~~2,5- OR 2,6 DISUBSTITUTED HYDROQUINONE DERIVATIVES WITH AT LEAST ONE CARBOXY, SULFO OR AMIDO GROUP USEFUL AS MEDICAMENTS~~ NOVEL HYDROQUINONE DERIVATIVES

FIELD OF THE INVENTION

This invention relates generally to novel hydroquinone derivatives, their preparation and to methods of treating disorders by administration of such compounds to a warm-blooded animal in need thereof. The present invention also relates to compounds that are useful in the prevention and/or treatment of autoimmune, immunological, rheumatology, vascular disorders, ophthalmologic disorders, fibrotic disorders, metabolic and gastro-intestinal disorders, neuroinflammatory and neurodegenerative diseases, neoplasms and cancer associated disorders, hormone related diseases and immunological disorders resulting from viral and bacterial infectious diseases, and complications thereof.

BACKGROUND OF THE INVENTION

Some hydroquinone-based derivatives like for example, 2,5-dihydroxybenzenesulfonic acid derivatives and specifically calcium dobesilate, ethamsylate and persilate are known in the art as active agents for the treatment of male sexual dysfunction and other vascular disorders of endothelial origin, both alone and in combination with other agents. For example, US Patent No. 6,147,112 describes a method for the use of 2,5-dihydroxybenzenesulfonic acid derivatives, preferably calcium dobesilate, ethamsylate and persilate. Calcium dobesilate or hydroquinone calcium sulfonate, with the chemical name 2,5-dihydroxybenzenesulfonic acid calcium salt, is being sold as Dexium (Delalande) and Doxium (Carrion), and a process for its preparation is described in US Patent No. 3,509,207.

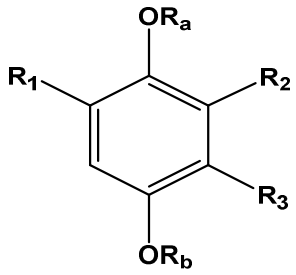
There are many drugs that contain phenol or catechol groups which suffer from premature metabolism at the hydroxy group during absorption after oral administration. Previous efforts to protect the hydroxy groups have been generally unsuccessful as the protecting groups employed are either too labile (O═COR or O═CR) or too stable (CH_3). It is thus an object of the present invention to provide novel derivatives of hydroquinones, their pharmaceutically acceptable salts and formulations. These novel hydroquinones derivatives have particularly potent anti-fibrotic, anti-inflammatory and anti-angiogenic properties.

International publication WO2018160618A1 discloses certain substituted hydroquinones, 1,4-quinones, catechols, 1,2-quinones, anthraquinones, and anthrahydroquinones for use as redox mediators in emerging technologies, such as in mediated fuel cells or organic-mediator flow batteries.

Richter et al, in Synthesis, 1976, 1976(3), 192-194 disclose Bis-N-arylcarbamates and 2,5-Dihydroxy-3,6-bis[N-arylcarboxamido]-1,4-benzoquinones and their preparation from 2,5-Dihydroxy-1,4-benzoquinone and Aryl Isocyanates.

CLAIMS

1. A substituted hydroquinone of formula (I):



(I)

wherein:

R_a, R_b = H, $C_{1\text{-}4}$acyl, aryl$C_{1\text{-}4}$alkyl, C_6-C_{10}arylCO, $HOOC(CH_2)_nCO$, C_1-C_7alkylNHCO, phosphono, phosphonooxymethyl, C_1-C_6acyloxymethyl, C_1-C_6acyloxy-1-ethyl, C_1-C_6alkoxycarbonyloxymethyl, or C_1-C_6alkoxycarbonyloxy-1-ethyl;

R_1 = $COOR_4$, $(CH_2)_nCOOR_4$, SO_3H, $(CH_2)_nSO_3H$, or CONH-$R_{10;}$

R_2 and R_3 are H or R_5, with the proviso that when one of R_2 and R_3 is R_5, the other is H and when one of R_2 and R_3 is H, the other is R_5;

R_4 = H, $C_{1\text{-}4}$alkyl, aryl$C_{1\text{-}4}$alkyl, functionalized C_1-C_6alkyl including morpholino-C_1-C_6alkyl, pyrrolidino-C_1-C_6alkyl, N-methylpiperazino-C_1-C_6alkyl, C_6-C_{10}aryl including *o*-methoxyphenyl (guaiacol ester), C_1-C_6acyloxymethyl, C_1-C_6acyloxy-1-ethyl, C_1-C_6alkoxycarbonyloxymethyl, C_1-C_6alkoxycarbonyloxy-1-ethyl, or (oxodioxolyl)methyl;

R_5 = R_6, R_7, or R_8

R_6 = CONH-R_9, $CONHCOR_9$, $CONH(CH_2)_n$-R_9, $CONHCH(COOR_4)(CH_2)_kR_{9,;}$ wherein k = 0-4;

R_7 = benzoheteroaryl substituted with at least one or more groups selected from: $COOR_4$, $(CH_2)_nCOOR_4$, SO_3H, $(CH_2)_nSO_3H$, OR_4, azoles [5-membered N-containing heterocycles], or fluorine;

R_8 = $(CH_2)_mX(CH_2)_pR_{9;}$

X = O, S, SO_2, NH, NAc, or $N(CH_2)_qR_9$;

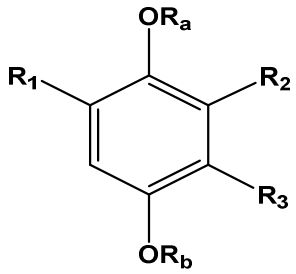
R_9 = aryl, heteroaryl, substituted with at least one or more groups selected from $COOR_4$, $(CH_2)_nCOOR_4$, $(CH_2)_nSO_3H$, OR_4, SO_3H, azoles [5-membered N-containing heterocycles], fluorine, C=O, or NHCO-R_{10};

R_{10} = aryl, heteroaryl, substituted with at least one or more groups selected from $COOR_4$, $(CH_2)_nCOOR_4$, $(CH_2)_nSO_3H$, OR_4, SO_3H, azoles [5-membered N-containing heterocycles], or fluorine;

wherein the aryl of R_9 and R_{10} is an aromatic group containing from 6 to 14 carbon atoms, selected among phenyl, naphthyl, biphenyl group; and the heteroaryl of R_9 and R_{10} is an aromatic group containing 1 to 14 carbon atoms and one or more nitrogen; and

n, m, p and q are independently 1-4.

2. The compound of formula (I):



(I)

wherein:

R_a, R_b = H, $C_{1\text{-}4}$acyl, aryl$C_{1\text{-}4}$alkyl, C_6-C_{10}arylCO, HOOC$(CH_2)_n$CO, C_1-C_7alkylNHCO, phosphono, phosphonooxymethyl, C_1-C_6acyloxymethyl, C_1-C_6acyloxy-1-ethyl, C_1-C_6alkoxycarbonyloxymethyl, or C_1-C_6alkoxycarbonyloxy-1-ethyl;

R_1 = $COOR_4$, $(CH_2)_nCOOR_4$, SO_3H, $(CH_2)_nSO_3H$, or CONH-$R_{10;}$

R_2 and R_3 are H or R_5, with the proviso that when one of R_2 and R_3 is R_5, the other is H and when one of R_2 and R_3 is H, the other is R_5;

R_4 = H, $C_{1\text{-}4}$alkyl, aryl$C_{1\text{-}4}$alkyl, functionalized C_1-C_6alkyl including morpholino-C_1-C_6alkyl, pyrrolidino-C_1-C_6alkyl, N-methylpiperazino-C_1-C_6alkyl, C_6-C_{10}aryl including *o*-methoxyphenyl (guaiacol ester), C_1-C_6acyloxymethyl, C_1-C_6acyloxy-1-ethyl, C_1-C_6alkoxycarbonyloxymethyl, C_1-C_6alkoxycarbonyloxy-1-ethyl, or (oxodioxolyl)methyl;

R_5 = R_6, or R_7,

R_6 = CONH-R_9, CONHCOR_9, CONH$(CH_2)_n$-R_9, or CONHCH$(COOR_4)(CH_2)_kR_{9;}$ wherein k = 0-4;

R_7 = benzoheteroaryl substituted with at least one or more groups selected from: $COOR_4$, $(CH_2)_nCOOR_4$, SO_3H, $(CH_2)_nSO_3H$, OR_4, azoles [5-membered N-containing heterocycles], or fluorine;

R_9 = aryl, heteroaryl, substituted with at least one or more groups selected from $COOR_4$, $(CH_2)_nCOOR_4$, $(CH_2)_nSO_3H$, OR_4, SO_3H, azoles [5-membered N-containing heterocycles], fluorine, C=O, or NHCO-R_{10};

R_{10} = aryl, heteroaryl, substituted with at least one or more groups selected from $COOR_4$, $(CH_2)_nCOOR_4$, $(CH_2)_nSO_3H$, OR_4, SO_3H, azoles [5-membered N-containing heterocycles], or fluorine; wherein the aryl of R_9 and R_{10} is an aromatic group containing from 6 to 14 carbon atoms, selected among phenyl,

naphthyl, biphenyl group; and the heteroaryl of R_9 and R_{10} is an aromatic group containing 1 to 14 carbon atoms and one or more nitrogen; and n, is independently 1-4.

