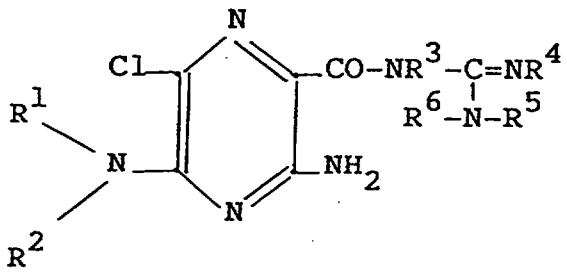
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New pyrazine derivatives, the preparation and use thereof

The invention relates to new tetra-substituted pyrazine derivatives, the preparation thereof by conventional methods and their use in the production of pharmaceutical substances or drugs.

The new compounds correspond to the formula



(I)

and may occur in the form of bases or salts with acids.

In formula I, independently of one another:

R^1 represents H or a (C_{1-8})alkyl group,

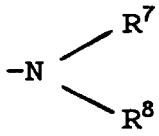
R^2 represents a 1-morpholinyl group,

a straight-chained or branched (C_{1-8})alkyl chain which may be substituted,

a) by a substituted or unsubstituted N,O,S-heterocyclic group,

b) by the phenyl group which is optionally mono- or polysubstituted by a (C_{1-4})alkoxy group, which may in turn be functionalised by a hydroxyl or alkylamino group of formula

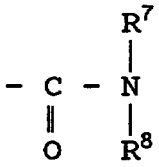
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(II),

wherein R^7 and R^8 independently of each other denote hydrogen or a (C_{1-4})alkyl group;

c) by an aminocarbonyl group of the formula

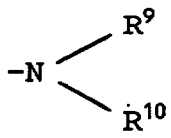


(III),

wherein R^7 and R^8 are defined as hereinbefore;

d) independently of one another by one or more (C_{1-4})alkoxy groups, the hydroxyl or a hydroxyl(C_{1-4})-alkyl group or a phenoxy group which may in turn be mono- or polysubstituted by halogen (F, Cl), a cyano group, (C_{1-4})alkyl, (C_{1-4})alkoxy or (C_{1-4})alkoxy-(C_{1-4})alkyl;

e) by an amino group of the formula



(IV),

wherein the groups R^9 and R^{10} independently of each other denote hydrogen, a mono- or polynuclear N,O,S-heterocyclic group, a mono- or polysubstituted phenyl group substituted either homogeneously or by a mixture of halogen (F, Cl), (C_{1-4})alkyl or a sulphonamide group, an N,O-heterocyclic acyl group, a di- or trichlorophenylsulphonyl group substituted

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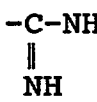
by an amide group, or a (C_{1-4})alkyl chain, which may be substituted independently of each other by the hydroxy group, or by a phenyl group which is optionally mono- or polysubstituted by halogen (F, Cl), hydroxy, (C_{1-4})alkyl or (C_{1-4})alkoxy-(C_{1-4})alkyl, or R^9 and R^{10} form a morpholine ring together with the nitrogen atom to which they are bound and an oxygen atom;

a 4-piperidinyl group which may be substituted in the 1-position

a) by the acyl group of an aliphatic, alicyclic, aromatic or heteroaromatic carboxylic acid;

b) by a (C_{1-8})alkyl chain which in turn is substituted, independently of each other, by the hydroxy group or by a (C_{1-4})alkoxy- or (C_{1-4})alkoxy-(C_{1-4})alkyl-substituted phenoxy group or by an α-naphthoxy group;

and amidino group of the formula



(V),

wherein R^{11} represents a phenyl group which is mono- or polysubstituted by halogen (F, Cl) or a (C_{1-4})alkyl group;

R^1 and R^2 together denote, together with the nitrogen atom to which they are bound, a piperazine ring which may be substituted

a) by an N,O,S-heterocyclic group,

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b) by the acyl group of an aliphatic, alicyclic, aromatic or heterocyclic carboxylic acid,

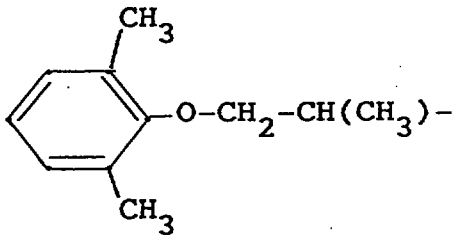
c) by a (C_{1-8})alkyl chain, which may in turn be substituted independently of one another, by the hydroxy group or by a (C_{1-4})alkoxy- or (C_{1-4})alkoxy-(C_{1-4})alkyl-substituted phenoxy group or an α-naphthoxy group;

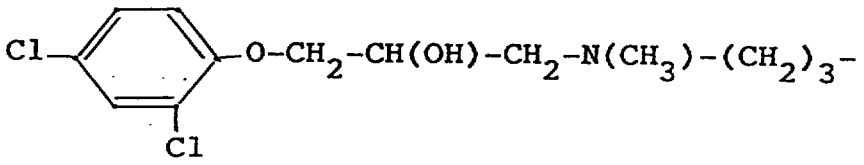
R^3, R^4, R^5 and R^6 have identical or different meanings and represent hydrogen, (C_{1-8})alkyl or benzyl.

