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(54) **Titre : FLUIDE THERAPEUTIQUE PERITONEAL**
(54) **Title: PERITONEAL THERAPEUTIC FLUID**

(57) **Abrégé/Abstract:**

Described is peritoneal therapeutic fluid comprising one or more of a biocompatibility enhancing agent (BCA) that is selected from the group consisting of a polyphenolic compound, a metabolite of a polyphenolic compound which is obtained by metabolization in the human or animal body, a salt of a polyphenolic compound, a glycoside of a polyphenolic compound, polyethylene glycol (PEG), or a derivative of a polyethylene glycol. The peritoneal therapeutic fluid may be obtained by metabolization in the human or animal body, a salt or a glycoside of a polyphenolic compound. The peritoneal therapeutic fluid may be used as a peritoneal dialysis fluid, or as a peritoneal therapeutic fluid with decreased cytotoxicity on human peritoneal mesothelial cells.

ABSTRACT

Described is peritoneal therapeutic fluid comprising one or more of a biocompatibility enhancing agent (BCA) that is selected from the group consisting of a polyphenolic compound, a metabolite of a polyphenolic compound which is obtained by metabolization in the human or animal body, a salt of a polyphenolic compound, a glycoside of a polyphenolic compound, polyethylene glycol (PEG), or a derivative of a polyethylene glycol. The peritoneal therapeutic fluid may be obtained by metabolization in the human or animal body, a salt or a glycoside of a polyphenolic compound. The peritoneal therapeutic fluid may be used as a peritoneal dialysis fluid, or as a peritoneal therapeutic fluid with decreased cytotoxicity on human peritoneal mesothelial cells.

Peritoneal therapeutic fluid

The present invention relates to a peritoneal therapeutic fluid showing increased biocompatibility.

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Different peritoneal therapies encompass peritoneal nutrition, peritoneal dialysis, peritoneal detoxification in case of liver failure or drug abuse, treatment of primary and secondary peritoneal cancer, treatment of peritoneal infections and peritonitis, pre- or post-
10 operative peritoneal treatment, or simply peritoneal administration of systemic treatments. They are carried out by applying peritoneal therapy fluids to the peritoneum.

Such fluids contain active pharmaceutical ingredients (APIs) and
15 compounds to establish physiological osmotic pressure. Commonly applied compounds to achieve physiological osmotic pressure in peritoneal therapy fluids are the same as those that are used as osmotic agents in the case of dialysis, at concentrations between 0.5 and 20%, such as salts, mono- or oligo-saccharides such as glucose and glucose-oligomers
20 or other saccharides, aminoacid mono- or multimers, PEGs or proteins, derivatives and/or compositions thereof.

Peritoneal dialysis (PD) is the most common peritoneal therapy applied to patients. It is a form of dialysis, representing an alternative to
25 extra-corporal hemodialysis (HD). It has the advantage of being independent from heavy instrumentation, and can be done at home. The process uses the patient's highly capillarized peritoneum in the abdomen as a membrane across which fluids and dissolved substances (electrolytes, urea, glucose and other small molecules) are exchanged
30 from the blood. To do so, peritoneal dialysis fluid is introduced through a permanent tube in the abdomen and flushed out either every night while the patient sleeps (automatic peritoneal dialysis) or via regular exchanges throughout the day (continuous ambulatory peritoneal dialysis). The specificity of Peritoneal dialysis lies in the fact that
35 the compound(s) that establish osmotic pressure represent at the same time the active pharmaceutical ingredient(s), since the goal of peritoneal dialysis is to eliminate fluid and waste products out of the blood into the peritoneal dialysate.

Currently available peritoneal dialysis fluids (PDFs) cause cyto-toxicity due to high glucose concentration, glucose uptake from dialysate, the presence of glucose degradation products (GDPs), a low pH
5 and supra-physiologic concentrations of lactate buffer. Bacterial "by-products" (Mangram et al. 1998) and infectious complications lead to inflammatory reactions (ter Wee et al. 2007). All these side-effects lead to fibrosis of the peritoneum, decreasing its dialysis efficiency over the long term. But even in absence of infections or inflammatory
10 responses, significant fibrotic activity in the peritoneum of PD-patients may be observed (Reimold et al. 2013). In vitro studies have shown cyto-toxicity of dialysis solutions on peritoneal mesothelial cells (Ha et al. 2000), which could be attributed to high osmolality, low pH, and GDPs.

15 GDPs form during heat sterilization of glucose containing solutions. Comparable degradation products form when heating any kind of sugar containing solutions. GDP formation during heat sterilization is greatly reduced, although not completely avoided, at acidic pH. Therefore, first
20 generation PD solution are equilibrated at pH 5 to 6, since GDP generation is reduced, and such a pH may be rapidly equilibrated in the patient's peritoneum. Lowest GDP formation occurs at pH 3 to 3.5. Therefore second generation PD solutions are supplied as two compartment application, one containing a glucose solution at pH 3 to 3.5, the
25 second compartment containing salts and buffers to establish a pH neutral solution by mixing the two compartments, shortly before application to peritoneal dialysis. GDPs or comparable degradation products may form advanced glycation end products (AGEs), which are carbohydrate proteins. AGEs are thought to be a factor in aging,
30 vascular complications, diabetes mellitus and inflammation.

A way to address high glucose concentrations of PDFs is the use of maltodextrins as alternative osmotic agents to glucose. Icodextrin is such a maltodextrin derived from starch; it is a mixture of glucose
35 polymers used as a colloidal solution in PDFs. Icodextrin-containing iso-osmolar PDFs are marketed under the trade name "Extraneal" (Baxter, USA). It is supplied under acidic pH, and significant elevation in PDF levels was detected in overnight effluent of PD patients, 6 months after

the switch to icodextrin PDF (Moriishi et al. 2008).

As the prior art shows, there is still a significant need for reducing side-effects of dialysis treatments. A reduction of general cytotoxicity would potentially decrease long term fibrosis, keep the peritoneum efficacious for dialysis, and thereby prolonge average peritoneal dialysis therapy time windows in the long run.

SUMMARY OF THE INVENTION

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The present invention provides with a peritoneal therapeutic fluid and a container or kit as defined in the claims and in the following description.

15 A peritoneal therapeutic fluid is disclosed, containing one or several biocompatibility enhancing agents (BCA). BCA may be characterized by reducing human peritoneal mesothelial cell-toxicity or peritoneal cell-toxicity. The peritoneal therapeutic fluid of the present invention can be used for the aforementioned purposes and other purposes mentioned in
20 this description.

According to one particular aspect the invention relates to a peritoneal therapeutic fluid comprising one or more of a biocompatibility enhancing agent (BCA) that is selected from the group consisting of a
25 polyphenolic compound, a metabolite of a polyphenolic compound which is obtained by metabolization in the human or animal body, a salt of a polyphenolic compound, a glycoside of a polyphenolic compound,

for use as a peritoneal dialysis fluid, or as a peritoneal therapeutic fluid with decreased cytotoxicity on human peritoneal
30 mesothelial cells.

According to another particular aspect the invention relates to the use of a peritoneal therapeutic fluid comprising one or more of a biocompatibility enhancing agent (BCA) as a peritoneal dialysis fluid, or as a peritoneal therapeutic fluid with decreased cytotoxicity on human
35 peritoneal mesothelial cells, wherein the biocompatibility enhancing

agent is selected from the group consisting of a polyphenolic compound, a metabolite of a polyphenolic compound which is obtained by metabolization in the human or animal body, a salt of a polyphenolic compound, and a glycoside of a polyphenolic compound.

- 5 According to another particular aspect the invention relates to the use of a peritoneal therapeutic fluid comprising one or more of a biocompatibility enhancing agent (BCA) as a peritoneal dialysis fluid, or as a peritoneal therapeutic fluid with decreased cytotoxicity on human peritoneal mesothelial cells, wherein the biocompatibility enhancing
- 10 agent is selected from the group consisting of a polyphenolic compound, a metabolite of a polyphenolic compound which is obtained by metabolization in the human or animal body, a salt of a polyphenolic compound, and a glycoside of a polyphenolic compound wherein the one or more BCA is/are present in a concentration of between 0.05 to 20 $\mu\text{Mol/L}$.
- 15 According to another particular aspect the invention relates to the use of a peritoneal therapeutic fluid comprising one or more of a biocompatibility enhancing agent (BCA) as a peritoneal dialysis fluid, or as a peritoneal therapeutic fluid with decreased cytotoxicity on human peritoneal mesothelial cells, wherein the biocompatibility enhancing
- 20 agent is selected from the group consisting of a polyphenolic compound, a metabolite of a polyphenolic compound which is obtained by metabolization in the human or animal body, a salt of a polyphenolic compound, and a glycoside of a polyphenolic compound, wherein the peritoneal therapeutic fluid comprises one or more of a saccharide, wherein the saccharide is
- 25 fructose, a disaccharide, an oligosaccharide, a polysaccharide, or any mixture thereof.

- According to another particular aspect the invention relates to the use of a peritoneal therapeutic fluid comprising one or more of a biocompatibility enhancing agent (BCA) as a peritoneal dialysis fluid,
- 30 or as a peritoneal therapeutic fluid with decreased cytotoxicity on human peritoneal mesothelial cells, wherein the biocompatibility enhancing agent is selected from the group consisting of a polyphenolic compound, a metabolite of a polyphenolic compound which is obtained by

metabolization in the human or animal body, a salt of a polyphenolic compound, and a glycoside of a polyphenolic compound, wherein the peritoneal dialysis fluid or peritoneal therapeutic fluid is used for decreasing expression of Vascular Endothelial Growth Factor (VEGF) in the
5 peritoneum.

According to another particular aspect the invention relates to the use of a peritoneal therapeutic fluid comprising one or more of a biocompatibility enhancing agent (BCA) as a peritoneal dialysis fluid, or as a peritoneal therapeutic fluid with decreased cytotoxicity on human
10 peritoneal mesothelial cells, wherein the biocompatibility enhancing agent is selected from the group consisting of a polyphenolic compound, a metabolite of a polyphenolic compound which is obtained by metabolization in the human or animal body, a salt of a polyphenolic compound, and a glycoside of a polyphenolic compound, wherein the peritoneal dialysis
15 fluid or peritoneal therapeutic fluid is used for decreasing long term fibrosis.

According to another particular aspect the invention relates to the use of a peritoneal therapeutic fluid comprising one or more of a biocompatibility enhancing agent (BCA) as a peritoneal dialysis fluid,
20 or as a peritoneal therapeutic fluid with decreased cytotoxicity on human peritoneal mesothelial cells, wherein the biocompatibility enhancing agent is selected from the group consisting of a polyphenolic compound, a metabolite of a polyphenolic compound which is obtained by metabolization in the human or animal body, a salt of a polyphenolic
25 compound, and a glycoside of a polyphenolic compound, wherein the peritoneal fluid is used in a peritoneal therapy which is selected from the group consisting of peritoneal nutrition, peritoneal detoxification in case of liver failure or drug abuse, treatment of primary and secondary peritoneal cancer, treatment of peritoneal infections and
30 peritonitis, and pre- or post-operative peritoneal treatment.

According to another particular aspect the invention relates to a peritoneal therapeutic fluid comprising one or more of a biocompatibility enhancing agent (BCA) that is selected from the group consisting of a polyphenolic compound, a metabolite of a polyphenolic compound which is

obtained by metabolization in the human or animal body, a salt of a polyphenolic compound, and a glycoside of a polyphenolic compound,

for use as a peritoneal dialysis fluid, or as a peritoneal therapeutic fluid with decreased cytotoxicity on human peritoneal mesothelial cells,

wherein the one or more BCA is/are present in a concentration of between 0.05 to 20 $\mu\text{Mol/L}$.

According to another particular aspect the invention relates to a peritoneal therapeutic fluid comprising one or more of a biocompatibility enhancing agent (BCA) that is selected from the group consisting of a polyphenolic compound, a metabolite of a polyphenolic compound which is obtained by metabolization in the human or animal body, a salt of a polyphenolic compound, and a glycoside of a polyphenolic compound,

for use as a peritoneal dialysis fluid, or as a peritoneal therapeutic fluid with decreased cytotoxicity on human peritoneal mesothelial cells,

wherein the peritoneal therapeutic fluid comprises one or more of a saccharide, wherein the saccharide is fructose, a disaccharide, an oligosaccharide, a polysaccharide, or any mixture thereof.

According to another particular aspect the invention relates to a peritoneal therapeutic fluid comprising one or more of a biocompatibility enhancing agent (BCA) that is selected from the group consisting of a polyphenolic compound, a metabolite of a polyphenolic compound which is obtained by metabolization in the human or animal body, a salt of a polyphenolic compound, and a glycoside of a polyphenolic compound,

for use as a peritoneal dialysis fluid, or as a peritoneal therapeutic fluid with decreased cytotoxicity on human peritoneal mesothelial cells,

wherein the peritoneal dialysis fluid or peritoneal therapeutic fluid is used for decreasing expression of Vascular Endothelial Growth Factor (VEGF) in the peritoneum.

According to another particular aspect the invention relates to a peritoneal therapeutic fluid comprising one or more of a biocompatibility

enhancing agent (BCA) that is selected from the group consisting of a polyphenolic compound, a metabolite of a polyphenolic compound which is obtained by metabolization in the human or animal body, a salt of a polyphenolic compound, and a glycoside of a polyphenolic compound,

5 for use as a peritoneal dialysis fluid, or as a peritoneal therapeutic fluid with decreased cytotoxicity on human peritoneal mesothelial cells,

 wherein the peritoneal dialysis fluid or peritoneal therapeutic fluid is used for decreasing long term fibrosis.

10 According to another particular aspect the invention relates to a peritoneal therapeutic fluid comprising one or more of a biocompatibility enhancing agent (BCA) that is selected from the group consisting of a polyphenolic compound, a metabolite of a polyphenolic compound which is obtained by metabolization in the human or animal body, a salt of a
15 polyphenolic compound, and a glycoside of a polyphenolic compound,

 for use as a peritoneal dialysis fluid, or as a peritoneal therapeutic fluid with decreased cytotoxicity on human peritoneal mesothelial cells,

 wherein the peritoneal fluid is used in a peritoneal therapy which is
20 selected from the group consisting of peritoneal nutrition, peritoneal detoxification in case of liver failure or drug abuse, treatment of primary and secondary peritoneal cancer, treatment of peritoneal infections and peritonitis, and pre- or post-operative peritoneal treatment.

25 Preferred BCAs are polyphenolic compounds or derivatives of polyphenolic compounds.

 Particularly suitable polyphenolic compounds are Resveratrol and Piceid
30 (Polydatin). Particularly these compounds show a cell-viability increasing effect, rescuing human peritoneal mesothelial cells (HPMC) from PDF induced cytotoxicity.

 The present invention provides a peritoneal therapeutic fluid comprising
35 one or more BCAs, selected from the group consisting of a polyphenolic

compound, a metabolite of a polyphenolic compound which is obtained by metabolization in the human or animal body, a salt of a polyphenolic compound, preferably a pharmaceutically acceptable salt, or a glycoside of a polyphenolic compound or a derivative of such compounds.

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Further BCAs according to the invention are polyethylene glycol (PEG), or a derivative of a polyethylene glycol, such as mPEG.

Some derivatives are specified on the example of resveratrol. A salt of a polyphenolic compound is obtained by deprotonation of a polyphenolic compound at one or more phenolic hydroxy-groups.

5

Aforementioned BCA is also called a "cytotoxicity reducing compound", a "cytotoxicity reducing agent" or a "cell-toxicity reducing compound", or simply "a (first) compound". So, in the present claims, the BCA can also be called a "compound". The term "cytotoxicity reducing" and "cell-toxicity reducing" were explained in more detail above in connection with the term BCA. "Cytotoxicity reducing" preferably means that a peritoneal therapeutic fluid of the invention shows lower cytotoxicity than a peritoneal therapeutic fluid not comprising the cytotoxicity reducing compound of the invention, and preferably having the same composition of other ingredients as the PTF of the invention. Particularly, a peritoneal therapeutic fluid of the invention shows higher viability of cells, preferably of human peritoneal mesothelial cells, in comparison to a peritoneal therapeutic fluid not comprising the cytotoxicity reducing compound of the invention.

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A preferred glycoside is a glucoside. In a glucoside, a glucose moiety is bound to the polyphenolic compound, preferably via a hydroxyl group.

The BCA, particularly a polyphenolic compound, in the peritoneal therapeutic fluid may be selected from the group of stilbenoids, phenolic acids, and flavonoids.

Stilbenoids are naturally occurring substances corresponding to the structure C6-C2-C6, preferably polyphenols or polyphenol derivatives, belonging to the family of phenylpropanoids. Well studied Stilbenes are resveratrol (trans-3,5,4'-trihydroxystilbene), pinosylvine, piceatannol, pterostilbene, and a glycoside, piceid (resveratrol-3-O- β -mono-D-glucoside, also named as trans-3,5,4'-trihydroxystilbene-3-O- β -D-glucopyranoside).

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In a specific embodiment, the BCA, preferably the polyphenolic compound, is selected from resveratrol, a resveratrol derivative, dihydro-resveratrol, and a glycoside thereof, such as astringin, piceid

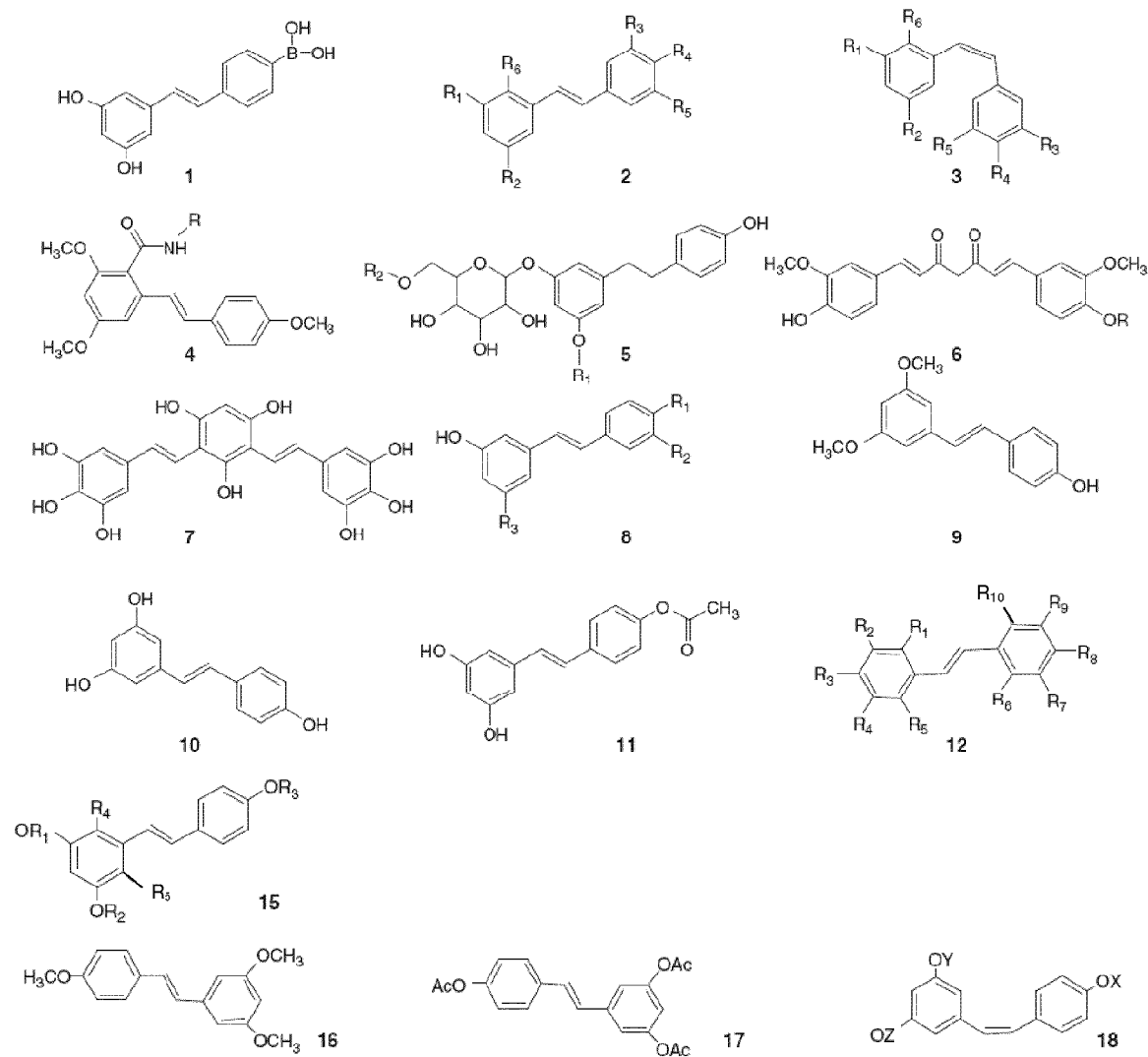
(polydatin), piceatannol, pterostilbene, piceid glucoside. These compounds are specific, but non limiting examples for stilbenoides. In piceid glucoside, at least one further glucose moiety is bound to resveratrol via another hydroxyl group, i.e. the 5-hydroxylgroup and/or
5 the 4'-hydroxylgroup of piceid.

In a further specific embodiment, the BCA, preferably the polyphenolic compound, is caffeic acid, which is a specific, but non limiting example for a phenolic acid.
10

In a further specific embodiment, the BCA, preferably the polyphenolic compound, is selected from luteolin or delphinidin, which are specific, but non limiting examples for a flavonoid.

15 Resveratrol derivatives are for example described in John M Pezzuto et al., Resveratrol derivatives: a patent review (2009 -- 2012), Expert Opin. Ther. Patents (2013) 23(12).

A resveratrol-derivative may be selected from the following compounds:
20



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wherein in compound 2 and compound 3

$R_1 = R_2 = R_4 = OH, R_3 = R_5 = R_6 = H$; or

10 $R_1 = R_2 = R_4 = OCH_3, R_3 = R_5 = R_6 = H$; or

$R_1 = R_2 = R_4 = OCH_3, R_3 = R_5 = H, R_6 = OH$; or

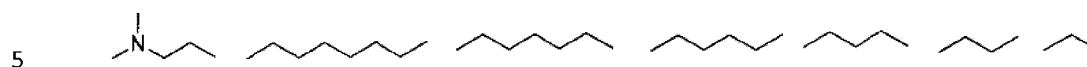
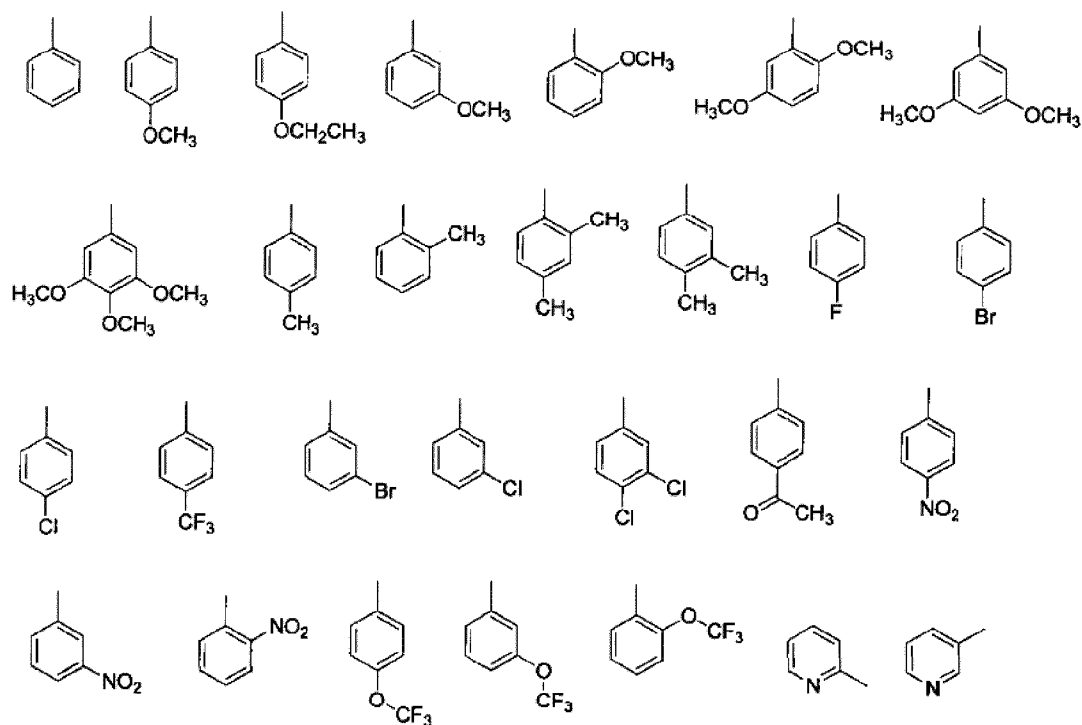
$R_1 = R_2 = R_3 = R_5 = OCH_3, R_4 = R_6 = H$; or

$R_1 = R_2 = R_3 = R_5 = OCH_3, R_4 = H, R_6 = OH$; or

$R_1 = R_2 = R_3 = R_4 = OCH_3, R_5 = R_6 = H$; or

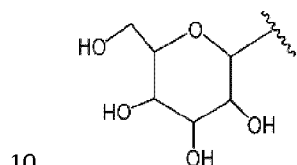
R1 = R2 = R3 = R4 = OCH₃, R5 = H, R6 = OH.

wherein in compound 4 R is one of the following moieties:



wherein in compound 5

R1 is hydrogen or a group of formula

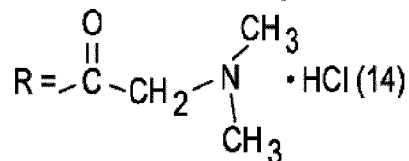
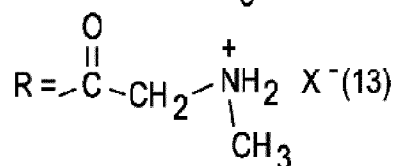
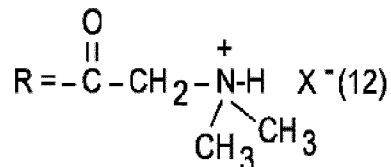
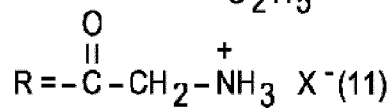
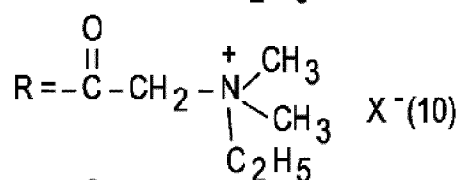
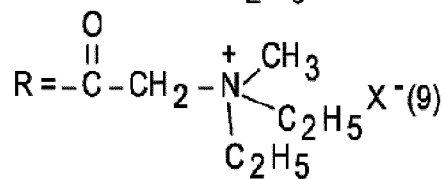
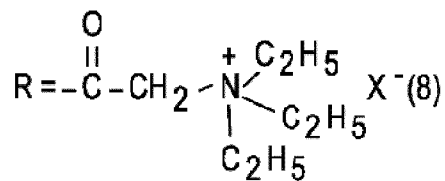
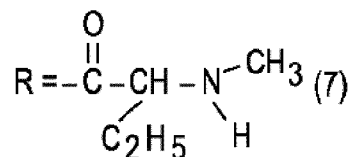
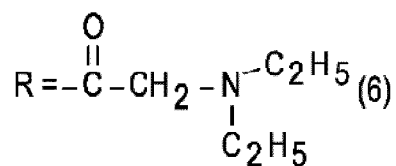
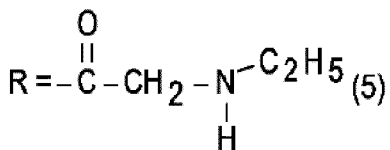
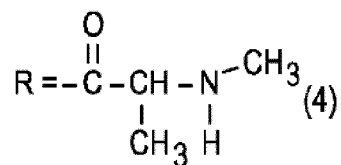
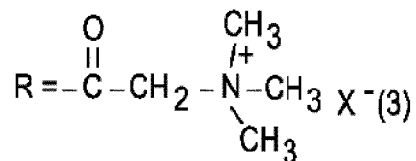
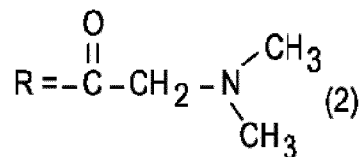
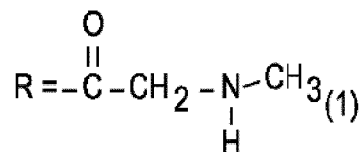