3. The compound according to claim 2, wherein:

(A)

R_a, R_b = H, C_{1-4}acyl, arylC_{1-4}alkyl, C_6-C_{10}arylCO, HOOC$(CH_2)_n$CO, C_1-C_7alkylNHCO, phosphono, phosphonooxymethyl, C_1-C_6acyloxymethyl, C_1-C_6acyloxy-1-ethyl, C_1-C_6alkoxycarbonyloxymethyl, or C_1-C_6alkoxycarbonyloxy-1-ethyl;

R_1 = $COOR_4$; R_4 = H, C_{1-4}alkyl, arylC_{1-4}alkyl, functionalized C_1-C_6alkyl including morpholino-C_1-C_6alkyl, pyrrolidino-C_1-C_6alkyl, N-methylpiperazino-C_1-C_6alkyl, C_6-C_{10}aryl including *o*-methoxyphenyl (guaiacol ester), C_1-C_6acyloxymethyl, C_1-C_6acyloxy-1-ethyl, C_1-C_6alkoxycarbonyloxymethyl, C_1-C_6alkoxycarbonyloxy-1-ethyl, or (oxodioxolyl)methyl;

R_2 = H; R_3 = R_5; and

R_5 = R_6 = CONH-R_9;

or

(B)

R_a, R_b = H, C_{1-4}acyl, arylC_{1-4}alkyl, C_6-C_{10}arylCO, HOOC$(CH_2)_n$CO, C_1-C_7alkylNHCO, phosphono, phosphonooxymethyl, C_1-C_6acyloxymethyl, C_1-C_6acyloxy-1-ethyl, C_1-C_6alkoxycarbonyloxymethyl, or C_1-C_6alkoxycarbonyloxy-1-ethyl;

R_1 = $COOR_4$; R_4 = H, C_{1-4}alkyl, arylC_{1-4}alkyl, functionalized C_1-C_6alkyl including morpholino-C_1-C_6alkyl, pyrrolidino-C_1-C_6alkyl, N-methylpiperazino-C_1-C_6alkyl, C_6-C_{10}aryl including *o*-methoxyphenyl (guaiacol ester), C_1-C_6acyloxymethyl, C_1-C_6acyloxy-1-ethyl, C_1-C_6alkoxycarbonyloxymethyl, C_1-C_6alkoxycarbonyloxy-1-ethyl, or (oxodioxolyl)methyl;

R_3 = H; R_2 = R_5; and

R_5 = R_6 = CONH-R_9;

or

wherein said compound is selected form the group consisting of:

4-(2-carboxyphenylaminocarbonyl)-2,5-dihydroxybenzoic acid;

4-(2-(1H-tetrazol-5-yl)phenylaminocarbonyl)-2,5-dihydroxybenzoic acid;

2,5-dihydroxy-4-(2-sulfophenylaminocarbonyl)benzoic acid;

4-(3-carboxyphenylaminocarbonyl)-2,5-dihydroxybenzoic acid;

4-(3-(1H-tetrazol-5-yl)phenylaminocarbonyl)-2,5-dihydroxybenzoic acid;

2,5-dihydroxy-4-(3-sulfophenylaminocarbonyl)benzoic acid;

4-(4-carboxyphenylaminocarbonyl)-2,5-dihydroxybenzoic acid;

4-(4-(1H-tetrazol-5-yl)phenylaminocarbonyl)-2,5-dihydroxybenzoic acid;

2,5-dihydroxy-4-(4-sulfophenylaminocarbonyl)benzoic acid;
4-(3-carboxy-4-hydroxyphenylaminocarbonyl)-2,5-dihydroxybenzoic acid;
4-(4-carboxy-3-hydroxyphenylaminocarbonyl)-2,5-dihydroxybenzoic acid;
4-(4-carboxy-2,5-dihydroxyphenylaminocarbonyl)-2,5-dihydroxybenzoic acid;
4-(2-carboxy-4-hydroxyphenylaminocarbonyl)-2,5-dihydroxybenzoic acid;
3,5-bis(2,5-dihydroxy-4-carboxybenzoylamino)benzoic acid;
3-(4-carboxy-2,5-dihydroxybenzamido)phthalic acid;
2-(4-carboxy-2,5-dihydroxybenzamido)terephthalic acid;
2-(4-carboxy-2,5-dihydroxybenzamido)isophthalic acid;
4-(4-carboxy-2,5-dihydroxybenzamido)phthalic acid;
5-(4-carboxy-2,5-dihydroxybenzamido)isophthalic acid;
2-(4-carboxy-2,5-dihydroxybenzamido)nicotinic acid;
2-(4-carboxy-2,5-dihydroxybenzamido)isonicotinic acid;
6-(4-carboxy-2,5-dihydroxybenzamido)nicotinic acid;
6-(4-carboxy-2,5-dihydroxybenzamido)picolinic acid;
2-(4-carboxy-2,5-dihydroxybenzamido)-5-fluoronicotinic acid;
6-(4-carboxy-2,5-dihydroxybenzamido)pyridine-2,5-dicarboxylic acid;
2-(4-carboxy-2,5-dihydroxybenzamido)pyridine-3,5-dicarboxylic acid;
3-(4-carboxy-2,5-dihydroxybenzamido)isonicotinic acid;
5-(4-carboxy-2,5-dihydroxybenzamido)nicotinic acid;
5-(4-carboxy-2,5-dihydroxybenzamido)picolinic acid;
3-(4-carboxy-2,5-dihydroxybenzamido)picolinic acid;
5-(4-carboxy-2,5-dihydroxybenzamido)-2-fluoroisonicotinic acid;
4-(4-carboxy-2,5-dihydroxybenzamido)nicotinic acid;
4-(4-carboxy-2,5-dihydroxybenzamido)picolinic acid;
4-(4-(carboxymethyl)phenylaminocarbonyl)-2,5-dihydroxybenzoic acid;
4-(3-(carboxymethyl)phenylaminocarbonyl)-2,5-dihydroxybenzoic acid;
2,5-dihydroxy-4-(3-(1-hydroxy-1H-pyrazol-4-yl)phenylaminocarbonyl)benzoic acid;
4-(2-(carboxymethyl)phenylaminocarbonyl)-2,5-dihydroxybenzoic acid;
ethyl 4-(2-(ethoxycarbonyl)phenylaminocarbonyl)-2,5-diacetoxybenzoate;
ethyl 4-(2-(ethoxycarbonyl)phenylaminocarbonyl)-2,5-dihydroxybenzoate;
ethyl 4-(2-(1H-tetrazol-5-yl)phenylaminocarbonyl)-2,5-diacetoxybenzoate;
ethyl 4-(2-(1H-tetrazol-5-yl)phenylaminocarbonyl)-2,5-dihydroxybenzoate;
ethyl 2,5-dihydroxy-4-(4-hydroxy-3-(methoxycarbonyl)phenylaminocarbonyl)benzoate;
ethyl 3,5-bis(2,5-diacetoxy-4-ethoxycarbonylbenzoylamino)benzoate;

ethyl 3,5-bis(2,5-dihydroxy-4-ethoxycarbonylbenzoylamino)benzoate;
ethyl 3-(4-(ethoxycarbonyl)-2,5-dihydroxybenzamido)isonicotinate;
Ethyl 4-(4-ethoxycarbonyl-2,5-dihydroxyphenylaminocarbonyl)-2,5-dihydroxybenzoate;
3-(2-carboxyphenylaminocarbonyl)-2,5-dihydroxybenzoic acid;
3-(2-(1H-tetrazol-5-yl)phenylaminocarbonyl)-2,5-dihydroxybenzoic acid;
2,5-dihydroxy-3-(2-sulfophenylaminocarbonyl)benzoic acid;
3-(3-carboxyphenylaminocarbonyl)-2,5-dihydroxybenzoic acid;
3-(3-(1H-tetrazol-5-yl)phenylaminocarbonyl)-2,5-dihydroxybenzoic acid;
2,5-dihydroxy-3-(3-sulfophenylaminocarbonyl)benzoic acid;
3-(4-carboxyphenylaminocarbonyl)-2,5-dihydroxybenzoic acid;
3-(4-(1H-tetrazol-5-yl)phenylaminocarbonyl)-2,5-dihydroxybenzoic acid;
2,5-dihydroxy-3-(4-sulfophenylaminocarbonyl)benzoic acid;
3-(3-carboxy-4-hydroxyphenylaminocarbonyl)-2,5-dihydroxybenzoic acid;
3-(4-carboxy-3-hydroxyphenylaminocarbonyl)-2,5-dihydroxybenzoic acid;
3-(2-carboxy-4-hydroxyphenylaminocarbonyl)-2,5-dihydroxybenzoic acid;
3,5-Bis(2,5-dihydroxy-3-carboxybenzoylamino)benzoic acid;
3-(3-carboxy-2,5-dihydroxybenzamido)phthalic acid;
2-(3-carboxy-2,5-dihydroxybenzamido)terephthalic acid;
2-(3-carboxy-2,5-dihydroxybenzamido)isophthalic acid;
4-(3-carboxy-2,5-dihydroxybenzamido)phthalic acid;
5-(3-carboxy-2,5-dihydroxybenzamido)isophthalic acid;
2-(3-carboxy-2,5-dihydroxybenzamido)nicotinic acid;
2-(3-carboxy-2,5-dihydroxybenzamido)isonicotinic acid;
6-(3-carboxy-2,5-dihydroxybenzamido)nicotinic acid;
6-(3-carboxy-2,5-dihydroxybenzamido)picolinic acid;
2-(3-carboxy-2,5-dihydroxybenzamido)-5-fluoronicotinic acid;
6-(3-carboxy-2,5-dihydroxybenzamido)pyridine-2,5-dicarboxylic acid;
2-(3-carboxy-2,5-dihydroxybenzamido)pyridine-3,5-dicarboxylic acid;
3-(3-carboxy-2,5-dihydroxybenzamido)isonicotinic acid;
5-(3-carboxy-2,5-dihydroxybenzamido)nicotinic acid;
5-(3-carboxy-2,5-dihydroxybenzamido)picolinic acid;
3-(3-carboxy-2,5-dihydroxybenzamido)picolinic acid
5-(3-carboxy-2,5-dihydroxybenzamido)-2-fluoroisonicotinic acid;
4-(3-carboxy-2,5-dihydroxybenzamido)nicotinic acid;
4-(3-carboxy-2,5-dihydroxybenzamido)picolinic acid;