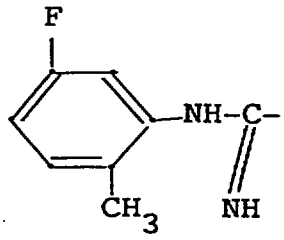
The phrase "N,O,S-heterocyclic group" denotes those ring systems which contain one or more identical or different heteroatoms of the type specified. The term "polynuclear heterocyclic groups" also refers to those ring systems which are made up of heterocyclic and carbocyclic rings, such as quinoline and quinazoline. These ring systems may contain one or more substituents such as C_{1-4}-alkyl, C_{1-4}-alkoxy and/or amino. Similarly, "N,O-heterocyclic group" encompasses both pure N-heterocyclic groups such as piperidine, piperazine and also morpholine. If the alkyl groups in the above definitions may contain up to 8 carbon atoms, those containing up to 4 carbon atoms are preferred; of the (C_{1-4})alkyl or alkoxy groups, those which are preferred are the ones which contain up to three carbon atoms. The preferred substituents in phenyl or phenoxy groups are alkyl or alkoxy groups having one or two carbon atoms as well as F and Cl. R^3 and R^5 preferably denote hydrogen, R^4 and R^6 preferably denote hydrogen, methyl or ethyl, and one of the two groups also denotes butyl or benzyl. The acyl groups of the aliphatic carboxylic acids contain up to 18 carbon atoms, those of the alicyclic carboxylic acid contain up to 8 carbon atoms. The short-chained aliphatic carboxylic acids may also be substituted by phenyl or heteroaryl, the aromatic

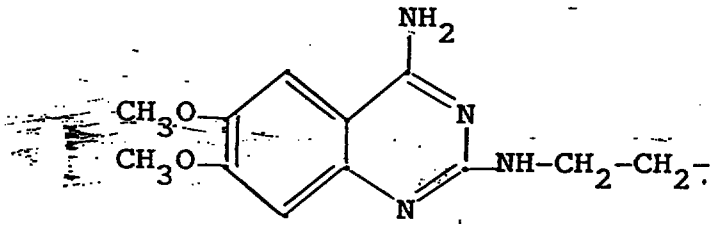
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carboxylic acids optionally contain substituted phenyl, and the heteroaromatic carboxylic acids are derived from monocyclic heterocyclic groups which contain N, O and/or S. Whereas R^1 is preferably hydrogen or methyl, R^2 preferably represents larger groups, e.g. those contained in the following Tables, for example:



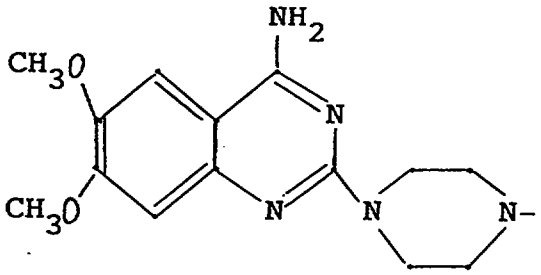


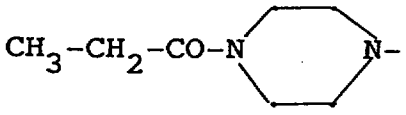


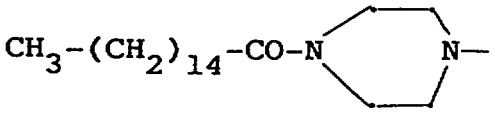


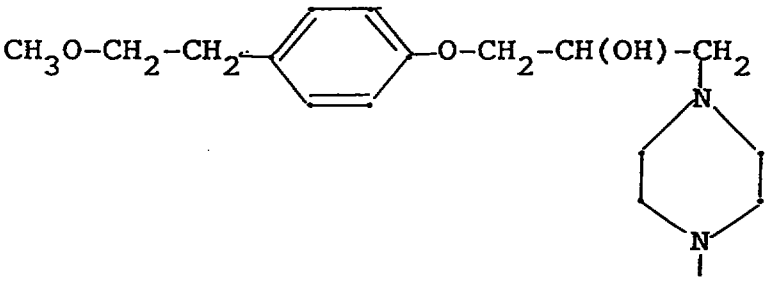
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or R^1 and R^2 form a substituted heterocyclic group with the nitrogen to which they are bound, e.g.









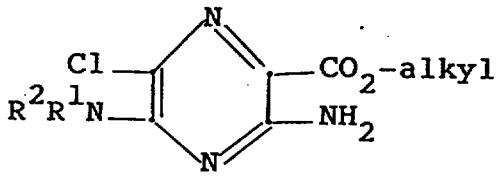
Methods of preparing the new compounds are known to those skilled in the art:

1) a lower alkylester of 3-amino-5,6-dichloropyrazine-2-carboxylic acid is reacted under anhydrous conditions with an amine of formula

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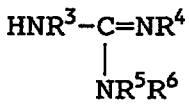
HNR^1R^2 (VI)

wherein R_1 and R_2 are as hereinbefore defined, and the resulting compound of formula



(VII)

(alkyl = (C_{1-4})alkyl)
is converted with a guanidine of formula



(VIII)

wherein R^3 to R^6 are as hereinbefore defined, into the desired end product.

