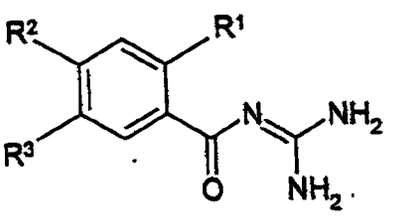
Use of benzoylguanidines for the treatment of non-insulin-dependent diabetes mellitus

The invention relates to the use of benzoylguanidines of the formula I



I

R^1		is A,
R^2		is Het, $C_nF_mH_{2n+1-m}O_p$, R^4, OR^4, OH, benzyl, CN, Hal, SO_q-R^5, Ph, O-Ph, O-Het, NH-Het, NH_2, NHA, NA_2 or NH-Ph,
R^3		is SO_2A',
R^4		is a straight-chain or branched alkyl radical having 1 to 8 C atoms or cycloalkyl having 3 to 8 C atoms which can be unsubstituted or mono-, di- or trisubstituted by A,
R^5		is A or Ph,
A, A'		in each case independently of one another are alkyl having 1 to 6 C atoms,
Het		is a mono- or bicyclic saturated, unsaturated or aromatic heterocycle having from 1 to 4 N, O and/or S atoms, which can be substituted once, twice or three times by Hal, CF_3, A, CN, NO_2, NH_2 and/or carbonyl oxygen,
Hal		is F, Cl, Br or I,
Ph		is unsubstituted phenyl or substituted once, twice or three times by A, OA, Hal, CF_3, NH_2, NHA or NA_2,
m		is 1, 2, 3, 4, 5, 6, 7, but at most 2n+1,
n		is 1, 2 or 3,
p		is 0 or 1,
q		is 0, 1 or 2,

and/or their physiologically acceptable salts and solvates for the production of a medicament for the treatment of non-insulin-dependent diabetes mellitus.

and/or their physiologically acceptable salts and solvates for the production of a medicament for the treatment of non-insulin-dependent diabetes mellitus.

The compounds of formula I are known from EP 0 699 666, EP 0 699 663, EP 0 743 301, EP 0 704 431, EP 0 758 644, EP 0 699 660, EP 0 725 062, EP 0 708 088, EP 0 694 537 and EP 0 723 963. They are potent inhibitors of the cellular sodium-proton-antiporter (Na^+/H^+-exchanger).

Benzoylguanidines with other substitution patterns are discribed e.g. in EP 0 589 336 as inhibitors of the cellular sodium-proton-antiporter, which shows an increased level in diabetes.

The use of pyrazinoylguanidines for the treatment of diabetes mellitus is disclosed in WO 97/21438.

The invention was based on the object of finding compounds having useful properties, in particular those which can be used for the production of medicaments.

It has been found that the compounds of the formula I and their salts have particularly useful pharmacological properties combined with good tolerability, as, in particular, they can be used for the production of a medicament for the treatment of non-insulin-dependent diabetes mellitus (NIDDM).

Moreover, the compounds of the formula I and their salts can be used for the production of a medicament for lowering and/or controlling the blood sugar levels of NIDDM persons.

Additionally, the compounds of the formula I and their salts can be used for the production of a medicament for lowering and/or controlling the levels of insulin, free fatty acids and triglycerides of NIDDM persons.

The activity of the compounds of formula I which can be used for the production of a medicament for the treatment of non-insulin-dependent diabetes mellitus was confirmed experimentally for some representative compounds of the formula I. The pharmacological test data are compiled in Table I.

The invention thus relates to the use of benzoylguanidines of the formula I wherein the compounds are selected from the group

a) N-diaminomethylene-2-methyl-4-(1-pyrrolyl)-5-methylsulfonyl-benzamide,

b) N-diaminomethylene-2-methyl-4-trifluoromethyl-5-methylsulfonyl-benzamide,

c) N-diaminomethylene-2-methyl-4-isopropyl-5-methylsulfonyl-benzamide,

and/or their physiologically acceptable salts and solvates for the production of a medicament for the treatment of non-insulin-dependent diabetes mellitus.