3-(4-(carboxymethyl)phenylaminocarbonyl)-2,5-dihydroxybenzoic acid;
3-(3-(carboxymethyl)phenylaminocarbonyl)-2,5-dihydroxybenzoic acid;
2,5-dihydroxy-3-(3-(1-hydroxy-1H-pyrazol-4-yl)phenylaminocarbonyl)benzoic acid;
3-(2-(carboxymethyl)phenylaminocarbonyl)-2,5-dihydroxybenzoic acid;
ethyl 3-(2-(1H-tetrazol-5-yl)phenylaminocarbonyl)-2,5-dihydroxybenzoate; and
ethyl 3-(2-(ethoxycarbonylmethyl)phenylaminocarbonyl)-2,5-dihydroxybenzoate;

4. The compound according to claim 2, wherein:
(A)
R_a, R_b = H;
$R_1 = SO_3H$;
R_2 = H; $R_3 = R_5$; and
$R_5 = R_6 = CONH\text{-}R_9$;
or
(B)
R_a, R_b = H;
$R_1 = SO_3H$;
R_3 = H; $R_2 = R_5$; and
$R_5 = R_6 = CONH\text{-}R_9$;
or
wherein said compound is selected form the group consisting of:
2-(2,5-dihydroxy-4-sulfobenzamido)benzoic acid;
2,5-dihydroxy-4-(2-sulfophenylaminocarbonyl)benzenesulfonic acid;
3-(2,5-dihydroxy-4-sulfobenzamido)benzoic acid;
2,5-dihydroxy-4-(3-sulfophenylaminocarbonyl)benzenesulfonic acid;
4-(2,5-dihydroxy-4-sulfobenzamido)benzoic acid;
2,5-dihydroxy-4-(4-sulfophenylaminocarbonyl)benzenesulfonic acid;
5-(2,5-dihydroxy-4-sulfobenzamido)-2-hydroxybenzoic acid;
4-(2,5-dihydroxy-4-sulfobenzamido)-2-hydroxybenzoic acid;
2-(2,5-dihydroxy-4-sulfobenzamido)-5-hydroxybenzoic acid;
3,5-bis(2,5-dihydroxy-4-sulfobenzamido)benzoic acid;
3-(2,5-dihydroxy-4-sulfobenzamido)phthalic acid;
2-(2,5-dihydroxy-4-sulfobenzamido)terephthalic acid;
2-(2,5-dihydroxy-4-sulfobenzamido)isophthalic acid;
4-(2,5-dihydroxy-4-sulfobenzamido)phthalic acid;

5-(2,5-dihydroxy-4-sulfobenzamido)isophthalic acid;
2-(2,5-dihydroxy-4-sulfobenzamido)nicotinic acid;
2-(2,5-dihydroxy-4-sulfobenzamido)isonicotinic acid;
6-(2,5-dihydroxy-4-sulfobenzamido)nicotinic acid;
6-(2,5-dihydroxy-4-sulfobenzamido)picolinic acid;
2-(2,5-dihydroxy-4-sulfobenzamido)-5-fluoronicotinic acid;
6-(2,5-dihydroxy-4-sulfobenzamido)pyridine-2,5-dicarboxylic acid;
2-(2,5-dihydroxy-4-sulfobenzamido)pyridine-3,5-dicarboxylic acid;
3-(2,5-dihydroxy-4-sulfobenzamido)isonicotinic acid;
5-(2,5-dihydroxy-4-sulfobenzamido)nicotinic acid;
5-(2,5-dihydroxy-4-sulfobenzamido)picolinic acid;
3-(2,5-dihydroxy-4-sulfobenzamido)picolinic acid;
5-(2,5-dihydroxy-4-sulfobenzamido)-2-fluoroisonicotinic acid;
4-(2,5-dihydroxy-4-sulfobenzamido)nicotinic acid;
4-(2,5-dihydroxy-4-sulfobenzamido)picolinic acid;
(4-(2,5-dihydroxy-4-sulfobenzamido)phenyl)acetic acid;
(3-(2,5-dihydroxy-4-sulfobenzamido)phenyl)acetic acid;
(2-(2,5-dihydroxy-4-sulfobenzamido)phenyl)acetic acid;
2-(2,5-dihydroxy-3-sulfobenzamido)benzoic acid;
2,5-dihydroxy-3-(2-sulfophenylaminocarbonyl)benzenesulfonic acid;
3-(2,5-dihydroxy-3-sulfobenzamido)benzoic acid;
2,5-dihydroxy-3-(3-sulfophenylaminocarbonyl)benzenesulfonic acid;
4-(2,5-dihydroxy-3-sulfobenzamido)benzoic acid;
2,5-dihydroxy-3-(4-sulfophenylaminocarbonyl)benzenesulfonic acid;
5-(2,5-dihydroxy-3-sulfobenzamido)-2-hydroxybenzoic acid;
4-(2,5-dihydroxy-3-sulfobenzamido)-2-hydroxybenzoic acid;
2-(2,5-dihydroxy-3-sulfobenzamido)-5-hydroxybenzoic acid;
3-(2,5-dihydroxy-3-sulfobenzamido)-5-(2,5-dihydroxy-4-sulfobenzamido)benzoic acid
3-(2,5-dihydroxy-3-sulfobenzamido)phthalic acid;
2-(2,5-dihydroxy-3-sulfobenzamido)terephthalic acid;
2-(2,5-dihydroxy-3-sulfobenzamido)isophthalic acid;
4-(2,5-dihydroxy-3-sulfobenzamido)phthalic acid;
5-(2,5-dihydroxy-3-sulfobenzamido)isophthalic acid;
2-(2,5-dihydroxy-3-sulfobenzamido)nicotinic acid;
2-(2,5-dihydroxy-3-sulfobenzamido)isonicotinic acid;

6-(2,5-dihydroxy-3-sulfobenzamido)nicotinic acid;
6-(2,5-dihydroxy-3-sulfobenzamido)picolinic acid;
2-(2,5-dihydroxy-3-sulfobenzamido)-5-fluoronicotinic acid;
6-(2,5-dihydroxy-3-sulfobenzamido)pyridine-2,5-dicarboxylic acid;
2-(2,5-dihydroxy-3-sulfobenzamido)pyridine-3,5-dicarboxylic acid;
3-(2,5-dihydroxy-3-sulfobenzamido)isonicotinic acid;
5-(2,5-dihydroxy-3-sulfobenzamido)nicotinic acid;
5-(2,5-dihydroxy-3-sulfobenzamido)picolinic acid;
3-(2,5-dihydroxy-3-sulfobenzamido)picolinic acid;
5-(2,5-dihydroxy-3-sulfobenzamido)-2-fluoroisonicotinic acid;
4-(2,5-dihydroxy-3-sulfobenzamido)nicotinic acid;
4-(2,5-dihydroxy-3-sulfobenzamido)picolinic acid;
(4-(2,5-dihydroxy-3-sulfobenzamido)phenyl)acetic acid;
(3-(2,5-dihydroxy-3-sulfobenzamido)phenyl)acetic acid; and
(2-(2,5-dihydroxy-3-sulfobenzamido)phenyl)acetic acid.