The reaction of the 3-amino-5,6-dichloropyrazine-2-carboxylic acid ester with the amine component VI to obtain the intermediate compounds of general formula VII is carried out using methods known from the literature in an inert solvent at elevated temperature in the presence of an acid acceptor. The amine component is generally used in equimolar amounts. However, it is also possible to use the amine component as the acid acceptor and solvent. Preferably, however, the solvent used is dimethylformamide or dimethylsulphoxide or mixtures thereof. The reaction temperature is not crucial. As a rule, the reaction is carried out at a

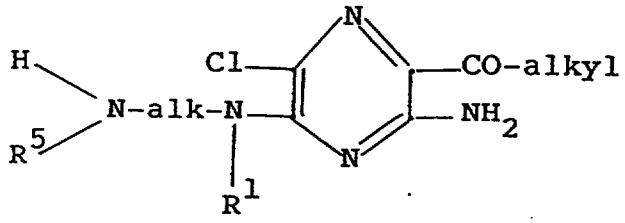
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temperature in the range from 80 - 100°C depending on the reactivity of the amine used. Under these conditions the reaction is finished after about 1 to 2 hours. Organic and inorganic bases may be used as acid acceptors. Preferably, tertiary amines such as pyridine, N-methylpiperidine, dimethylaniline or triethylamine are used.

The 3,5-diaminopyrazine carboxylic acid esters of formula VII prepared in this way may, if desired, be subjected to subsequent treatment, e.g. a reaction of acylation or alkylation.

Acylation is carried out by known methods, e.g. by reacting a diamine of formula VII with a reactive carboxylic acid derivative.

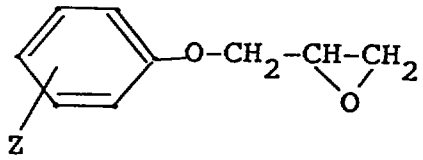
The alkylation is used, for example, in the preparation of corresponding phenoxypropanolamine derivatives. For this purpose, a diamino compound of the substructure IX of formula VII:



(IX)

(alk = (C_{1-8})alkylene, alkyl, R^5 as above) is reacted in a suitable solvent e.g. with a phenoxypropyleneoxide of general formula

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(X)

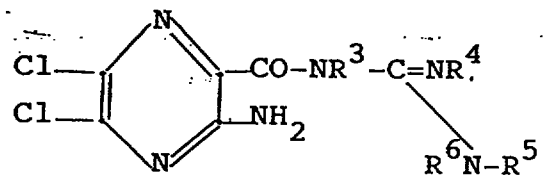
Z = (C_{1-4})alkoxy,
(C_{1-4})alkoxy-(C_{1-4})alkyl

at ambient temperature or slightly elevated temperature. Generally, the reaction is complete in about 0.5 to 1 hour.

However, the direct method of synthesis described above is preferred.

In order to prepare the end products of formula I the 3,5-diaminopyrazine carboxylic acid esters of formula VII are reacted with a guanidine of formula VIII in a suitable solvent with heating. Simple alcohols are particularly suitable as the solvent. Preferably, the reaction is carried out in methanol at boiling temperature. Under these conditions the reaction is generally complete after about 30 to 90 minutes.

2) Reaction of a pyrazine derivative of formula



(XI),

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wherein R^3 to R^6 are as hereinbefore defined, with an amine of formula

$$HNR^1R^2 \qquad (VI),$$

wherein R^1 and R^2 are as hereinbefore defined.

The reaction is preferably carried out at elevated temperature in a polar solvent, if possible anhydrous, e.g. dimethylformamide, dimethylsulphoxide.

The starting compounds of formula XI are obtained by conventional methods. They may for example be obtained according to process 1) if pyrazine carboxylic acid esters are used which are of similar construction to the esters of formula VII but contain a chlorine atom instead of NR^1R^2 in the 5-position.

The compounds of formula I may be used as active substances in pharmaceutical preparations or may be used as intermediate products for preparing such active substances. The new compounds inhibit the Na^+/H^+- and Na^+/Li^+-exchange, inter alia. The active substances according to the invention may be used as antihypertensives, mucolytics, diuretics and cancerostatics; they may also be used in diseases connected with ischaemia (for example: cardiac, cerebral, gastrointestinal, pulmonary and renal ischaemia, ischaemia of the liver, ischaemia of the skeletal musculature). Corresponding diseases include, for example, coronary heart disease, angina pectoris, embolisms in the circulation of the lungs, acute or chronic kidney failure, chronic kidney insufficiency, cerebral infarct, chronic circulatory disorders of the brain. During reperfusion of the ischaemic heart (e.g.

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after an attack of angina pectoris or a cardiac infarct) irreversible damage may occur to cardiomyocytes in the affected region. The compounds according to the invention may be used in such cases for cardioprotection.

The prevention of damage which may occur as a result of reduced circulation during transplants should also be included in the field of ischaemia.

The active substances may be administered in conventional forms, e.g. plain or coated tablets, capsules, granules, injectable solutions, and possibly nasally administered preparations, the active substance generally being present in an amount of 1 to 200 mg, preferably 20 to 100 mg per dosage unit. These pharmaceutical preparations are produced in a manner known per se.