Solvates means addition compounds with e.g. water or alcoholes.

For all radicals which occur several times, such as, for example, A, it holds true that their meanings are independent of one another.

Alkyl has 1 to 6, preferably 1, 2, 3, 4; 5 or 6 C atoms. Alkyl is therefore in particular, for example, methyl, furthermore ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl or tert-butyl, further also pentyl, 1-, 2- or 3-methylbutyl, 1,1-, 1,2- or 2,2-dimethylpropyl, 1-ethylpropyl, hexyl, 1-, 2-, 3- or 4-

methylpentyl, 1,1-, 1,2-, 1,3-, 2,2-, 2,3- or 3,3-dimethylbutyl, 1- or 2-ethylbutyl, 1-ethyl-1-methylpropyl, 1-ethyl-2-methylpropyl, 1,1,2- or 1,2,2-trimethylpropyl.

R^1 preferably means alkyl having 1-6 C atoms, preferably e.g. methyl, ethyl, propyl or isopropyl, most preferably methyl.
R^3 means SO_2A', wherein A' preferably is e.g. methyl, ethyl, propyl, isopropyl or butyl, most preferably R^3 means SO_2CH_3.

Het is preferably 2- or 3-furyl, 2- or 3-thienyl, 1-, 2- or 3-pyrrolyl, 1-, 2, 4- or 5-imidazolyl, 1-, 3-, 4- or 5-pyrazolyl, 2-, 4- or 5-oxazolyl, 3-, 4- or 5-isoxazolyl, 2-, 4- or 5-thiazolyl, 3-, 4- or 5-isothiazolyl, 2-, 3- or 4-pyridyl, 2-, 4-, 5- or 6-pyrimidinyl, furthermore preferably 1,2,3-triazol-1-, -4- or -5-yl, 1,2,4-triazol-1-, -3- or -5-yl, 1- or 5-tetrazolyl, 1,2,3-oxadiazol-4- or -5-yl, 1,2,4-oxadiazol-3- or 5-yl, 1,3,4-thiadiazol-2- or -5-yl, 1,2,4-thiadiazol-3- or -5-yl, 1,2,3-thiadiazol-4- or -5-yl, 2-, 3-, 4-, 5- or 6-2H-thiopyranyl, 2-, 3- or 4-4-H-thiopyranyl, 3- or 4-pyridazinyl, pyrazinyl, 2-, 3-, 4-, 5- 6- or 7-benzofuryl, 2-, 3-, 4-, 5-, 6- or 7-benzothienyl, 1-, 2-, 3-, 4-, 5-, 6- or 7-indolyl, 1-, 2-, 4- or 5-benzimidazolyl, 1-, 3-, 4-, 5-, 6- or 7-benzopyrazolyl, 2-, 4-, 5-, 6- or 7-benzoxazolyl, 3-, 4-, 5-, 6- or 7-benzoisoxazolyl, 2-, 4-, 5-, 6- or 7-benzothiazolyl, 2-, 4-, 5-, 6- or 7-benzisothiazolyl, 4-, 5-, 6- or 7-benzo-2,1,3-oxadiazolyl, 2-, 3-, 4-, 5-, 6-, 7- or 8-quinolyl, 1-, 3-, 4-, 5-, 6-, 7- or 8-isoquinolyl, 3-, 4-, 5-, 6-, 7- or 8-quinolinyl, 2-, 4-, 5-, 6-, 7- or 8-quinazolinyl. The heterocyclic radicals can also be partially or completely hydrogenated. Het can thus, for example, also be 2,3-dihydro-2-, -3-, -4- or -5-furyl, 2,5-dihydro-2-, -3-, -4- or 5-furyl, tetrahydro-2- or -3-furyl, 1,3-dioxolan-4-yl, tetrahydro-2- or -3-thienyl, 2,3-dihydro-1-, -2-, -3-, -4- or -5-pyrrolyl, 2,5-dihydro-1-, -2-, -3-, -4- or -5-pyrrolyl, 1-, 2- or 3-pyrrolidinyl, tetrahydro-1-, -2- or -4-imidazolyl, 2,3-dihydro-1-, -2-, -3-, -4- or -5-pyrazolyl, tetrahydro-1-, -3- or -4-pyrazolyl, 1,4-dihydro-1-, -2-, -3- or -4-pyridyl, 1,2,3,4-tetrahydro-1-, -2-, -3-, -4-, -5- or -6-pyridyl, 1-, 2-, 3- or 4-piperidinyl, 2-, 3- or 4-morpholinyl, tetrahydro-2-, -3- or -4-pyranyl, 1,4-