5. The compound according to claim 2, wherein:

(A)

R_a, R_b = H,

$R_1 = (CH_2)_nCOOR_4$; R_4 = H, $C_{1\text{-}4}$alkyl, aryl$C_{1\text{-}4}$alkyl, functionalized C_1-C_6alkyl including morpholino-C_1-C_6alkyl, pyrrolidino-C_1-C_6alkyl, N-methylpiperazino-C_1-C_6alkyl, C_6-C_{10}aryl including *o*-methoxyphenyl (guaiacol ester), C_1-C_6acyloxymethyl, C_1-C_6acyloxy-1-ethyl, C_1-C_6alkoxycarbonyloxymethyl, C_1-C_6alkoxycarbonyloxy-1-ethyl, or (oxodioxolyl)methyl;

R_2 = H or R_5, $R_3 = R_5$; and

$R_5 = R_6 = CONH\text{-}R_9$;

Or

(B)

R_a, R_b = H;

$R_1 = (CH_2)_nCOOR_4$; R_4 = H, $C_{1\text{-}4}$alkyl, aryl$C_{1\text{-}4}$alkyl, functionalized C_1-C_6alkyl including morpholino-C_1-C_6alkyl, pyrrolidino-C_1-C_6alkyl, N-methylpiperazino-C_1-C_6alkyl, C_6-C_{10}aryl including *o*-methoxyphenyl (guaiacol ester), C_1-C_6acyloxymethyl, C_1-C_6acyloxy-1-ethyl, C_1-C_6alkoxycarbonyloxymethyl, C_1-C_6alkoxycarbonyloxy-1-ethyl, or (oxodioxolyl)methyl;

R_3 = H; $R_2 = R_5$; and

$R_5 = R_6 = CONH\text{-}R_9$;

or wherein said compound is selected form the group consisting of:

2-(4-(carboxymethyl)-2,5-dihydroxybenzamido)benzoic acid;
(2-(1H-tetrazol-5-yl)phenylaminocarbonyl)-2,5-dihydroxyphenyl)acetic acid;
(2,5-dihydroxy-4-(2-sulfophenylaminocarbonyl)phenyl)acetic acid;
3-(4-(carboxymethyl)-2,5-dihydroxybenzamido)benzoic acid;
(2,5-dihydroxy-4-(3-sulfophenylaminocarbonyl)phenyl)acetic acid;
4-(4-(carboxymethyl)-2,5-dihydroxybenzamido)benzoic acid;
2-(2,5-dihydroxy-4-(4-sulfophenylaminocarbonyl)phenyl)acetic acid;
5-(4-(carboxymethyl)-2,5-dihydroxybenzamido)-2-hydroxybenzoic acid;
4-(4-(carboxymethyl)-2,5-dihydroxybenzamido)-2-hydroxybenzoic acid;
2-(4-(carboxymethyl)-2,5-dihydroxybenzamido)-5-hydroxybenzoic acid;
3,5-Bis(2,5-dihydroxy-4-carboxymethylbenzoylamino)benzoic acid
3-(4-(carboxymethyl)-2,5-dihydroxybenzamido)phthalic acid;
2-(4-(carboxymethyl)-2,5-dihydroxybenzamido)terephthalic acid;
2-(4-(carboxymethyl)-2,5-dihydroxybenzamido)isophthalic acid;
4-(4-(carboxymethyl)-2,5-dihydroxybenzamido)phthalic acid;
5-(4-(carboxymethyl)-2,5-dihydroxybenzamido)isophthalic acid;
2-(4-(carboxymethyl)-2,5-dihydroxybenzamido)nicotinic acid;
2-(4-(carboxymethyl)-2,5-dihydroxybenzamido)isonicotinic acid;
6-(4-(carboxymethyl)-2,5-dihydroxybenzamido)nicotinic acid;
6-(4-(carboxymethyl)-2,5-dihydroxybenzamido)picolinic acid;
2-(4-(carboxymethyl)-2,5-dihydroxybenzamido)-5-fluoronicotinic acid;
6-(4-(carboxymethyl)-2,5-dihydroxybenzamido)pyridine-2,5-dicarboxylic acid;
2-(4-(carboxymethyl)-2,5-dihydroxybenzamido)pyridine-3,5-dicarboxylic acid;
3-(4-(carboxymethyl)-2,5-dihydroxybenzamido)isonicotinic acid;
5-(4-(carboxymethyl)-2,5-dihydroxybenzamido)nicotinic acid;
5-(4-(carboxymethyl)-2,5-dihydroxybenzamido)picolinic acid;
3-(4-(carboxymethyl)-2,5-dihydroxybenzamido)picolinic acid;
5-(4-(carboxymethyl)-2,5-dihydroxybenzamido)-2-fluoroisonicotinic acid;
4-(4-(carboxymethyl)-2,5-dihydroxybenzamido)nicotinic acid;
4-(4-(carboxymethyl)-2,5-dihydroxybenzamido)picolinic acid;
(4-(4-(carboxymethyl)-2,5-dihydroxybenzamido)phenyl)acetic acid;
(3-(4-(carboxymethyl)-2,5-dihydroxybenzamido)phenyl)acetic acid;
(2-(4-(carboxymethyl)-2,5-dihydroxybenzamido)phenyl)acetic acid;
methyl 2-(4-(ethoxycarbonylmethyl)-2,5-dihydroxybenzamido)benzoate;
ethyl (4-(2-(1H-tetrazol-5-yl)phenylaminocarbonyl)-2,5-dihydroxyphenyl)acetate;

diethyl 5-(4-(ethoxycarbonylmethyl)-2,5-dihydroxybenzamido)isophthalate;
methyl 3,5-bis(4-(ethoxycarbonylmethyl)-2,5-dihydroxybenzamido)benzoate;
2-(3-(carboxymethyl)-2,5-dihydroxybenzamido)benzoic acid;
(2,5-dihydroxy-3-(2-sulfophenylaminocarbonyl)phenyl)acetic acid;
3-(3-(carboxymethyl)-2,5-dihydroxybenzamido)benzoic acid;
(2,5-dihydroxy-3-(3-sulfophenylaminocarbonyl)phenyl)acetic acid;
4-(3-(carboxymethyl)-2,5-dihydroxybenzamido)benzoic acid;
(2,5-dihydroxy-3-(4-sulfophenylaminocarbonyl)phenyl)acetic acid;
5-(3-(carboxymethyl)-2,5-dihydroxybenzamido)-2-hydroxybenzoic acid;
4-(3-(carboxymethyl)-2,5-dihydroxybenzamido)-2-hydroxybenzoic acid;
2-(3-(carboxymethyl)-2,5-dihydroxybenzamido)-5-hydroxybenzoic acid;
3,5-Bis(2,5-dihydroxy-3-carboxymethylbenzoylamino)benzoic acid
3-(3-(carboxymethyl)-2,5-dihydroxybenzamido)phthalic acid;
2-(3-(carboxymethyl)-2,5-dihydroxybenzamido)terephthalic acid;
2-(3-(carboxymethyl)-2,5-dihydroxybenzamido)isophthalic acid;
4-(3-(carboxymethyl)-2,5-dihydroxybenzamido)phthalic acid;
5-(3-(carboxymethyl)-2,5-dihydroxybenzamido)isophthalic acid;
2-(3-(carboxymethyl)-2,5-dihydroxybenzamido)nicotinic acid;
2-(3-(carboxymethyl)-2,5-dihydroxybenzamido)isonicotinic acid;
6-(3-(carboxymethyl)-2,5-dihydroxybenzamido)nicotinic acid;
6-(3-(carboxymethyl)-2,5-dihydroxybenzamido)picolinic acid;
2-(3-(carboxymethyl)-2,5-dihydroxybenzamido)-5-fluoronicotinic acid;
6-(3-(carboxymethyl)-2,5-dihydroxybenzamido)pyridine-2,5-dicarboxylic acid;
2-(3-(carboxymethyl)-2,5-dihydroxybenzamido)pyridine-3,5-dicarboxylic acid;
3-(3-(carboxymethyl)-2,5-dihydroxybenzamido)isonicotinic acid;
5-(3-(carboxymethyl)-2,5-dihydroxybenzamido)nicotinic acid;
5-(3-(carboxymethyl)-2,5-dihydroxybenzamido)picolinic acid;
3-(3-(carboxymethyl)-2,5-dihydroxybenzamido)picolinic acid;
5-(3-(carboxymethyl)-2,5-dihydroxybenzamido)-2-fluoroisonicotinic acid;
4-(3-(carboxymethyl)-2,5-dihydroxybenzamido)nicotinic acid;
4-(3-(carboxymethyl)-2,5-dihydroxybenzamido)picolinic acid;
(4-(3-(carboxymethyl)-2,5-dihydroxybenzamido)phenyl)acetic acid;
(3-(3-(carboxymethyl)-2,5-dihydroxybenzamido)phenyl)acetic acid; and
(2 -(3-(carboxymethyl)-2,5-dihydroxybenzamido)phenyl)acetic acid.

6. The compound according to claim 2, wherein:

(A)

R_a, R_b = H, C_{1-4}acyl, arylC_{1-4}alkyl, C_6-C_{10}arylCO, HOOC$(CH_2)_n$CO, C_1-C_7alkylNHCO, phosphono, phosphonooxymethyl, C_1-C_6acyloxymethyl, C_1-C_6acyloxy-1-ethyl, C_1-C_6alkoxycarbonyloxymethyl, or C_1-C_6alkoxycarbonyloxy-1-ethyl;

R_1 = CONH-R_{10}; R_4 = H, C_{1-4}alkyl, arylC_{1-4}alkyl, functionalized C_1-C_6alkyl including morpholino-C_1-C_6alkyl, pyrrolidino-C_1-C_6alkyl, N-methylpiperazino-C_1-C_6alkyl, C_6-C_{10}aryl including *o*-methoxyphenyl (guaiacol ester), C_1-C_6acyloxymethyl, C_1-C_6acyloxy-1-ethyl, C_1-C_6alkoxycarbonyloxymethyl, C_1-C_6alkoxycarbonyloxy-1-ethyl, or (oxodioxolyl)methyl;

R_2 = H; R_3 = R_5; and

R_5 = R_6 = CONH-R_9;

Or

(B)

R_a, R_b = H, C_{1-4}acyl, arylC_{1-4}alkyl, C_6-C_{10}arylCO, HOOC$(CH_2)_n$CO, C_1-C_7alkylNHCO, phosphono, phosphonooxymethyl, C_1-C_6acyloxymethyl, C_1-C_6acyloxy-1-ethyl, C_1-C_6alkoxycarbonyloxymethyl, or C_1-C_6alkoxycarbonyloxy-1-ethyl;