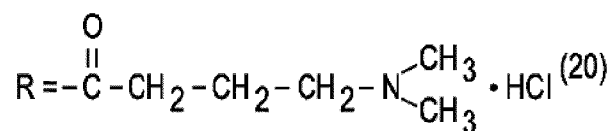
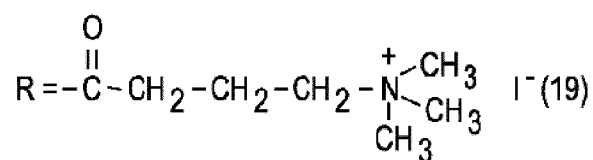
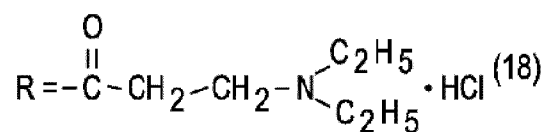
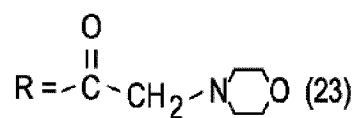
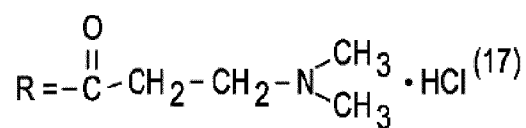
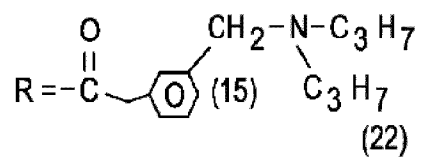
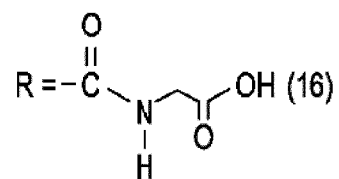
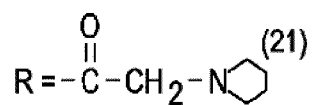
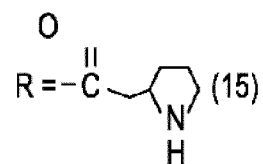
R2 is hydrogen or forms together with the oxygen to which it is bound an acyl group (-OCO-R3), wherein R3 is a C1-C22 alkyl group or a C2-C22 alkenyl group,

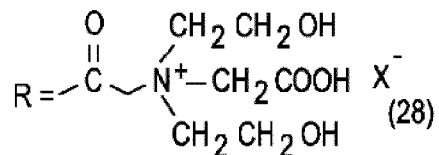
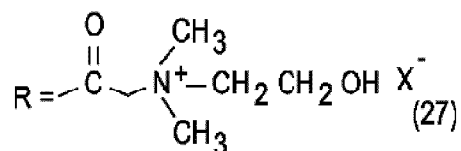
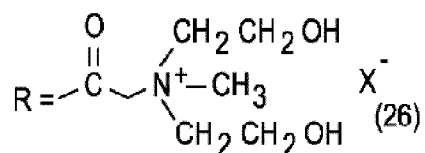
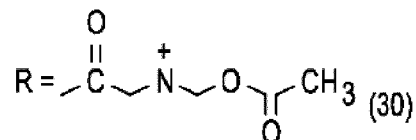
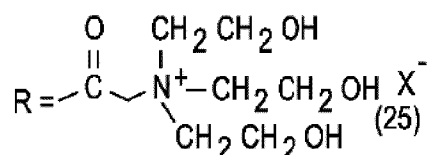
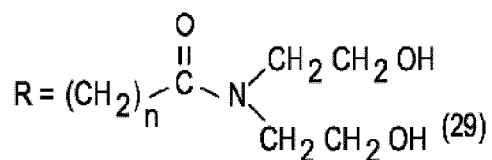
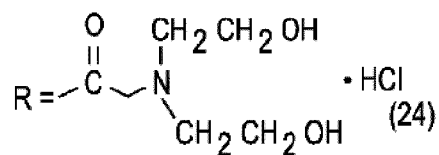
wherein, if R2 is hydrogen R1 forms a group of above-shown formula,

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wherein in compound 6, R is one of the following moieties:







wherein X^- is a free soluble anion;

5 wherein in compound 8

$\text{R1} = \text{OCH}_3$, $\text{R2} = \text{OH}$, $\text{R3} = \text{O-Glucose}$; or

$\text{R1} = \text{OCH}_3$, $\text{R2} = \text{H}$, $\text{R3} = \text{O-Glucose}$; or

$\text{R1} = \text{OCH}_3$, $\text{R2} = \text{OH}$, $\text{R3} = \text{OH}$; or

$\text{R1} = \text{OCH}_3$, $\text{R2} = \text{H}$, $\text{R3} = \text{OH}$; or

10 $\text{R1} = \text{OH}$, $\text{R2} = \text{OH}$, $\text{R3} = \text{O-Glucose}$; or

$\text{R1} = \text{OH}$, $\text{R2} = \text{OH}$, $\text{R3} = \text{OH}$;

wherein in compound 12

R1 , R2 , R3 , R4 , R5 , R6 , R7 , R8 , R9 , and R10 are independently chosen

15 from hydrogen, hydroxyl, hydrocarbyl, substituted hydrocarbyl,

hydrocarbyloxy, substituted hydrocarbyloxy, and sulfoxy; provided that at least one of the R groups is a hydroxyl or substituted hydroxyl group; and provided that if compound 12 is monomeric, then compound 12 is other than resveratrol,

5

wherein in compound 15

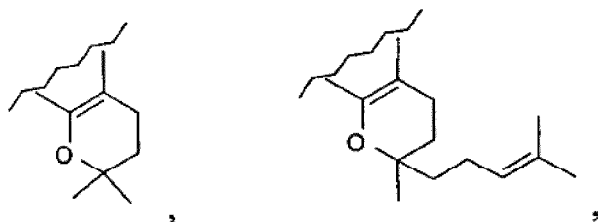
R1, R2 and R3, independently from one another, represent H or (C1-C3)alkyl; R4 and R5 are identical or different and represent hydrogen, linear or branched (C1-C5)alkyl,

10

a prenyl group $-\text{CH}_2-\text{CH}=\text{C}(\text{CH}_3)_2$,

a geranyl group $-\text{CH}_2-\text{CH}=\text{C}(\text{CH}_3)(\text{CH}_2)_2\text{CH}=\text{C}(\text{CH}_3)_2$

or R4 and R1, and independently R5 and R2, together with the atoms they are linked to, form one of the following groups:



15

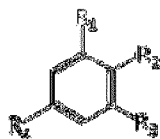
with the provisos that R4 and R5 are not both hydrogen and that when $\text{R}_1=\text{R}_2=\text{R}_3=\text{H}$, R4 and R5 are not a prenyl group and hydrogen, respectively,

wherein in compound 18 X, Y, and Z are either hydrogen or a protective group, provided that at least one of X, Y, and Z is the protective

20

group.

A BCA may be a compound of formula 19:

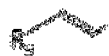


19

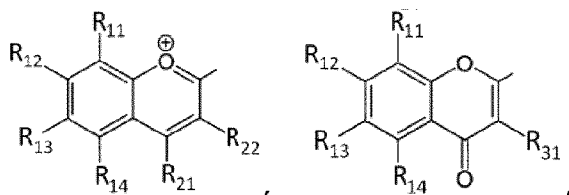
25

wherein in compound 19

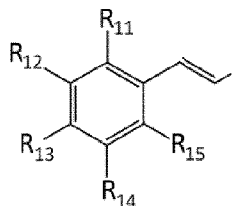
R4 is selected from one of the following groups



, which is a suitable group to constitute a phenolic acid,



which are suitable groups to constitute a flavonoid,



or , which is a suitable group to constitute a stilbenoid or a stilbenoid derivative,

wherein at least 2 of R1, R2, R3, R12, and R14 are -OH,

wherein R1, R2, R3, R5, R11, R12, R13, R14, R15, R21, R22 and R31 are independently from each other selected from

-H, -OH, -O-R_{Alk}, -CHO, -COR_{Alk}, -COOH, -COO-R_{Alk}, -CO-NH-C_nH_{2n}-COOH, -CO-NH-C_nH_{2n}-COO⁻,

-CN, -Cl, -Br, -I, -NO₂,

-C_nH_{2n}CN, -C_nH_{2n}-Cl, -C_nH_{2n}-Br, -C_nH_{2n}-I, -C_nH_{2n}-NO₂,

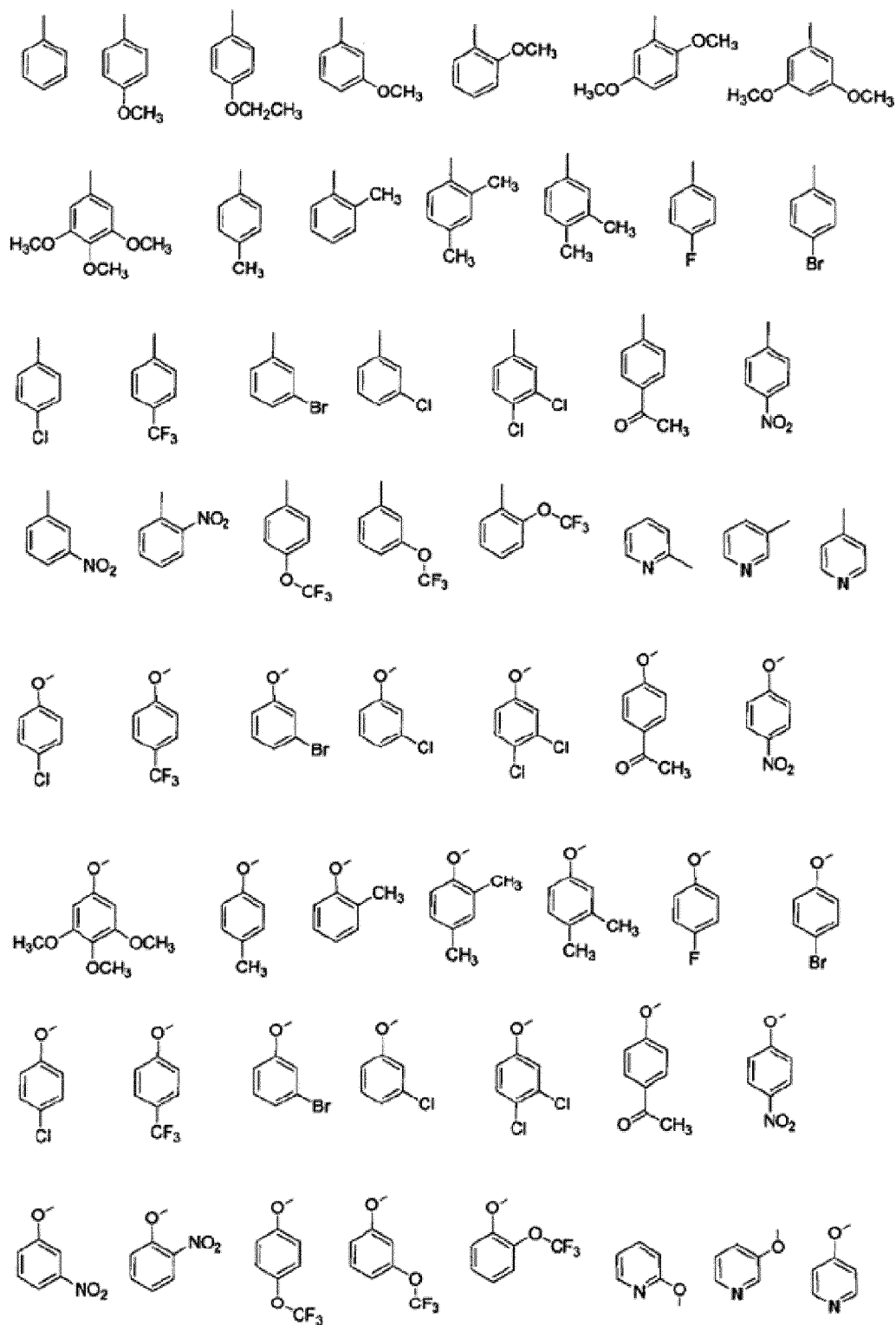
-O-PO₃²⁻, -O-PO₃H⁻, -O-PO₃H₂, -NH₂, -NHR_{Alk}, -NR_{Alk1}R_{Alk2}, -N⁺H₃, -N⁺H₂R_{Alk}, -N⁺HR_{Alk1}R_{Alk2}, -N⁺R_{Alk1}R_{Alk2}R_{Alk3},

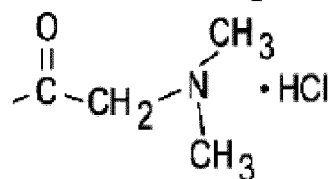
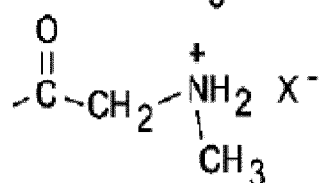
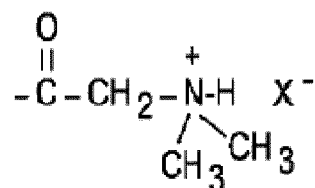
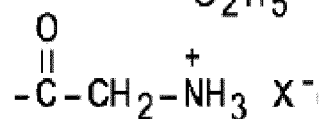
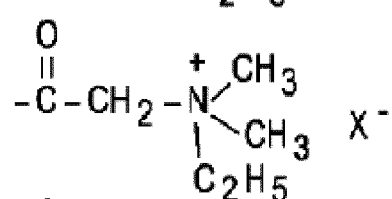
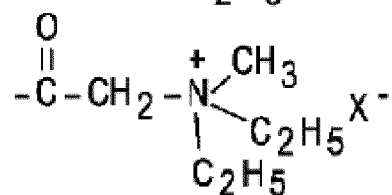
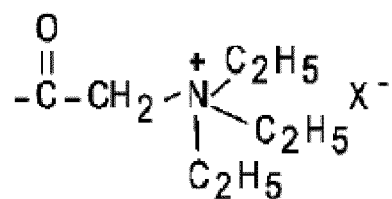
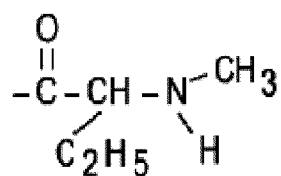
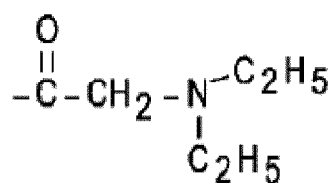
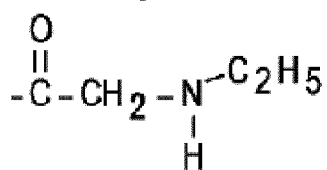
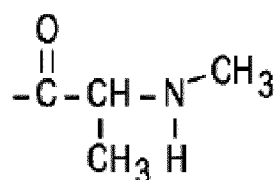
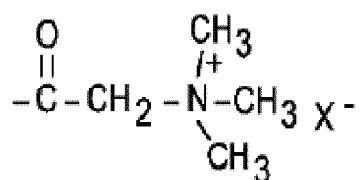
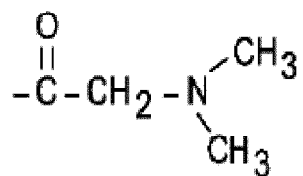
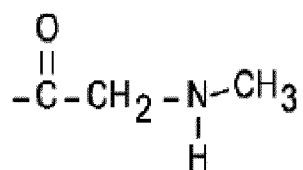
-B(OH)₂, -OCHO, -O-COR_{Alk}, -OCF₃, -O-CN, -OCH₂CN,

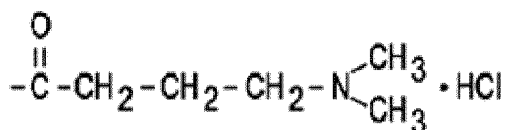
wherein R_{Alk}, R_{Alk1}, R_{Alk2}, and R_{Alk3} are alkyl residues which are independently selected from each other, preferably CH₃, C₂H₅, C₃H₇ or C₄H₉,

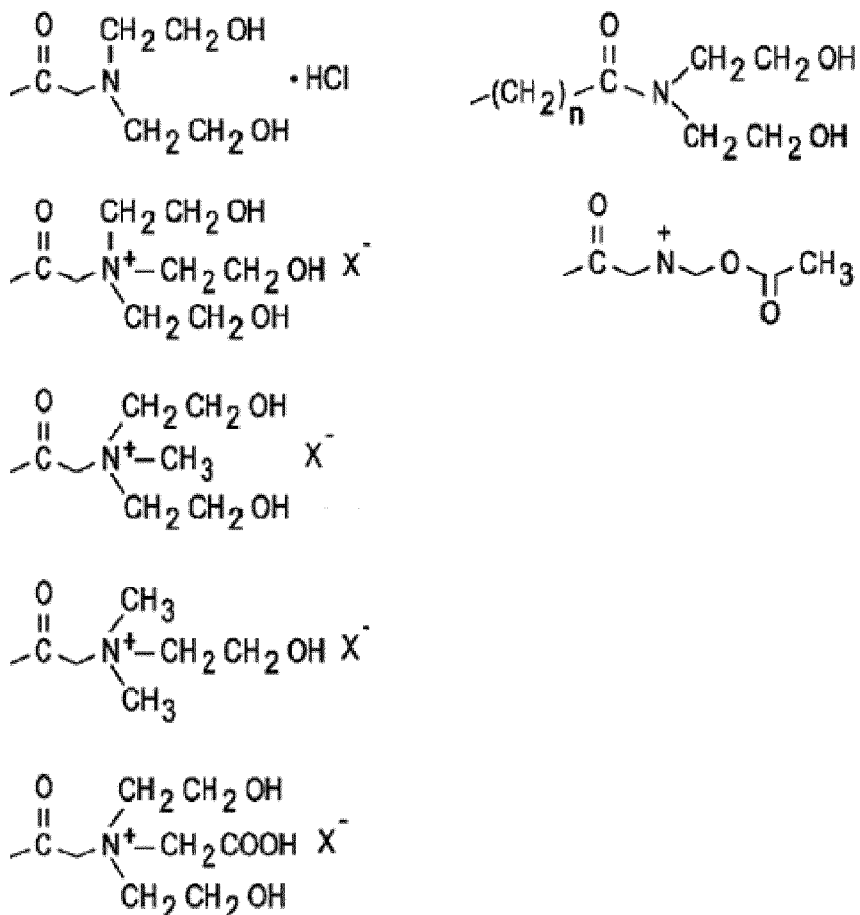
wherein in C_nH_{2n} n is an integer, and C_nH_{2n} preferably is CH₂, C₂H₄, C₃H₆, C₄H₈;

or wherein R1, R2, R3, R5, R11, R12, R13, R14, R15, R21, R22 and R31 are, independently from each other, one of the following moieties:









wherein X^- is a free soluble anion,

or wherein R_{11} , R_{12} , R_{13} , R_{14} or R_{15} are a mono or oligo saccharide-residue,

with the proviso that

at least 2 of R_1 , R_2 , R_3 , R_{11} , R_{12} , R_{13} , R_{14} and R_{15} are independently selected from $-\text{OH}$, $-\text{O}-\text{R}_{1k}$, $-\text{O}-\text{COR}_{1k}$, $-\text{OCF}_3$, $-\text{O}-\text{CN}$, and $-\text{OCHO}$.

Alternatively, at least 2 of existing R_1 , R_2 , R_3 , R_{11} , R_{12} , R_{13} , R_{14} may be $-\text{OH}$, to form a polyphenol.

Alternatively, at least one of existing R_1 , R_2 , R_3 , R_{11} , R_{12} , R_{13} , R_{14} or R_{15} may be $-\text{OH}$ to form a stilbenoid.

Alternatively, at least one of existing R1, R2, R3, R11, R12, R13, R14 or R15 may be -O-R41 to give non limiting examples of a stilbenoid derivative.

5

The BCA, preferably the polyphenolic compound, may be selected from the group comprising:

- epsilon-viniferin, pallidol, trans-diplotindonesin B, hopeaphenol, oxyresveratrol, piceatannol, pterostilbene, or 4'-methoxy-(E)-
- 10 resveratrol 3-O-rutinoside, phenolic acids such as gallic acid, ellagic acid, vanillic acid; propyl gallate, protocatechuic acid, p-coumaric acid, caffeic acid, danielone, syringic acid, salicylic acid, gentisic acid, p-hydroxy benzoic acid, rosmarinic acid, rosmanol, quinic acid, sinapic acid, epi-isorosmanol, isorosmanol, E-anethol, 3,4-
- 15 dimethoxycinnamic acid, ferulic acid; phenolic diterpenes such as carnosol and carnosic acid; coumarines such as coumarin, umbelliferone, herniarine, esculetin, scopoletin, scopanone, fraxetin and their glucosides such as 7-O-glucosyl-umbelliferone, 6-O-glucosyl-esculetin, 7-O-glucosyl-esculetin, 7-O-Glucosyl-6-methoxycoumarin,
- 20 dihydroxyisocoumarins such as 6-methoxymellein, as well as prenyloxyisocoumarins such as 7-geranyloxy coumarin, 7-methoxy-6-(3-methyl-2-butenyl)-coumarin, 7-methoxy-8-(3-methyl-2-butenyl)-coumarin; naphthoquinones such as 1,2-naphthoquinone, 1,4-Naphthoquinone, 2,6-Naphthoquinone, alkanin, hexahydroxy-1,4-naphthalenedione, juglone,
- 25 lapachol, lawsone, menatetrenone, 2-methoxy-1,4-naphthoquinone, nigrosprin B, 2,3,5,7-tetrahydroxy-1,4-naphthalenedione, menadione, 5,8-Dihydroxy-1,4-naphthoquinone and other dihydroxynaphthoquinones, atovaquone; flavonoids: anthoxanthins including flavonols such as quercetin, kaempferol, myricetin, fisetin, galangin, isorhamnetin, pachypodol, rhamnazin pyranoflavonols and furanoflavonols, flavones such as apigenin, luteolin and tangeritin, flavonoides including flavanones such as hesperetin and naringenin, eriodictyol, homoeriodictyol and sakuranetin, flavanols such as taxifolin, dihydrolquercetin and dihydrokaempferol, flavans such as flavan-3-ol (including Catechin,
- 30 Gallocatechin, catechin 3'-gallate, gallocatechin 3-gallate, epicatechin, epigallocatechin, epicatechin 3-gallate, Epigallocatechin 3-gallate, theaflavin, theaflavin-3-gallate, theaflavin-3,3'-digallate, thearubigin, proanthocyanidins, flavan-4-ol and flavan-3,4-diol;

anthocyanins such as cyanidin, delphinidin, malvidin, pelargonidin, peonidin, petunidin, cyanin-3-rutinoside and delphinidin-3-rutinoside; isoflavonoides including isoflavones such as genistein, glycitein and daidzein, further including isoflavanes, isoflavenes, coumestans and
5 pterocarpan stilbenoides including stilbene and aglycones such as piceatannol, pinosylvin, pterostilbene.

The BCA in the peritoneal therapeutic fluid may be solubilized by complexation to a cyclodextrin, or by conjugation to a soluble moiety,
10 which means a water soluble moiety, or by contacting with nanoparticles, preferably water soluble nanoparticles.

The BCA in the peritoneal therapeutic fluid may be emulsified, for example by addition of a suitable surfactant.

15 The BCA in the peritoneal therapeutic fluid may be suspended, for example treatment of the compound of the PTF by ultrasound, thereby breaking larger particles of the compound into smaller particles.

20 The BCA in the peritoneal therapeutic fluid may be solubilized through chemical binding to a highly soluble moiety. Preferentially, the BCA in the peritoneal therapeutic fluid, if it is not PEG or a derivative of PEG, may be solubilized through pegylation with Polyethyleneglycol (PEG) or Methoxy-Polyethyleneglycol (mPEG).

25 As mentioned before, the BCA may be a polyethylene glycol (PEG), or a derivative of a polyethylene glycol, such as mPEG. So, a PEG or PEG derivative may be present in the PTF of the invention as a BCA on its own.

30 The following description relates to a) PEG or PEG derivative as an autonomous BCA and also to b) PEG or PEG derivative as a compound that is used for pegylation.

35 The PEG or mPEG may have a molecular weight above 400 Da.

The PEG or the mPEG may be selected from the group comprising PEG 600, mPEG 600, PEG 1000 , mPEG 1000, PEG 1450, mPEG 1450, PEG 3350 and mPEG

3350, or the like.

In the Peritoneal therapeutic fluid, one or more BCAs may be present in a concentration of 0.001 mg/L to 5g/L, preferentially between 0.001 mg
5 and 1g/l further preferred between 0.01 and 500 mg/L. These concentrations, and other concentrations for BCA that are given in g/L, relate to the total concentration of all BCA if more than one BCA is present.

10 In the Peritoneal therapeutic fluid, one or more BCAs may be present in a concentration of 0.05 to 60 $\mu\text{Mol/L}$, preferentially between 0.05 to 40 $\mu\text{Mol/L}$ further preferred between 0.05 to 20 $\mu\text{Mol/L}$. These concentrations, and other concentrations for BCA that are given in $\mu\text{Mol/L}$, relate to the total concentration of all BCA if more than one
15 BCA is present.

The term "between" is intended to include the lower and upper limit of the respective range, if not otherwise indicated. So, if a range is disclosed as "between X and Y", X and Y are included.

20

In the Peritoneal therapeutic fluid the one or more BCAs may be present in a concentration of 0.02 μM to 315 μM , preferentially 0.07 μM to 100 μM further preferred 0.2 μM to 50 μM . Said molar concentration relates to each individual BCA if more than one BCA is present.

25

The peritoneal therapeutic fluid may be used as a peritoneal dialysis fluid, as a peritoneal therapeutic fluid with decreased cytotoxicity on human peritoneal mesothelial cells. The peritoneal therapy fluids of the present invention are particularly suitable for use as peritoneal
30 dialysis fluids.

35

The peritoneal therapeutic fluid may comprise one or more of an ingredient which is selected from the following: alkali metal ions, alkaline earth metal ions, an osmotic agent, and/or a pH-buffer. In one embodiment, the peritoneal therapeutic fluid comprises an osmotic agent and/or a pH-buffer, and preferably also alkali metal ions and/or alkaline earth metal ions. An osmotic agent is an agent capable of increasing osmolality of a solution. An osmotic agent is preferably

biocompatible.

The peritoneal therapeutic fluid may comprise at least one saccharide, which may be a mono-, oligo- or polysaccharide. Examples are fructose,
5 glucose, maltose or maltodextrin.

The invention is also directed to a peritoneal therapeutic fluid container or kit comprising at least one liquid containing compartment, wherein liquid of at least one compartment contains a compound as
10 mentioned above, wherein the compound is solubilized.

The Peritoneal therapeutic fluid container or kit may comprise at least two compartments, which after mixation generates a peritoneal therapeutic fluid as defined above, wherein at least one compartment
15 contains a solubilized BCA as mentioned above.

The Peritoneal therapeutic fluid container or kit may comprise at least two compartments, which after mixation generate a peritoneal therapeutic fluid as defined above, wherein at least one compartment contains a dry
20 and unsolubilized BCA (for example in powder form) as mentioned above, that maybe solubilized by contacting liquid from one of the other compartments, just before application.

The peritoneal dialysis fluid container or kit may comprise one or
25 several compartments, wherein at least one compartment contains a part of a dialysis fluid comprising an osmotic driver such as glucose, maltodextrin or other sugars or sugar polymers, aminoacids, cyclodextrins, Polyethylene glycols (PEGs) or other osmotic drivers, or derivatives of such osmotic drivers or a mixture of the described
30 osmotic driver compounds and/or their derivatives.

The peritoneal dialysis fluid container or kit may comprise one or several compartments, wherein at least one compartment contains a BCA as described before in dry or solubilized form, for example as a part of a
35 dialysis fluid comprising the BCA in a solubilized formulation.

The Peritoneal therapeutic fluid container or kit may be used in peritoneal dialysis.

A BCA, in the present application, is preferably a polyphenolic compound or derivative thereof that presents a PDF induced cyto-toxicity decreasing activity. BCAs also include metabolized derivatives of polyphenolic compounds that exhibit cyto-toxicity decreasing activity in
5 presence of fluids for peritoneal treatment.

DETAILED DESCRIPTION OF THE INVENTION

10 Further embodiments of the present invention are provided hereunder.

The term polyphenolic compound comprises compounds that are characterized by at least two phenolic hydroxyl groups. In other words, a polyphenol comprises at least two hydroxyl groups which are bound to
15 one or more aromatic rings.

The term "glycoside of a polyphenolic compound" is used in the present application to refer to a polyphenolic compound to which a sugar moiety is bound via a glycosidic bond. The sugar moiety is preferably bound to
20 a hydroxyl group of the polyphenolic compound via a glycosidic bond, thereby forming an acetal of the sugar moiety. The sugar moiety may be a monosaccharide, a disaccharide, a trisaccharide, or an oligosaccharide. In a glycoside of a polyphenolic compound, one or more sugar moieties may be bound to a polyphenolic compound, respectively, preferably via
25 one or more hydroxyl groups.

The term "bio-compatibility enhancing agents" ("BCA") is particularly used in the present application to refer to a polyphenolic compound, a metabolite of a polyphenolic compound which is obtained by
30 metabolization in the human or animal body, a salt of a polyphenolic compound, a glycoside of a polyphenolic compound, derivatives of such compounds, or a polyphenolic compound that is chemically linked to a solubilizing moiety, such as a pegylated polyphenolic compound. So, in the present invention the aforementioned compound are also designated as
35 BCAs. Preferred BCAs are stilbenoids and derivatives thereof, even more preferred resveratrol and derivatives thereof, such as piceid (polydatin), piceid glucosides, Piceatannol, and Pterostilbene.

BCAs in the present application may include, and may be characterized as, cyto-toxicity reducing agents. Polyphenols and derivatives thereof, preferred stilbenoids and derivatives thereof, even more preferred resveratrol and derivatives thereof, such as piceid, piceid glucosides, 5 Piceatannol, and Pterostilbene; or solubilized polyphenols and derivatives thereof, which may be modified by complexation to solubilizing agents such as cyclodextrins, or modified through conjugation to highly soluble molecules, preferentially conjugated to a Polyethylene glycol (PEG), are further included in the scope of BCAs as 10 defined in the present specification.