dioxanyl, 1,3-dioxan-2-, -4- or -5-yl, hexahydro-1-, -3- or -4-pyridazinyl, hexahydro-1-, -2-, -4- or -5-pyrimidinyl, 1-, 2- or 3-piperazinyl, 1,2,3,4-tetrahydro-1-, -2-, -3-, -4-, -5-, -6-, -7- or -8-quinolyl, 1,2,3,4-tetrahydro-1-, -2-, -3-, -4-, -5-, -6-, -7- or -8-isoquinolyl.

Most preferably, Het means 1-imidazolyl, 1-piperazinyl, 1-piperidyl, 1-pyrrolidinyl, 1-pyrrolyl, pyridyl, oxodihydropyridyl or benzimidazolyl; the most preferred meaning is 1-pyrrolyl.

$C_nF_mH_{2n+1-m}O_p$ is preferably OCF_3, OCH_2F, $OCHF_2$, CF_3 C_2F_5 or partially fluorinated alkyl having 1-4 C atoms, CH_2F, CHF_2, C_2HF_4, $C_2H_2F_3$ or C_2H_4F.

R^4 is preferably a straight-chain or branched alkyl radical having 1 to 8 C atoms or cycloalkyl having 3 to 8 C atoms. If R^4 is noncyclic, the radical is then, preferably, one of the alkyl radicals which are also preferred for A. Particularly preferred cycloalkyl radicals which can be R^4 are cyclopropyl, cyclobutyl, cyclopentyl or cyclohexyl, or their derivatives which are substituted once by A, in particular methyl, ethyl or isopropyl.

R^2 is preferably e.g. F, Cl, Br, methyl, ethyl, propyl, iso-propyl, 2-butyl, $-(CH_2)_4-CH_3$, cyclobutyl, cyclohexyl, p-tolyl, 4-chlorophenyl, 2,4-dichloro-phenyl, 4-fluorophenyl, 3,5-bis(trifluoromethyl)phenyl, 3,5-dichlorophenyl, phenyl, 2-furyl, SMe, SEt, SPr, S-iso-propyl, S-tert.-butyl, S-(3-chloro-phenyl), S-(2-chlorophenyl), S-(4-chlorophenyl), S-phenyl, S-(4-pyridyl), benzyloxy, OH, methoxy, ethoxy, iso-propyloxy, cyclopentyloxy, cyclohexyloxy, tert.-butyloxy, phenoxy, 2-chlorophenoxy, 3-chlorophenoxy, 4-chlorophenoxy, 3-pyridyloxy, 1-pyrrolidinyl, 1-piperidinyl, 3-hydroxy-1-piperidinyl, 4-amino-1-piperidinyl, 1-imidazolyl, 1-benzimidazolyl, 2-methyl-1-imidazolyl, 1-pyrazolyl, 1-pyrrolyl, amino, anilino, 2-pyridylamino or 2-pyrimidylamino.

For the whole invention, it holds true that all radicals which occur several times can be identical or different, i.e. are independent of one another.