R1 = CONH-R_{10}; R_4 = H, C_{1-4}alkyl, arylC_{1-4}alkyl, functionalized C_1-C_6alkyl including morpholino-C_1-C_6alkyl, pyrrolidino-C_1-C_6alkyl, N-methylpiperazino-C_1-C_6alkyl, C_6-C_{10}aryl including *o*-methoxyphenyl (guaiacol ester), C_1-C_6acyloxymethyl, C_1-C_6acyloxy-1-ethyl, C_1-C_6alkoxycarbonyloxymethyl, C_1-C_6alkoxycarbonyloxy-1-ethyl, or (oxodioxolyl)methyl;

R_3 = H; R_2 = R_5; and

R_5 = R_6 = CONH-R_9.

or

wherein said compound is selected form the group consisting of:

5-(4-(2-(1H-tetrazol-5-yl)phenylaminocarbonyl)-2,5-dihydroxybenzamido)-2-hydroxybenzoic acid;

N_1,N_4-bis(2-(1H-tetrazol-5-yl)phenyl)-2,5-dihydroxyterephthalamide;

5-(4-(3-carboxy-4-hydroxyphenylaminocarbonyl)-2,5-dihydroxybenzamido)-2-hydroxybenzoic acid;

5-(2,5-dihydroxy-4-(4-hydroxy-3-sulfophenylaminocarbonyl)benzamido)-2-hydroxybenzenesulphonic acid;

4-(4-(4-carboxy-3-hydroxyphenylaminocarbonyl)-2,5-dihydroxybenzamido)-2-hydroxybenzoic acid;

4-(2,5-dihydroxy-4-(3-hydroxy-4-sulfophenylaminocarbonyl)benzamido)-2-hydroxybenzenesulphonic acid;

2-(2,5-dihydroxy-4-(4-hydroxy-2-carboxyphenylaminocarbonyl)benzamido)-5-hydroxybenzoic acid;

2-(2,5-dihydroxy-4-(4-hydroxy-2-sulfophenylaminocarbonyl)benzamido)-5-hydroxybenzene sulphonic acid;

methyl 5-(4-(2-(1H-tetrazol-5-yl)phenylaminocarbonyl)-2,5-dihydroxybenzamido)-2-hydroxybenzoate;

methyl 5-(2,5-diacetoxy-4-(4-acetoxy-3-(methoxycarbonyl)phenylaminocarbonyl)benzamido)-2-acetoxybenzoate;

methyl 5-(2,5-dihydroxy-4-(4-hydroxy-3-(methoxycarbonyl)phenylaminocarbonyl)benzamido)-2-hydroxybenzoate;

methyl 2-(2,5-dihydroxy-4-(4-hydroxy-2-(methoxycarbonyl)phenylaminocarbonyl)benzamido)-5-hydroxybenzoate;

1-(2,2-dimethylpropanoyloxy)ethyl 5-[[4-[[3-[1-(2,2-dimethylpropanoyloxy)ethoxycarbonyl]-4-hydroxy-phenyl]aminocarbonyl]-2,5-dihydroxy-benzoyl]amino]-2-hydroxybenzoate

5-(3-(3-carboxy-4-hydroxyphenylaminocarbonyl)-2,5-dihydroxybenzamido)-2-hydroxybenzoic acid;

5-(2,5-dihydroxy-3-(4-hydroxy-3-sulfophenylaminocarbonyl)benzamido)-2-hydroxybenzenesulphonic acid;

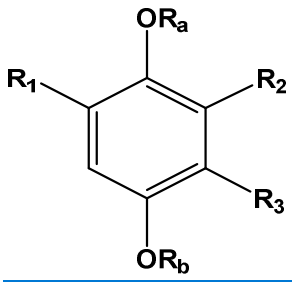
4-(3-(3-hydroxy-4-carboxyphenylaminocarbonyl)-2,5-dihydroxybenzamido)-2-hydroxybenzoic acid;

4-(2,5-dihydroxy-3-(3-hydroxy-4-sulfophenylaminocarbonyl)benzamido)-2-hydroxybenzenesulphonic acid;

2-(3-(2-carboxy-4-hydroxyphenylaminocarbonyl)-2,5-dihydroxybenzamido)-5-hydroxylbenzoic acid; and

2-(2,5-dihydroxy-3-(4-hydroxy-2-sulfophenylaminocarbonyl)benzamido)-5-hydroxybenzenesulphonic acid.

7. The compound according to claim 2 having the formula (I):



(I)

wherein:

R_a, R_b = H;

R_1 = CONH-R_{10};

R_{10} = phenyl substituted with $COOR_4$ and with OR_4;

R_2 = H;

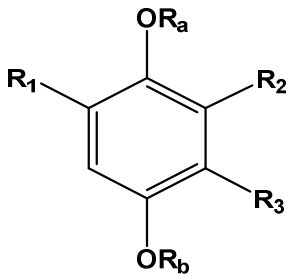
R_3 = CONH-R_9;

R_9 = phenyl substituted with $COOR_4$ and with OR_4; and

R_4 = H;

and wherein said compound is 5-(4-(3-carboxy-4-hydroxyphenylaminocarbonyl)-2,5-dihydroxybenzamido)-2-hydroxybenzoic acid.

8. The compound according to claim 2 having the formula (I):



(I)

wherein:

R_a, R_b = H;

R_1 = CONH-R_{10};

R_{10} = phenyl substituted with $COOR_4$ and with OR_4;

R_2 = CONH-R_9;

R_3 = H;

R_9 = phenyl substituted with $COOR_4$ and with OR_4; and

R_4 = H;

and wherein said compound is 5-(3-(3-carboxy-4-hydroxyphenylaminocarbonyl)-2,5-dihydroxybenzamido)-2-hydroxybenzoic acid.

9. The compound according to claim 2, wherein:

(A)

R_a, R_b = H;

R1 = $COOR_4$; $(CH_2)_nCOOR_4$; R_4 = H, $C_{1\text{-}4}$alkyl, aryl$C_{1\text{-}4}$alkyl, functionalized C_1-C_6alkyl including morpholino-C_1-C_6alkyl, pyrrolidino-C_1-C_6alkyl, N-methylpiperazino-C_1-C_6alkyl, C_6-C_{10}aryl including *o*-methoxyphenyl (guaiacol ester), C_1-C_6acyloxymethyl, C_1-C_6acyloxy-1-ethyl, C_1-C_6alkoxycarbonyloxymethyl, C_1-C_6alkoxycarbonyloxy-1-ethyl, or (oxodioxolyl)methyl;

R_2 = H; R_3 = R_5; and

R_5 = R_6 = $CONHCOR_9$;

or

(B)

R_a, R_b = H;

R^1 = $COOR_4$; $(CH_2)_nCOOR_4$; R_4 = H, $C_{1\text{-}4}$alkyl, aryl$C_{1\text{-}4}$alkyl, functionalized C_1-C_6alkyl including morpholino-C_1-C_6alkyl, pyrrolidino-C_1-C_6alkyl, N-methylpiperazino-C_1-C_6alkyl, C_6-C_{10}aryl including *o*-methoxyphenyl (guaiacol ester), C_1-C_6acyloxymethyl, C_1-C_6acyloxy-1-ethyl, C_1-C_6alkoxycarbonyloxymethyl, C_1-C_6alkoxycarbonyloxy-1-ethyl, or (oxodioxolyl)methyl;

R_3 = H; R_2 = R_5; and

R_5 = R_6 = $CONHCOR_9$;

or wherein said compound is selected form the group consisting of:

N-(1,3,4,5-tetrahydroxycyclohexylcarbonyl) 4-carboxy-2,5-dihydroxybenzamide;

N-(4-carboxy-2,5-dihydroxybenzoyl) 4-carboxy-2,5-dihydroxy-benzamide;

N-(3-carboxy-2,5-dihydroxybenzoyl) 4-carboxy-2,5-dihydroxy-benzamide;

N-(3,4-dihydroxybenzoyl) 4-carboxy-2,5-dihydroxybenzamide;

N-(3,5-dihydroxybenzoyl) 4-carboxy-2,5-dihydroxybenzamide;

N-(1,3,4,5-tetrahydroxycyclohexylcarbonyl) 3-carboxy-2,5-dihydroxybenzamide;

N-(4-carboxy-2,5-dihydroxybenzoyl) 3-carboxy-2,5-dihydroxy-benzamide;

N-(3-carboxy-2,5-dihydroxybenzoyl) 3-carboxy-2,5-dihydroxy-benzamide;

N-(3,4-dihydroxybenzoyl) 3-carboxy-2,5-dihydroxybenzamide;

N-(3,5-dihydroxybenzoyl) 3-carboxy-2,5-dihydroxybenzamide;

N-(1,3,4,5-tetrahydroxycyclohexylcarbonyl) 4-carboxymethyl-2,5-dihydroxybenzamide;

N-(4-carboxy-2,5-dihydroxybenzoyl) 4-carboxymethyl-2,5-dihydroxy-benzamide;

N-(3-carboxy-2,5-dihydroxybenzoyl) 4-carboxymethyl-2,5-dihydroxy-benzamide;

N-(3,4-dihydroxybenzoyl) 4-carboxymethyl-2,5-dihydroxybenzamide;

N-(3,5-dihydroxybenzoyl) 4-carboxymethyl-2,5-dihydroxybenzamide;

N-(1,3,4,5-tetrahydroxycyclohexylcarbonyl) 3-carboxymethyl-2,5-dihydroxybenzamide;

N-(4-carboxy-2,5-dihydroxybenzoyl) 3-carboxymethyl-2,5-dihydroxy-benzamide;

N-(3-carboxy-2,5-dihydroxybenzoyl) 3-carboxymethyl-2,5-dihydroxy-benzamide;

N-(3,4-dihydroxybenzoyl) 3-carboxymethyl-2,5-dihydroxybenzamide; and

N-(3,5-dihydroxybenzoyl) 3-carboxymethyl-2,5-dihydroxybenzamide.