A stated above, also polyethylene glycol (PEG), or a derivative of a polyethylene glycol, such as mPEG can be a BCA on its own.

15 The PEG that is used for binding to another BCA may be activated. Activation preferably means that PEG comprises a functional group that allows coupling to another compound. Examples are given below.

In the present specification, the terms "polyethylene glycol 600", 20 "polyethylene glycol 1000", "polyethylene glycol 1450", "polyethylene glycol 3350" refer to linear polyethylene glycols that are generally known and commercially available for example as Carbowax PEGs.

In order to link the PEGs to a polyphenol, preferentially a stilbenoid, 25 more preferentially resveratrol, a piceid or a piceid glucoside, PEGs have to be covalently bound to the BCAs, a process known as pegylation. To allow pegylation, PEG has to be activated. For example "activated PEGs" can be coupled to polyphenolic Compounds, as a means of attaching bound biocompatibility enhancing additive to fixed supports or to 30 solubilize them in aqueous fluids. Commercially available examples for "activated PEGs" are:

Methoxy PEG Hydrazide: $\text{CH}_3\text{O}-(\text{CH}_2\text{CH}_2\text{O})_n-\text{CH}_2-\text{CO}-\text{NH}-\text{NH}_2$,
 Methoxy PEG Amine HCl Salt: $\text{CH}_3\text{O}-(\text{CH}_2\text{CH}_2\text{O})_n-\text{CH}_2-\text{CH}_2-\text{NH}_2\text{HCl}$,
 Methoxy PEG Propionaldehyde : $\text{CH}_3\text{O}-(\text{CH}_2\text{CH}_2\text{O})_n-\text{CH}_2-\text{CH}_2-\text{CHO}$,
 35 Methoxy PEG Thiols: $\text{CH}_3\text{O}-(\text{CH}_2\text{CH}_2\text{O})_n-\text{CH}_2-\text{CH}_2-\text{SH}$,
 Methoxy PEG Vinylsulfone: $\text{CH}_3\text{O}-(\text{CH}_2\text{CH}_2\text{O})_n-\text{CH}_2-\text{CH}_2-\text{SO}_2-\text{CH}=\text{CH}_2$,
 Methoxy PEG Maleimide,
 Methoxy PEG Nitrophenyl Carbonate: $\text{CH}_3\text{O}-(\text{CH}_2\text{CH}_2\text{O})_n-\text{CO}-\text{O}-\text{C}_6\text{H}_4-\text{NO}_2$,

Methoxy PEG Succinimidyl Carbonate,
 Methoxy PEG Succinimidyl Carboxymethyl Ester,
 Methoxy PEG Succinimidyl Carboxyl Ester,
 Methoxy PEG Succinimidyl Carboxypentyl Ester,
 5 Aminoalkyl PEGs: $\text{CH}_3\text{O}-(\text{CH}_2\text{CH}_2\text{O})_n-(\text{CH}_2)_n'-\text{NH}_2$.

The terms "peritoneal therapy fluid" (PTF) is used in the present application to refer to a fluid that can be used in a peritoneal therapy. Peritoneal therapies encompass, for example, peritoneal
 10 nutrition, peritoneal dialysis, peritoneal detoxification in case of liver failure or drug abuse, treatment of primary and secondary peritoneal cancer, treatment of peritoneal infections and peritonitis, pre- or post-operative peritoneal treatment, or peritoneal administration of systemic treatments. A "peritoneal dialysis fluid"
 15 (PDF) is a "peritoneal therapy fluid" (PTF) that is used for peritoneal dialysis.

Peritoneal therapy is carried out by applying a peritoneal therapeutic fluid to the peritoneum. As an active ingredient, a Peritoneal
 20 therapeutic fluid of the invention may comprise a polyphenolic compound, a metabolite of a polyphenolic compound which is obtained by metabolization in the human or animal body, or a glycoside of a polyphenolic compound, or a derivative of these compounds. Further possible ingredients are disclosed in this description.

25 The terms "peritoneal therapy fluid" (PTF), and "peritoneal dialysis fluid" (PDF) are particularly used in the present application to refer to an aqueous solution comprising physiological amounts of various electrolytes in concentrations comparable to those in the blood.

30 The peritoneal therapy fluid (PTF) may comprise one or more of the following components:

- sodium, preferably in an amount of (about) 90 to (about) 150 mEq/L;
- potassium, preferably in an amount of (about) 0 to about 5 mEq/L;
- 35 • calcium, preferably in an amount of (about) 0 to (about) 6 mEq/L;
- magnesium, preferably in an amount of (about) 0 to (about) 4 mEq/L;
- alkali equivalent, such as lactate, acetate, citrate, bicarbonate or phosphate, preferably in an amount of (about) 25 to (about) 50 mEq/L;

Alkali equivalents may also be called pH buffers. The PTF of the invention may contain lactate at a concentration between 10 and 100 mM and/or bicarbonate at a concentration between 5 and 100 mM, or other physiologically acceptable pH buffers.

- 5 • an "osmotic agent", such as glucose and maltodextrin or other mono- and/or polymeric sugar molecules, amino-acids, cyclodextrins, PEGs, or other biocompatible compounds, that may be administered at concentrations sufficient to increase osmolality, derivatives of such compounds and mixtures of such compounds and/or their derivatives,
10 preferably at a total concentration between 0.5 and 20 % (by weight). Commonly applied osmotic agents are salts, glucose, dextrose or oligosaccharides obtained from limited hydrolysis of poly-saccharides and derivatives thereof, preferably at concentrations between 0.5 and 20%. Other osmotic agents may be glucose polymers, aminoacid mono- or
15 multimers, cyclodextrins, PEGs or proteins, or compositions thereof.

A "peritoneal therapeutic fluid" (PTF) or a "peritoneal dialysis fluid" (PDF) is introduced and maintained in the peritoneal cavity of a patient in need of such treatment or of dialysis, for a time period of usually 1
20 to 24 hours. After treatment has occurred, the fluid is removed from the patient's peritoneal cavity.

Peritoneal therapeutic fluids preferably contain one or a mixture of several "osmotic agents", to establish physiological osmolality. In case
25 of Peritoneal dialysis fluids, in many cases osmolality is higher than physiological osmolality in order to draw liquid and small molecular weight "waste molecules" out of the patient's blood into the dialysate. PDFs are usually applied at osmolalities between about 280 and 500 mOsm/kg.

30

In a further embodiment, a peritoneal therapeutic fluid of the invention comprises one or more of a saccharide, wherein the saccharide may be a monosaccharide, a disaccharide, an oligosaccharide or a polysaccharide, or any mixture thereof, preferably a mono- or oligo-saccharide, which is
35 an ingredient of the PTF. In the present invention it was found that solubility and stability of a polyphenolic compound, of a metabolite of a polyphenolic compound, of a salt or of a derivative of a polyphenolic compound such as a glycoside of a polyphenolic compound, or of

derivative of these compounds, can be increased when a peritoneal therapy fluid comprises one or a mixture of mono- and/or oligo-saccharides. Preferred saccharides are selected from biologically metabolizable or biologically inactive saccharides such as fructose,
 5 glucose, sucrose, maltose or dextrans. Further embodiment related to saccharides are described in the following paragraphs.

The saccharide preferably has a maximum molecular weight of 50 kD. 1 D (Dalton) corresponds to 1 g/mol. More preferably, the molecular weight is in a range of 90D - 50 kD. Said molecular weight is range of a
 10 molecular weight of molecules present in the saccharide. The saccharide can be a mixture of saccharides of different chain lengths (different numbers of monosaccharide units). So, the saccharide preferably has a molecular weight distribution in the range of 90D - 50 kD.

15 The molecular weight of oligo/poly-saccharides may vary widely:
 In one embodiment, the at least one saccharide has a molecular weight of 90D to 500 D. (1 D = 1 g/mol).

In one embodiment, the at least one saccharide has a molecular weight of 90D to 1.5 kD.

20 In one embodiment, the at least one saccharide has a molecular weight of 1.5kD to 50kD.

In another embodiment, the at least one saccharide has a molecular weight of 350D to 50kD.

25 As mentioned, the saccharide may be a monosaccharide, a disaccharide, an oligosaccharide or a polysaccharide, wherein an oligo- or polysaccharide, or a mixture of different mono-, di-, oligo- and/or poly-saccharides. A polysaccharide preferably comprises, or is composed of, up to 500 monosaccharide units in maximum.

30

A mono-saccharide may be selected from a triose such as glyceraldehyde and glucerone, a tetrose, such as erythroses, threose and erythrulose, a pentose, such as ribose, arabinose, xylose, lyxose, ribulose and xylulose, or a hexose, such as allose, altrose, glucose, mannose,
 35 gulose, idose, galactose, talose, psicose, fructose, sorbose and tagatose, and may also be defined as a saccharide of a molecular weight of roughly 90 to 200 D.

The term saccharide may be selected from derivatives of mono-saccharide, such as aminoglycosides, such as glucosamine, galactosamine, N-acetylglucosamine, N-acetylgalactosamine, which may not or may be sulfated to different degrees.

5

A mono-saccharide may be further selected from uronic sugars, such as glucuronic acid or iduronic acid.

10 A di-saccharide may be selected from sucrose, Gentiobiulose, Laminaribiose, Gentiobiose, Rutinulose, Xylobiose, trehalose, β,β -Trehalose, α,β -Trehalose, lactulose, sophorose, lactose, cellobiose, chitobiose, or from reducing alpha-disaccharides such as maltose, Kojibiose, Nigerose, Isomaltose, Turanose, Maltulose, Palatinose (Isomaltulose), Mannobiose, Melibiose, Melibiulose, Rutinose, and may
15 also be defined as a saccharide of a molecular weight of about 150 to 400 D.

The term di-saccharide may further comprise glycosaminoglycan-di-saccharides", preferably glucosaminoglucan-di-saccharides, composed of
20 an aminoglucoside and a monosaccharide, which may be acetylated or sulfated to different degrees.

An oligo-saccharide may be Trisaccharides or saccharides of higher degree of polymerization, selected from an oligomer of above cited
25 saccharides, a product of limited hydrolysis of a linear or branched homo-polysaccharide, such as a amylose, amylopectin, fructan such as inulin, glucan, galactan and mannan, cellulose, arabic gum, amylose, amylopectin, glycogen, dextran, and hemicellulose, a product of limited hydrolysis of a hetero-polysaccharide, such as hemi-cellulose,
30 arabinoxyllose, or pectine, or a product of limited hydrolysis of a mixed polysaccharide, such as starch.

In a more specific embodiment a oligo-saccharide may be an alpha-glucan, preferably a reducing alpha glucan, with a degree of polymerization of 3
35 or higher, exemplified by, but not limited to isomaltotriose, nigerotriose, maltotriose, melezitose; maltotriulose, raffinose, kestose, maltodextrins of different molecular weight or other hydrolysis products from alpha glucans, such as Dextran, glycogen, pullulan,

floridean starch, starches, amylose, amylopectine, hydrolyzed starches, and mixtures thereof, preferably with molecular weights between 300D and 300KD.

5 The term "saccharide" also comprises derivatives of a saccharide. So, the saccharide may be a derivative of a saccharide, such as an oxidized saccharide, such as a saccharic acid, or another acidic saccharide, such as a sulfuric ester groups containing saccharide, a deoxy-saccharide, an acetylated saccharide or an amylylated saccharide, and corresponding homo-
10 and hetero-oligo-saccharides.

The term saccharide may further comprise oligo- and/or poly-saccharides composed of composed of "glycosaminoglycan-disaccharides", also called Glycosaminoglycans or mucopolysaccharides.

15

In a specific embodiment, alpha-Glucosaminoglycans, such as Heparins, are selected.

In one embodiment, the saccharide is selected from glucose, fructose,
20 sucrose, maltose, a homo-oligomer thereof, a hetero-oligomer thereof, or a mixture thereof.

In another embodiment the saccharide is selected from glucose, icodextrin, or a mixture thereof.

25

In another embodiment the saccharide is selected from a reducing alpha-glucan, and/or a reducing derivated alpha-glucan, exemplified but not limited to a heparin or a heparin derivate, and one or several saccharide mono- and di-mers.

30

In the frame of this application oligo-saccharides and polysaccharides cover saccharides composed of between 3 and 500 monosaccharide-units, preferably 3 to 300 monosaccharide-units. In another definition, oligo-saccharides and polysaccharides have to a molecular weight between 250D
35 and 50 KD. Preferably, an oligosaccharide means saccharides composed of between 3 to 20 monosaccharide-units. Preferably, a polysaccharide means saccharides composed of between 21 to 500 monosaccharide-units.

Icodextrin, which is a type of maltodextrin or can be derived from maltodextrin, is a polydisperse mixture of polymers with varying chain lengths (2 - 300 linked glucose molecules corresponding to a molecular weight of 350 to 50kD), its molecular weight is characterized by both a number average (Mn) and a weight average (Mw) molecular weight. The number average molecular weight Mn for icodextrin, ranges from 5000 to 6500 Da and the weight average molecular weight Mw ranges from 13 000 to 19000 Da (Garcia-Lopez et al., Peritoneal Dialysis International, Vol. 29, p370).

As for oligo-saccharides, MW of polysaccharides is very heterogeneous. For example, the Mw (Berry method) of starch from waxy corn is 2.27×10^8 Da, waxy rice 8.9×10^7 Da, cassava 5.7×10^7 Da, Hylon V 2.7×10^7 Da, Hylon VII 4.8×10^6 Da, and potato amylose 1.9×10^5 Da (Yokoyama et al., Cereal chemistry, volume: 75, 530).

In certain applications, such as "power-drinks" artificial polysaccharides of a size of up to 700 KD are advertised.

The at least one saccharide may be present in a total concentration of ≥ 0.02 % by weight (200mg/L). It has been shown that a concentration as low as this concentration enhances polyphenol stability.

The at least one saccharide may be present in a total concentration of ≥ 0.75 % by weight (7.5 g/L). It has been shown that such concentration enhances polyphenol stability and/or solubility of polyphenol.

The at least one saccharide may be present in a total concentration of ≥ 2.4 % by weight. It has been shown that such concentration further enhances polyphenol stability and/or solubility of polyphenol.

The at least one saccharide may be present in a total concentration of ≥ 5 % by weight. It has been shown that such concentration further enhances polyphenol stability and/or solubility of polyphenol.

The at least one saccharide may be present in a total concentration of $\geq 7.5\%$ by weight (75g/L). It has been shown that such concentration enhances polyphenol stability and solubility of polyphenol.

The at least one saccharide may be present in a total concentration of $\geq 20\%$ by weight (200g/L). It has been shown that such concentration further enhances polyphenol stability and solubility of polyphenol.

The upper limit of concentration of the at least one saccharide is

preferably the concentration of saturation. Another possible upper limits, that could be combined with any of the lower limits in this description, are 45%, 40%, 30% by weight.

In a more specific embodiment, the at least one saccharide of a
5 molecular weight of 90D to 500 D and is present in a total concentration of $\geq 0.02\%$ (200 mg/L) minimum, thereby enhancing polyphenols solubility and/or stability.

In a more specific embodiment, the at least one saccharide of a
10 molecular weight of 90D to 500 D is present in a total concentration of $\geq 0.75\%$ (7.5g/L) minimum, thereby enhancing polyphenols solubility and/or stability.

In a further specific embodiment, the at least one saccharide of a
15 molecular weight of 90D to 500 D is present in a total concentration of $\geq 7.5\%$ (75g/L) minimum, thereby enhancing polyphenols solubility and stability.

In a more specific embodiment the at least one saccharide of a molecular
weight of 350 D to 50kD is present in a total concentration of $\geq 0.02\%$ by
weight (200 mg/L), thereby minimum enhancing polyphenol solubility
and/or stability.

20 In a further specific embodiment, at least one saccharide of a molecular weight of 350 D to 50kD is present in a total concentration of $\geq 0.2\%$ by weight (2g/L), thereby enhancing polyphenol solubility and/or stability.

In a further specific embodiment, at least one saccharide of a molecular
25 weight of 350 D to 50kD is present in a total concentration of $\geq 2\%$ by weight (20 g/L), thereby enhancing polyphenol solubility and/or stability.

In a further specific embodiment, at least one saccharide of a molecular
weight of 350 D to 50kD is present in a total concentration of $\geq 5\%$ by
30 weight (50 g/L), thereby enhancing polyphenol solubility and/or stability.

In a further specific embodiment, at least one saccharide of a molecular
weight of 350 kD to 50kD is present in a total concentration of $\geq 7.5\%$ by
weight (75 g/L), thereby enhancing polyphenol solubility and/or
35 stability.

Different concentrations of the at least one saccharide may be employed.
If more than one saccharide, i.e. more than one type of saccharide, is

present, the concentration refers to the total concentration of all saccharides present in the solution.

If in this description concentrations are given in percent by weight, 1%
5 by weight corresponds to 10g/L.

A concentration of said mono- or oligo-saccharide of 0.02% (200mg/L) significantly increases polyphenol stability. A concentration of ≥ 0.75 %, preferably ≥ 7.5 %, further preferably ≥ 20 % of saccharides, preferably
10 of molecular weight of 50D to 1.5 kD, enhances polyphenol stability and solubility. A concentration of ≥ 0.02 % (200mg/L), preferably ≥ 0.75 % (7.5g/L), more preferably ≥ 2.4 % (24g/L), further preferably ≥ 5 % (50g/L) enhances polyphenol solubility and stability.

15 The concentration ranges for saccharide can be combined with any concentration ranges described herein for a BCA. A sugar can also fulfill the function of an osmotic agent, as described herein. The sugar is not covalently bound to the BCA, i.e. the cytotoxicity reducing agent. The sugar is preferably a dissolved component of a PTF.

20 Solubility of Polyphenolic BCAs may also be increased by amino acids, and therefore such BCAs may also be applied to amino acid containing peritoneal therapeutic or dialysis solutions. The Peritoneal therapeutic fluid may therefore comprise at least one amino acid. One or more amino
25 acids may be present individually or as mixtures at concentrations between 0.01 and 10 % for therapeutic liquids, or at higher concentrations, if highly concentrated BCA shall be formulated.

The present invention provides and claims peritoneal therapy fluids
30 (PTFs) comprising bio-compatibility enhancing additives (BCAs), as addressed in the definitions.

Bio-compatibility enhancing additives are preferably used at concentrations between 0.001 mg/L and 5 g/L in the dialysis fluid, a
35 concentration of 0.001 mg/L to 1g/L is further preferred, a concentration of 0.01 to 500 mg/L is especially preferred.

Concentrations of BCA in the present invention are preferably measured after 1 hour stirring at room temperature (which is preferably 20-23°C, more preferably 22°C), particularly if the BCA is a polyphenolic compound, a metabolite of a polyphenolic compound which is obtained by
5 metabolization in the human or animal body, a salt of a polyphenolic compound, a glycoside of a polyphenolic compound, or derivative of these compounds. So, concentrations of said compound correspond to measured solubility after 1 hour stirring at room temperature. Concentration is measured in a PTF of the invention. So, BCA can be dissolved in water.
10 Other ingredients of a PTF, which are mentioned in this description, are preferably present. If not specifically indicated, or if not specifically indicated otherwise, the time of stirring is one hour. In some cases, other stirring times are indicated, such as 12 hours. The fact that solubility after one hour stirring cannot be equated with a
15 maximum or absolute concentration is illustrated by the fact that for example the concentration of resveratrol after 1 hour stirring between 10 and 15 mg/L evolves above 24 mg/L after 12 hours.

Bio-compatibility enhancing agents may be polyphenols, preferentially
20 stilbenoids, such as resveratrol; or derivatives thereof, preferentially glucoside-stilbenoids such as piceid or piceid glucosides, Piceatannol, or Pterostilbene; or solubilized Polyphenols through complexation, such as cyclodextrin-polyphenol complexes or through conjugation with a highly soluble moiety such as PEG, resulting in pegylated polyphenols,
25 preferentially pegylated stilbenoids, more preferentially pegylated resveratrol, piceid, piceid glucoside, Piceatannol, and Pterostilbene.

In another embodiment, the invention provides PTFs comprising any combination of above described BCAs.
30

In another embodiment of the present invention, it is preferred that the PTF is a peritoneal dialysis fluid.

In another embodiment of the present invention, one BCA, or multiple
35 BCAs in combination, are present in a concentration of 0.001 mg/L to 5 g/L. The present inventor has surprisingly found that these BCAs or BCA combinations reduce cyto-toxicity of commonly applied peritoneal dialysis fluids, thereby increasing biocompatibility of PTFs.

In a preferable embodiment of the invention, one BCA, or multiple BCAs in combination, are present in a concentration of 0.001 to 1 g/L.

The present inventor has surprisingly found that these BCAs or BCA
5 combinations reduce cyto-toxicity of commonly applied peritoneal dialysis fluids, thereby increasing biocompatibility of PTFs.

In a further preferable embodiment of the invention, one BCA, or multiple BCAs in combination, are present in a concentration of 0.01 to
10 500 mg /L.

The present inventor has surprisingly found that these BCAs or BCA combinations reduce cyto-toxicity of commonly applied peritoneal dialysis fluids, thereby increasing biocompatibility of PTFs.

15

In another aspect, the invention provides a process for manufacturing of a PTF herein described, using methods known to the one of ordinary skill in the art.

20 In a further aspect, the invention provides with a peritoneal therapeutic fluid container or kit comprising at least one liquid containing compartment, wherein liquid of at least one compartment contains a BCA as mentioned before, wherein the BCA is solubilized. The liquid containing compartment may comprise a saccharide as disclosed
25 before, wherein the saccharide is preferably selected from glucose, an alpha-glucan, glucose di- tri- or oligo-mers, maltodextrin, icodextrin, or alpha-glucan polysaccharide hydrolysate of higher average molecular weight, or a mixture thereof. In this aspect, the peritoneal dialysis container or kit may contain a BCA solubilized in the PTF, or in one of
30 the fluids composing the final PTF.

In a further aspect, the invention provides with a Peritoneal therapeutic fluid container or kit comprising at least two compartments, also called multicompartment container, wherein at least one compartment
35 contains a BCA as mentioned before, wherein the BCA may be in solid form or in liquid solution, solubilized or in suspension. At least one compartment may comprise a solubilized BCA in concentrated form.

A multicompartment container preferably comprises at least one dry compartment, containing one or several BCAs in solid form, preferably powder form, to be solubilized just before application of the PD solution. At least one further compartment may comprise a liquid. A
5 solid BCA in a first compartment maybe solubilized by contacting with a liquid from one of the other compartments, just before application. A liquid from one of the other compartments may comprise a saccharide as disclosed before, wherein the saccharide is preferably selected from glucose, maltodextrin, icodextrin, or a mixture thereof, or one of the
10 other saccharides as mentioned before.

In a further aspect, a PTF container or kit is described, comprising one or multiple compartments, wherein at least one compartment contains a part of a dialysis fluid comprising glucose, maltodextrin, aminoacids
15 PEGs, cyclodextrins or alternative osmotic drivers, or a derivative of such osmotic drivers, or a mixture of any such molecules, in a dialysis fluid as described above.

In yet another aspect, a multi-compartment container or kit may contain
20 at least one compartment containing a sugar or sugar polymer derived osmotic agent under acidic conditions (pH between 1 and 6). The container or kit may further be characterized in that at least one second compartment contains a further part of the dialysis fluid at basic pH, which, upon mixture with the fluid from the first compartment,
25 reconstitutes a PTF with a pH between 6.5 to 8, preferably between 6.8 and 7.5.

Molecular weight in the present invention is preferably measured by gel permeation chromatography (GPC), preferably gel permeation
30 chromatography with light scattering and refractive index detection (GPC-RI-MALLS). A number of polysaccharide units, which corresponds to a degree of polymerization, can be determined with these methods. A more detailed, but non-limiting, method is given in the examples.

35 BRIEF DESCRIPTION OF FIGURES

Fig. 1 Comparative testing of PDFs after 48 hours results in decreased resazurin to reorufin conversion;

- Fig. 2 Results of resazurin to reorufin conversion, Resveratrol, Polydatin, PEG, PD solution #1;
- 5 Fig. 3 Results of resazurin to reorufin conversion, Resveratrol, Polydatin, PEG, PD solution #2;
- Fig. 4 Results of resazurin to reorufin conversion, Resveratrol, Polydatin, PEG, PD solution #3;
- 10 Fig. 5 Results with Medium control;
- Fig. 6 Results of resazurin to reorufin conversion, Resveratrol in different PD solutions;
- 15 Fig. 7 Results of resazurin to reorufin conversion, Piceatannol in different PD solutions;
- Fig. 8 Results of resazurin to reorufin conversion, Pterostilbene in different PD solutions;
- 20 Fig. 9a,b Results of resazurin to reorufin conversion, Piceid in different PD solutions;
- 25 Fig. 10 Results of resazurin to reorufin conversion, Caffeic acid in different PD solutions;
- Fig. 11 Results of resazurin to reorufin conversion, Luteolin in different PD solutions;
- 30 Fig. 12 Results of resazurin to reorufin conversion, Delphinidin in different PD solutions;
- 35 Fig. 13 Results of peritoneal VEGF expression in Sprague-Dawley rats after 2 to 4 weeks Peritoneal Dialysis with PD solution #4 in absence or presence of Resveratrol 40 μ M (average concentrations and standard deviations).

The following Examples illustrate embodiments of the present invention:

EXAMPLES

5

Molecular weight measurement:

The saccharides are dissolved in extra-pure water in a concentration of 0.5% (w/v). The solutions are heated at 95°C for 30 minutes. The polymers are analyzed using the following devices: Alliance chromatography system (Waters corporation, Milford, Massachusetts, USA),
10 DAWN-EOS light scattering detector (Wyatt Technology, Santa Barbara, USA) with $\lambda_0 = 658$ nm and 16 detectors in the range of angles from 14.4 to 163.3°, K5 flow cell. The polymers are fractionated on a precolumn and three columns having the separation ranges 300-10⁴, 5×10^4 - 2×10^6
15 and 10⁶-10⁸ (SUPREMA-Gel, PSS Polymer Standards Service GmbH, Mainz, Germany). 100 µl of solution are injected. The fractionation takes place at a temperature of 30°C and a flow rate of 0.8 ml/min with 0.05M NaNO₃ as eluent. The Astra V 5.1.8.0 program (from Wyatt Technology, Santa Barbara, USA) is used to analyze the molecular weight distribution of
20 the samples. Same procedure can be used when molecular weight of other compounds than saccharides are measured.

Dialysis solutions:

In accordance with this invention, peritoneal dialysis fluids are
25 provided, containing an osmolality sufficient to cause diffusion of water and waste products across the peritoneum after infusion of the peritoneal dialysis fluid into the peritoneal cavity of a patient. In addition to an osmotic agent or a combination of osmotic agents, the present peritoneal dialysis fluid contains amounts of various
30 physiologically important electrolytes in concentrations comparable to those in plasma. A suitable peritoneal dialysis fluid has been described in the definitions part of this patent.

TABLE I:

PD Sol	PD#1 StaySafe®	PD#2 Physioneal®	PD#3 Extraneal®	PD#4 StaySafe®
Osmolality (mOsm/kg)	346	485	284	486
Osmotic Agent (%) w/v	Glu 1.25	Glu 3.86	Ico 7,5	Glu 4.25
Sodium (mEq/L)	132	132	133	132
Calcium (mEq/L)	3,5	1.75	3,5	3,5
Magnesium	0,5	0.25	0,5	0,5
Chloride	96	101	96	96
Lactate	40	10	40	40
Bicarbonate		25		
	pH5.5	pH7	pH5.5	pH5.5
tested BCA	/, R, P, PE	/, R, P, PE	/, R, P, PE Pa,Pt,CA,Lu,De	/, P, Pa,Pt,CA,Lu,De

Legend to Table I:

- 5 Solutions tested for their application as peritoneal dialysis fluids.
Abbreviations: Glu, glucose; Ico, icodextrin; OsAg, osmotic agent; BCA, added "biocompatibility enhancing agent". Concentrations in % (w/v) and mEq/L; osmolality in mOsm/kg. Tested BCAs are:
The stilbenoids Resveratrol (R), Piceid (Polydatin) (P), Piceatannol
10 (Pa), Pterostilbene (Pt);
the phenolic acid Cafeic Acid (CA),
the flavonoides Luteolin (Lu), Quercetin (Qu), Delphinidin (De).
PEG 1450 Carbowax (PE).

15

Legend to Table I:

- Solutions tested for their application as peritoneal dialysis fluids.
Abbreviations: Glu, glucose; Ico, icodextrin; OsAg, osmotic agent; BCA, added "biocompatibility enhancing agent". Concentrations in % (w/v) and
20 mEq/L; osmolality in mOsm/kg. Tested BCAs are: R Resveratrol, P Piceid and PE PEG 1450 Carbowax.

- Table 1 shows peritoneal dialysis fluids, compared for testing the effect of reduction of cytotoxicity by addition of tested BCAs. The
25 study involves evaluation of additions of BCAs at different concentrations to PD solutions.

StaySafe 1.25 solution was chosen to show impact of acidic pH at low Glucose concentration in an environment of high lactate buffer. Physioneal 3.86 was chosen to show the impact of high glucose concentration at physiological pH in an environment of low lactate buffer. StaySafe 4.25 was chosen to show combined challenge of acidic pH and high glucose concentration. Extraneal was chosen to compare the difference of glucose and maltodextrin at acidic pH and at high lactate concentration.