Accordingly, the invention relates in particular to the use of those compounds of the formula I in which at least one of the radicals mentioned has one of the preferred meanings indicated above. Some preferred groups of compounds can be expressed by the following subformulae Ia to 1i, which correspond to the formula I and in which the radicals not described in greater detail have the meaning indicated in the formula I, but in which

in Ia R^1 is methyl or ethyl;

in Ib R^3 is SO_2CH_3;

in Ic R^1 is methyl or ethyl,
R^3 is SO_2CH_3;

in Id Het is 1-imidazolyl, 1-piperazinyl, 1-piperidyl, 1-pyrrolidinyl, 1-pyrrolyl, pyridyl, oxodihydropyridyl or benzimidazolyl;

in Ie R^1 is methyl or ethyl,
R^3 is SO_2CH_3;
R^2 is 1-imidazolyl, 1-piperazinyl, 1-piperidyl, 1-pyrrolidinyl, 1-pyrrolyl, pyridyl, oxodihydropyridyl or benzimidazolyl;

in If R^1 is methyl or ethyl,
R^3 is SO_2A^1;
R^2 Het, $C_nF_mH_{2n+1-m}O_p$, R^4, OR^4, OH, benzyl, CN, F, Cl, SO_qR^5, Ph, O-Ph, O-Het, NH-Het, NH_2, NHA, NA_2 or NH-Ph;

R^4 is a straight-chain or branched alkyl radical having 1 to 6 C atoms or cycloalkyl having 3 to 6 C atoms which can be unsubstituted or monosubstituted by A,

R^5 is A or Ph,

A, A' is alkyl having 1 to 6 C atoms,

Het is a mono- or bicyclic saturated, unsaturated or aromatic heterocycle having from 1 to 4 N, O and/or S atoms, which can be substituted once, twice or three times by Hal, CF_3, A, CN, NO_2, NH_2 and/or carbonyl oxygen,

Hal is F, Cl, Br or I,

Ph is unsubstituted phenyl or substituted once, twice or three times by A, OA, Hal, CF_3, NH_2, NHA or NA_2,

m is 1, 2, 3, 4, 5, 6, 7, but at most 2n+1,

n is 1, 2 or 3,

p is 0 or 1;

q is 0 or 2;

in Ig R^1 is methyl or ethyl,

R^3 is SO_2CH_3;

R^2 is 1-imidazolyl, 1-piperazinyl, 1-piperidyl, 1-pyrrolidinyl, 1-pyrrolyl, pyridyl, oxodihydropyridyl, benzimidazolyl, $C_nF_mH_{2n+1-m}O_p$ or R^4;

R^4 is a straight-chain or branched alkyl radical having 1 to 6 C atoms or cycloalkyl having 3 to 6 C atoms which can be unsubstituted or monosubstituted by A,

A is alkyl having 1 to 6 C atoms,

m is 1, 2, 3, 4, 5, 6, 7, but at most 2n+1,

n is 1, 2 or 3,

p is 0 or 1;

in Ih R^1 is methyl or ethyl,

R^3 is SO_2CH_3;

R^2 is 1-imidazolyl, 1-piperazinyl, 1-piperidyl, 1-pyrrolidinyl, 1-pyrrolyl, pyridyl, oxodihydropyridyl or benzimidazolyl, CF_3, OCF_3 or alkyl having 1 to 6 C atoms;

in Ii R^1 is methyl or ethyl,
R^3 is SO_2CH_3;
R^2 is 1-pyrrolyl, CF_3, OCF_3 or alkyl having 1 to 4 C atoms

in Ij R^1 is methyl or ethyl,
R^3 is SO_2A;
R^2 is Het, $C_nF_mH_{2n+1-m}O_p$, R^4, OR^4, OH, benzyl, CN, F, Cl, SO_qR^5, Ph, O-Ph, O-Het, NH-Het, NH_2, NHA, NA_2 or NH-Ph;
R^4 is a straight-chain or branched alkyl radical having 1 to 6 C atoms or cycloalkyl having 3 to 6 C atoms which can be unsubstituted or monosubstituted by A,
R^5 is A or Ph,
A, A' is alkyl having 1 to 6 C atoms,
Het is 1-imidazolyl, 1-piperazinyl, 1-piperidyl, 1-pyrrolidinyl, 1-pyrrolyl, pyridyl, oxodihydropyridyl, benzimidazolyl, which can be substituted once, twice or three times by Hal, CF_3, A, CN, NO_2, NH_2 and/or carbonyl oxygen,
Hal is F, Cl, Br or I,
Ph is unsubstituted phenyl or substituted once, twice or three times by A, OA, Hal, CF_3, NH_2, NHA or NA_2,
m is 1, 2, 3, 4, 5, 6, 7, but at most 2n+1,
n is 1, 2 or 3,
p is 0 or 1;
q is 0 or 2;

and/or their physiologically acceptable salts and solvates.