~~8~~10. A compound according to claim 2, wherein

(A)

R_a, R_b = H;

R_1 = $COOR_4$; $(CH_2)_nCOOR_4$; R_4 = H, $C_{1\text{-}4}$alkyl, aryl$C_{1\text{-}4}$alkyl, functionalized C_1-C_6alkyl including morpholino-C_1-C_6alkyl, pyrrolidino-C_1-C_6alkyl, N-methylpiperazino-C_1-C_6alkyl, C_6-C_{10}aryl including *o*-methoxyphenyl (guaiacol ester), C_1-C_6acyloxymethyl, C_1-C_6acyloxy-1-ethyl, C_1-C_6alkoxycarbonyloxymethyl, C_1-C_6alkoxycarbonyloxy-1-ethyl, or (oxodioxolyl)methyl;

R_2 = H; R_3 = R_5; and

R_5 = R_6 = $CONH(CH_2)_n$-R_9;

Or

(B)

R_a, R_b = H;

R_1 = $COOR_4$; $(CH_2)_nCOOR_4$; R_4 = H, $C_{1\text{-}4}$alkyl, aryl$C_{1\text{-}4}$alkyl, functionalized C_1-C_6alkyl including morpholino-C_1-C_6alkyl, pyrrolidino-C_1-C_6alkyl, N-methylpiperazino-C_1-C_6alkyl, C_6-C_{10}aryl including *o*-methoxyphenyl (guaiacol ester), C_1-C_6acyloxymethyl, C_1-C_6acyloxy-1-ethyl, C_1-C_6alkoxycarbonyloxymethyl, C_1-C_6alkoxycarbonyloxy-1-ethyl, or (oxodioxolyl)methyl;

R_3 = H; R_2 = R_5; and

R_5 = R_6 = $CONH(CH_2)_n$-R_9;

or wherein said compound is selected form the group consisting of:

4-(3,4-dihydroxyphenylmethylaminocarbonyl)-2,5-dihydroxybenzoic acid;

4-(2-(3,4-dihydroxyphenyl)ethylaminocarbonyl)-2,5-dihydroxybenzoic acid;

4-(3,5-dihydroxyphenylmethylaminocarbonyl)-2,5-dihydroxybenzoic acid;

4-((4,5-dihydroxy-3-oxocyclohex-1-enyl)methylaminocarbonyl)-2,5-dihydroxybenzoic acid;

2,5-dihydroxy-4-((3,4,5-trihydroxycyclohexyl)methylaminocarbonyl)benzoic acid;

4-(2-carboxyphenylmethylaminocarbonyl)-2,5-dihydroxybenzoic acid;

4-(3-carboxyphenylmethylaminocarbonyl)-2,5-dihydroxybenzoic acid;

4-(4-carboxyphenylmethylaminocarbonyl) 2,5-dihydroxybenzoic acid;

3-(3,4-dihydroxyphenylmethylaminocarbonyl)-2,5-dihydroxybenzoic acid;

3-(2-(3,4-dihydroxyphenyl)ethylaminocarbonyl)-2,5-dihydroxybenzoic acid;

3-(3,5-dihydroxyphenylmethylaminocarbonyl)-2,5-dihydroxybenzoic acid;

3-((4,5-dihydroxy-3-oxocyclohex-1-enyl)methylaminocarbonyl)-2,5-dihydroxybenzoic acid;

2,5-dihydroxy-3-((3,4,5-trihydroxycyclohexyl)methylaminocarbonyl)benzoic acid;

3-(2-carboxyphenylmethylaminocarbonyl)-2,5-dihydroxybenzoic acid;

3-(3-carboxyphenylmethylaminocarbonyl)-2,5-dihydroxybenzoic acid;

3-(4-carboxyphenylmethylaminocarbonyl)-2,5-dihydroxybenzoic acid;

(4-(3,4-dihydroxyphenylmethylaminocarbonyl)-2,5-dihydroxyphenyl)acetic acid;

(4-(3,5-dihydroxyphenylmethylaminocarbonyl)-2,5-dihydroxyphenyl)acetic acid;

(4-((4,5-dihydroxy-3-oxocyclohex-1-enyl)methylaminocarbonyl)-2,5-dihydroxyphenyl)acetic acid;

(2,5-dihydroxy-4-((3,4,5-trihydroxycyclohexyl)methylaminocarbonyl)phenyl)acetic acid;
(4-(2-carboxyphenylmethylaminocarbonyl)-2,5-dihydroxyphenyl)acetic acid;
(4-(3-carboxyphenylmethylaminocarbonyl)-2,5-dihydroxyphenyl)acetic acid;
(4-(4-carboxyphenylmethylaminocarbonyl)-2,5-dihydroxyphenyl)acetic acid;
(3-(3,4-dihydroxyphenylmethylaminocarbonyl)-2,5-dihydroxyphenyl)acetic acid;
(3-(3,5-dihydroxyphenylmethylaminocarbonyl)-2,5-dihydroxyphenyl)acetic acid;
(3-((4,5-dihydroxy-3-oxocyclohex-1-enyl)methylaminocarbonyl)-2,5-dihydroxyphenyl)acetic acid;
(2,5-dihydroxy-3-((3,4,5-trihydroxycyclohexyl)methylcarbonylamino)phenyl)acetic acid;
(3-(2-carboxyphenylmethylaminocarbonyl)-2,5-dihydroxyphenyl)acetic acid;
(3-(3-carboxyphenylmethylaminocarbonyl)-2,5-dihydroxyphenyl)acetic acid; and
(3-(4-carboxyphenylmethylaminocarbonyl)-2,5-dihydroxyphenyl)acetic acid.

~~9~~11. A compound according to claim 2, wherein:
R_a, R_b = H;
$R_1 = SO_3H$;
R_2 = H; $R_3 = R_5$; and
$R_5 = R_6 = CONH(CH_2)_n\text{-}R_9$;
or wherein said compound is selected form the group consisting of:
2-((2,5-dihydroxy-4-sulfobenzamido)methyl)benzoic acid;
3-((2,5-dihydroxy-4-sulfobenzamido)methyl)benzoic acid; and
4-((2,5-dihydroxy-4-sulfobenzamido)methyl)benzoic acid.

~~10~~12. The compound according to claim 2, wherein:
(A)
R_a, R_b = H;
$R_1 = COOR_4$; $(CH_2)_nCOOR_4$; R_4 = H, $C_{1\text{-}4}$alkyl, aryl$C_{1\text{-}4}$alkyl, functionalized C_1-C_6alkyl including morpholino-C_1-C_6alkyl, pyrrolidino-C_1-C_6alkyl, N-methylpiperazino-C_1-C_6alkyl, C_6-C_{10}aryl including *o*-methoxyphenyl (guaiacol ester), C_1-C_6acyloxymethyl, C_1-C_6acyloxy-1-ethyl, C_1-C_6alkoxycarbonyloxymethyl, C_1-C_6alkoxycarbonyloxy-1-ethyl, or (oxodioxolyl)methyl;
R_2 = H; $R_3 = R_5$; and
$R_5 = R_6 = CONHCH(COOR_4)(CH_2)_kR_9$;
or
(B)
R_a, R_b = H;

R_1 = $COOR_4$; $(CH_2)_nCOOR_4$; R_4 = H, $C_{1\text{-}4}$alkyl, aryl$C_{1\text{-}4}$alkyl, functionalized C_1-C_6alkyl including morpholino-C_1-C_6alkyl, pyrrolidino-C_1-C_6alkyl, N-methylpiperazino-C_1-C_6alkyl, C_6-C_{10}aryl including *o*-methoxyphenyl (guaiacol ester), C_1-C_6acyloxymethyl, C_1-C_6acyloxy-1-ethyl, C_1-C_6alkoxycarbonyloxymethyl, C_1-C_6alkoxycarbonyloxy-1-ethyl, or (oxodioxolyl)methyl;

R_3 = H; R_2 = R_5; and

R_5 = R_6 = $CONHCH(COOR_4)(CH_2)_kR_9$;

or wherein said compound is selected form the group consisting of:

4-(1-carboxy-2-(3,4-dihydroxyphenyl)ethylaminocarbonyl)-2,5-dihydroxybenzoic acid;

4-(carboxy(3,4-dihydroxyphenyl)methylaminocarbonyl)-2,5-dihydroxybenzoic acid;

3-(1-carboxy-2-(3,4-dihydroxyphenyl)ethylaminocarbonyl)-2,5-dihydroxybenzoic acid

3-(carboxy(3,4-dihydroxyphenyl)methylaminocarbonyl)-2,5-dihydroxybenzoic acid;

(4-(carboxy(3,4-dihydroxyphenyl)methylaminocarbonyl)-2,5-dihydroxyphenyl)acetic acid; and

(3-(carboxy(3,4-dihydroxyphenyl)methylaminocarbonyl)-2,5-dihydroxyphenyl)acetic acid.