10

The examples show that addition of specifically selected BCAs increase biocompatibility of currently marketed PDFs. Those skilled in the art readily understand that addition of such "biocompatibility enhancing agents" will increase long term biocompatibility of any peritoneal therapeutic and/or dialysis solution, more specifically of such solutions containing sugar and/or sugar polymer-derived osmotic agents or such, and this even in cases and models where certain dialysis solutions do not show immediate cytotoxicity and/or very low AGE formation.

20

Solutions are applied to different toxicity experiments in absence or presence of specifically selected BCAs, to show that BCAs, exemplifying the present invention, decrease cytotoxic side-effects, and thereby increasing biocompatibility, as compared to reference solutions without such BCAs.

25

Toxicity:

The following experiments compare the cytotoxicity of reference solutions in absence or presence of BCAs of this invention, to show increased biocompatibility of dialysis solutions in presence of BCAs of this invention.

30

Examples 1, 2, 3, and 4

35

Experimental comparison of different dialysis solution with respect to their effect on human peritoneal mesothelial cells, applying the following protocol.

Cell Culture

Experimental Procedure:

5 Human peritoneal mesothelial cells (HPMC) were purchased from Zen Bio Inc. and cultured in cell culture flasks using suppliers media. Near confluent HPMC were harvested by trypsinization, seeded into collagen-coated 96-well tissue culture plates (Corning) and allowed to adhere overnight. The medium was changed to twice diluted with dialysis
10 solution for 48 up to 72 hours.

Cell viability was established applying the promega resazurin assay, following the suppliers protocol. Living cells are metabolically active and are able to reduce the non-fluorescent dye resazurin to the strongly-fluorescent dye resorufin. The fluorescence output is
15 proportional to the number of viable cells over a wide concentration range. This also allows the calculation of the proliferation rate for cells capable of consecutive cell division. Resazurin is effectively reduced in mitochondria making it also useful to assess mitochondrial metabolic activity. For the dose-response relationship, relative
20 viability was plotted against the test item concentrations.

In the case of Piceid, the intra-cellular ATP level was determined with the CTG assay. For this, media was completely removed from all wells by
25 aspiration, 60 µl of CTG reagent was added to each well, and incubated for 5 min at RT while softly shaking (50 rpm). Using a Victor3 1420 Multilabel Counter, the emitted luminescence produced in the CTG assay was measured. For the dose-response relationship, absolute luminescence (background subtracted) was related to the negative (medium) control and
30 relative viability values were plotted against the test item concentrations. For the dose-response relationship, absolute luminescence (background subtracted) was related to the negative (medium) control and relative viability values in presence of BCA were plotted against the BCA concentrations.

35 All assays were conducted in a duplex format using the same cell culture.

Results:

Example 1:

Comparative testing of PDFs after 48 hours results in decreased
5 resazurin to reorufin conversion, which translates to decreased cell-
viability. See Fig. 1.

10 Example 2:

Addition of selected BCAs of this invention partially reestablished
reszurin to reorufin conversion, , which is interpreted as a result of a
decreased cytotoxicity, due to the application of the tested BCAs.
15 Compounds were added at 9 dilutions (Cmax=500 µM) together with tested
PD solutions or Medium cotrol. Incubation was 48 hours.
Results with PD-Solution #1 are presented in Fig. 2

Resveratrol improves cell viability of HPMC cells up to 20 %. Piceid
20 (polydatin) shows minor improvements.

Results with PD-Solution #2 are presented in Fig. 3.

Resveratrol improves cell viability of HPMC cells up to 40 %. Piceid
25 (polydatin) shows minor improvements.

Results with PD-Solution #3 are presented in Fig. 4.

Resveratrol improves cell viability of HPMC cells up to 40 %. PEG shows
30 minor improvements.

Medium Control is presented in Fig. 5:

In control medium, without cytotoxic stress, resveratrol, piceid
35 (polydatin) and PEG have no significant effect on cell viability until
Cmax.

In conclusion, we obtained a strong effect of Resveratrol reducing cyto-

toxicity of all three tested peritoneal dialysis solutions and a minor effect of piceid. A possible explanation for a relatively weaker effect of piceid is, that piceid has first to be converted to resveratrol or another biological active compound by enzymes that are present in the peritoneum. We therefore shall show a stronger effect of piceid in an animal model.

For PD-solution #3 we observed a cytotoxicity decreasing effect of PEG. We had used PEG simply as a control in our experiments and have no explanation for this observation.

Example 3:

Addition of selected BCA resveratrol partially reestablished resazurin to reorufin conversion, in a triplicate assay, which is interpreted as a result of a decreased cytotoxicity, due to the application of the tested BCA. In this series, Resveratrol was added 5 minutes in advance to application of test-solutions, at 9 dilutions (Cmax=500 µM). Incubation was 72 hours. Results are presented in Fig. 6.

Resveratrol improves viability of HPMC cells exposed to PD-Solution #1 by up to 84%. Resveratrol improves viability of HPMC cells exposed to PD-Solution #2 by up to 28%. Resveratrol improves viability of HPMC cells exposed to PD-Solution #3 by up to 105%.

Example 4:

Addition of selected BCAs, namely of the stilbenoids Piceatannol (Pa), Pterostilbene (Pt), Piceid (Polydatin) (P); the phenolic acid Cafeic Acid (CA); the flavonoides Luteolin (Lu), Delphinidin (De); partially reestablished resazurin to reorufin conversion, or partly re-established intracellular ATP-level, which is interpreted as a result of a decreased cytotoxicity, due to the application of the tested BCA. Test items were tested at 3 replicates per concentration. All assays were conducted in a duplex format using the same cell culture. Incubation was 72 hours.

Results with Piceatannol are presented in Fig. 7

Piceatanol improves cell viability of HPMC cells, when exposed to PD-Solution #3 by up to 44 %, and when exposed to PD-Solution #4 by up to 40 %.

5

Results with Pterostilbene are presented in Fig. 8

Pterostilbene improves cell viability of HPMC cells, when exposed to PD-Solution #3 by 183 %, and when exposed to PD-Solution #4 by 118 %.

- 10 Results with Piceid (Polydatin) are presented in figures 9a. and b. In this experimental series, Piceid improved viability of HPMC cells measured by resazurin to resorufin transformation, when exposed to Solution #3 by up to 32 %, when exposed to PD-Solution #4 by up to 17% (Fig. 9a). Measured by ATP-level re-establishment, Piceid improves
- 15 viability of HPMC cells exposed to PD-Solution #4 by 51 %.

Results with Cafeic Acid are presented in Fig. 10.

Cafeic Acid improves cell viability of HPMC cells, when exposed to PD-Solution #3, up to 32 %. Cell viability improvement is minor when HPMC

20 cells are exposed to PD-Solution #4.

Results with Luteolin are presented in Fig. 11.

Luteolin improves cell viability of HPMC cells, when exposed to PD-Solution #3 by up to 56 %, and when exposed to PD-Solution #4 by up to

25 21 %.

Results with Delphinidin are represented in Fig. 12.

Delphinidin improves cell viability of HPMC cells, when exposed to PD-Solution #3 by up to 57 %. No cell viability improvement du to

30 Delphinidin was observed under the applied experimental conditions, when testing HPMC cells expose to PD-Solution #4.

- 35 Taken together, results from examples 1 to 4 indicate a general effect of tested BCAs by increasing cell-viability of HPMC cells, when exposed to PD-Solutions. For most BCAs the concentration of maximal activity varies between 0.08 μ M and 18.5 μ M, but in some cases concentrations of 167 or even 500 μ M were highly efficacious. For those skilled in the art such variability of concentration with highest efficacy is not

surprising, reflecting different bioavailabilities and target affinities. Nevertheless, such a general impact of so many representatives of given classes of naturally occurring compounds within the same model is a striking discovery.

5

All tested compounds (Polyphenols) showed some improvement of HPMCs when exposed to at least one of the 4 tested PD-Solutions. All tested Stilbenoids (Resveratrol, Piceid, Piceatanol and Pterostilben) increased cell viability as well on Glucose based as on Icodextrin based PD-

10

Solutions. The phenolic acid Cafeic Acid, and flavanoides Luteolin and Delphinidin mainly improved Icodextrin based dialysis solutions.

15

Those, skilled in the art understand that a toxicity cell model is a relatively fragile model, and that measurable cell-culture toxicity decrease is already dependent on measurable cell-toxicity in the first place. Nevertheless we observed overall higher stress due to Icodextrin based PTFs as compared to Glucose Based PTFs, under the applied experimental conditions. Such stronger toxicity challenge enabled us to show BCA activity of tested compounds over a larger range of concentrations. The results of Piceid show highest variation of all tested compounds. We believe that the need of metabolization of piceid, dependent on metabolic capacity of cultured cells, might be a reason for such variability. In example 4 we succeeded to show reproducible BCA activity of Piceid in 3 different experimental set-ups

20

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Example 5:

30

Animal Studies have been carried out as described in Lee et al. 2012:

Experimental procedure:

Peritoneal access ports were inserted in male Sprague-Dawley rats. After one week, rats started to received peritoneal treatment: 10 rats receive once daily 20 ml of Sol #4, 10 rats received 20 ml of Sol #4 with addition of selected BCA (resveratrol), during 2 hour infusions. After 2 to 4 weeks, the abdomen was opened, the peritoneum was recovered and submitted to protein extraction. Tissue VEGF concentration was

35

established by ELISA (Abcam Rat VEGF ELISA Kit, ab100787) on obtained protein preparations (pg/ml).

Results:

- 5 Increased VEGF expression after chronic peritoneal dialysis has been reported in humans and rat-models, and is related to fibrosis and angiogenesis as side effects of long term peritoneal dialysis treatment (Zweers, 2001; Park, 2004). Results of example 5 (table II and Figure 13) show that addition of selected BCA (resveratrol) decreases
10 expression of VEGF in the peritoneum of standard PDF treated rats, indicating improved biocompatibility of BCA supplemented PDFs in the animal model.

TABLE II:

- 15 VEGF expression in peritoneal tissue after 2 or 4 weeks of peritoneal dialysis wit Solution #4 in absence or presence of Resveratrol 40 μ M. Values between 2 and 4 weeks were highly reproducible and therefore combined for the statistical analysis.

PD Solution	Treatment (weeks)	Animal	VEGF concentration (pg/mL) in prot. prep.	Statistical results
Sol #4	2	1	81.64	Average 95.18 Stand.Dev. 20.08
		2	80.21	
		3	93.52	
		4	92.56	
		5	84.42	
	4	6	84.42	
		7	136.91	
		8	95.72	
		9	77.05	
		10	125.32	
Sol #4 + 40µM Resveratrol	2	11	50.21	Average 60.94 Stand.Dev. 10.65
		12	39.99	
		13	70.88	
		14	77.84	
		15	60.12	
	4	16	62.02	
		17	63.71	
		18	57.91	
		19	68.45	
		20	58.23	
t-test pval				0.00065

5 References:

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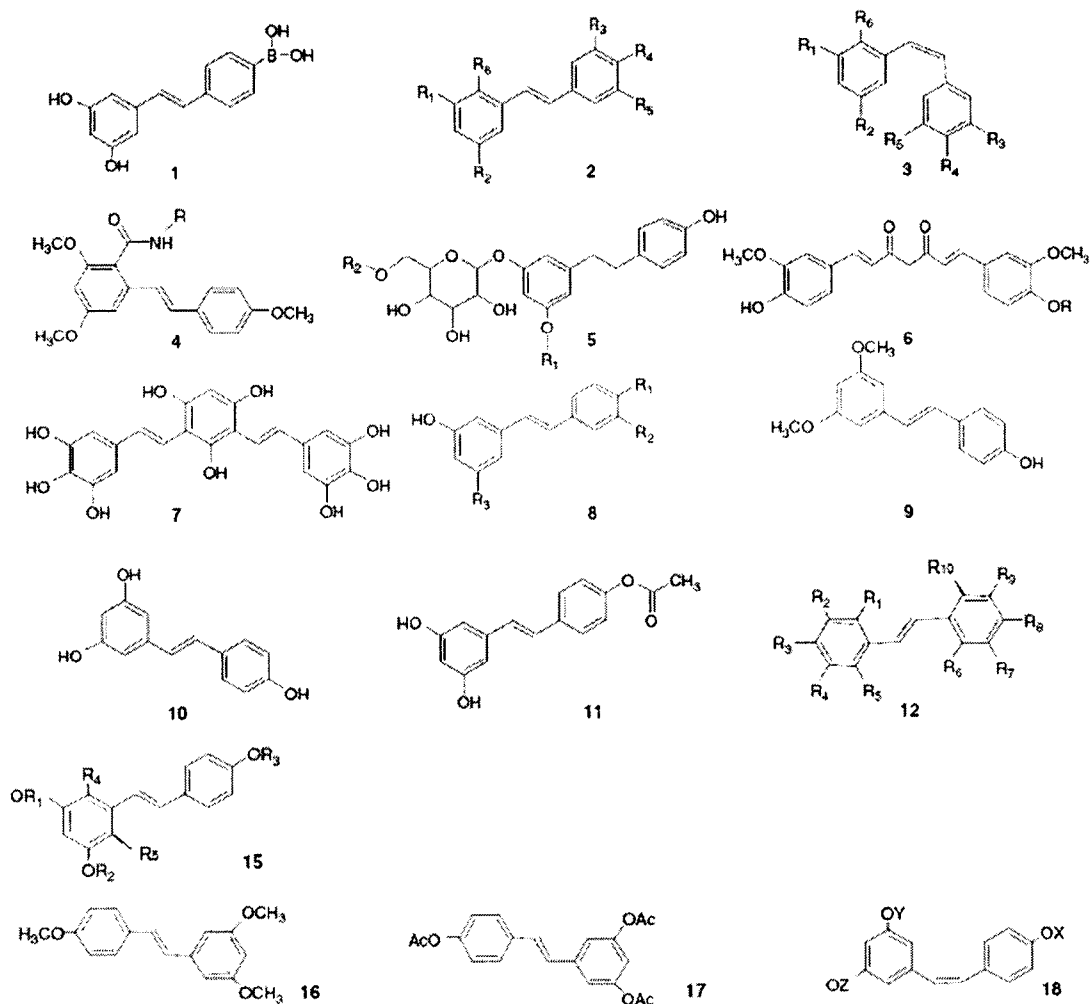
Mangram, Archibald, Hupert, Tokars, Silver, Brennan, Arduino, Peterson,

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CLAIMS:

1. Peritoneal therapeutic fluid comprising one or more of a biocompatibility enhancing agent (BCA) that is selected from the group consisting of a polyphenolic compound, a metabolite of a polyphenolic compound which is obtained by metabolization in the human or animal body, a salt of a polyphenolic compound, and a glycoside of a polyphenolic compound,
for use as a peritoneal dialysis fluid, or as a peritoneal therapeutic fluid with decreased cytotoxicity on human peritoneal mesothelial cells.
2. Peritoneal therapeutic fluid according to claim 1, wherein the biocompatibility enhancing agent is selected from the group of stilbenoids, phenolic acids, flavonoids, flavones, anthocyanidins, a salt of said biocompatibility enhancing agent, and a glycoside of said biocompatibility enhancing agent.
3. Peritoneal therapeutic fluid according to one of claims 1 or 2, wherein the biocompatibility enhancing agent is resveratrol, dihydro-resveratrol, piceid, piceatannol, pterostilbene, piceid glucoside, caffeic acid, luteolin, or delphinidin.
4. Peritoneal therapeutic fluid according to claim 1 or 2, wherein the biocompatibility enhancing agent is selected from following compounds 1-12, 15, 16, 17, 18:



wherein in compound 2 and compound 3

R1 = R2 = R4 = OH, R3 = R5 = R6 = H; or

R1 = R2 = R4 = OCH3, R3 = R5 = R6 = H; or

R1 = R2 = R4 = OCH3, R3 = R5 = H; R6 = OH; or

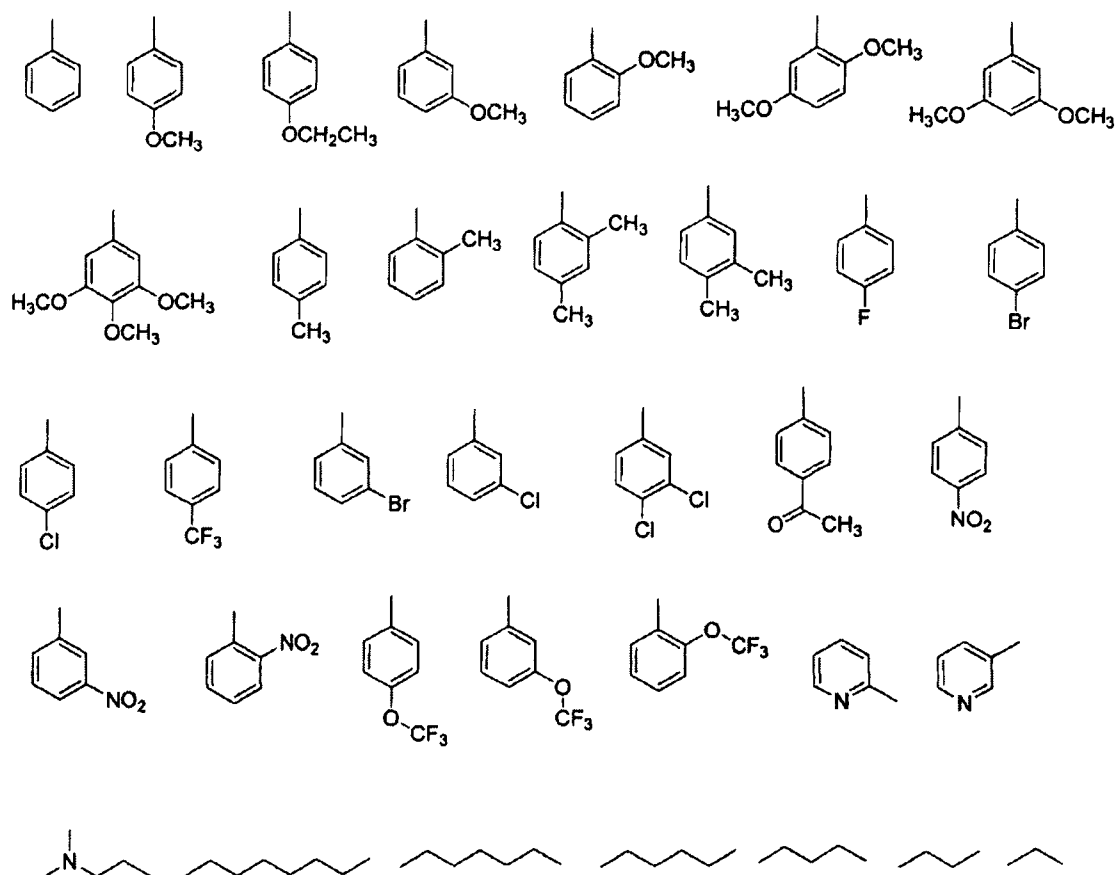
R1 = R2 = R3 = R5 = OCH3, R4 = R6 = H; or

R1 = R2 = R3 = R5 = OCH3, R4 = H, R6 = OH; or

R1 = R2 = R3 = R4 = OCH3, R5 = R6 = H; or

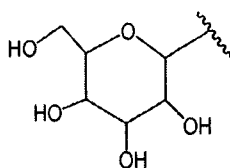
R1 = R2 = R3 = R4 = OCH3, R5 = H, R6 = OH;

wherein in compound 4 R is one of the following moieties:



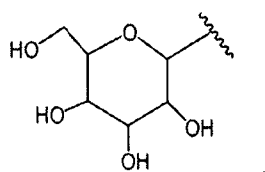
wherein in compound 5

R1 is hydrogen or a group of formula

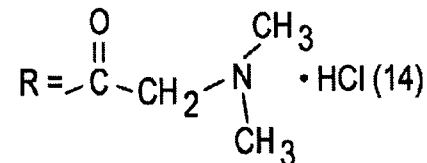
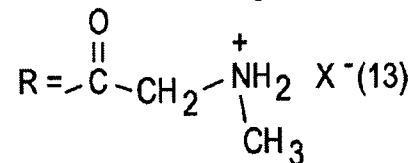
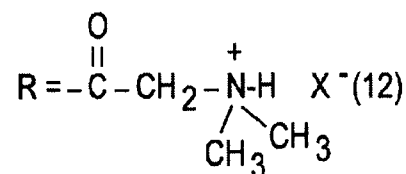
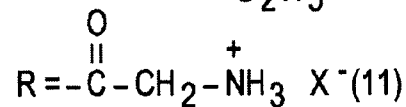
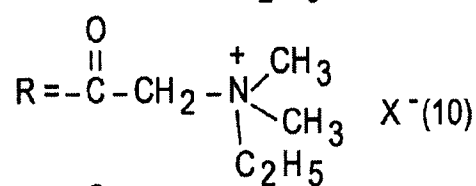
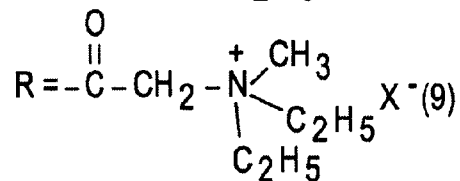
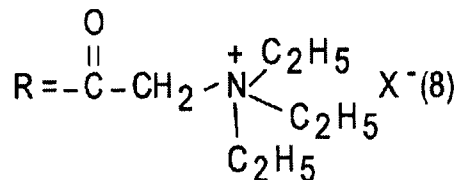
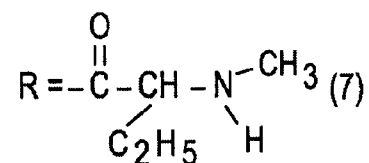
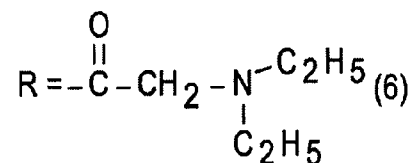
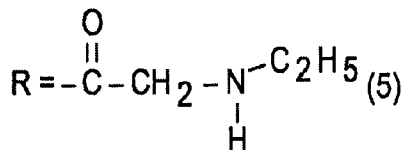
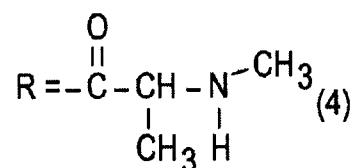
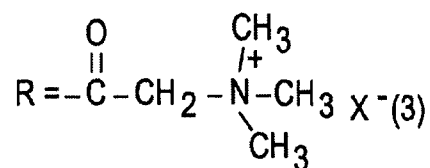
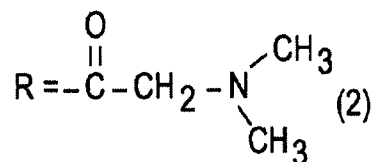
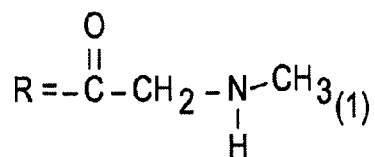


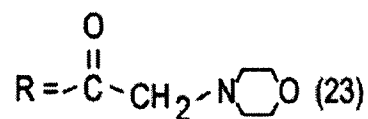
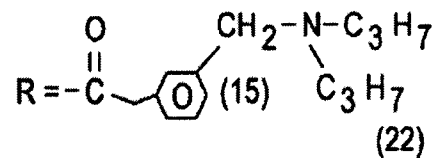
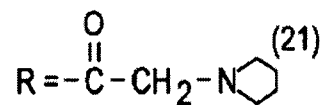
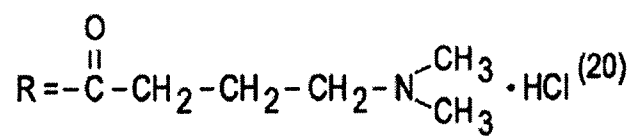
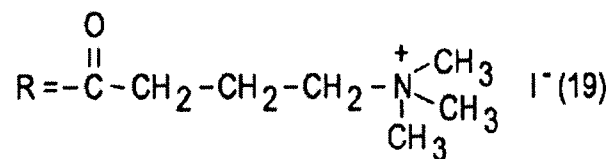
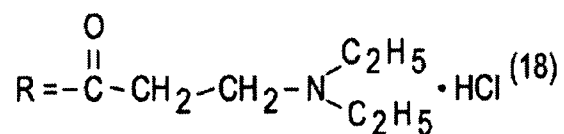
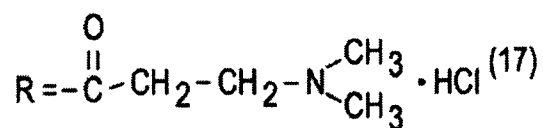
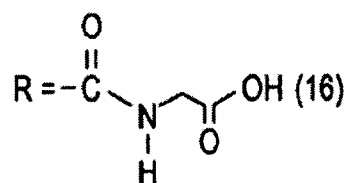
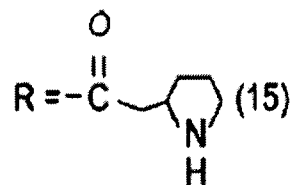
R2 is hydrogen or forms together with the oxygen to which it is bound an acyl group ($-\text{OCO}-\text{R}_3$), wherein R3 is a C1-C22 alkyl group or a C2-C22 alkenyl group,

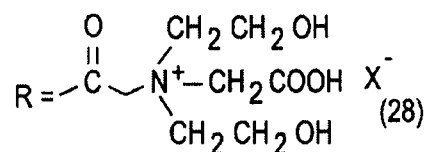
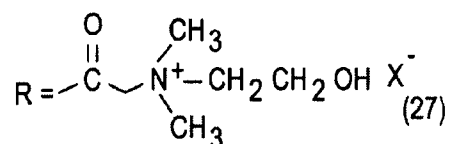
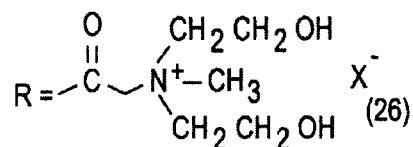
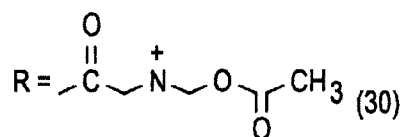
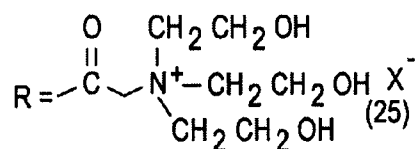
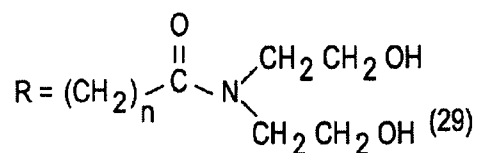
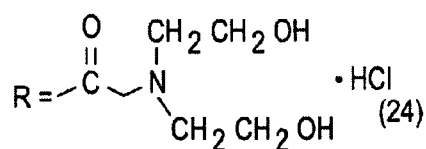
wherein, if R2 is hydrogen R1 forms a group of formula



wherein in compound 6, R is one of the following moieties:







wherein X^- is a free soluble anion,

wherein in compound 8

$\text{R1} = \text{OCH}_3$, $\text{R2} = \text{OH}$, $\text{R3} = \text{O-Glucose}$; or

$\text{R1} = \text{OCH}_3$, $\text{R2} = \text{H}$, $\text{R3} = \text{O-Glucose}$; or

$\text{R1} = \text{OCH}_3$, $\text{R2} = \text{OH}$, $\text{R3} = \text{OH}$; or

$\text{R1} = \text{OCH}_3$, $\text{R2} = \text{H}$, $\text{R3} = \text{OH}$; or

$\text{R1} = \text{OH}$, $\text{R2} = \text{OH}$, $\text{R3} = \text{O-Glucose}$; or

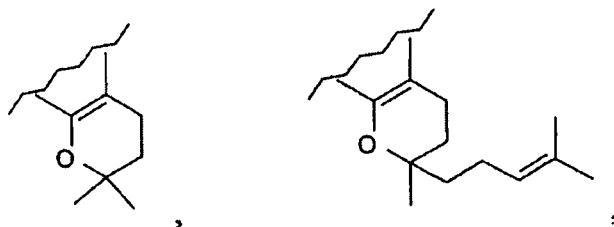
$\text{R1} = \text{OH}$, $\text{R2} = \text{OH}$, $\text{R3} = \text{OH}$;

wherein in compound 12

R1 , R2 , R3 , R4 , R5 , R6 , R7 , R8 , R9 , and R10 are independently chosen from hydrogen, hydroxyl, hydrocarbyl, substituted hydrocarbyl, hydrocarbyloxy, substituted hydrocarbyloxy, and sulfoxy; provided that at least one of the R groups is a hydroxyl or substituted hydroxyl group; and provided that if compound 12 is monomeric, then compound 12 is other than resveratrol,

wherein in compound 15

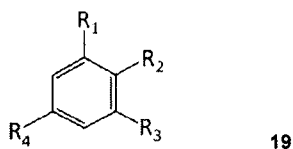
R1 , R2 and R3, independently from one another, represent H or (C1-C3)alkyl; R4 and R5 are identical or different and represent hydrogen, linear or branched (C1-C5)alkyl, a prenyl group $-\text{CH}_2-\text{CH}=\text{C}(\text{CH}_3)_2$, a geranyl group $-\text{CH}_2-\text{CH}=\text{C}(\text{CH}_3)(\text{CH}_2)_2\text{CH}=\text{C}(\text{CH}_3)_2$ or R4 and R1, and independently R5 and R2, together with the atoms they are linked to, form one of the following groups:



with the provisos that R4 and R5 are not both hydrogen and that when $\text{R1}=\text{R2}=\text{R3}=\text{H}$, R4 and R5 are not a prenyl group and hydrogen, respectively,

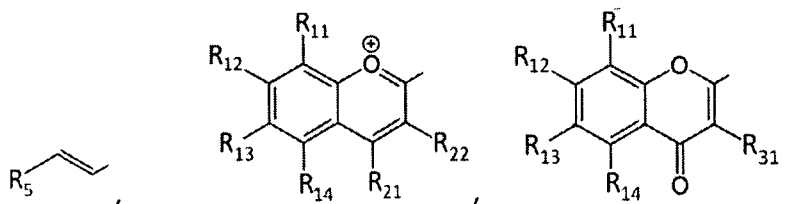
wherein in compound 18 X, Y, and Z are either hydrogen or a protective group, provided that at least one of X, Y, and Z is the protective group.