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Examples

1. Tablets (Composition)

Compound according to Example	40.0 mg
Corn starch	144.0 mg
Sec. calcium phosphate	115.0 mg
Magnesium stearate	1.0 mg
	300.0 mg

2. Gelatine capsules

The contents of a capsule consist of 50.0 mg of a compound according to the invention and 150.0 mg of corn starch.

Note: Under the headings "Form" the Tables which follow indicate whether the preparation is a salt (HCl = hydrochloride, 2.HCl = dihydrochloride, etc.) or the base (BS).

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Example 1

a) Methyl 3-amino-6-chloro-5-(2-[1-(1,6-dimethyl-phenoxy)]propylamino)-pyrazine-2-carboxylate

4.44 g (20 mmol) of methyl 3-amino-5,6-dichloropyrazine-2-carboxylate, 3.6 g (20 mmol) of 2-amino-1-(2,6-dimethylphenoxy)propane and 2.2 g (22 mmol) of triethylamine are heated to 95 - 100°C in 40 ml of anhydrous dimethylformamide for 1½ hours. After the solvent has been distilled off in vacuo the residue is purified on silica gel (eluant: ethyl acetate/isopropanol/NH_3 (70:30:1). Yield 7.3 g

b) N-amidino-3-amino-6-chloro-5-(2-[1-(2,6-dimethylphenoxy)]propylamino)pyrazine-2-carboxamide-hydrochloride

7.3 g (0.02 mmol) of pyrazine carboxylic acid ester from Example 1a) are dissolved in 50 ml of methanol and heated with 80 ml of a 1 molar methanolic guanidine solution for 45 minutes over a boiling water bath. The solvent is distilled off in vacuo and the residue is purified over a silica gel column (eluant: ethyl acetate/isopropanol/NH_3 (70:30:5) and the hydrochloride of the end product is prepared.
Yield 4.9 g; melting point 267 - 270°C.

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Example 2

a) Methyl 3-amino-6-chloro-2-[N'-(5-fluoro-2-methyl)phenyl]-guanidino-pyrazine-2-carboxylate

13.3 g (60 mmol) of methyl 3-amino-5,6-dichloropyrazine-2-carboxylate, 15 g (90 mmol) of (5-fluoro-2-methyl)-phenylguanidine and 6 g of triethylamine are stirred into 100 ml of DMSO for 2 hours at 90°C. After cooling, 100 ml of CH_2Cl_2 are added. 100 ml of water are added dropwise, with cooling, the CH_2Cl_2 phase is separated off and the aqueous phase is extracted with 150 ml of CH_2Cl_2. The CH_2Cl_2 phases collected are washed with a little water, dried over $MgSO_4$ and concentrated by evaporation. The residue is purified over silica gel (eluant: ethyl acetate/isopropanol (95:5). Yield: 12.6 g

b) N-Amidino-3-amino-6-chloro-2-[N'-(5-fluoro-2-methyl)-phenyl]guanidino-pyrazine-2-carboxamide

5.5 g of 2-methylpyrazinecarboxylate from Example 2a) are dissolved in 25 ml of anhydrous dimethylformamide, 50 ml of a 1.2 molar methanolic guanidine solution are added and the resulting mixture is refluxed for 30 minutes. Then the methanol is distilled off and the residue is purified on silica gel (eluant: ethyl acetate/isopropanol/NH_3 (70:30:5)) and the reaction product is converted into the hydrochloride. Yield: 8.7 g; m.p. 242°C.

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Example 3

N-Amidino-3-amino-6-chloro-5-(4-[2-(3-methoxy-phenoxy)ethyl-1-piperazinyl)-pyrazine-2-carboxamide-dihydrobromide

858 mg (3 mmol) of N-amidino-3-amino-5,6-dichloropyrazine-2-carboxamide, 924 (3 mmol) of N-[2-(3-methoxyphenoxy)ethyl]piperazine and 1.2 g (12 mmol) of triethylamine are heated to 95 - 100°C for 75 minutes. The solvent is distilled off in vacuo, the residue is purified over silica gel (eluant: ethyl acetate/isopropanol/NH_3 (7:3:1)) and the reaction product obtained is converted into the dihydrobromide.
Yield: 1.13 g; m.p.: 159 - 162°C.

Example 4

a) Methyl 3-amino-6-chloro-5-[N-(2-pyrrolocarbonyl-amino)ethyl-N-methylamino]-pyrazine-2-carboxylate

2.73 g (10 mmol) of ethyl 3-amino-6-chloro-5-[N-(2-amino)ethyl-N-methyl]amino-pyrazine-2-carboxylate, 1.35 g (10 mmol) of 1-hydroxy-1H-benzotriazole-hydrate and 1.11 g (10 mmol) of pyrrolo-2-carboxylic acid are dissolved in 50 ml of anhydrous tetrahydrofuran and stirred with 2.06 g (10 mmol) of dicyclohexylcarbodiimide for 15 hours at ambient temperature, whilst cooling with ice. The reaction product is isolated in the usual way and purified over silica gel (eluant: ethyl acetate/isopropanol (7:3).
Yield: 3.09 g

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b) N-Amidino-3-amino-6-chloro-5-[N-[2-(pyrrolyl-carbonylamino)ethyl]-N-methyl]aminopyrazine-2-carboxamide hydrochloride

Prepared analogously to Example 1.
3.09 g (10 mmol) of methyl pyrazine-2-carboxylate from Example 3 yield 1.65 g of the title compound; m.p. 181 - 184°C.