The compounds of formula I can be used in the form of salts derived from inorganic or organic acids or bases.

A base of the formula I can be converted into the associated acid addition salt using an acid, for example by reaction of equivalent amounts of the base and of the acid in an inert solvent such as ethanol and subsequent evaporation. For this reaction, possible acids are in particular those which yield physiologically acceptable salts. Thus inorganic acids can be used, e.g. sulfuric acid, nitric acid, hydrohalic acids such as hydrochloric acid or hydrobromic acid, phosphoric acids such as orthophosphoric acid, sulfamic acid, further organic acids, in particular aliphatic, alicyclic, araliphatic, aromatic or heterocyclic mono- or polybasic carboxylic, sulfonic or sulfuric acids, e.g. formic acid, acetic acid, propionic acid, pivalic acid, diethylacetic acid, malonic acid, succinic acid, pimelic acid, fumaric acid, maleic acid, lactic acid, tartaric acid, malic acid, citric acid, gluconic acid, ascorbic acid, nicotinic acid, isonicotinic acid, methane- or ethane- sulfonic acid, ethanedisulfonic acid, 2-hydroxyethane-sulfonic acid, benzenesulfonic acid, p-toluenesulfonic acid, naphthalenemono- and disulfonic acids, and laurylsulfuric acid. Salts with physiologically unacceptable acids, e.g. picrates, can be used for the isolation and/or purification of the compounds of the formula I.
On the other hand, compounds of the formula I can be converted using bases (e.g. sodium or potassium hydroxide or carbonate) into the corresponding metal salts, in particular alkali metal or alkaline earth metal salts, or into the corresponding ammonium salts.

The test results of the antidiabetic activity of some representative compounds of the formula I are compiled in Table I which follows.
The compounds were administered by oral route on an animal model of diabetes (NOSTZ rats) showing a moderate diabetic state.

Experiments were carried out on adult male rats 300-500 g, housed in groups of 5 under standard conditions.

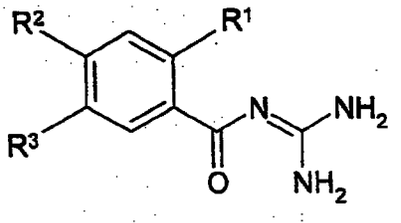
Diabetes was induced by injection of streptozotocin (100 mg/ kg body weight intravenously) on day of birth. As adult, NOSTZ rats present a NIDDM with the following characteristics (Portha - Diabetologia 17, 313-377, 1979):

- fasting hyperglycemia 180-200 mg/dl
- glucose intolerance
- specific failure of insulin secretion in response to glucose.

All drugs tested were suspended in an arabic gum solution and administered by oral route once a day during 4 days.
The compounds were studied using the procedure that is: determination of basal glycemia, lactatemia and insulinemia before treatment day 0, 2 hours after acute (day 1) and 2 hours after the last administration of the chronic treatment (once a day during 4 days) of the compounds at 20 mg/kg.

Table I

Antidiabetic activity of representative compounds of the formula I on NOSTZ diabetic rats (20 mg/kg p.o., effects [%])



I

R^1	R^2	R^3	Glycemia		Insulinemia		Lactatemia	
			D1	D4	D1	D4	D1	D4
CH_3	CF_3	$-SO_2CH_3$	-19	-21	-39	-22	-26	-20
CH_3	1-pyrrolyl	$-SO_2CH_3$	-16	-29	-17	-43	-15	-22
CH_3	isopropyl	$-SO_2CH_3$	-14	-25	19	-14	7	5

The pharmacological data confirm that the tested compounds at 20 mg/kg decreased significantly the fasting plasma glucose after acute and chronic treatment.