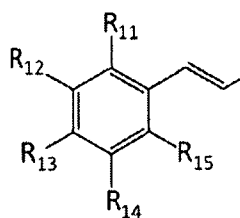
5. Peritoneal therapeutic fluid according to any one of claims 1, 2 and 4, wherein the biocompatibility enhancing agent is a compound of formula 19:



wherein in compound 19

R4 is selected from one of the following groups





or

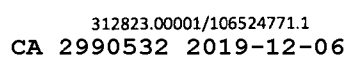
wherein at least 2 of R1, R2, R3, R12, and R14 are -OH,

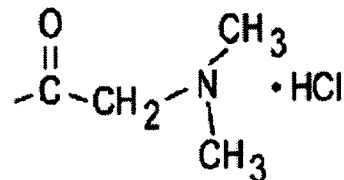
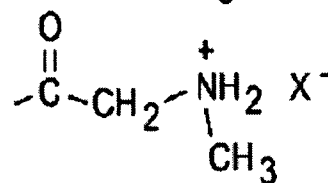
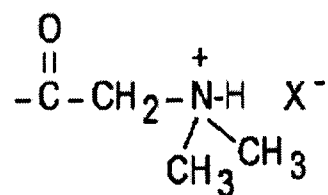
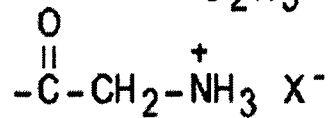
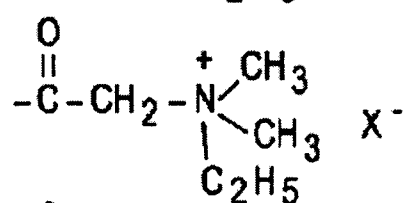
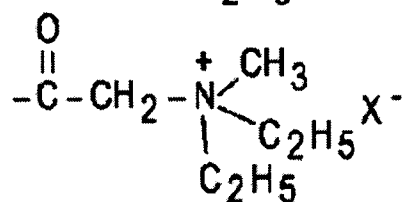
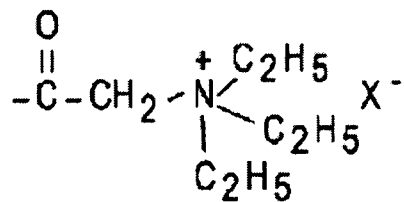
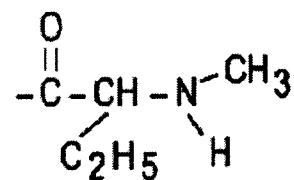
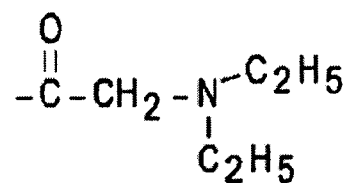
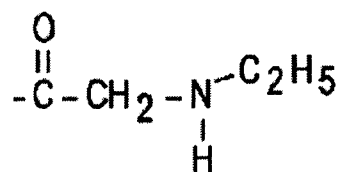
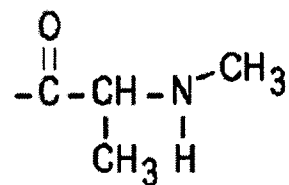
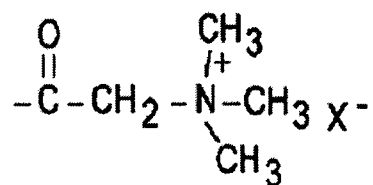
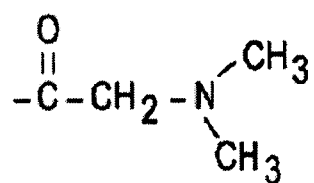
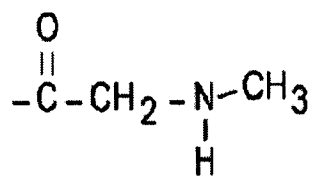
wherein R1, R2, R3, R5, R11, R12, R13, R14, R15, R21, R22 and R31 are independently from each other selected from

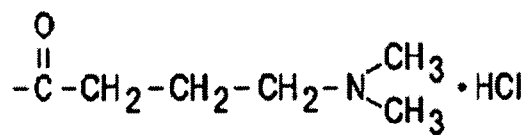
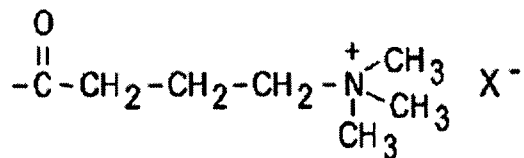
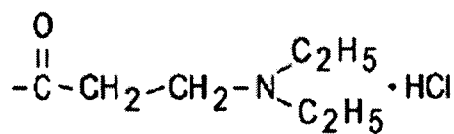
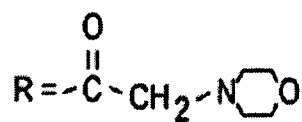
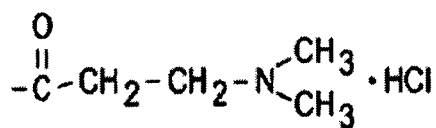
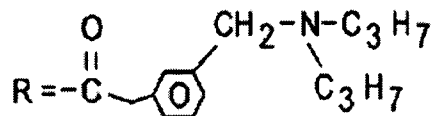
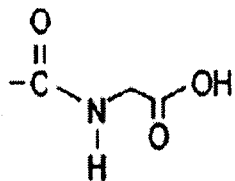
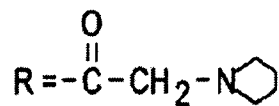
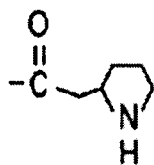
-H, -OH, -O-R_{Alk}, -CHO, -COR_{Alk}, -COOH, -COO-R_{Alk}, -CO-NH-C_nH_{2n}-COOH, -CO-NH-C_nH_{2n}-COO⁻,
 -CN, -Cl, -Br, -I, -NO₂,
 -C_nH_{2n}CN, -C_nH_{2n}-Cl, -C_nH_{2n}-Br, -C_nH_{2n}-I, -C_nH_{2n}-NO₂,
 -O-PO₃²⁻, -O-PO₃H⁻, -O-PO₃H₂, -NH₂, -NHR_{Alk}, -NR_{Alk1}R_{Alk2}, -N⁺H₃, -N⁺H₂R_{Alk}, -N⁺HR_{Alk1}R_{Alk2}, -N⁺R_{Alk1}R_{Alk2}R_{Alk3},
 -B(OH)₂, -OCHO, -O-COR_{Alk}, -OCF₃, -O-CN, -OCH₂CN,

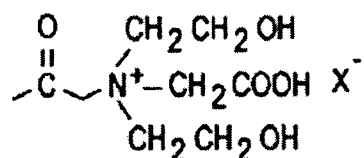
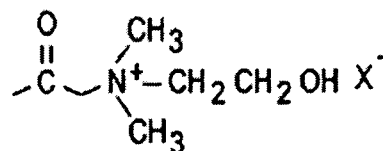
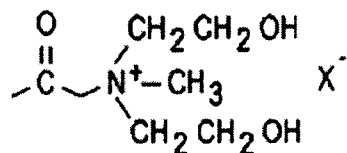
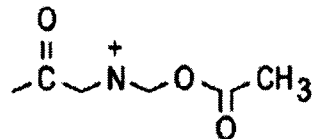
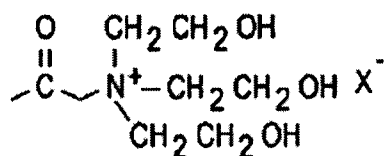
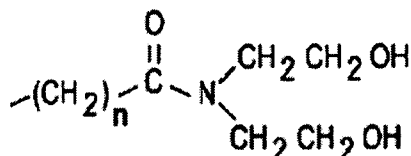
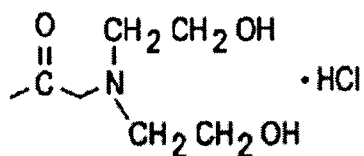
wherein R_{Alk}, R_{Alk1}, R_{Alk2}, and R_{Alk3} are independently alkyl residues,
 wherein in C_nH_{2n} n is an integer;

or wherein R1, R2, R3, R5, R11, R12, R13, R14, R15, R21, R22 and R31 are, independently from each other, one of the following moieties:









wherein X^- is a free soluble anion,

or wherein R_{11} , R_{12} , R_{13} , R_{14} or R_{15} are a mono or oligo saccharide-residue,

with the proviso that at least two of R_1 , R_2 , R_3 , R_{11} , R_{12} , R_{13} , R_{14} and R_{15} are independently selected from $-\text{OH}$, $-\text{O}-\text{R}_{\text{Alk}}$, $-\text{O}-\text{COR}_{\text{Alk}}$, $-\text{OCF}_3$, $-\text{O}-\text{CN}$, and $-\text{OCHO}$.

6. Peritoneal therapeutic fluid according to claim 5, wherein said alkyl residue is selected from CH_3 , C_2H_5 , C_3H_7 and C_4H_9 .
7. Peritoneal therapeutic fluid according to claim 5 or 6, wherein C_nH_{2n} is CH_2 , C_2H_4 , C_3H_6 , or C_4H_8 .

8. Peritoneal therapeutic fluid according to claim 1, wherein the biocompatibility enhancing agent is selected from the group consisting of:

epsilon-viniferin, pallidol, trans-diptoindonesin B, hopeaphenol, oxyresveratrol, 4'-methoxy-(E)-resveratrol 3-O-rutinoside, phenolic acids; phenolic diterpenes; coumarines, coumarines glucosides, dihydroxyisocoumarins, prenyloxy coumarines, naphthoquinones, atovaquone; flavonols, flavones, flavonoides, eriodictoyl, homoeriodictoyl, sakuranetin, flavanonols, flavans; anthocyanins; isoflavonoides, stilbenoides, aglycones; and mixtures of two or more thereof.

9. Peritoneal therapeutic fluid according to claim 8, wherein:

- said phenolic acids are selected from gallic acid, ellagic acid, vanillic acid, propyl gallate, protocatechuic acid, p-coumaric acid, danielone, syringic acid, salicylic acid, gentisic acid, p-hydroxy benzoic acid, rosmarinic acid, rosmanol, quinic acid, sinapic acid, epi-,isorosmanol, E-anethol, 3,4-dimethoxycinnamic acid, and ferulic acid;
- said phenolic diterpenes are selected from carnosol and carnosic acid;
- said coumarines are selected from coumarin, ombelliferon, herniarine, esculedol, scopoletol, scopanone, and fraxetol;
- said coumarines glucosides are selected from 7-O-glucosyl-ombelliferone, 6-O-glucosyl-esculetol, 7-O-glucosyl-esculetol, and 7-O-Glucosyl-6-methoxycoumarine;
- said dihydroxyisocoumarin is 6-methoxymellein;
- said prenyloxy coumarines are selected from 7-geranyloxy coumarine, 7-methoxy-6-(3-methyl-2-butenyl)-coumarine, and 7-methoxy-8-(3-methyl-2-butenyl)-coumarine;
- said naphthoquinones are selected from 1,2-naphthoquinone, 1,4-Naphthoquinone, 2,6-Naphthoquinone, alkannin, hexahydroxy-1,4-naphthalenedione, juglone, lapachol, lawsone, menatetrenone, 2-methoxy-1,4-naphthoquinone, nigrosprin B, 2,3,5,7-tetrahydroxy-1,4-naphthalenedione, menadione, 5,8-Dihydroxy-1,4-naphthoquinone and other dihydroxynaphthoquinones;

- said flavonols are selected from quercetin, kaempferol, myricetin, fisetin, galangin, isorhamnetin, pachypodol, rhamnazin pyranoflavonols and furanoflavonols;
 - said flavones are selected from apigenin, and tangeritin;
 - said flavonoides are selected from hesperetin, naringenin, eriodictoyl, homoeriodictoyl and sakuranetin;
 - said flavanonols are selected from taxifolin, dihydrolquercetin and dihydrokaempferol;
 - said flavans are selected from flavan-3ol including Catechin, Gallocatechin, catechin 3'-gallate, gallocatechin 3-gallate, epicatechin, epigallocatechin, epicatechin 3-gallate, Epigallocatechin 3-gallate, theaflavin, theaflavin-3-gallate, theaflavin-3,3'-digallate, thearubigin, proanthocyanidins, flavan-4-ol and flavan-3,4-diol;
 - said anthocyanins are selected from cyanidin, malvidin, pelargonidin, peonidin, petunidin, cyanin-3-rutinoside and delphinidin-3-rutinoside;
 - said isoflavonoides are selected from isoflavones, isoflavanes, isoflavenes, coumestans and pterocarpanes;
 - said stilbenoides is a stilbene; and
 - said aglycones are selected from piceatannol, pinosylvin and pterostilbene.
10. Peritoneal therapeutic fluid according to any one of claims 1-9, wherein the biocompatibility enhancing agent is solubilized through pegylation with Polyethyleneglycol (PEG) or Methoxy-Polyethyleneglycol (mPEG).
11. Peritoneal therapeutic fluid according to any one of claims 1 to 10, wherein the one or more biocompatibility enhancing agent is/are present in a concentration of 0.001 mg/L to 5g/L.
12. Peritoneal therapeutic fluid according to any one of claims 1 to 11, further comprising one or more of an ingredient which is selected from the following: alkali metal ions, alkaline earth metal ions, an osmotic agent, and/or a pH-buffer.

13. Peritoneal therapeutic fluid according to any one of claims 1 to 12, further comprising one or more of a saccharide, wherein the saccharide is fructose, a disaccharide, an oligosaccharide, a polysaccharide, or any mixture thereof.
14. Peritoneal therapeutic fluid container or kit comprising at least one liquid containing compartment, wherein liquid of at least one compartment contains a biocompatibility enhancing agent as mentioned in any one of claims 1 to 10, wherein the biocompatibility enhancing agent is solubilized.
15. Peritoneal therapeutic fluid container or kit comprising at least two compartments, wherein at least one compartment contains a biocompatibility enhancing agent as mentioned in any one of claims 1 to 10, wherein the biocompatibility enhancing agent may be in solubilized form or may be solubilized by contacting with a liquid from one of the other compartments.
16. Peritoneal therapeutic fluid container or kit according to claim 14 or 15, for use in peritoneal dialysis.
17. Peritoneal therapeutic fluid according to any one of claims 1 to 13, wherein the one or more BCA is/are be present in a concentration of between 0.05 to 20 $\mu\text{Mol/L}$.
18. Peritoneal therapeutic fluid according to any one of claims 1 to 13, further comprising glucose as osmotic agent.
19. Peritoneal therapeutic fluid according to claim 18, wherein the concentration of glucose is 0.5 to 20% by weight.
20. Peritoneal therapeutic fluid according to claim 13, wherein the disaccharide is selected from the group consisting of sucrose, Gentiobiulose, Laminaribiose, Gentiobiose, Rutinulose, Xylobiose, trehalose, β,β -Trehalose, α,β -Trehalose, lactulose, sophorose, lactose, cellobiose, chitobiose, maltose, Kojibiose, Nigerose, Isomaltose, Turanose, Maltulose, Palatinose (Isomaltulose), Mannobiose, Melibiose, Melibiulose, and Rutinose.
21. Peritoneal therapeutic fluid according to claim 13, wherein the oligosaccharide is a product of limited hydrolysis of one of more

of the following: starch, amylose, amylopectin, fructan, glucan, galactan, mannan, cellulose, arabic gum, amylose, glycogen, dextran, hemicellulose, arabinoxylose, and pectin.

22. Peritoneal therapeutic fluid according to claim 13, wherein the oligo-saccharide is an alpha-glucan with a degree of polymerization of 3 or higher.
23. Peritoneal therapeutic fluid according to claim 13, wherein the saccharide is selected from the group consisting of isomaltotriose, nigerotriose, maltotriose, melezitose, maltotriulose, raffinose, kestose, maltodextrin, dextrans, heparin, Dextran, glycogen, pullulan, starch, amylose, amylopectine, icodextrin, and mixtures thereof.
24. Peritoneal therapeutic fluid according to claim 13, wherein the one or more saccharide has a molecular weight in a range of 90D-50kD.
25. Peritoneal therapeutic fluid according to claim 13, wherein the one or more of a saccharide has a molecular weight of 90D to 500D.
26. Peritoneal therapeutic fluid according to claim 13, wherein the one or more of a saccharide has a molecular weight of 90D to 1.5kD.
27. Peritoneal therapeutic fluid according to claim 13, wherein the one or more of a saccharide has a molecular weight of 1.5kD to 50kD.
28. Peritoneal therapeutic fluid according to claim 13, wherein the one or more of a saccharide has a molecular weight of 350D to 50kD.
29. Peritoneal therapeutic fluid according to claim 13, wherein the one or more of a saccharide has a molecular weight between 250D and 50kD.
30. Peritoneal therapeutic fluid according to claim 13, wherein the one or more of a saccharide has a molecular weight of 150D to 400D.

31. Peritoneal therapeutic fluid according to claim 13, wherein the one or more of a saccharide is present in a total concentration of $\geq 0.02\%$ by weight.
32. Peritoneal therapeutic fluid according to claim 13, wherein the one or more of a saccharide is present in a total concentration of $\geq 0.75\%$ by weight.
33. Peritoneal therapeutic fluid according to claim 13, wherein the one or more of a saccharide is present in a total concentration of $\geq 2.4\%$ by weight.
34. Peritoneal therapeutic fluid according to claim 13, wherein the one or more of a saccharide is present in a total concentration of $\geq 5\%$ by weight.
35. Peritoneal therapeutic fluid according to claim 13, wherein the one or more of a saccharide is present in a total concentration of $\geq 7.5\%$ by weight.
36. Peritoneal therapeutic fluid according to claim 13, wherein the one or more of a saccharide is present in a total concentration of $\geq 20\%$ by weight.
37. Peritoneal therapeutic fluid according to any one of claims 1 to 36, wherein the peritoneal dialysis fluid or peritoneal therapeutic fluid is for use for decreasing expression of Vascular Endothelial Growth Factor (VEGF) in the peritoneum.
38. Peritoneal therapeutic fluid according to any one of claims 1 to 36, wherein the peritoneal dialysis fluid or peritoneal therapeutic fluid is for use in decreasing long term fibrosis.
39. Peritoneal therapeutic fluid according to any one of claims 1 to 36, wherein the peritoneal fluid is used in a peritoneal therapy which is selected from the group consisting of peritoneal nutrition, peritoneal detoxification in case of liver failure or drug abuse, treatment of primary and secondary peritoneal cancer, treatment of peritoneal infections and peritonitis, and pre- or post-operative peritoneal treatment.

40. Use of a peritoneal therapeutic fluid comprising one or more of a biocompatibility enhancing agent (BCA) as a peritoneal dialysis fluid, or as a peritoneal therapeutic fluid with decreased cytotoxicity on human peritoneal mesothelial cells, wherein the biocompatibility enhancing agent is selected from the group consisting of a polyphenolic compound, a metabolite of a polyphenolic compound which is obtained by metabolization in the human or animal body, a salt of a polyphenolic compound, and a glycoside of a polyphenolic compound.
41. Use of a peritoneal therapeutic fluid comprising one or more of a biocompatibility enhancing agent (BCA) as a peritoneal dialysis fluid, or as a peritoneal therapeutic fluid with decreased cytotoxicity on human peritoneal mesothelial cells, wherein the biocompatibility enhancing agent is selected from the group consisting of a polyphenolic compound, a metabolite of a polyphenolic compound which is obtained by metabolization in the human or animal body, a salt of a polyphenolic compound, and a glycoside of a polyphenolic compound wherein the one or more BCA is/are present in a concentration of between 0.05 to 20 $\mu\text{Mol/L}$.
42. Use of a peritoneal therapeutic fluid comprising one or more of a biocompatibility enhancing agent (BCA) as a peritoneal dialysis fluid, or as a peritoneal therapeutic fluid with decreased cytotoxicity on human peritoneal mesothelial cells, wherein the biocompatibility enhancing agent is selected from the group consisting of a polyphenolic compound, a metabolite of a polyphenolic compound which is obtained by metabolization in the human or animal body, a salt of a polyphenolic compound, and a glycoside of a polyphenolic compound, wherein the peritoneal therapeutic fluid comprises one or more of a saccharide, wherein the saccharide is fructose, a disaccharide, an oligosaccharide, a polysaccharide, or any mixture thereof.
43. Use of a peritoneal therapeutic fluid comprising one or more of a biocompatibility enhancing agent (BCA) as a peritoneal dialysis fluid, or as a peritoneal therapeutic fluid with decreased cytotoxicity on human peritoneal mesothelial cells, wherein the biocompatibility enhancing agent is selected from the group consisting of a polyphenolic compound, a metabolite of a

polyphenolic compound which is obtained by metabolization in the human or animal body, a salt of a polyphenolic compound, and a glycoside of a polyphenolic compound, wherein the peritoneal dialysis fluid or peritoneal therapeutic fluid is used for decreasing expression of Vascular Endothelial Growth Factor (VEGF) in the peritoneum.

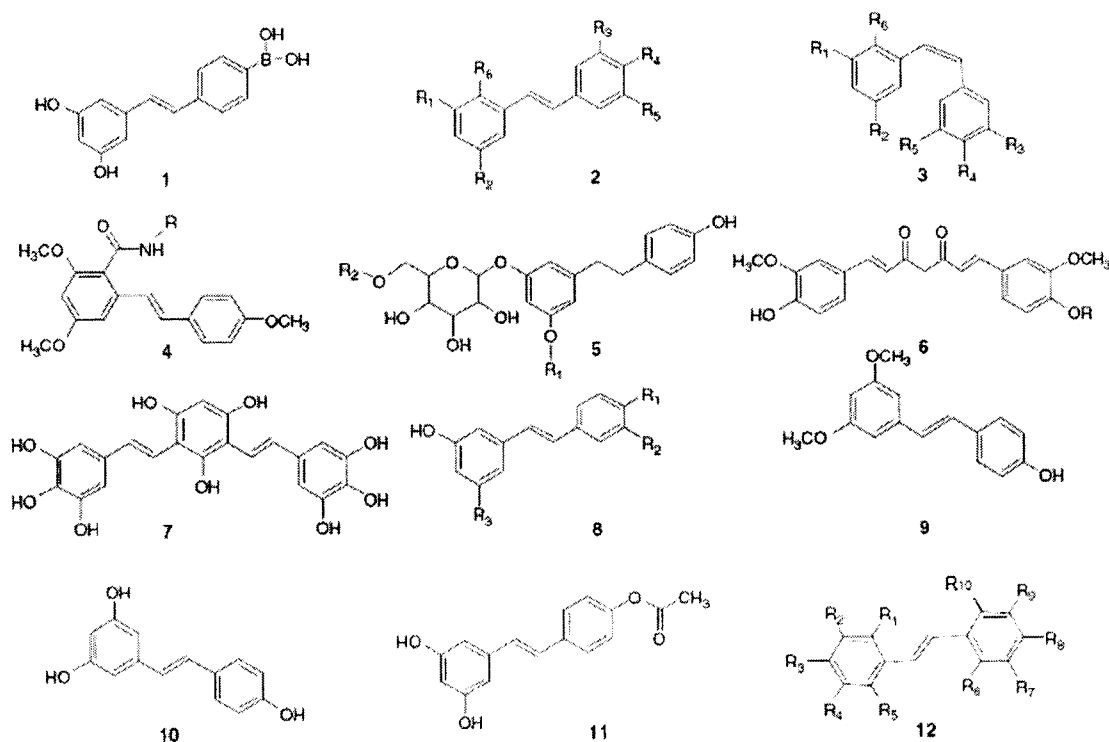
44. Use of a peritoneal therapeutic fluid comprising one or more of a biocompatibility enhancing agent (BCA) as a peritoneal dialysis fluid, or as a peritoneal therapeutic fluid with decreased cytotoxicity on human peritoneal mesothelial cells, wherein the biocompatibility enhancing agent is selected from the group consisting of a polyphenolic compound, a metabolite of a polyphenolic compound which is obtained by metabolization in the human or animal body, a salt of a polyphenolic compound, and a glycoside of a polyphenolic compound, wherein the peritoneal dialysis fluid or peritoneal therapeutic fluid is used for decreasing long term fibrosis.
45. Use of a peritoneal therapeutic fluid comprising one or more of a biocompatibility enhancing agent (BCA) as a peritoneal dialysis fluid, or as a peritoneal therapeutic fluid with decreased cytotoxicity on human peritoneal mesothelial cells, wherein the biocompatibility enhancing agent is selected from the group consisting of a polyphenolic compound, a metabolite of a polyphenolic compound which is obtained by metabolization in the human or animal body, a salt of a polyphenolic compound, and a glycoside of a polyphenolic compound, wherein the peritoneal fluid is used in a peritoneal therapy which is selected from the group consisting of peritoneal nutrition, peritoneal detoxification in case of liver failure or drug abuse, treatment of primary and secondary peritoneal cancer, treatment of peritoneal infections and peritonitis, and pre- or post-operative peritoneal treatment.
46. The use according to any one of claims 40 and 42 to 45, wherein the one or more BCA is/are present in a concentration of between 0.05 to 20 $\mu\text{Mol/L}$.
47. The use according to any one of claims 40, 41 and 43 to 46, further comprising one or more of a saccharide, wherein the

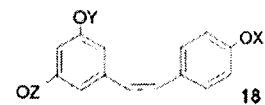
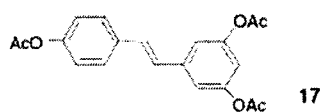
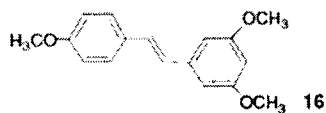
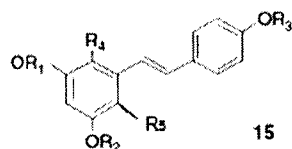
saccharide is fructose, a disaccharide, an oligosaccharide, a polysaccharide, or any mixture thereof.

48. The use according to claim 42 or claim 47, wherein the disaccharide is selected from the group consisting of sucrose, Gentiobiulose, Laminaribiose, Gentiobiose, Rutinulose, Xylobiose, trehalose, β,β -Trehalose, α,β -Trehalose, lactulose, sophorose, lactose, cellobiose, chitobiose, maltose, Kojibiose, Nigerose, Isomaltose, Turanose, Maltulose, Palatinose (Isomaltulose), Mannobiose, Melibiose, Melibiulose, and Rutinose.
49. The use according to claim 42 or claim 47, wherein the oligosaccharide is a product of limited hydrolysis of one of more of the following: starch, amylose, amylopectin, fructan, glucan, galactan, mannan, cellulose, arabic gum, amylose, glycogen, dextran, hemicellulose, arabinoxyllose, and pectin.
50. The use according to claim 42 or claim 47, wherein the oligosaccharide is an alpha-glucan with a degree of polymerization of 3 or higher.
51. The use according to claim 42 or claim 47, wherein the saccharide is selected from the group consisting of isomaltotriose, nigerotriose, maltotriose, melezitose, maltotriulose, raffinose, kestose, maltodextrin, dextrans, heparin, Dextran, glycogen, pullulan, starch, amylose, amylopectine, icodextrin, and mixtures thereof.
52. The use according to claim 42 or claim 47, wherein the one or more saccharide has a molecular weight in a range of 90D to 50 kD, 90D to 500 D, 90D to 1.5 kD, 1.5kD to 50kD, 350D to 50kD, 250D to 50 kD, or 150D to 400D.
53. The use according to claim 42 or claim 47, wherein the one or more of a saccharide is present in a total concentration of ≥ 0.02 % by weight, ≥ 0.75 % by weight, ≥ 2.4 % by weight, ≥ 5 % by weight, ≥ 7.5 % by weight, or ≥ 20 % by weight.
54. The use according to any one of claims 40 to 42 and 44 to 53, wherein the peritoneal dialysis fluid or peritoneal therapeutic

fluid is used for decreasing expression of Vascular Endothelial Growth Factor (VEGF) in the peritoneum.