Example 5

N-Amidino-3-amino-6-chloro-5-[4-[(4-amino-6,7-dimethoxy)-2-quinazolinyl]-1-piperazinyl]-pyrazine-2-carboxamide-dihydrochloride

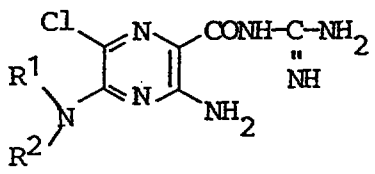
13.1 g (45.3 mmol) of N-[(4-amino-6,7-dimethoxy)-2-quinazolinyl]-piperazine, 10 g (45.3 mmol) of methyl 3-amino-5,6-dichloropyrazine-2-carboxylate and 7 ml of triethylamine are reacted in 60 ml of dimethylsulphoxide for 2 hours at 80°C. After cooling, the reaction product is precipitated by the addition of 100 ml of water, suction filtered, dried and converted into the end product without any further purification using the method described in Example 1a) by reacting with guanidine.
Yield: 10.5 g; m.p. > 290°C.

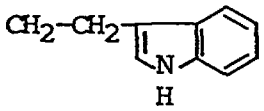
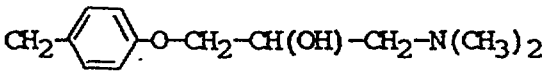
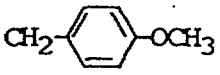
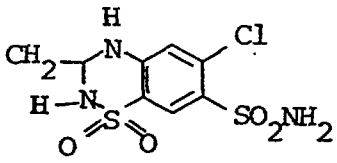
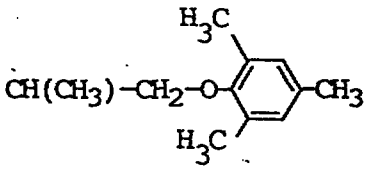
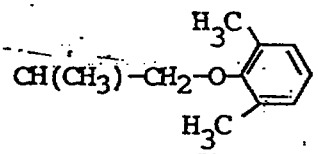
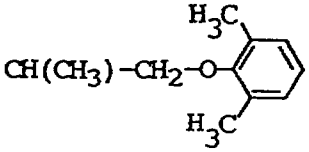
The compounds listed in the Tables which follow may be obtained analogously to the Examples and in accordance with the remarks in the specification. If the compounds take the form of the base the abbreviation BS appears in the column "Form", otherwise the acid with which the salt is formed is specified.

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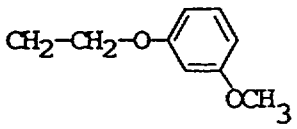
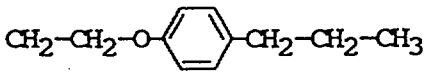
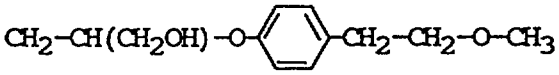
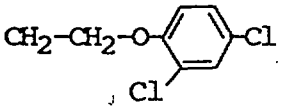
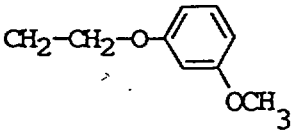
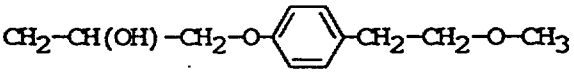
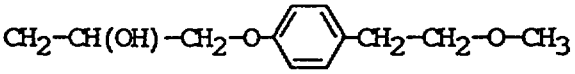
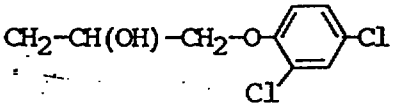
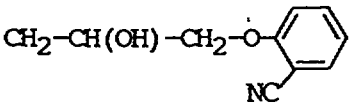
Table 1