The invention further relates to the use of the compounds of the formula I and/or their physiologically acceptable salts for the production of pharmaceutical preparations for the treatment of non-insulin-dependent diabetes mellitus, in particular in a non-chemical way. In this context, they can be brought into a suitable dose form together with at least one solid, liquid and/or semiliquid excipient or auxiliary and if appropriate in combination with one or more of the further active compounds.

The invention further relates to a pharmaceutical preparation for the treatment of non-insulin-dependent diabetes mellitus containing at least one compound of the formula I and/or one of its physiologically acceptable salts or solvates.

The invention further relates to a pharmaceutical preparation for the treatment of non-insulin-dependent diabetes mellitus, characterized in that it contains at least one compound selected from the group

a) N-diaminomethylene-2-methyl-4-(1-pyrrolyl)-5-methylsulfonyl-enzamide,

b) N-diaminomethylene-2-methyl-4-trifluoromethyl-5-methylsulfonyl-benzamide,

c) N-diaminomethylene-2-methyl-4-isopropyl-5-methylsulfony-benzamide,

and/or one of its physiologically salts or solvates.

These preparations can be used as medicaments in human or veterinary medicine. Possible excipients are organic or inorganic substances which are suitable for enteral (e.g. oral) or parenteral administration or topical application and do not react with the novel compounds, for example water,

vegetable oils, benzyl alcohols, alkylene glycols, polyethylene glycols, glycerol triacetate, gelatin, carbohydrates such as lactose or starch, magnesium stearate, talc and petroleum jelly. Tablets, pills, coated tablets, capsules, powders, granules, syrups, juices or drops are used in particular for oral administration, suppositories are used for rectal administration, solutions, preferably oily or aqueous solutions, and in addition suspensions, emulsions or implants are used for parentaral administration, and ointments, creams or powders are used for topical application. The compounds of formula I can also be lyophilized and the lyophilizates obtained used, for example, for the production of injection preparations. The preparations indicated can be sterilized and/or can contain auxiliaries such as lubricants, preservatives, stabilizers and/or wetting agents, emulsifiers, salts for affecting the osmotic pressure, buffer substances, colourants, flavourings and/or one or more further active compounds, e.g. one or more vitamins.

The compounds of formula I according to the invention are generally administered in analogy to other known commercially available preparations for the indications claimed (e.g. metformine or amiloride), preferably in doses of between 0.1 mg and 500 mg, in particular between 5 and 300 mg per dose unit. The daily dose is preferably between approximately 0.01 and 250 mg/kg, in particular between 0.02 and 100 mg/kg of body weight.

In this case, the substances according to the formula I are generally preferably administered in doses of between approximately 1 and 500 mg, in particular between 5 and 100 mg per dose unit. The daily dose is preferably between approximately 0.02 and 10 mg/kg of body weight. The specific dose for each patient, however, depends on all sorts of factors, for example on the efficacy of the specific compound employed, on the age, body weight, general state of health, sex, on the diet, on the time and route of administration, and on the excretion rate, pharmaceutical combination

and severity of the particular disorder to which the therapy relates. Oral administration is preferred.

The following examples relate to pharmaceutical preparations:

Example A: Injection vials

A solution of 100 g of an active compound of the formula I and 5 g of disodium hydrogen phosphate is adjusted to pH 6.5 in 3 l of double-distilled water using 2 N hydrochloric acid, sterile-filtered, filled into injection vials and lyophilized under sterile conditions, and the vials are aseptically sealed. Each injection vial contains 5 mg of active compound.

Example B: Suppositories

A mixture of 20 g of an active compound of the formula I is fused with 100 g of soya lecithin and 1400 g of cocoa butter, poured into moulds and allowed to cool. Each suppository contains 20 mg of active compound.

Example C: Solution

A solution is prepared from 1 g of an active compound of the formula I, 9.38 g of $NaH_2PO_4.2H_2O$, 28.48 g of $Na_2HPO_4.12H_2O$ and 0.1 g of benzalkonium chloride in 940 ml of double-distilled water. The pH is adjusted to 6.8, and the solution is made up to 1 l and sterilized by irradiation.