~~11~~13. The compound according to claim 2, wherein:

(A)

R_a, R_b = H;

R_1 = $COOR_4$, $(CH_2)_nCOOR_4$, SO_3H, $(CH_2)_nSO_3H$, $CONH\text{-}R_{10}$;

R_4 = H, $C_{1\text{-}4}$alkyl, aryl$C_{1\text{-}4}$alkyl, functionalized C_1-C_6alkyl including morpholino-C_1-C_6alkyl, pyrrolidino-C_1-C_6alkyl, N-methylpiperazino-C_1-C_6alkyl, C_6-C_{10}aryl including *o*-methoxyphenyl (guaiacol ester), C_1-C_6acyloxymethyl, C_1-C_6acyloxy-1-ethyl, C_1-C_6alkoxycarbonyloxymethyl, C_1-C_6alkoxycarbonyloxy-1-ethyl, or (oxodioxolyl)methyl;

R_2 = H; R_3 = R_5; and

R_5 = R_7 = benzoheteroaryl substituted with at least one or more groups selected from: $COOR_4$, $(CH_2)_nCOOR_4$, SO_3H, $(CH_2)_nSO_3H$, OR_4, azoles [5-membered N-containing heterocycles], or fluorine;

or

(B)

R_a, R_b = H;

R_1 = $COOR_4$, $(CH_2)_nCOOR_4$, SO_3H, $(CH_2)_nSO_3H$, $CONH\text{-}R_{10}$;

R_4 = H, $C_{1\text{-}4}$alkyl, aryl$C_{1\text{-}4}$alkyl, functionalized C_1-C_6alkyl including morpholino-C_1-C_6alkyl, pyrrolidino-C_1-C_6alkyl, N-methylpiperazino-C_1-C_6alkyl, C_6-C_{10}aryl including *o*-methoxyphenyl (guaiacol ester), C_1-C_6acyloxymethyl, C_1-C_6acyloxy-1-ethyl, C_1-C_6alkoxycarbonyloxymethyl, C_1-C_6alkoxycarbonyloxy-1-ethyl, or (oxodioxolyl)methyl;

R_3 = H; R_2 = R_5; and

R_5= R_7 = benzoheteroaryl substituted with at least one or more groups selected from: COOR4, (CH2)nCOOR4, SO3H, (CH2)nSO3H, OR4, azoles [5-membered N-containing heterocycles], or fluorine;

or wherein said compound is selected form the group consisting of:

2-(4-Carboxy-2,5-dihydroxyphenyl)-1H-benzo[d]imidazole-4-carboxylic acid;

Methyl 2-(4-ethoxycarbonyl-2,5-dihydroxyphenyl)-1H-benzo[d]imidazole-4-carboxylate;

2-(2,5-Dihydroxy-4-sulfophenyl)-1H-benzo[d]imidazole-4-carboxylic acid;

2-(4-Carboxy-2,5-dihydroxyphenyl)-1H-benzo[d]imidazole-5-carboxylic acid;

2-(2,5-Dihydroxy-4-sulfophenyl)-1H-benzo[d]imidazole-5-carboxylic acid;

2-(3-Carboxy-2,5-dihydroxyphenyl)-1H-benzo[d]imidazole-4-carboxylic acid;

2-(2,5-Dihydroxy-3-sulfophenyl)-1H-benzo[d]imidazole-4-carboxylic acid;

2-(3-Carboxy-2,5-dihydroxyphenyl)-1H-benzo[d]imidazole-5-carboxylic acid;

2-(2,5-Dihydroxy-3-sulfophenyl)-1H-benzo[d]imidazole-5-carboxylic acid;

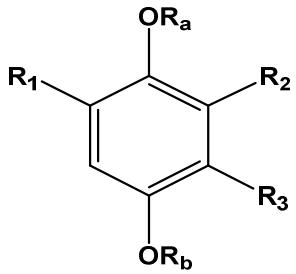
2-(4-(Carboxymethyl)-2,5-dihydroxyphenyl)-1H-benzo[d]imidazole-4-carboxylic acid;

2-(4-(Carboxymethyl)-2,5-dihydroxyphenyl)-1H-benzo[d]imidazole-5-carboxylic acid;

2-(3-(Carboxymethyl)-2,5-dihydroxyphenyl)-1H-benzo[d]imidazole-4-carboxylic acid; and

2-(3-(Carboxymethyl)-2,5-dihydroxyphenyl)-1H-benzo[d]imidazole-5-carboxylic acid.

~~12~~14. A compound of formula (I):



(I)

wherein:

R_a, R_b = H, $C_{1\text{-}4}$acyl, aryl$C_{1\text{-}4}$alkyl, C_6-C_{10}arylCO, HOOC$(CH_2)_n$CO, C_1-C_7alkylNHCO, phosphono, phosphonooxymethyl, C_1-C_6acyloxymethyl, C_1-C_6acyloxy-1-ethyl, C_1-C_6alkoxycarbonyloxymethyl, or C_1-C_6alkoxycarbonyloxy-1-ethyl;

R_1 = $COOR_4$, $(CH_2)_nCOOR_4$, SO_3H, $(CH_2)_nSO_3H$, or CONH-$R_{10;}$

R_2 and R_3 are H or R_5, with the proviso that when one of R_2 and R_3 is R_5, the other is H and when one of R_2 and R_3 is H, the other is R_5;

R_4 = H, $C_{1\text{-}4}$alkyl, aryl$C_{1\text{-}4}$alkyl, functionalized C_1-C_6alkyl including morpholino-C_1-C_6alkyl, pyrrolidino-C_1-C_6alkyl, N-methylpiperazino-C_1-C_6alkyl, C_6-C_{10}aryl including *o*-methoxyphenyl (guaiacol ester), C_1-C_6acyloxymethyl, C_1-C_6acyloxy-1-ethyl, C_1-C_6alkoxycarbonyloxymethyl, C_1-C_6alkoxycarbonyloxy-1-ethyl, or (oxodioxolyl)methyl;

R_5 = R_8

R_8 = $(CH_2)_mX(CH_2)_pR_9$;

X = O, S, SO_2, NH, NAc, or $N(CH_2)_qR_9$;

R_9 = aryl, heteroaryl, substituted with at least one or more groups selected from $COOR_4$, $(CH_2)_nCOOR_4$, $(CH_2)_nSO_3H$, OR_4, SO_3H, azoles [5-membered N-containing heterocycles], fluorine, C=O, or NHCO-R_{10};

R_{10} = aryl, heteroaryl, substituted with at least one or more groups selected from $COOR_4$, $(CH_2)_nCOOR_4$, $(CH_2)_nSO_3H$, OR_4, SO_3H, azoles [5-membered N-containing heterocycles], or fluorine;

wherein the aryl of R_9 an R_{10} is an aromatic group containing from 6 to 14 carbon atoms, selected among phenyl, naphthyl, or biphenyl group; and

the heteroaryl R_9 an R_{10} is an aromatic group containing 1 to 14 carbon atoms and one or more nitrogen; and

n, m, p and q are an integer independently equal to 1-4.

~~13~~15. The compound according to claim 1~~2~~4, wherein:

(A)

R_a, R_b = H, $C_{1\text{-}4}$acyl, aryl$C_{1\text{-}4}$alkyl, C_6-C_{10}arylCO, $HOOC(CH_2)_nCO$, C_1-C_7alkylNHCO, phosphono, phosphonooxymethyl, C_1-C_6acyloxymethyl, C_1-C_6acyloxy-1-ethyl, C_1-C_6alkoxycarbonyloxymethyl, or C_1-C_6alkoxycarbonyloxy-1-ethyl;

R_1 = $COOR_4$, $(CH_2)_nCOOR_4$, SO_3H, $(CH_2)_nSO_3H$, CONH-R_{10};

R_4 = H, $C_{1\text{-}4}$alkyl, aryl$C_{1\text{-}4}$alkyl, functionalized C_1-C_6alkyl including morpholino-C_1-C_6alkyl, pyrrolidino-C_1-C_6alkyl, N-methylpiperazino-C_1-C_6alkyl, C_6-C_{10}aryl including *o*-methoxyphenyl (guaiacol ester), C_1-C_6acyloxymethyl, C_1-C_6acyloxy-1-ethyl, C_1-C_6alkoxycarbonyloxymethyl, C_1-C_6alkoxycarbonyloxy-1-ethyl, or (oxodioxolyl)methyl;

R_2 = H; R_3 = R_5; and

R_5 = R_8 = $(CH_2)_mX(CH_2)pR_9$;

wherein X = O, S, SO_2, NH, NAc, or $N(CH_2)_qR_9$;

or

(B)

R_a, R_b = H, C_{1-4}acyl, arylC_{1-4}alkyl, C_6-C_{10}arylCO, HOOC$(CH_2)_n$CO, C_1-C_7alkylNHCO, phosphono, phosphonooxymethyl, C_1-C_6acyloxymethyl, C_1-C_6acyloxy-1-ethyl, C_1-C_6alkoxycarbonyloxymethyl, or C_1-C_6alkoxycarbonyloxy-1-ethyl;

R1 = $COOR_4$, (CH_2)nCOOR4, SO3H, $(CH_2)_nSO_3H$, CONH-R_{10};

