 1-(2,4-dichlorophenyl)-5-(4-bromophenyl)-4-methyl-N-(piperidin-1-yl)-1H-pyrazole-3-carboxamide;
- 1-(2,4-dichlorophenyl)-5-(4-chlorophenyl)-4-ethyl-N-(piperidin-1-yl)-1H-pyrazole-3-carboxamide;
- 1-(2,4-dichlorophenyl)-5-(4-bromophenyl)-4-ethyl-N-(piperidin-1-yl)-1H-pyrazole-3-carboxamide;
- 1-(2,4-dichlorophenyl)-5-(4-chlorophenyl)-N-(piperidin-1-yl)-1H-pyrazole-3-carboxamide or
- 1-(2,4-dichlorophenyl)-5-(4-bromophenyl)-N-(piperidin-1-yl)-1H-pyrazole-3-carboxamide

each optionally in the form of a corresponding N-oxide, a corresponding salt or a corresponding solvate.

34. Use of a compound of general formula I, or II described in claims 1 to 20 or of a combination of compounds described in claims 21 to 33 with at least one compound according to formulas I or II and at least one compound according to general formula X for the manufacture of a Medicament for the treatment of the metabolic syndrome.

35. Use according to claim 34, characterized in that the metabolic syndrome is weight independent.

36. Use according to claim 34 or 35, characterized in that the medicament is influencing/treating the blood parameters, especially the lipid parameters.

37. Use according to claim 34, characterized in that the medicament is for the treatment of diabetes, especially type II, glucose intolerance and insulin resistance.

38. Use of a compound of general formula I or II described in claims 1 to 20 or of a combination of compounds described in claims 21 to 33 of at least one compound according to formulas I or II and at least one compound according to general formula X for the manufacture of a Medicament for the treatment of diabetes, especially type II, glucose intolerance and insulin resistance.