55. The use according to any one of claims 40 to 43 and 45 to 54, wherein the peritoneal dialysis fluid or peritoneal therapeutic fluid is used for decreasing long term fibrosis.
56. The use according to any one of claims 40 to 44 and 46 to 55, wherein the peritoneal fluid is used in a peritoneal therapy which is selected from the group consisting of peritoneal nutrition, peritoneal detoxification in case of liver failure or drug abuse, treatment of primary and secondary peritoneal cancer, treatment of peritoneal infections and peritonitis, and pre- or post-operative peritoneal treatment.
57. The use according to any one of claims 40 to 56, wherein the biocompatibility enhancing agent is resveratrol, a resveratrol derivative, dihydro-resveratrol, piceid, piceatannol, pterostilbene, piceid glucoside, caffeic acid, luteolin, or delphinidin, and wherein the resveratrol derivative is selected from following compounds 1-12, 15, 16, 17, 18:





wherein in compound 2 and compound 3

$R_1 = R_2 = R_4 = OH$, $R_3 = R_5 = R_6 = H$; or

$R_1 = R_2 = R_4 = OCH_3$, $R_3 = R_5 = R_6 = H$; or

$R_1 = R_2 = R_4 = OCH_3$, $R_3 = R_5 = H$; $R_6 = OH$; or

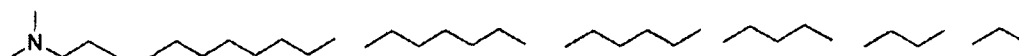
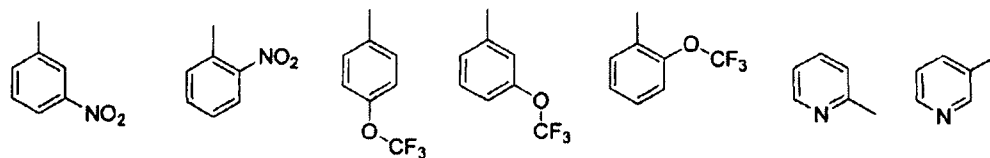
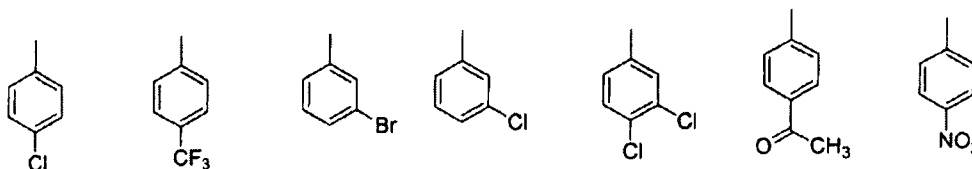
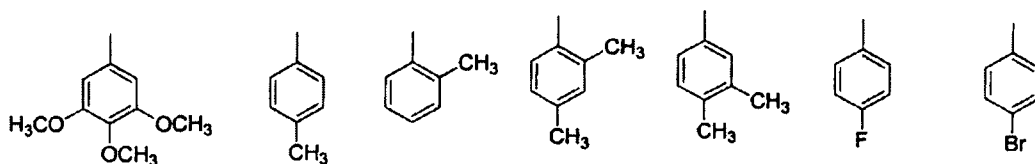
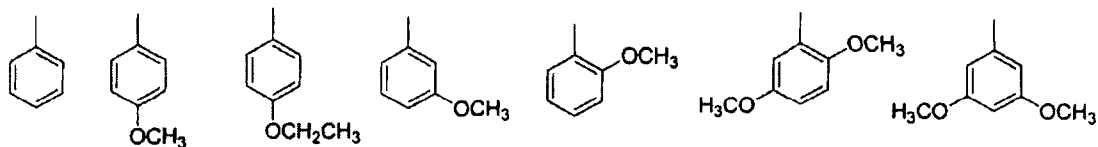
$R_1 = R_2 = R_3 = R_5 = OCH_3$, $R_4 = R_6 = H$; or

$R_1 = R_2 = R_3 = R_4 = OCH_3$, $R_5 = R_6 = H$; or

$R_1 = R_2 = R_3 = R_4 = OCH_3$, $R_5 = H$, $R_6 = OH$;

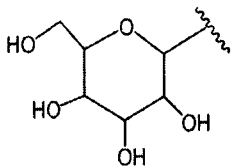
$R_1 = R_2 = R_3 = R_4 = OCH_3$, $R_5 = H$, $R_6 = OH$;

wherein in compound 4 R is one of the following moieties:



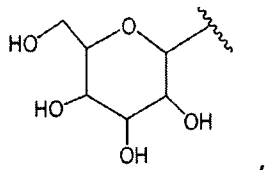
wherein in compound 5

R1 is hydrogen or a group of formula

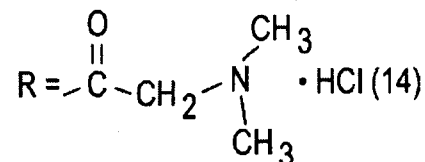
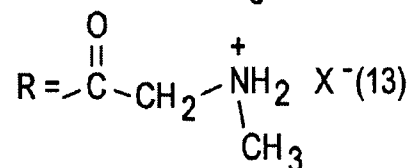
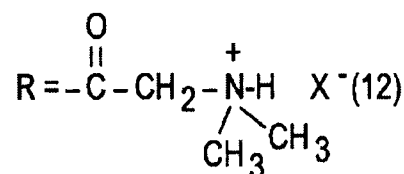
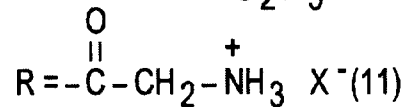
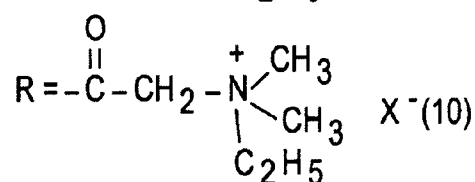
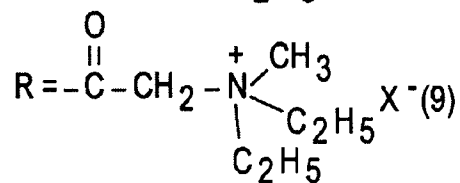
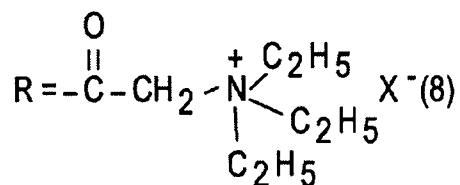
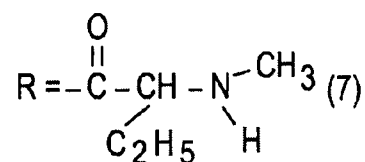
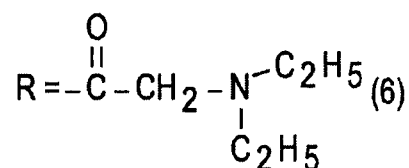
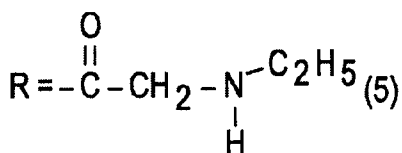
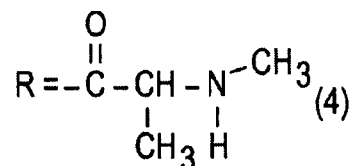
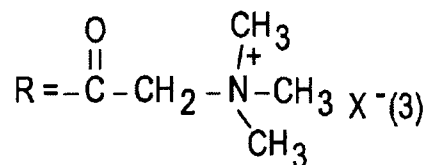
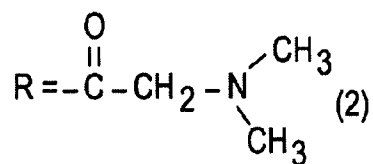
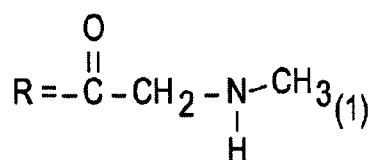


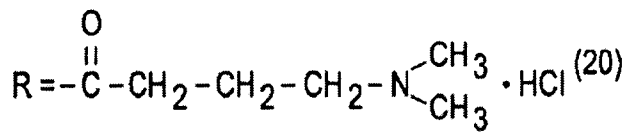
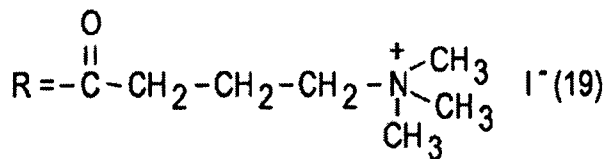
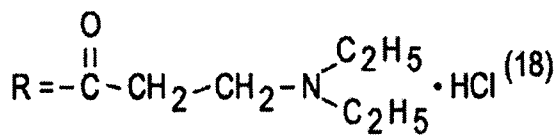
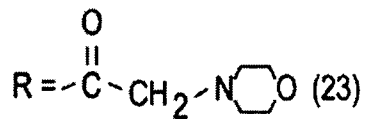
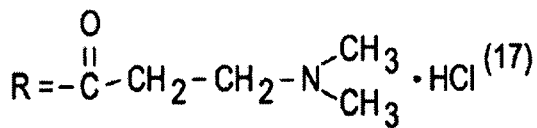
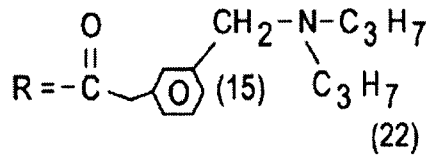
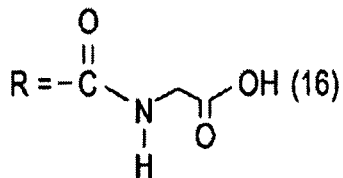
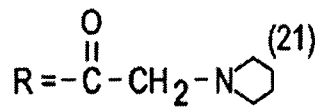
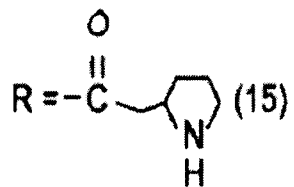
R2 is hydrogen or forms together with the oxygen to which it is bound an acyl group (-OCO-R3), wherein R3 is a C1-C22 alkyl group or a C2-C22 alkenyl group,

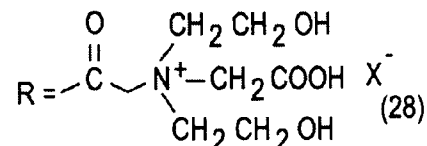
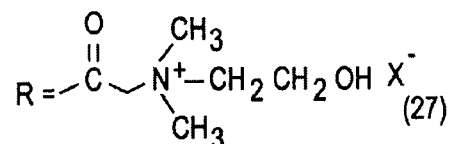
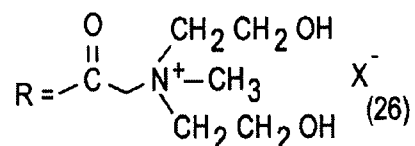
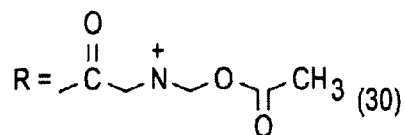
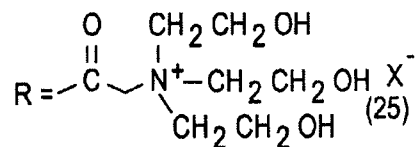
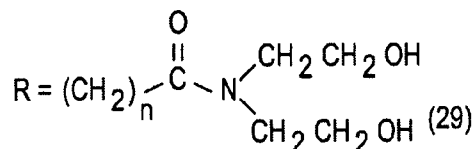
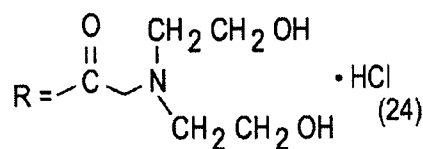
wherein, if R2 is hydrogen R1 forms a group of formula



wherein in compound 6, R is one of the following moieties:







wherein X^- is a free soluble anion,

wherein in compound 8

$\text{R1} = \text{OCH}_3$, $\text{R2} = \text{OH}$, $\text{R3} = \text{O-Glucose}$; or

$\text{R1} = \text{OCH}_3$, $\text{R2} = \text{H}$, $\text{R3} = \text{O-Glucose}$; or

$\text{R1} = \text{OCH}_3$, $\text{R2} = \text{OH}$, $\text{R3} = \text{OH}$; or

$\text{R1} = \text{OCH}_3$, $\text{R2} = \text{H}$, $\text{R3} = \text{OH}$; or

$\text{R1} = \text{OH}$, $\text{R2} = \text{OH}$, $\text{R3} = \text{O-Glucose}$; or

$\text{R1} = \text{OH}$, $\text{R2} = \text{OH}$, $\text{R3} = \text{OH}$;

wherein in compound 12

R1 , R2 , R3 , R4 , R5 , R6 , R7 , R8 , R9 , and R10 are independently chosen from hydrogen, hydroxyl, hydrocarbyl, substituted hydrocarbyl, hydrocarbyloxy, substituted hydrocarbyloxy, and sulfoxy; provided that at least one of the R groups is a hydroxyl or substituted hydroxyl group; and provided that if compound 12 is monomeric, then compound 12 is other than resveratrol,

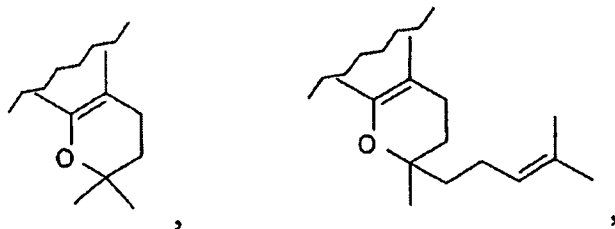
wherein in compound 15

R1 , R2 and R3, independently from one another, represent H or (C1-C3)alkyl; R4 and R5 are identical or different and represent hydrogen, linear or branched (C1-C5)alkyl,

a prenyl group $-\text{CH}_2-\text{CH}=\text{C}(\text{CH}_3)_2$,

a geranyl group $-\text{CH}_2-\text{CH}=\text{C}(\text{CH}_3)(\text{CH}_2)_2\text{CH}=\text{C}(\text{CH}_3)_2$

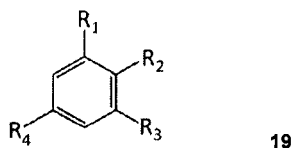
or R4 and R1, and independently R5 and R2, together with the atoms they are linked to, form one of the following groups:



with the provisos that R4 and R5 are not both hydrogen and that when R1=R2=R3=H, R4 and R5 are not a prenyl group and hydrogen, respectively,

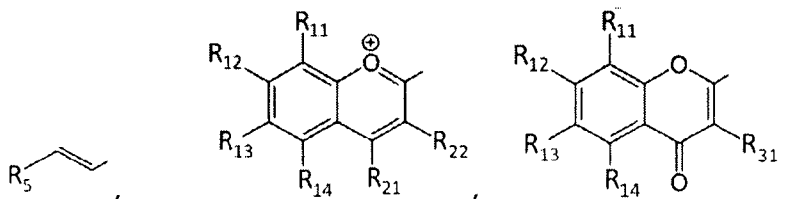
wherein in compound 18 X, Y, and Z are either hydrogen or a protective group, provided that at least one of X, Y, and Z is the protective group.

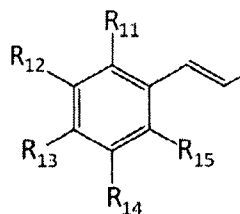
58. The use according to any one of claims 40 to 56, wherein the biocompatibility enhancing agent is a compound of formula 19:



wherein in compound 19

R4 is selected from one of the following groups





or

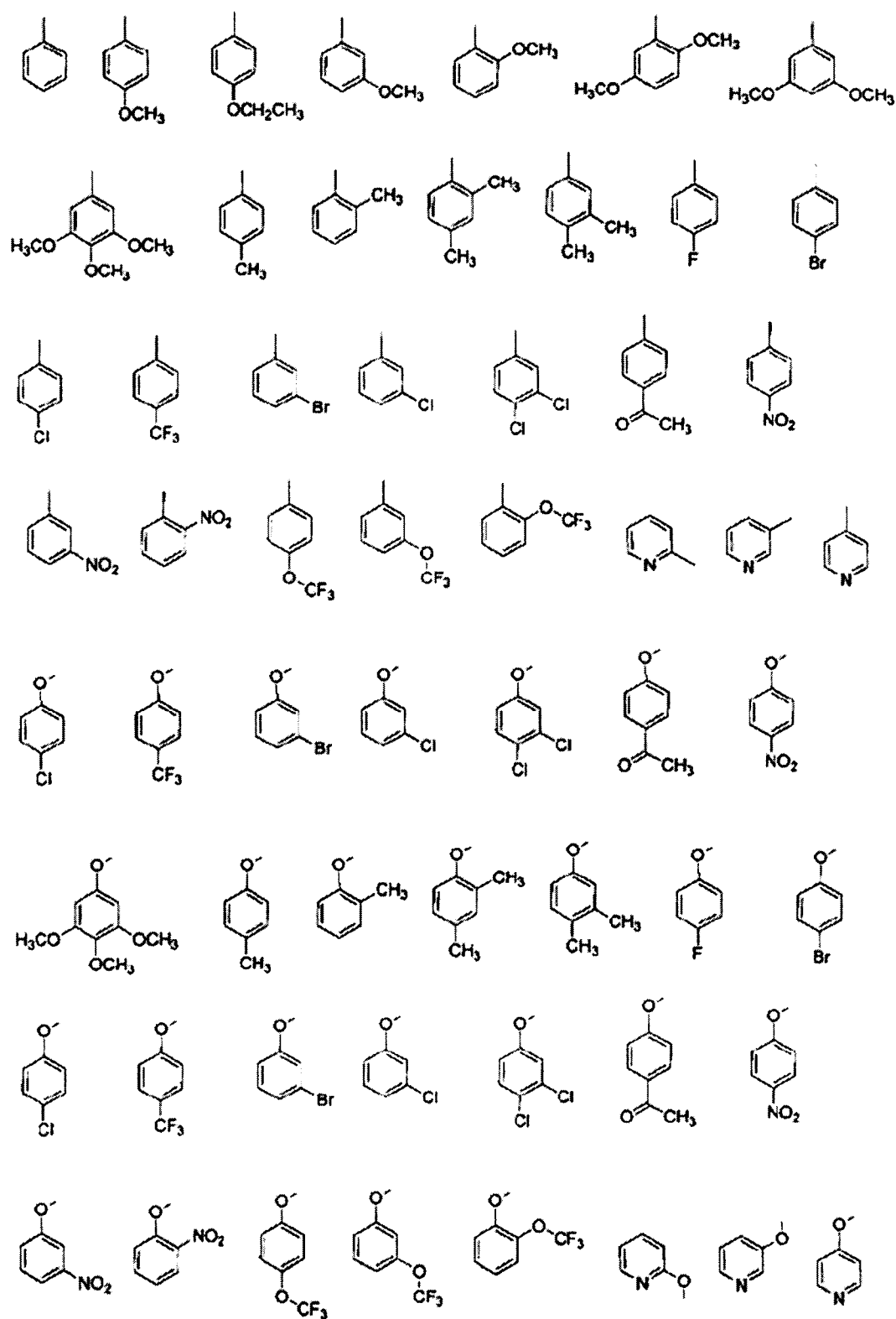
wherein at least 2 of R1, R2, R3, R12, and R14 are -OH,

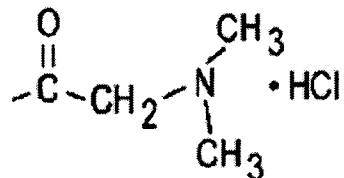
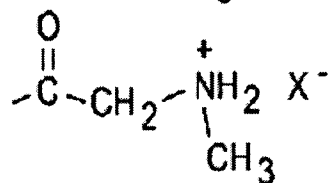
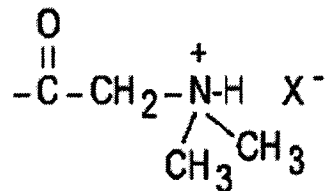
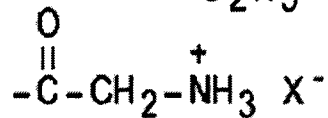
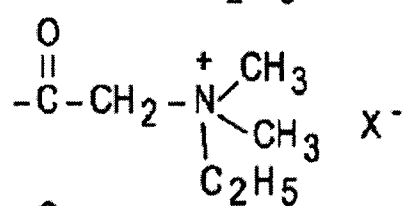
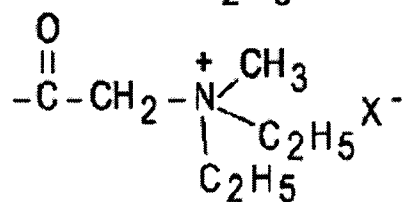
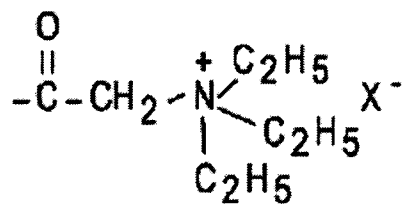
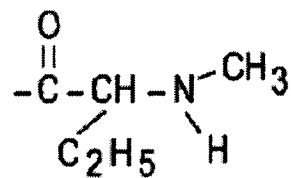
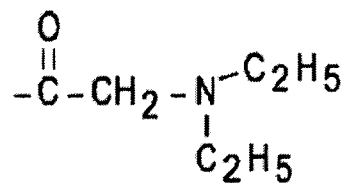
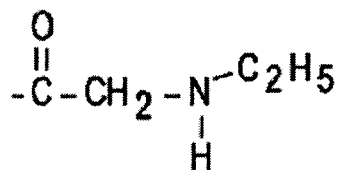
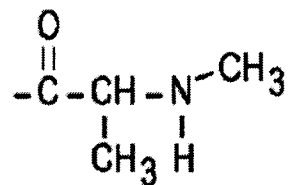
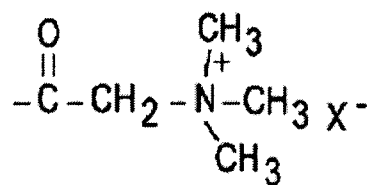
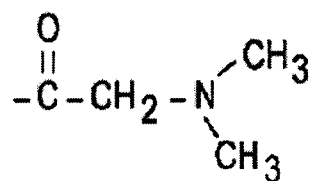
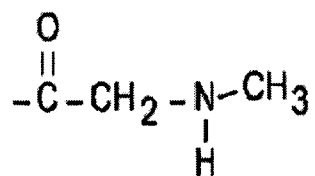
wherein R1, R2, R3, R5, R11, R12, R13, R14, R15, R21, R22 and R31 are independently from each other selected from

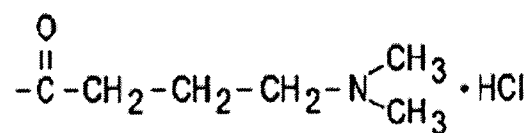
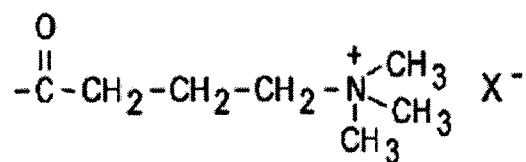
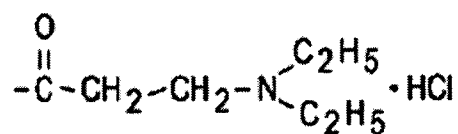
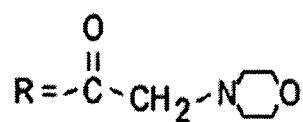
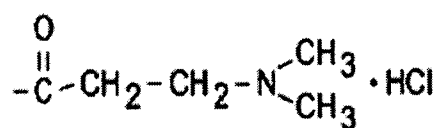
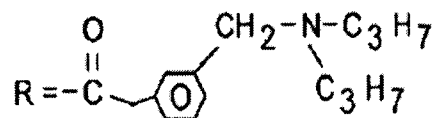
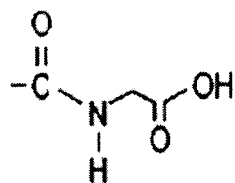
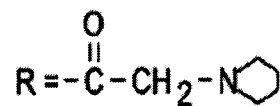
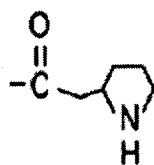
-H, -OH, -O-R_{Alk}, -CHO, -COR_{Alk}, -COOH, -COO-R_{Alk}, -CO-NH-C_nH_{2n}-COOH, -CO-NH-C_nH_{2n}-COO⁻,
 -CN, -Cl, -Br, -I, -NO₂,
 -C_nH_{2n}CN, -C_nH_{2n}-Cl, -C_nH_{2n}-Br, -C_nH_{2n}-I, -C_nH_{2n}-NO₂,
 -O-PO₃²⁻, -O-PO₃H⁻, -O-PO₃H₂, -NH₂, -NHR_{Alk}, -NR_{Alk1}R_{Alk2}, -N⁺H₃, -N⁺H₂R_{Alk}, -N⁺HR_{Alk1}R_{Alk2}, -N⁺R_{Alk1}R_{Alk2}R_{Alk3},
 -B(OH)₂, -OCHO, -O-COR_{Alk}, -OCF₃, -O-CN, -OCH₂CN,

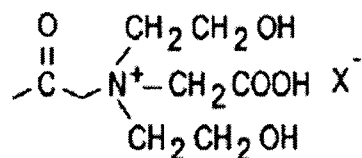
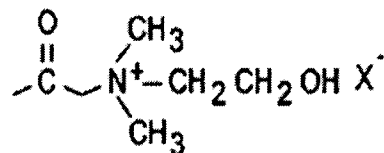
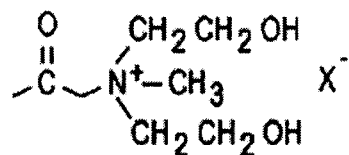
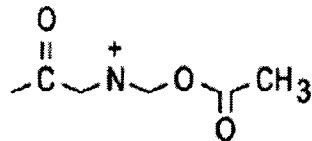
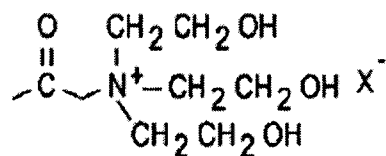
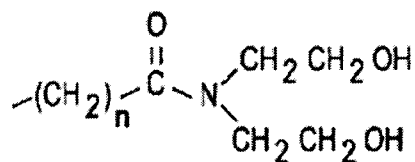
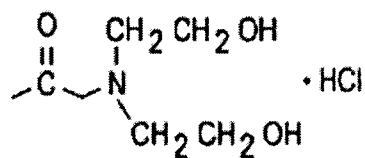
wherein R_{Alk}, R_{Alk1}, R_{Alk2}, and R_{Alk3} are independently alkyl residues, wherein in C_nH_{2n} n is an integer;

or wherein R1, R2, R3, R5, R11, R12, R13, R14, R15, R21, R22 and R31 are, independently from each other, one of the following moieties:









wherein X^- is a free soluble anion,

or wherein R_{11} , R_{12} , R_{13} , R_{14} or R_{15} are a mono or oligo saccharide-residue,

with the proviso that at least two of R_1 , R_2 , R_3 , R_{11} , R_{12} , R_{13} , R_{14} and R_{15} are independently selected from $-\text{OH}$, $-\text{O-R}_{\text{Alk}}$, $-\text{O-COR}_{\text{Alk}}$, $-\text{OCF}_3$, $-\text{O-CN}$, and $-\text{OCHO}$.

59. The use according to claim 58, wherein the alkyl residues are selected from the group consisting of CH_3 , C_2H_5 , C_3H_7 and C_4H_9 .
60. The use according to claim 58, wherein C_nH_{2n} is CH_2 , C_2H_4 , C_3H_6 or C_4H_8 .
61. The use according to claim 40, wherein the biocompatibility enhancing agent is selected from the group consisting of:

epsilon-viniferin, oxyresveratrol, gallic acid, vanillic acid, protocatechuic acid, p-coumaric acid, danielone, syringic acid, salicylic acid, gentisic acid, p-hydroxy benzoic acid, rosmanol, quinic acid, sinapic acid, 3,4-dimethoxycinnamic acid, ferulic acid, apigenin, tangeritin, cyanidin, malvidin, pelargonidin, peonidin, petunidin, piceatannol, pinosylvin, pterostilbene, and mixtures of two or more thereof.

62. The use according to any one of claims 40 to 61, wherein the biocompatibility enhancing agent is solubilized through pegylation with Polyethyleneglycol (PEG) or Methoxy-Polyethyleneglycol (mPEG).
63. The use according to any one of claims 40 to 62, wherein the one or more biocompatibility enhancing agent is/are present in a concentration of 0.001 mg/L to 5g/L.
64. The use according to any one of claims 40 to 63, further comprising one or more of an ingredient which is selected from the following: alkali metal ions, alkaline earth metal ions, an osmotic agent, and/or a pH-buffer.
65. The use according to any one of claims 40 to 64, further comprising glucose as osmotic agent.
66. The use to claim 65, wherein the concentration of glucose is 0.5 to 20% by weight.
67. The use according to any one of claims 40 to 66, wherein the biocompatibility enhancing agent is contained in a compartment of a container or kit, and wherein a liquid is contained in a further compartment of the container or kit, and wherein, before application, the biocompatibility enhancing agent is solubilized by contacting it with the liquid to produce the peritoneal therapeutic fluid.
68. The use according to any one of claims 40 to 67 wherein the biocompatibility agent is selected from the group consisting of stilbenoids, phenolic acids, flavonoids, flavones, anthocyanidins,

a salt of such said biocompatibility enhancing agent, and a glycoside of such said biocompatibility enhancing agent.