Compounds of formula

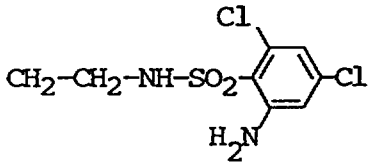
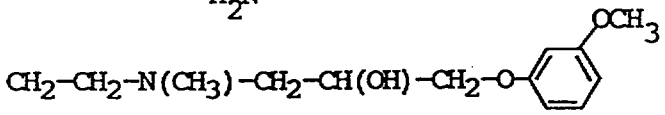
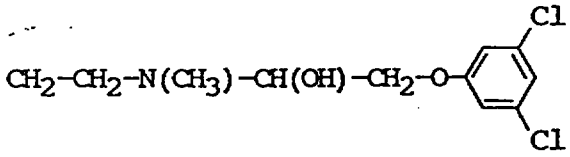
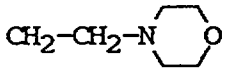
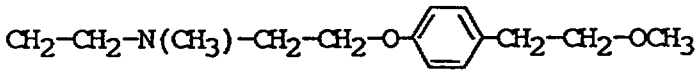
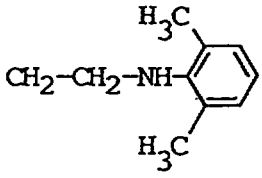
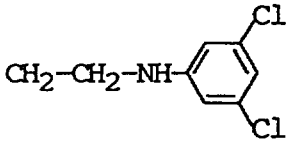
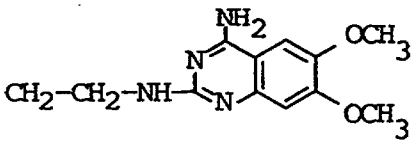
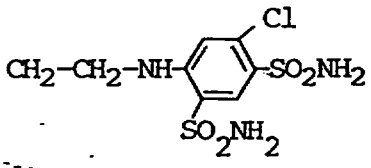
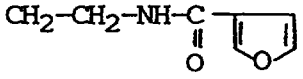
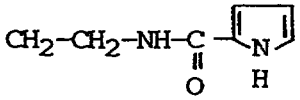


Nr.	R^1	R^2	Form	mp [°C]
1	CH_3	CH_3	HCl	>280
2	H		BS	188-189
3	H	$CH_2-CH_2-C(=O)-N(CH_3)_2$	HCl	262-264
4	H		2 · HCl	amorph
5	H		2 · HCl	amorph
6	H		HCl	252-253
7	H		HCl	250-253
8	H		HCl	278
9	CH_3		HCl	232-235

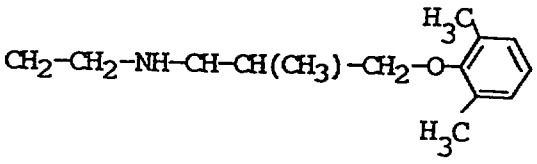
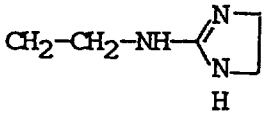
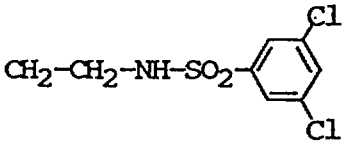
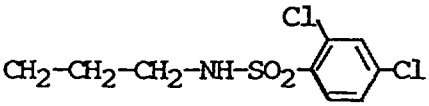
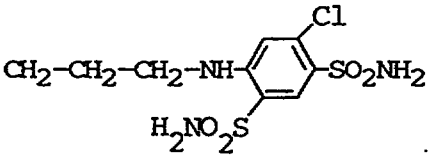
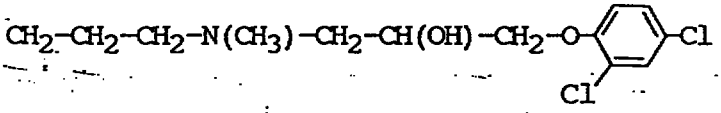
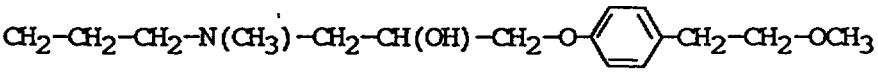
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Nr.	R^1	R^2	Form	mp. [°C]
10	H		HCl	145-148
11	H		HCl	117-119
12	H		HCl	197-200
13	H		2 · HCl	122-125
14	CH_3		HCl	141-143
15	H	$CH_2-CH(OCH_3)_2$	BS	205-207
16	CH_3		HCl	amorph
17	H		HCl	116-119
18	CH_3		HCl	112-115
19	CH_3		BS	207-209

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Nr.	R^1	R^2	Form	mp.[°C]
20	H		HCl	187-191
21	H		2 · HCl	118-120
22	H		BS	83-87
23	H		BS	200-202
24	CH_3		BS	95-97
25	H		BS	210-215
26	H		BS	225-228
27	H		2 · HCl	230-235
28	H		2 · HCl	>250
29	CH_3		BS	140-142
30	CH_3		HCl	183-186

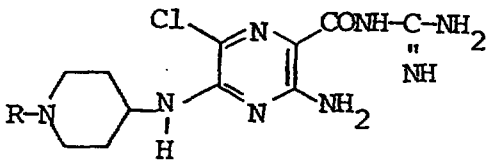
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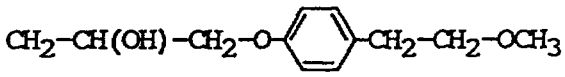
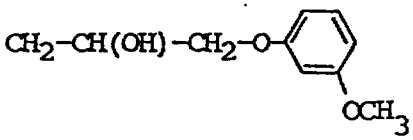
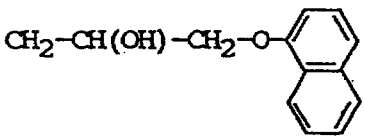
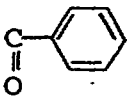
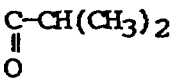
Nr.	R^1	R^2	Form	mp [°C]
31	H		2 · HCl	amorph
32	H	$CH_2-CH_2-NH_2$	2 · HCl	>270
33	H		3 · HCl	195–200
34	H		2 · HCl	168–171
35	H		HCl	250–252
36	H		HCl	211–215
37	H	$CH_2-CH_2-CH_2-N(CH_3)_2$	2 · HCl	268–270
38	H		BS	amorph
39	H		2 · HCl	amorph