Example D: Ointment

500 mg of an active compound of the formula I are mixed with 99.5 g of petroleum jelly under aseptic conditions.

Example E: Tablets

A mixture of 1 kg of active compound of the formula I, 4 kg of lactose, 1.2 kg of potato starch, 0.2 kg of talc and 0.1 kg of magnesium stearate is compressed in a customary manner to give tablets in such a way that each tablet contains 10 mg of active compound.

Example F: Coated tablets

Analogously to Example E, tablets are pressed which are then coated in a customary manner with a coating of sucrose, potato starch, talc, tragacanth and colourant.

Example G: Capsules

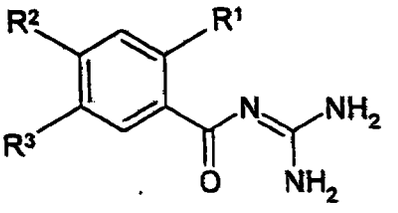
2 kg of active compound of the formula I are filled in a customary manner into hard gelatin capsules such that each capsule contains 20 mg of the active compound.

Example H: Ampoules

A solution of 1 kg of active compound of the formula I in 60 l of double-distilled water is sterile- filtered, filled into ampoules and lyophilized under sterile conditions, and the ampoules are aseptically sealed. Each ampoule contains 10 mg of active compound.

Patent Claims

1. Use of benzoylguanidines of the formula I



I

wherein

R^1 is A,

R^2 is Het, $C_nF_mH_{2n+1-m}O_p$, R^4, OR^4, OH, benzyl, CN, Hal, SO_q-R^5, Ph, O-Ph, O-Het, NH-Het, NH_2, NHA, NA_2 or NH-Ph,

R^3 is SO_2A',

R^4 is a straight-chain or branched alkyl radical having 1 to 8 C atoms or cycloalkyl having 3 to 8 C atoms which can be unsubstituted or mono-, di- or trisubstituted by A,

R^5 is A or Ph,

A, A' in each case independently of one another are alkyl having 1 to 6 C atoms,

Het is a mono- or bicyclic saturated, unsaturated or aromatic heterocycle having from 1 to 4 N, O and/or S atoms, which can be substituted once, twice or three times by Hal, CF_3, A, CN, NO_2, NH_2 and/or carbonyl oxygen,

Hal is F, Cl, Br or I,

Ph is unsubstituted phenyl or substituted once, twice or three times by A, OA, Hal, CF_3, NH_2, NHA or NA_2,

m is 1, 2, 3, 4, 5, 6, 7, but at most 2n+1,

n is 1, 2 or 3,

p is 0 or 1,

q is 0, 1 or 2,

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and/or their physiologically acceptable salts and solvates for the production of a medicament for the treatment of non-insulin-dependent diabetes mellitus.

2. Use of benzoylguanidines of the formula I according to claim 1 wherein the compounds are selected from the group

a) N-diaminomethylene-2-methyl-4-(1-pyrrolyl)-5-methylsulfonylbenzamide,

b) N-diaminomethylene-2-methyl-4-trifluoromethyl-5-methylsulfonylbenzamide,

c) N-diaminomethylene-2-methyl-4-isopropyl-5-methylsulfonylbenzamide,

and/or their physiologically acceptable salts and solvates for the production of a medicament for the treatment of non-insulin-dependent diabetes mellitus.

3. Phamaceutical preparation for the treatment of non-insulin-dependent diabetes mellitus, characterized in that it contains at least one compound of the general formula I according to claim 1 and/or one of its physiologically salts or solvates.

4. Phamaceutical preparation according to claim 3 for the treatment of non-insulin-dependent diabetes mellitus, characterized in that it contains at least one compound selected from the group

a) N-diaminomethylene-2-methyl-4-(1-pyrrolyl)-5-methylsulfonylbenzamide,

b) N-diaminomethylene-2-methyl-4-trifluoromethyl-5-methylsulfonylbenzamide,

c) N-diaminomethylene-2-methyl-4-isopropyl-5-methylsulfonylbenzamide,

and/or one of its physiologically salts or solvates.

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