69. The use according to any one of claims 40 to 67, wherein the biocompatibility enhancing agent is selected from the group consisting of:

epsilon-viniferin, pallidol, trans-diptoindonesin B, hopeaphenol, oxyresveratrol, 4'-methoxy-(E)-resveratrol 3-O-rutinoside, phenolic acids; phenolic diterpenes; coumarines, coumarines glucosides, dihydroxyisocoumarins, prenyloxy coumarines, naphthoquinones, atovaquone; flavonols, flavones, flavonoides, eriodictoyl, homoeriodictoyl, sakuranetin, flavanonols, flavans; anthocyanins; isoflavonoides, stilbenoides, aglycones; and mixtures of two or more thereof.

70. The use according to claim 69, wherein:

- said phenolic acids are selected from gallic acid, ellagic acid, vanillic acid, propyl gallate, protocatechuic acid, p-coumaric acid, danielone, syringic acid, salicylic acid, gentisic acid, p-hydroxy benzoic acid, rosmarinic acid, rosmanol, quinic acid, sinapic acid, epi-,isorosmanol, E-anethol, 3,4-dimethoxycinnamic acid, and ferulic acid;
- said phenolic diterpenes are selected from carnosol and carnosic acid;
- said coumarines are selected from coumarin, ombelliferon, herniarine, esculedol, scopoletol, scopanone, and fraxetol;
- said coumarines glucosides are selected from 7-O-glucosyl-ombelliferone, 6-O-glucosyl-esculetol, 7-O-glucosyl-esculetol, and 7-O-Glucosyl-6-methoxycoumarine;
- said dihydroxyisocoumarin is 6-methoxymellein;
- said prenyloxy coumarines are selected from 7-geranyloxy coumarine, 7-methoxy-6-(3-methyl-2-butenyl)-coumarine, and 7-methoxy-8-(3-methyl-2-butenyl)-coumarine;
- said naphthoquinones are selected from 1,2-naphthoquinone, 1,4-Naphthoquinone, 2,6-Naphthoquinone, alkannin, hexahydroxy-1,4-naphthalenedione, juglone, lapachol, lawsone, menatetrenone, 2-methoxy-1,4-naphthoquinone, nigrosprin B, 2,3,5,7-tetrahydroxy-

1,4-naphtalenedione, menadione, 5,8-Dihydroxy-1,4-naphtoquinone and other dihydroxynophtoquinones;

- said flavonols are selected from quercetin, kaempferol, myricetin, fisetin, galangin, isorhamnetin, pachypodol, rhamnazin pyranoflavonols and furanoflavonols;
- said flavones are selected from apigenin, and tangeritin;
- said flavonoides are selected from hesperetin, naringenin, eriodictoyl, homoeriodictoyl and sakuranetin;
- said flavanonols are selected from taxifolin, dihydrolquercitin and dihydrokaempferol;
- said flavans are selected from flavan-3ol including Catechin, Gallocatechin, catechin 3'-gallate, gallocatechin 3-gallate, epicatechin, epigallocatechin, epicatechin 3-gallate, Epigallocatechin 3-gallate, theaflavin, theaflavin-3-gallate, theaflavin-3,3'-digallate, thearubigin, proanthocyanidins, flavan-4-ol and flavan-3,4-diol;
- said anthocyanins are selected from cyanidin, malvidin, pelargonidin, peonidin, petunidin, cyanin-3-rutinoside and delphinidin-3-rutinoside;
- said isoflavonoides are selected from isoflavones, isoflavanes, isoflavones, coumestans and pterocarpanes;
- said stilbenoide is a stilbene; and
- said aglycones are selected from piceatannol, pinosylvin and pterostilbene.

71. Peritoneal therapeutic fluid comprising one or more of a biocompatibility enhancing agent (BCA) that is selected from the group consisting of a polyphenolic compound, a metabolite of a polyphenolic compound which is obtained by metabolization in the human or animal body, a salt of a polyphenolic compound, and a glycoside of a polyphenolic compound,

for use as a peritoneal dialysis fluid, or as a peritoneal therapeutic fluid with decreased cytotoxicity on human peritoneal mesothelial cells,

wherein the one or more BCA is/are present in a concentration of between 0.05 to 20 $\mu\text{Mol/L}$.

72. Peritoneal therapeutic fluid comprising one or more of a biocompatibility enhancing agent (BCA) that is selected from the group consisting of a polyphenolic compound, a metabolite of a polyphenolic compound which is obtained by metabolization in the human or animal body, a salt of a polyphenolic compound, and a glycoside of a polyphenolic compound,

for use as a peritoneal dialysis fluid, or as a peritoneal therapeutic fluid with decreased cytotoxicity on human peritoneal mesothelial cells,

wherein the peritoneal therapeutic fluid comprises one or more of a saccharide, wherein the saccharide is fructose, a disaccharide, an oligosaccharide, a polysaccharide, or any mixture thereof.

73. Peritoneal therapeutic fluid comprising one or more of a biocompatibility enhancing agent (BCA) that is selected from the group consisting of a polyphenolic compound, a metabolite of a polyphenolic compound which is obtained by metabolization in the human or animal body, a salt of a polyphenolic compound, and a glycoside of a polyphenolic compound,

for use as a peritoneal dialysis fluid, or as a peritoneal therapeutic fluid with decreased cytotoxicity on human peritoneal mesothelial cells,

wherein the peritoneal dialysis fluid or peritoneal therapeutic fluid is used for decreasing expression of Vascular Endothelial Growth Factor (VEGF) in the peritoneum.

74. Peritoneal therapeutic fluid comprising one or more of a biocompatibility enhancing agent (BCA) that is selected from the group consisting of a polyphenolic compound, a metabolite of a polyphenolic compound which is obtained by metabolization in the human or animal body, a salt of a polyphenolic compound, and a glycoside of a polyphenolic compound,

for use as a peritoneal dialysis fluid, or as a peritoneal therapeutic fluid with decreased cytotoxicity on human peritoneal mesothelial cells,

wherein the peritoneal dialysis fluid or peritoneal therapeutic fluid is used for decreasing long term fibrosis.

75. Peritoneal therapeutic fluid comprising one or more of a biocompatibility enhancing agent (BCA) that is selected from the group consisting of a polyphenolic compound, a metabolite of a polyphenolic compound which is obtained by metabolization in the human or animal body, a salt of a polyphenolic compound, and a glycoside of a polyphenolic compound,

for use as a peritoneal dialysis fluid, or as a peritoneal therapeutic fluid with decreased cytotoxicity on human peritoneal mesothelial cells,

wherein the peritoneal fluid is used in a peritoneal therapy which is selected from the group consisting of peritoneal nutrition, peritoneal detoxification in case of liver failure or drug abuse, treatment of primary and secondary peritoneal cancer, treatment of peritoneal infections and peritonitis, and pre- or post-operative peritoneal treatment.

76. Peritoneal therapeutic fluid according to any one of claims 72 to 75, wherein the one or more BCA is/are present in a concentration of between 0.05 to 20 $\mu\text{Mol/L}$.

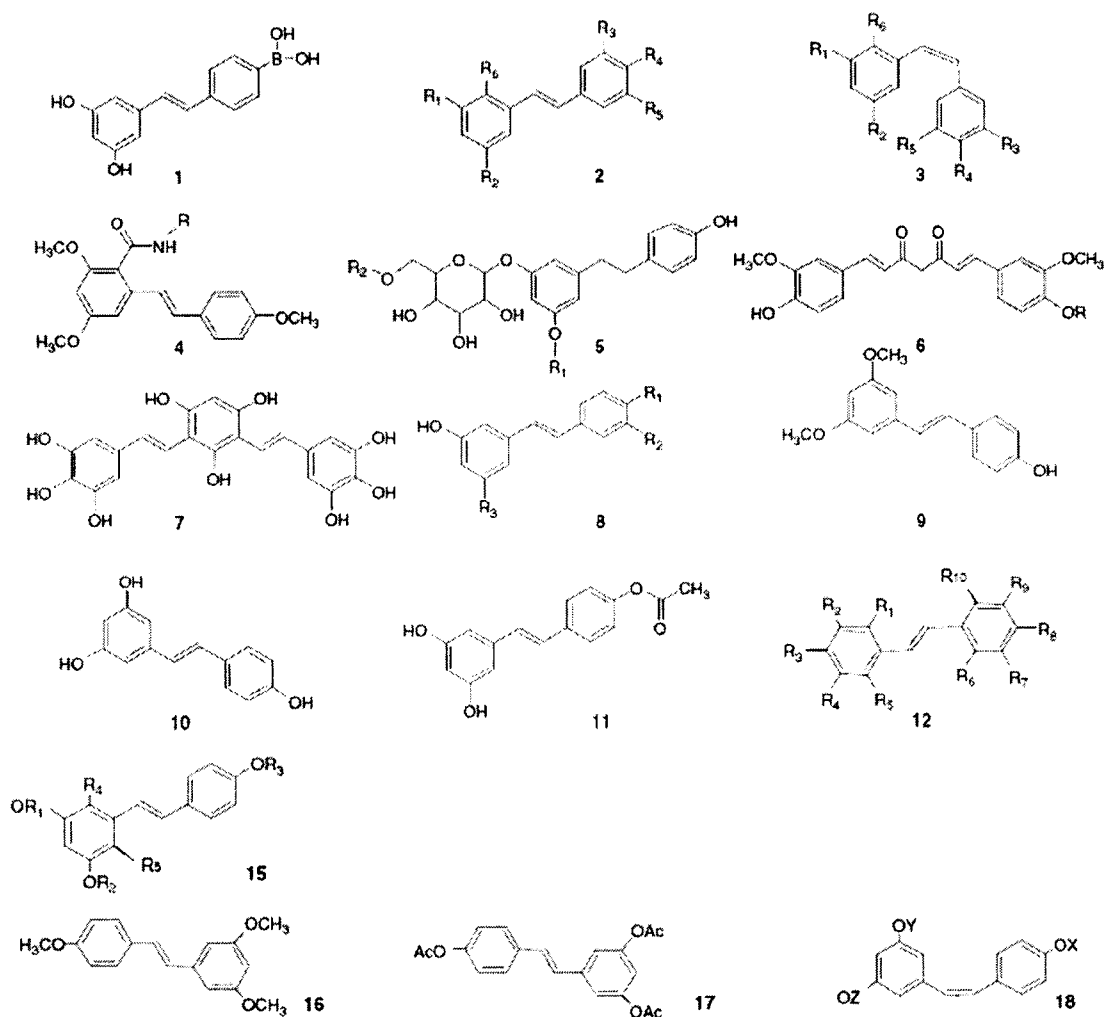
77. Peritoneal therapeutic fluid according to any one of claims 71 and 73 to 76, further comprising one or more of a saccharide, wherein the saccharide is fructose, a disaccharide, an oligosaccharide, a polysaccharide, or any mixture thereof.

78. Peritoneal therapeutic fluid according to claim 72 or claim 77, wherein the disaccharide is selected from the group consisting of sucrose, Gentiobiulose, Laminaribiose, Gentiobiose, Rutinulose, Xylobiose, trehalose, β,β -Trehalose, α,β -Trehalose, lactulose, sophorose, lactose, cellobiose, chitobiose, maltose, Kojibiose, Nigerose, Isomaltose, Turanose, Maltulose, Palatinose (Isomaltulose), Mannobiose, Melibiose, Melibiulose, and Rutinose.

79. Peritoneal therapeutic fluid according to claim 72 or claim 77, wherein the oligosaccharide is a product of limited hydrolysis of one of more of the following: starch, amylose, amylopectin, fructan, glucan, galactan, mannan, cellulose, arabic gum, amylose, glycogen, dextran, hemicellulose, arabinoxyllose, and pectin.

80. Peritoneal therapeutic fluid according to claim 72 or claim 77, wherein the oligo-saccharide is an alpha-glucan with a degree of polymerization of 3 or higher.
81. Peritoneal therapeutic fluid according to claim 72 or claim 77, wherein the saccharide is selected from the group consisting of isomaltotriose, nigerotriose, maltotriose, melezitose, maltotriulose, raffinose, kestose, maltodextrin, dextrans, heparin, Dextran, glycogen, pullulan, starch, amylose, amylopectine, icodextrin, and mixtures thereof.
82. Peritoneal therapeutic fluid according to claim 72 or claim 77, wherein the one or more saccharide has a molecular weight in a range of 90D to 50 kD, 90D to 500 D, 90D to 1.5 kD, 1.5kD to 50kD, 350D to 50kD, 250D to 50 kD, or 150D to 400D.
83. Peritoneal therapeutic fluid according to claim 72 or claim 77, wherein the one or more of a saccharide is present in a total concentration of ≥ 0.02 % by weight, ≥ 0.75 % by weight, ≥ 2.4 % by weight, ≥ 5 % by weight, ≥ 7.5 % by weight, or ≥ 20 % by weight.
84. Peritoneal therapeutic fluid according to any one of claims 71, 72 and 74 to 83, wherein the peritoneal dialysis fluid or peritoneal therapeutic fluid is used for decreasing expression of Vascular Endothelial Growth Factor (VEGF) in the peritoneum.
85. Peritoneal therapeutic fluid according to any one of claims 71 to 73 and 75 to 84, wherein the peritoneal dialysis fluid or peritoneal therapeutic fluid is used for decreasing long term fibrosis.
86. Peritoneal therapeutic fluid according to any one of claims 71 to 74 and 76 to 85, wherein the peritoneal fluid is used in a peritoneal therapy which is selected from the group consisting of peritoneal nutrition, peritoneal detoxification in case of liver failure or drug abuse, treatment of primary and secondary peritoneal cancer, treatment of peritoneal infections and peritonitis, and pre- or post-operative peritoneal treatment.
87. Peritoneal therapeutic fluid according to any one of claims 71 to 86, wherein the biocompatibility enhancing agent is resveratrol,

a resveratrol derivative, dihydro-resveratrol, piceid, piceatannol, pterostilbene, piceid glucoside, caffeic acid, luteolin, or delphinidin, and wherein the resveratrol derivative is selected from following compounds 1-12, 15, 16, 17, 18:



wherein in compound 2 and compound 3

R1 = R2 = R4 = OH, R3 = R5 = R6 = H; or

R1 = R2 = R4 = OCH3, R3 = R5 = R6 = H; or

R1 = R2 = R4 = OCH3, R3 = R5 = H; R6 = OH; or

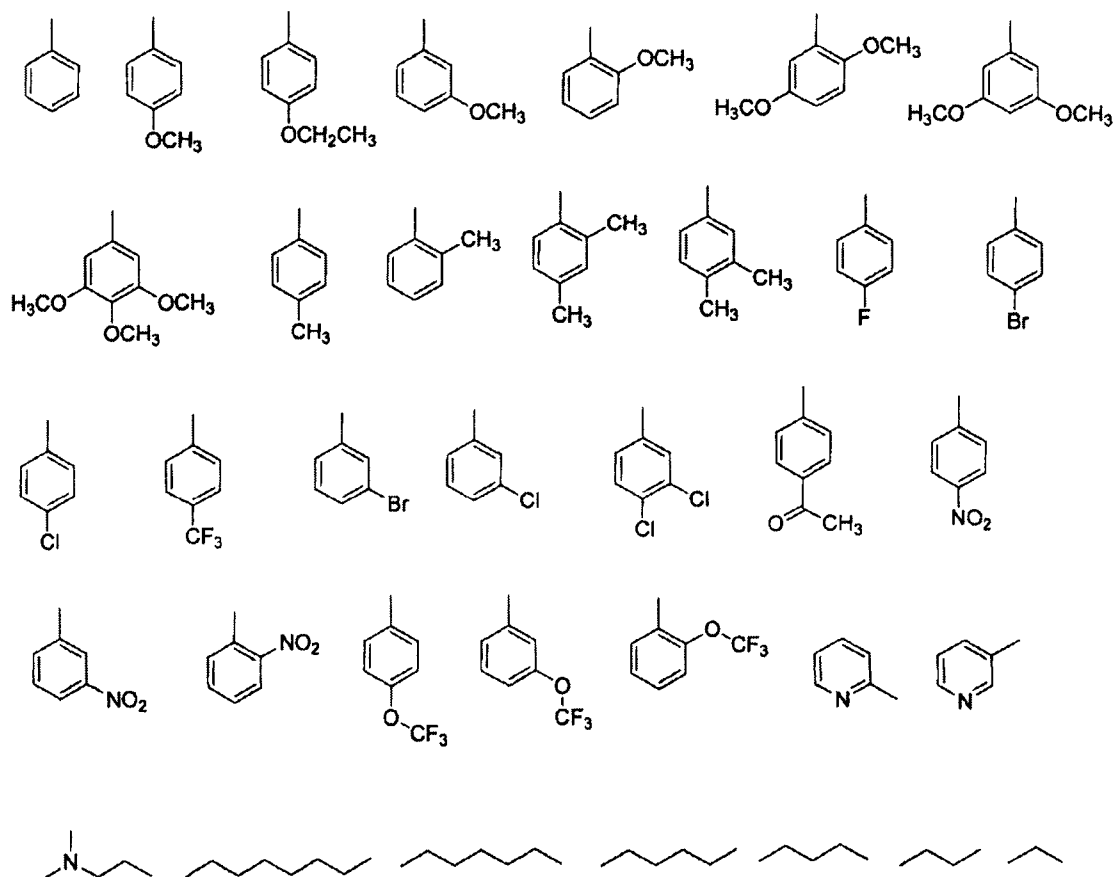
R1 = R2 = R3 = R5 = OCH3, R4 = R6 = H; or

R1 = R2 = R3 = R5 = OCH3, R4 = H, R6 = OH; or

R1 = R2 = R3 = R4 = OCH3, R5 = R6 = H; or

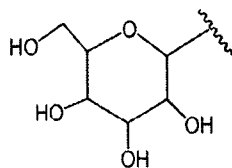
R1 = R2 = R3 = R4 = OCH3, R5 = H, R6 = OH;

wherein in compound 4 R is one of the following moieties:



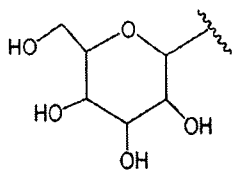
wherein in compound 5

R1 is hydrogen or a group of formula

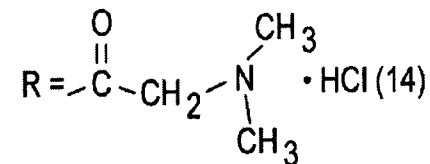
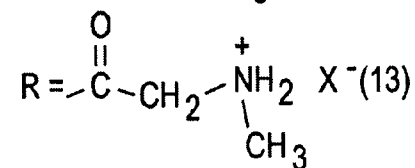
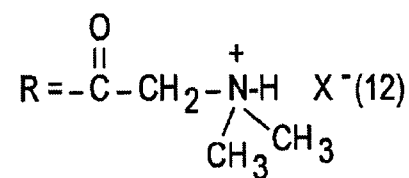
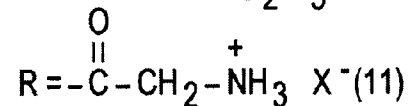
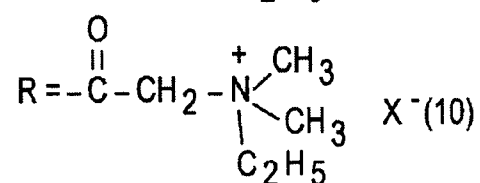
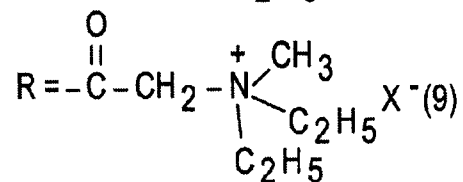
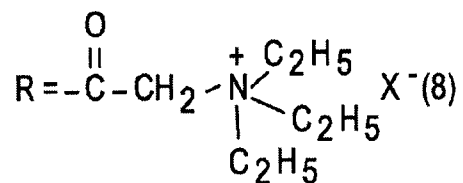
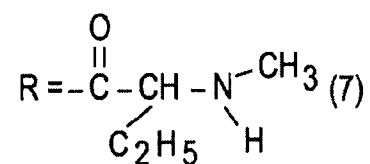
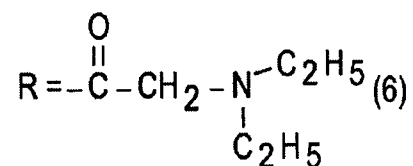
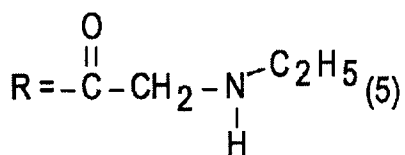
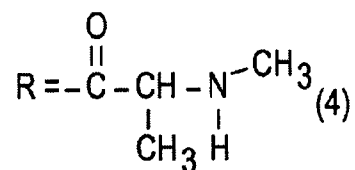
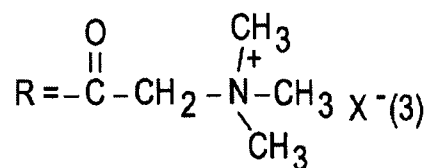
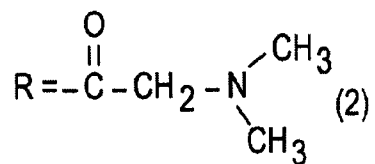
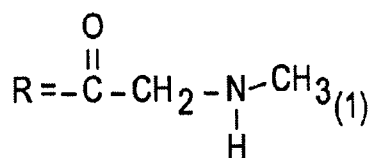


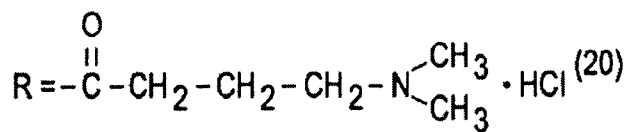
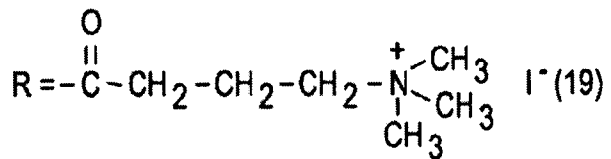
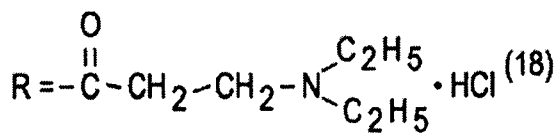
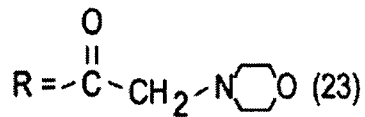
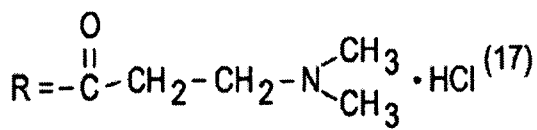
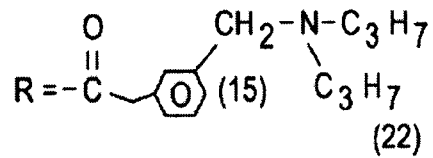
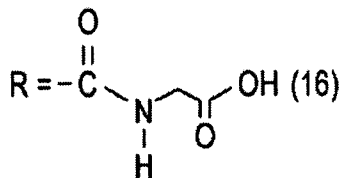
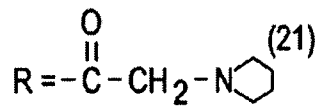
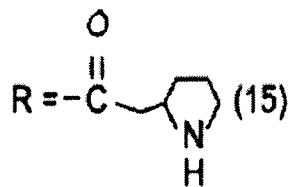
R2 is hydrogen or forms together with the oxygen to which it is bound an acyl group (-OCO-R3), wherein R3 is a C1-C22 alkyl group or a C2-C22 alkenyl group,

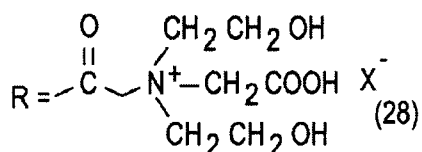
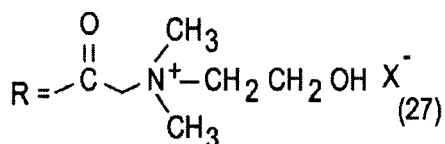
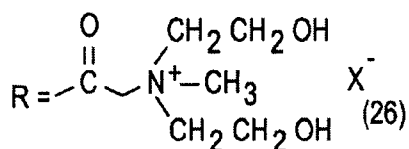
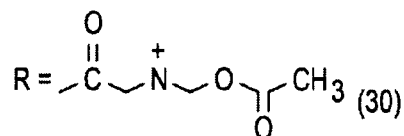
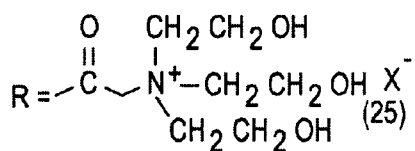
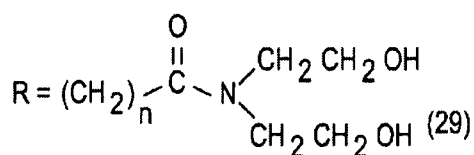
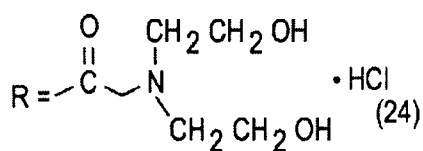
wherein, if R2 is hydrogen R1 forms a group of formula



wherein in compound 6, R is one of the following moieties:







wherein X⁻ is a free soluble anion,

wherein in compound 8

R1 = OCH3, R2 = OH, R3 = O-Glucose; or

R1 = OCH3, R2 = H, R3 = O-Glucose; or

R1 = OCH3, R2 = OH, R3 = OH; or

R1 = OCH3, R2 = H, R3 = OH; or

R1 = OH, R2 = OH, R3 = O-Glucose; or

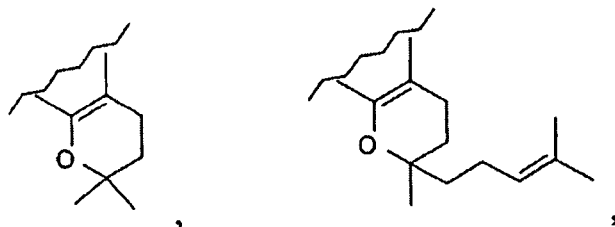
R1 = OH, R2 = OH, R3 = OH;

wherein in compound 12

R1, R2, R3, R4, R5, R6, R7, R8, R9, and R10 are independently chosen from hydrogen, hydroxyl, hydrocarbyl, substituted hydrocarbyl, hydrocarbyloxy, substituted hydrocarbyloxy, and sulfoxy; provided that at least one of the R groups is a hydroxyl or substituted hydroxyl group; and provided that if compound 12 is monomeric, then compound 12 is other than resveratrol,

wherein in compound 15

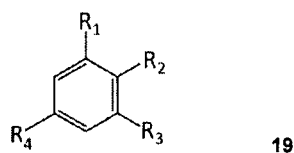
R1 , R2 and R3, independently from one another, represent H or (C1-C3)alkyl; R4 and R5 are identical or different and represent hydrogen, linear or branched (C1-C5)alkyl, a prenyl group $-\text{CH}_2-\text{CH}=\text{C}(\text{CH}_3)_2$, a geranyl group $-\text{CH}_2-\text{CH}=\text{C}(\text{CH}_3)(\text{CH}_2)_2\text{CH}=\text{C}(\text{CH}_3)_2$ or R4 and R1, and independently R5 and R2, together with the atoms they are linked to, form one of the following groups:



with the provisos that R4 and R5 are not both hydrogen and that when R1=R2=R3=H, R4 and R5 are not a prenyl group and hydrogen, respectively,

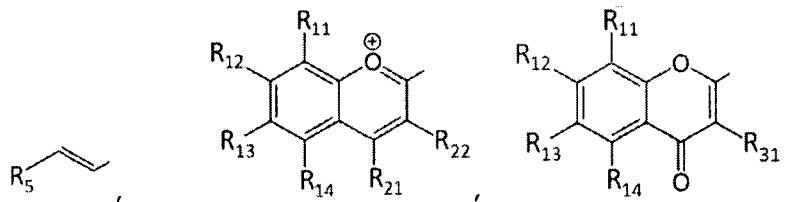
wherein in compound 18 X, Y, and Z are either hydrogen or a protective group, provided that at least one of X, Y, and Z is the protective group.