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Table 2

Compounds of formula

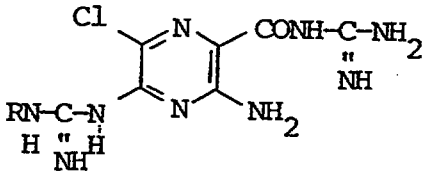


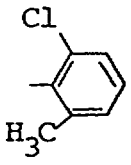
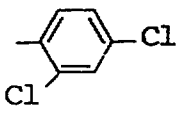
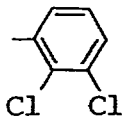
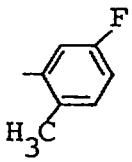
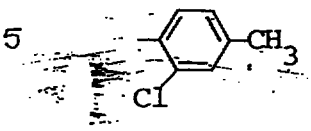
Nr.	R	Form	m.p. [°C]
1		BS	184-187
2		BS	163-167
3		BS	amorph
4		BS	187-190
5		BS	218-220

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Table 3

Compounds of formula



Nr.	R	Form	Mp. [°C]
1		2 · HCl	237-240
2		2 · HCl	264-267
3		2 · HCl	239-242
4		2 · HCl	242
5		BS	177-180

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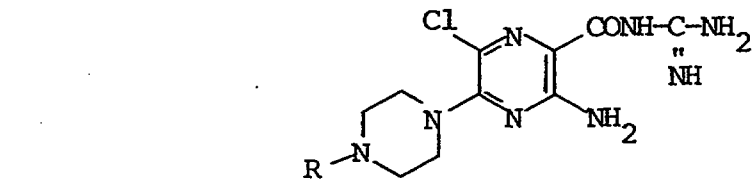
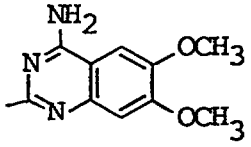
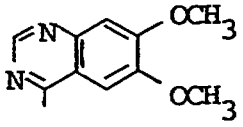
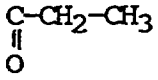
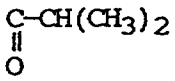
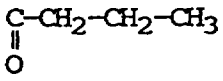
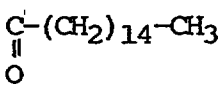
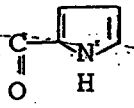
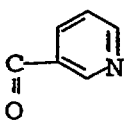
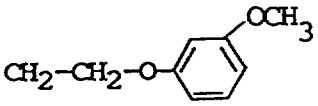
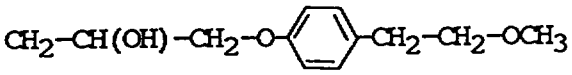
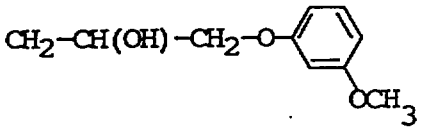
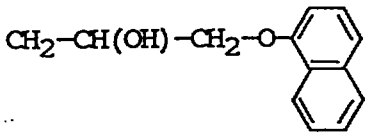
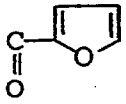


Table 4

Compounds of formula

Nr.	R	Form	mp. [°C]
1		2 · HCl	274
2		2 · HCl	225-230
3		HCl	211-213
4		BS	143-145
5		HCl	231-233
6		2 · HCl	165-167
7		HCl	181-184
8		BS	210-213
9	H	2 · HCl	>290

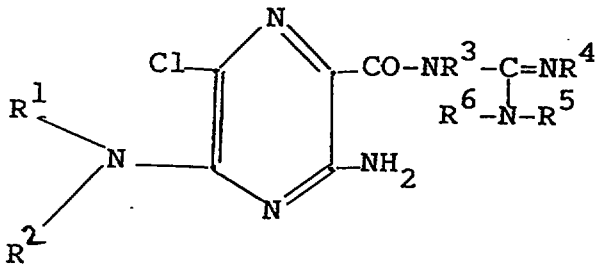
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Nr.	R	Form	mp. [°C]
10		2 · HBr	159–162
11		BS	180–182
12		2 · HCl	268–270
13		2 · HCl	287–290
14		BS	196–198

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Claims

1. Compounds of formula



(I)

wherein

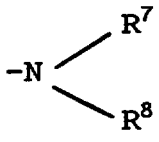
R^1 represents H or a (C_{1-8})alkyl group,

R^2 represents a 1-morpholinyl group,

a straight-chained or branched (C_{1-8})alkyl chain which may be substituted,

a) by a substituted or unsubstituted N,O,S-heterocyclic group,

b) by the phenyl group which is optionally mono- or polysubstituted by a (C_{1-4})alkoxy group, which may in turn be functionalised by a hydroxyl or alkylamino group of formula



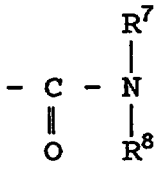
(II),

wherein R^7 and R^8 independently of each other denote hydrogen or a (C_{1-4})alkyl group;