R_4 = H, C_{1-4}alkyl, arylC_{1-4}alkyl, functionalized C_1-C_6alkyl including morpholino-C_1-C_6alkyl, pyrrolidino-C_1-C_6alkyl, N-methylpiperazino-C_1-C_6alkyl, C_6-C_{10}aryl including *o*-methoxyphenyl (guaiacol ester), C_1-C_6acyloxymethyl, C_1-C_6acyloxy-1-ethyl, C_1-C_6alkoxycarbonyloxymethyl, C_1-C_6alkoxycarbonyloxy-1-ethyl, or (oxodioxolyl)methyl;

R_3 = H; R_2 = R_5; and

R_5 = R_8 = $(CH_2)_mX(CH_2)_pR_9$;

wherein X = O, S, SO_2, NH, NAc, or $N(CH_2)_qR_9$;

or wherein said compound is selected form the group consisting of:

Bis(4-carboxy-2,5-dihydroxyphenylmethyl)amine;

4-((2,5-Dihydroxy-4-sulfophenylmethylamino)methyl)-2,5-dihydroxybenzoic acid;

4-((2,5-Dihydroxy-3-sulfophenylmethylamino)methyl)-2,5-dihydroxybenzoic acid;

Bis(2,5-dihydroxy-4-sulfophenylmethyl)amine;

N,N-Bis(4-carboxy-2,5-dihydroxyphenylmethyl)acetamide;

N-(2,5-dihydroxy-4-sulfophenylmethyl) N-(4-carboxy-2,5-dihydroxyphenylmethyl)acetamide;

N-(2,5-dihydroxy-3-sulfophenylmethyl) N-(4-carboxy-2,5-dihydroxyphenylmethyl)acetamide;

N,N-Bis(2,5-dihydroxy-4-sulfophenylmethyl)acetamide;

4-((2,5-Dihydroxy-4-carboxyphenyl)methylthiomethyl)-2,5-dihydroxybenzoic acid;

4-((2,5-Dihydroxy-4-sulfophenyl)methylthiomethyl)-2,5-dihydroxybenzoic acid;

4-((2,5-Dihydroxy-3-sulfophenyl)methylthiomethyl)-2,5-dihydroxybenzoic acid;

4-((2,5-Dihydroxy-4-sulfophenyl)methylthiomethyl)-2,5-dihydroxybenzenesulfonic acid;

4-((2,5-Dihydroxy-4-carboxyphenyl)methylsulfonylmethyl)-2,5-dihydroxybenzoic acid;

4-((2,5-Dihydroxy-4-sulfophenyl)methylsulfonylmethyl)-2,5-dihydroxybenzoic acid;

4-((2,5-Dihydroxy-3-sulfophenyl)methylsulfonylmethyl)-2,5-dihydroxybenzoic acid;

4-((2,5-Dihydroxy-4-sulfophenyl)methylsulfonylmethyl)-2,5-dihydroxybenzenesulfonic acid;

4-((2,5-Dihydroxy-4-carboxyphenyl)methoxymethyl)-2,5-dihydroxybenzoic acid;

4-((2,5-dihydroxy-4-sulfophenyl)methoxymethyl)-2,5-dihydroxybenzoic acid;

4-((2,5-dihydroxy-3-sulfophenyl)methoxymethyl)-2,5-dihydroxybenzoic acid;

4-((2,5-Dihydroxy-4-sulfophenyl)methoxymethyl)-2,5-dihydroxybenzenesulfonic acid;

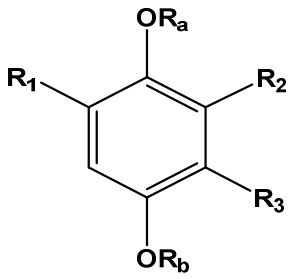
Tris (4-carboxy-2,5-dihydroxyphenylmethyl)amine;

Tris (4-ethoxycarbonyl-2,5-dihydroxyphenylmethyl)amine;

Bis(3-carboxy-2,5-dihydroxyphenylmethyl)amine;

3-((2,5-Dihydroxy-3-sulfophenylmethylamino)methyl)-2,5-dihydroxybenzoic acid;
3-((2,5-Dihydroxy-4-sulfophenylmethylamino)methyl)-2,5-dihydroxybenzoic acid;
Bis(2,5-dihydroxy-3-sulfophenylmethyl)amine;
N,N-Bis(3-carboxy-2,5-dihydroxyphenylmethyl)acetamide;
N-(2,5-dihydroxy-3-sulfophenylmethyl) N-(3-carboxy-2,5-dihydroxyphenylmethyl)acetamide;
N-(2,5-dihydroxy-4-sulfophenylmethyl) N-(3-carboxy-2,5-dihydroxyphenylmethyl)acetamide;
N,N-Bis(2,5-dihydroxy-3-sulfophenylmethyl)acetamide;
3-((2,5-Dihydroxy-3-carboxyphenyl)methylthiomethyl)-2,5-dihydroxybenzoic acid;
3-((2,5-Dihydroxy-3-sulfophenyl)methylthiomethyl)-2,5-dihydroxybenzoic acid;
3-((2,5-Dihydroxy-4-sulfophenyl)methylthiomethyl)-2,5-dihydroxybenzoic acid;
3-((2,5-Dihydroxy-3-sulfophenyl)methylthiomethyl)-2,5-dihydroxybenzenesulfonic acid;
3-((2,5-Dihydroxy-3-carboxyphenyl)methylsulfonylmethyl)-2,5-dihydroxybenzoic acid;
3-((2,5-Dihydroxy-3-sulfophenyl)methylsulfonylmethyl)-2,5-dihydroxybenzoic acid;
3-((2,5-Dihydroxy-4-sulfophenyl)methylsulfonylmethyl)-2,5-dihydroxybenzoic acid;
3-((2,5-Dihydroxy-3-sulfophenyl)methylsulfonylmethyl)-2,5-dihydroxybenzenesulfonic acid;
3-((2,5-Dihydroxy-3-carboxyphenyl)methoxymethyl)-2,5-dihydroxybenzoic acid;
3-((2,5-dihydroxy-3-sulfophenyl)methoxymethyl)-2,5-dihydroxybenzoic acid;
3-((2,5-dihydroxy-4-sulfophenyl)methoxymethyl)-2,5-dihydroxybenzoic acid;
3-((2,5-Dihydroxy-3-sulfophenyl)methoxymethyl)-2,5-dihydroxybenzenesulfonic acid;
Methyl 3-((2,5-diacetoxy-3-methoxycarbonylphenyl)methylsulfonylmethyl)-2,5-diacetoxybenzoate;
Methyl 3-((2,5-dihydroxy-3-methoxycarbonylphenyl)methylsulfonylmethyl)-2,5-hydroxybenzoate;
2-Morpholinoethyl 3-((2,5-dihydroxy-3-(2-morpholinoethoxycarbonyl)phenyl)methylsulfonylmethyl)-2,5-hydroxybenzoate;
Tris (3-carboxy-2,5-dihydroxyphenylmethyl)amine; and
Tris (3-ethoxycarbonyl-2,5-dihydroxyphenylmethyl)amine.

~~14~~16. The compound according to claim 2, having the formula (I):



(I)

wherein:

R_a, R_b = H;

R1 = $COOR_4$;

R_2 = H;

R_3 = R_8;

R_4 = H;

R_8 = $(CH_2)_mX(CH_2)_pR_9$;

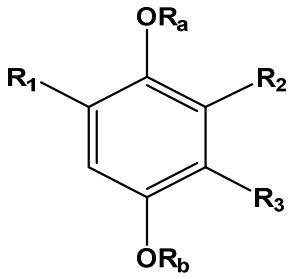
R_9 = phenyl substituted with $COOR_4$ and with OR_4;

X = $N(CH_2)_qR_9$; and

m, p and q = 1; and

wherein said compound is Tris (4-carboxy-2,5-dihydroxyphenylmethyl)amine.

17. The compound according to claim 2, having the formula (I):



(I)

wherein:

R_a, R_b = H;

R_1 = $COOR_4$;

R_2 = $(CH_2)_mX(CH_2)_pR_9$

R_3 = H;

R_9 = phenyl substituted with $COOR_4$ and with OR_4;

R_4 = H;

X = SO_2; and

m and p = 1;

and said compound is 3-((2,5-Dihydroxy-3-carboxyphenyl)methylsulfonylmethyl)-2,5-dihydroxybenzoic acid.

18. A pharmaceutical composition comprising a therapeutically effective amount of the compound according to any one of claims 1-~~13~~ 17 or a pharmaceutically acceptable salt, or stereoisomer thereof, and a pharmaceutically acceptable excipient.

~~15~~19. Use of ~~A~~a compound according to any one of the claims 1-~~13~~ 17 in the manufacture of pharmaceutical composition for ~~use in a method of~~ treating and/or preventing autoimmune, immunological, rheumatology, vascular disorders, ophthalmologic disorders, fibrotic disorders, metabolic and gastro-intestinal disorders, neuroinflammatory and neurodegenerative diseases, neoplasms and cancer associated disorders, hormone related diseases, or immunological disorders resulting from viral and/or bacterial infectious diseases and/or complications thereof.

20. Intermediates in the synthesis of compounds according to claim 2, said intermediates being chosen among 2,5-bis(benzyloxy)-4-(ethoxycarbonyl)benzoic acid; 2,5-bis(benzyloxy)isophthalaldehyde; 2,5-bis(benzyloxy)isophthalic acid; ethyl 2,5-bis(benzyloxy)-4-(hydroxymethyl)benzoate; or 2,5-bis(benzyloxy)-3-(hydroxymethyl)benzoate.