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c) by an aminocarbonyl group of the formula

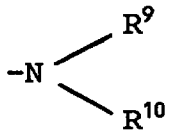


(III),

wherein R^7 and R^8 are defined as hereinbefore;

d) independently of one another by one or more (C_{1-4})alkoxy groups, the hydroxyl or a hydroxyl(C_{1-4})-alkyl group or a phenoxy group which may in turn be mono- or polysubstituted by halogen (F, Cl), a cyano group, (C_{1-4})alkyl, (C_{1-4})alkoxy or (C_{1-4})alkoxy-(C_{1-4})alkyl;

e) by an amino group of the formula



(IV),

wherein the groups R^9 and R^{10} independently of each other denote hydrogen, a mono- or polynuclear N,O,S-heterocyclic group, a mono- or polysubstituted phenyl group substituted either homogeneously or by a mixture of halogen (F, Cl), (C_{1-4})alkyl or a sulphonamide group, an N,O-heterocyclic acyl group, a di- or trichlorophenylsulphonyl group substituted by an amine group, or a (C_{1-4})alkyl chain, which may be substituted independently of each other by the hydroxy group, or by a phenyl group which is optionally mono- or polysubstituted by halogen (F, Cl), hydroxy, (C_{1-4})alkyl or (C_{1-4})alkoxy-(C_{1-4})alkyl, or R^9 and R^{10} form a morpholine ring together with the nitrogen atom to which they are bound and an

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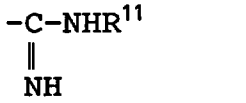
oxygen atom;

a 4-piperidinyl group which may be substituted in the 1-position

a) by the acyl group of an aliphatic, alicyclic, aromatic or heteroaromatic carboxylic acid;

b) by a (C_{1-8})alkyl chain which in turn is substituted, independently of each other, by the hydroxy group or by a (C_{1-4})alkoxy- or (C_{1-4})alkoxy-(C_{1-4})alkyl-substituted phenoxy group or by an α-naphthoxy group;

and amidino group of the formula



(V),

wherein R^{11} represents a phenyl group which is mono- or polysubstituted by halogen (F, Cl) or a (C_{1-4})alkyl group; or wherein

R^1 and R^2 may together represent a piperidine or a piperazine ring, which may be N-substituted:

a) by an N,O,S-heterocyclic group,

b) by the acyl group of an aliphatic, alicyclic, aromatic or heterocyclic carboxylic acid,

c) by a (C_{1-8})alkyl chain, which may in turn be substituted independently of one another, by the hydroxy group or by a (C_{1-4})alkoxy- or (C_{1-4})alkoxy-(C_{1-4})alkyl-substituted phenoxy group or an α-naphthoxy group;

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in the form of the bases or in the form of acid addition salts.

2. N-Amidino-3-amino-6-chloro-5-[4-[(4-amino-6,7-dimethoxy)-2-quinazolinyl]-1-piperazinyl]-pyrazine-2-carboxamide and the acid addition salts thereof.

3. N-Amidino-3-amino-6-chloro-2-[N'-(5-fluoro-2-methyl)-phenyl]guanidinopyrazine-2-carboxamide and the acid addition salts thereof.

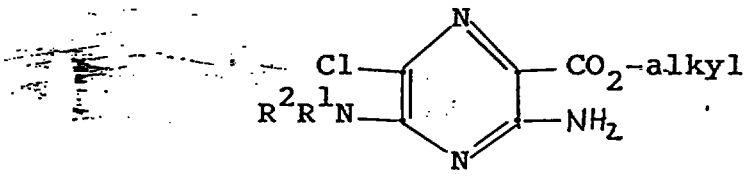
4. N-Amidino-3-amino-6-chloro-5-[2-[1-(2,6-dimethyl-phenoxy)]propylamino]pyrazine-2-carboxamide and the acid addition salts thereof.

5. Pharmaceutical compositions, characterised in that they contain a compound according to one of claims 1 to 4 together with conventional excipients and/or carriers.

6. Use of compounds according to claim 1, 2, 3 or 4 in the preparation of pharmaceutical compositions having an antihypertensive, mucolytic, diuretic, cancerostatic and PAF-antagonistic activity.

7. Process for preparing compounds according to claim 1, 2, 3 or 4 by methods known <u>per se</u>, characterised in that

a) a pyrazine carboxylic acid ester of formula

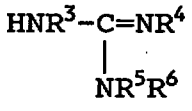


(VII)

(alkyl = (C_{1-4})alkyl)

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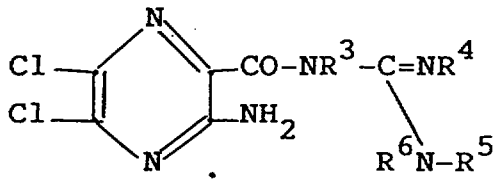
is reacted with a guanidine of formula



(VIII)

or

b) a pyrazine derivative of formula



(XI),

wherein R^3 to R^6 are as hereinbefore defined, is reacted with an amine of formula



(VI),

wherein R^1 and R^2 are as hereinbefore defined

and if desired the bases of formula I obtained are converted into acid addition salts.