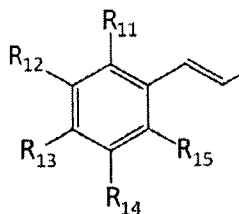
88. Peritoneal therapeutic fluid according to any one of claims 71 to 86, wherein the biocompatibility enhancing agent is a compound of formula 19:



wherein in compound 19

R4 is selected from one of the following groups





or

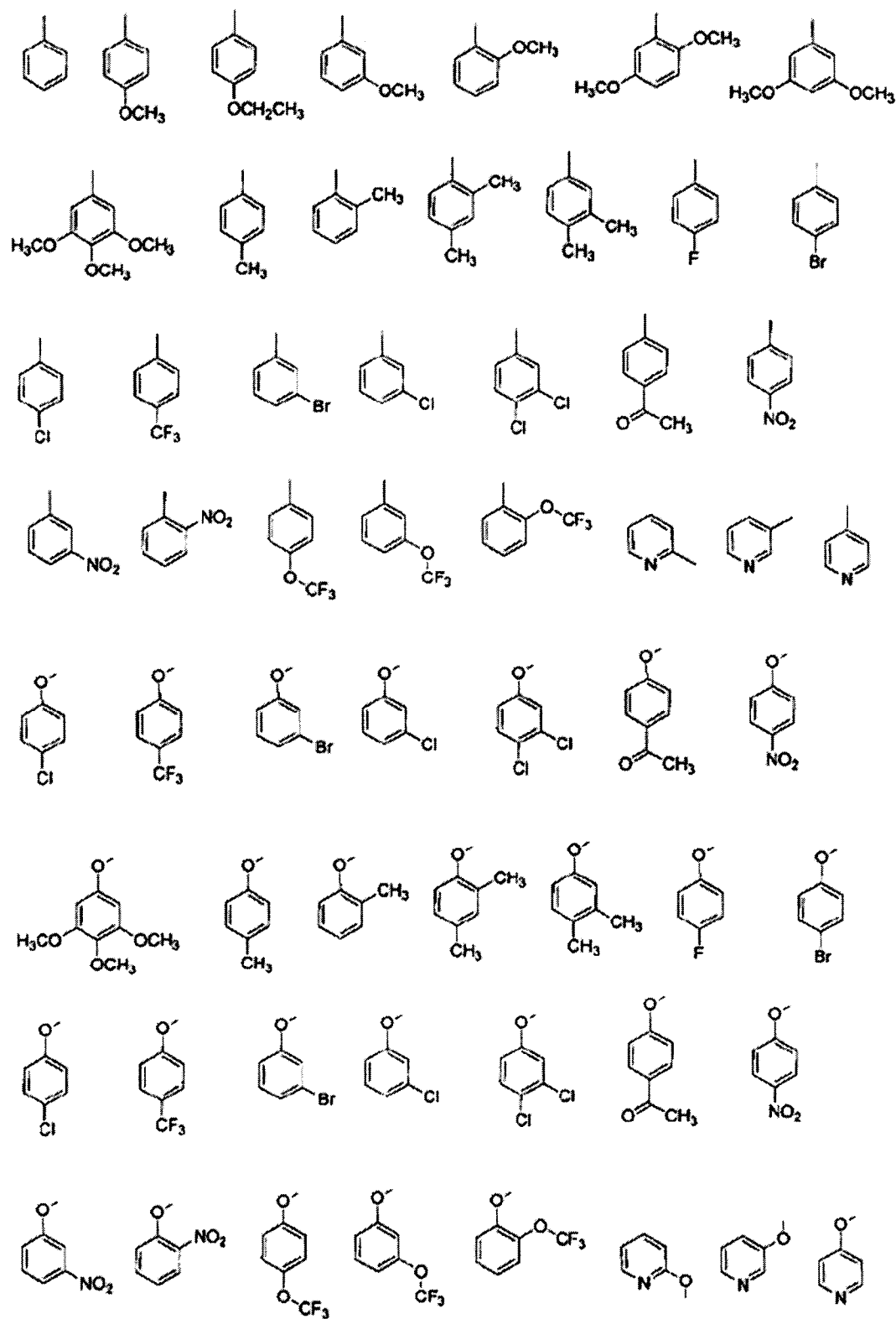
wherein at least 2 of R1, R2, R3, R12, and R14 are -OH,

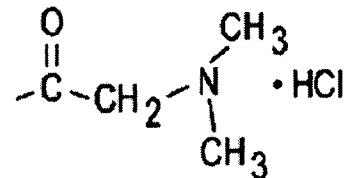
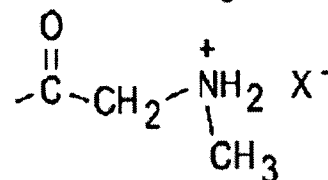
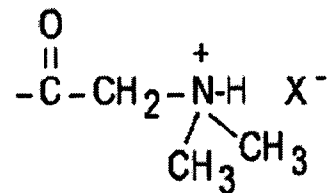
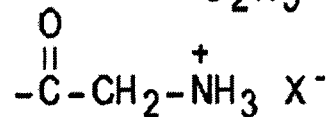
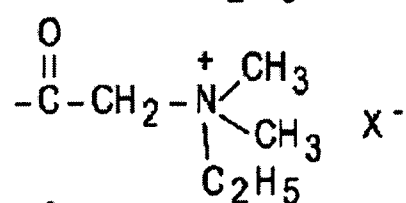
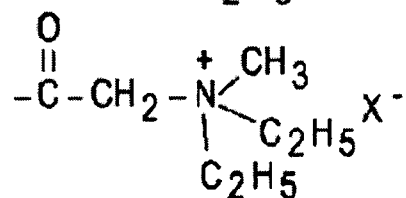
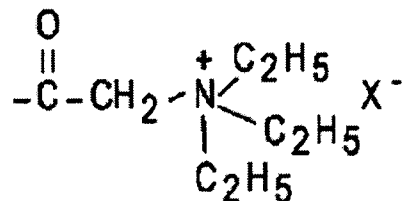
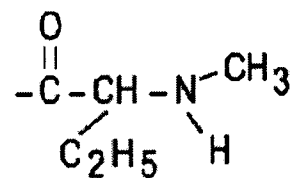
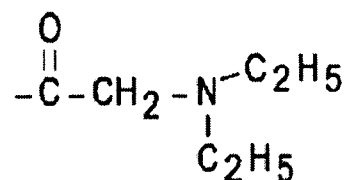
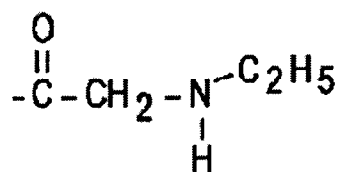
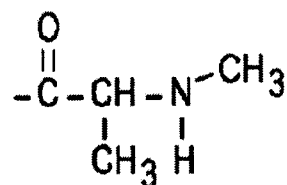
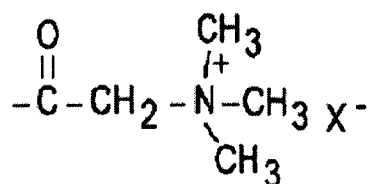
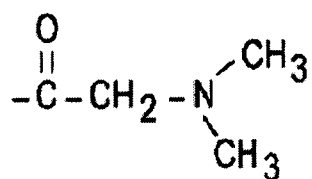
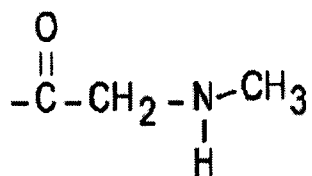
wherein R1, R2, R3, R5, R11, R12, R13, R14, R15, R21, R22 and R31 are independently from each other selected from

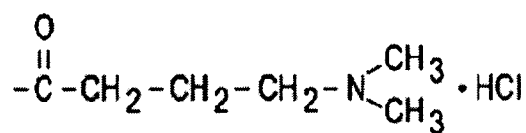
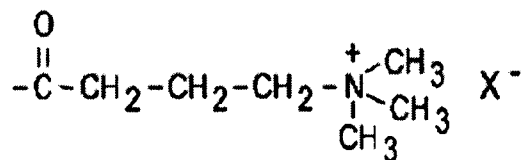
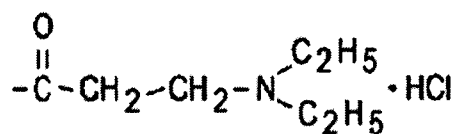
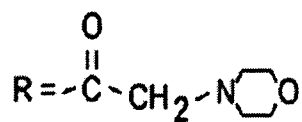
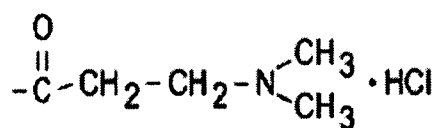
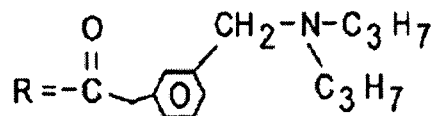
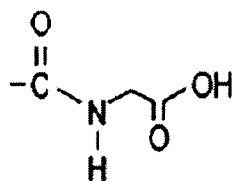
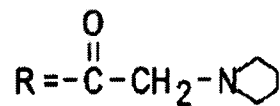
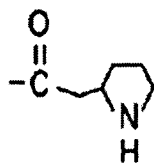
-H, -OH, -O-R_{Alk}, -CHO, -COR_{Alk}, -COOH, -COO-R_{Alk}, -CO-NH-C_nH_{2n}-COOH, -CO-NH-C_nH_{2n}-COO⁻,
 -CN, -Cl, -Br, -I, -NO₂,
 -C_nH_{2n}CN, -C_nH_{2n}-Cl, -C_nH_{2n}-Br, -C_nH_{2n}-I, -C_nH_{2n}-NO₂,
 -O-PO₃²⁻, -O-PO₃H⁻, -O-PO₃H₂, -NH₂, -NHR_{Alk}, -NR_{Alk1}R_{Alk2}, -N⁺H₃, -N⁺H₂R_{Alk}, -N⁺HR_{Alk1}R_{Alk2}, -N⁺R_{Alk1}R_{Alk2}R_{Alk3},
 -B(OH)₂, -OCHO, -O-COR_{Alk}, -OCF₃, -O-CN, -OCH₂CN,

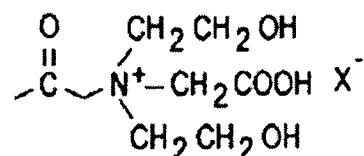
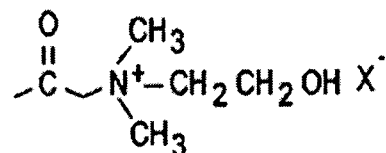
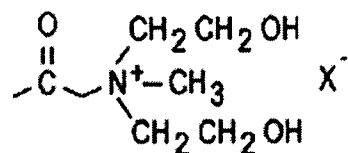
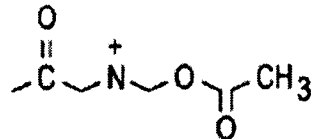
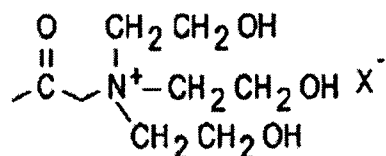
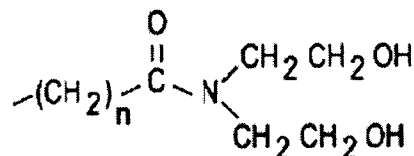
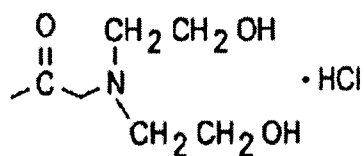
wherein R_{Alk}, R_{Alk1}, R_{Alk2}, and R_{Alk3} are independently alkyl residues, wherein in C_nH_{2n} n is an integer;

or wherein R1, R2, R3, R5, R11, R12, R13, R14, R15, R21, R22 and R31 are, independently from each other, one of the following moieties:









wherein X^- is a free soluble anion,

or wherein R_{11} , R_{12} , R_{13} , R_{14} or R_{15} are a mono or oligo saccharide-residue,

with the proviso that at least two of R_1 , R_2 , R_3 , R_{11} , R_{12} , R_{13} , R_{14} and R_{15} are independently selected from $-\text{OH}$, $-\text{O}-\text{R}_{\text{Alk}}$, $-\text{O}-\text{COR}_{\text{Alk}}$, $-\text{OCF}_3$, $-\text{O}-\text{CN}$, and $-\text{OCHO}$.

89. Peritoneal therapeutic fluid according to claim 88, wherein the alkyl residues are selected from the group consisting of CH_3 , C_2H_5 , C_3H_7 and C_4H_9 .

90. Peritoneal therapeutic fluid according to claim 88, wherein C_nH_{2n} is CH_2 , C_2H_4 , C_3H_6 or C_4H_8 .

91. Peritoneal therapeutic fluid according to any one of claims 71 to 90, wherein the biocompatibility enhancing agent is solubilized through pegylation with Polyethyleneglycol (PEG) or Methoxy-Polyethyleneglycol (mPEG).
92. Peritoneal therapeutic fluid according to any one of claims 71 to 91, wherein the one or more biocompatibility enhancing agent is/are present in a concentration of 0.001 mg/L to 5g/L.
93. Peritoneal therapeutic fluid according to any one of claims 71 to 92, further comprising one or more of an ingredient which is selected from the following: alkali metal ions, alkaline earth metal ions, an osmotic agent, and/or a pH-buffer.
94. Peritoneal therapeutic fluid according to any one of claims 71 to 93, further comprising glucose as osmotic agent.
95. Peritoneal therapeutic fluid according to claim 94, wherein the concentration of glucose is 0.5 to 20% by weight.
96. Peritoneal therapeutic fluid according to any one of claims 71 to 95, wherein the biocompatibility enhancing agent is contained in a compartment of a container or kit, and wherein a liquid is contained in a further compartment of the container or kit, and wherein, before application, the biocompatibility enhancing agent is solubilized by contacting it with the liquid to produce the peritoneal therapeutic fluid.
97. Peritoneal therapeutic fluid according to any one of claims 71 to 95 wherein the biocompatibility agent is selected from the group consisting of stilbenoids, phenolic acids, flavonoids, flavones, anthocyanidins, a salt of such said biocompatibility enhancing agent, and a glycoside of such said biocompatibility enhancing agent.
98. Peritoneal therapeutic fluid according to any one of claims 71 to 96, wherein the biocompatibility enhancing agent is selected from the group consisting of:
epsilon-viniferin, pallidol, trans-diploterone B, hopeaphenol,

oxyresveratrol, 4'-methoxy-(E)-resveratrol 3-O-rutinoside, phenolic acids; phenolic diterpenes; coumarines, coumarines glucosides, dihydroxyisocoumarins, prenyloxy coumarines, naphthoquinones, atovaquone; flavonols, flavones, flavonoides, eriodictoyl, homoeriodictoyl, sakuranetin, flavanonols, flavans; anthocyanins; isoflavonoides, stilbenoides, aglycones; and mixtures of two or more thereof.

99. Peritoneal therapeutic fluid according to claim 98, wherein:

- said phenolic acids are selected from gallic acid, ellagic acid, vanillic acid, propyl gallate, protocatechuic acid, p-coumaric acid, danielone, syringic acid, salicylic acid, gentisic acid, p-hydroxy benzoic acid, rosmarinic acid, rosmanol, quinic acid, sinapic acid, epi-,isorosmanol, E-anethol, 3,4-dimethoxycinnamic acid, and ferulic acid;
- said phenolic diterpenes are selected from carnosol and carnosic acid;
- said coumarines are selected from coumarin, umbelliferone, herniarine, esculetin, scopoletin, scopanone, and fraxetin;
- said coumarines glucosides are selected from 7-O-glucosyl-umbelliferone, 6-O-glucosyl-esculetin, 7-O-glucosyl-esculetin, and 7-O-Glucosyl-6-methoxycoumarin;
- said dihydroxyisocoumarin is 6-methoxymellein;
- said prenyloxy coumarines are selected from 7-geranyloxy coumarin, 7-methoxy-6-(3-methyl-2-butenyl)-coumarin, and 7-methoxy-8-(3-methyl-2-butenyl)-coumarin;
- said naphthoquinones are selected from 1,2-naphthoquinone, 1,4-Naphthoquinone, 2,6-Naphthoquinone, alkanin, hexahydroxy-1,4-naphthalenedione, juglone, lapachol, lawsone, menatetrenone, 2-methoxy-1,4-naphthoquinone, nigrospin B, 2,3,5,7-tetrahydroxy-1,4-naphthalenedione, menadione, 5,8-Dihydroxy-1,4-naphthoquinone and other dihydroxynaphthoquinones;
- said flavonols are selected from quercetin, kaempferol, myricetin, fisetin, galangin, isorhamnetin, pachypodol, rhamnazin pyranoflavonols and furanoflavonols;
- said flavones are selected from apigenin, and tangeretin;
- said flavonoides are selected from hesperetin, naringenin, eriodictoyl, homoeriodictoyl and sakuranetin;

- said flavanonols are selected from taxifolin, dihydrolquercitin and dihydrokaempferol;
- said flavans are selected from flavan-3ol including Catechin, Gallocatechin, catechin 3'-gallate, gallocatechin 3-gallate, epicatechin, epigallocatechin, epicatechin 3-gallate, Epigallocatechin 3-gallate, theaflavin, theaflavin-3-gallate, theaflavin-3,3'-digallate, thearubigin, proanthocyanidins, flavan-4-ol and flavan-3,4-diol;
- said anthocyanins are selected from cyanidin, malvidin, pelargonidin, peonidin, petunidin, cyanin-3-rutinoside and delphinidin-3-rutinoside;
- said isoflavonoides are selected from isoflavones, isoflavanes, isoflavones, coumestans and pterocarpanes;
- said stilbenoid is a stilbene; and
- said aglycones are selected from piceatannol, pinosylvin and pterostilbene.

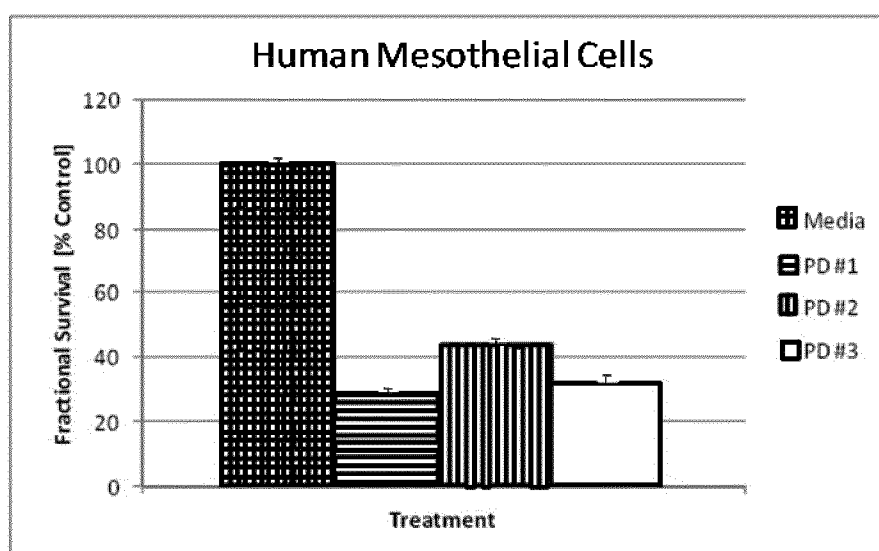


Fig. 1

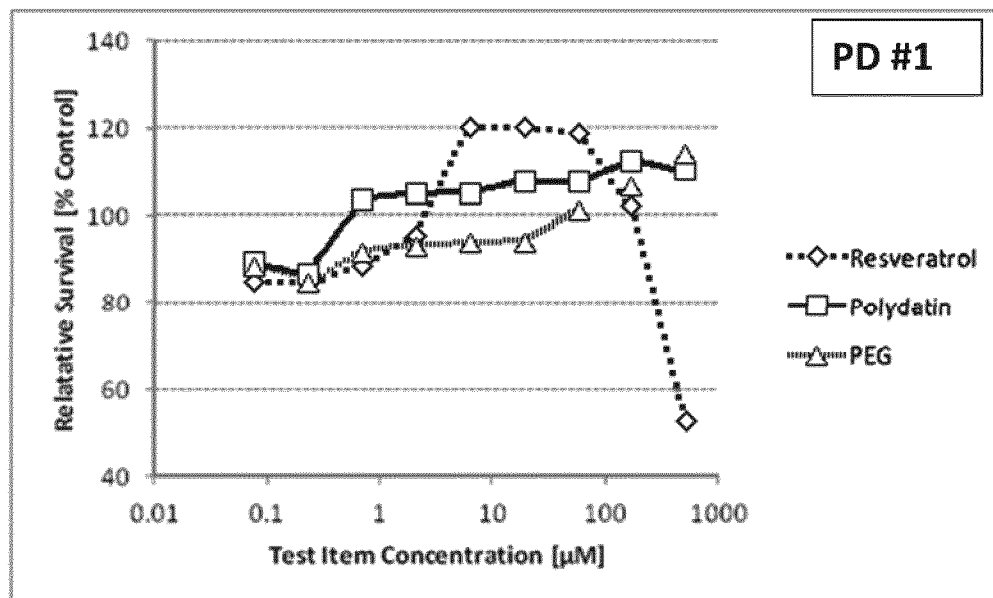


Fig. 2

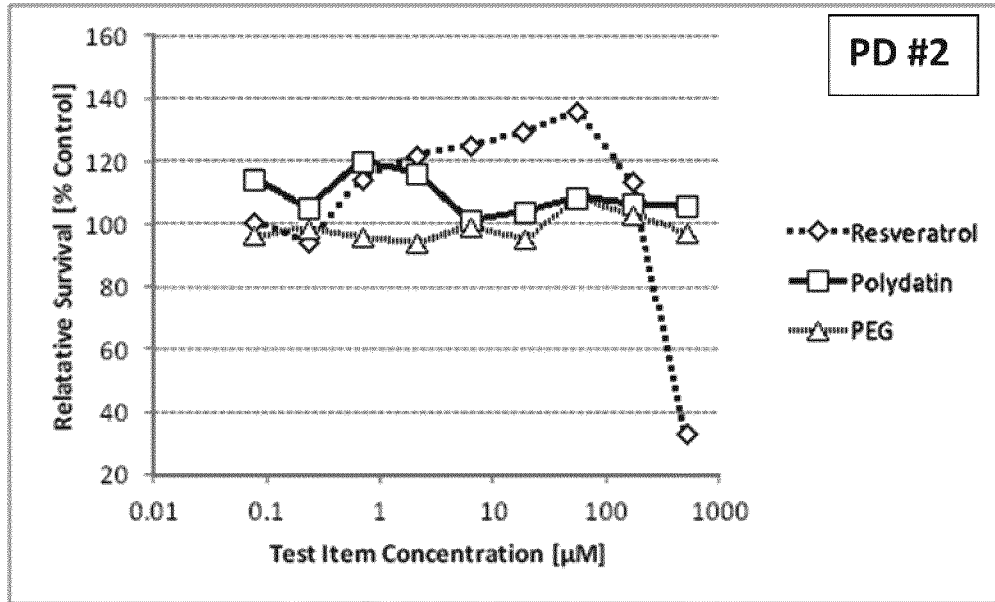


Fig. 3

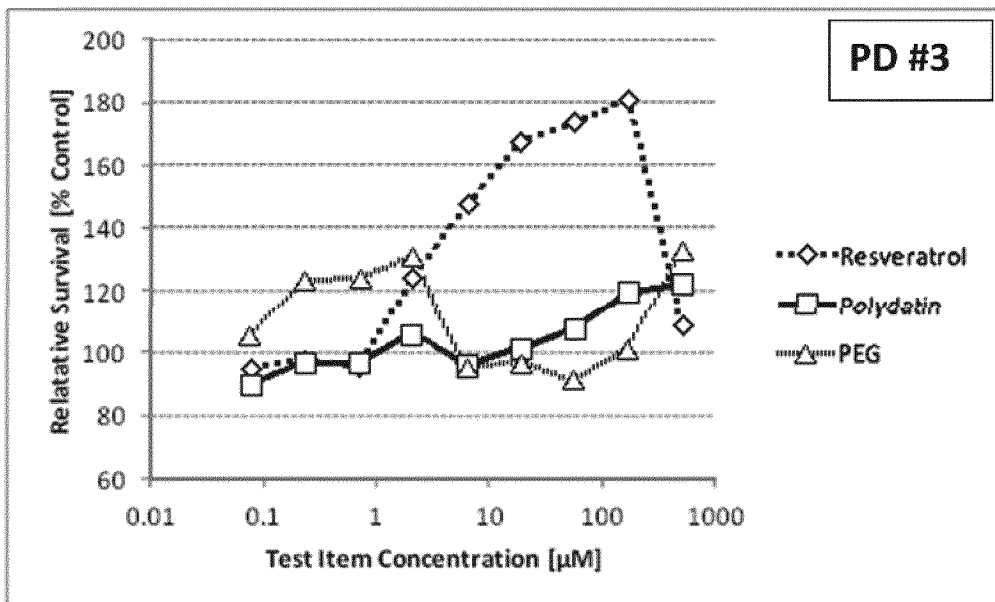


Fig. 4

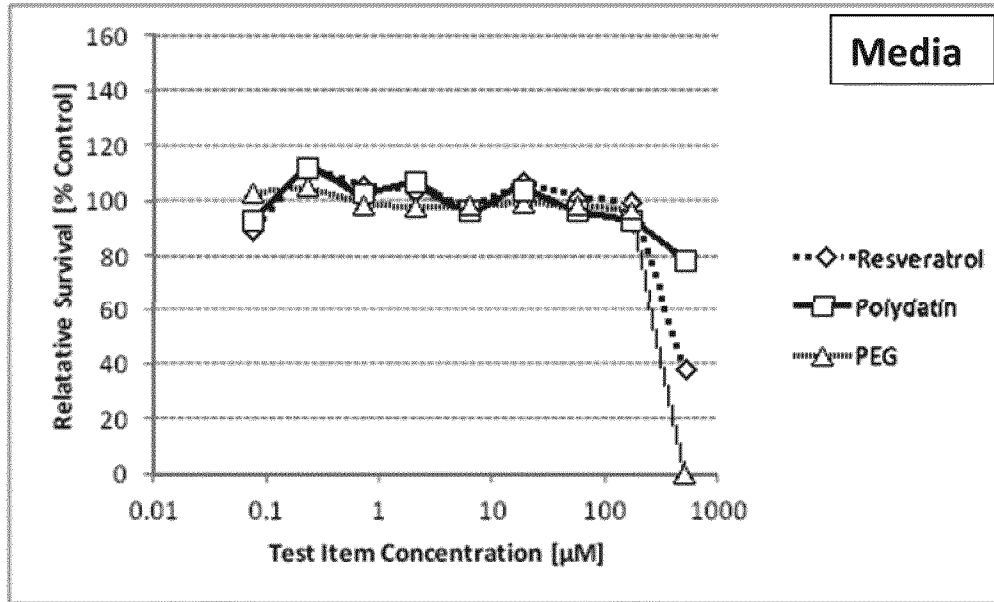


Fig. 5

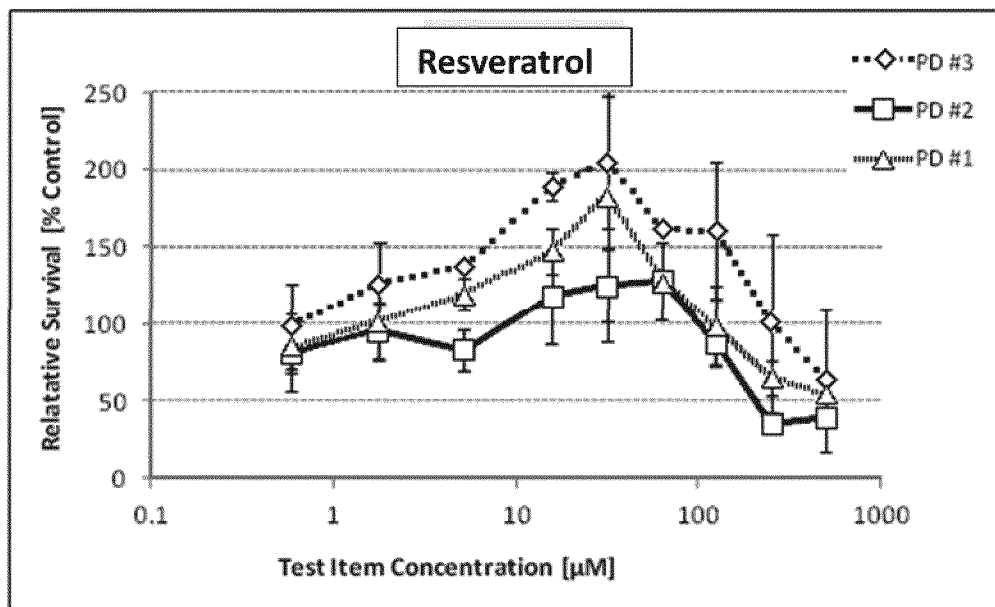


Fig. 6

Fig. 7:

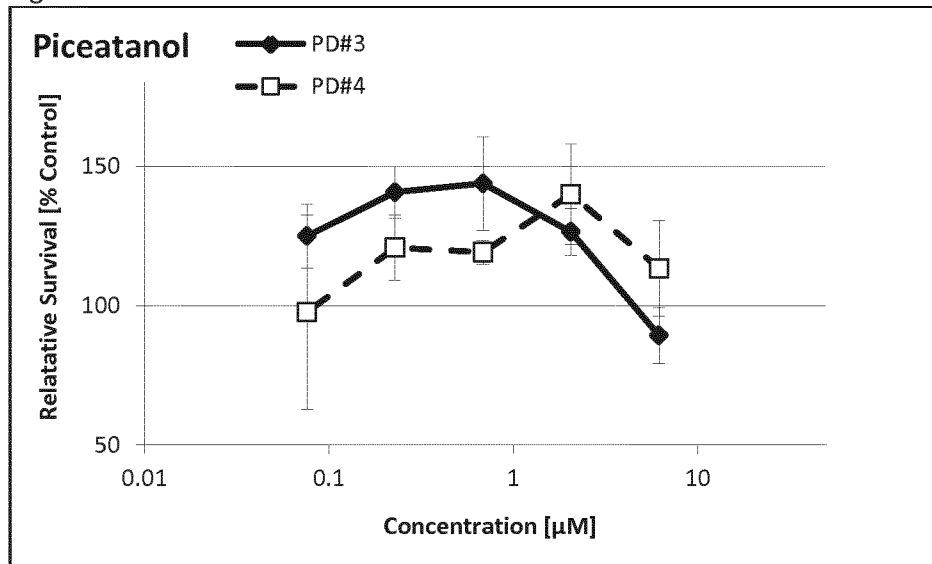


Fig. 8:

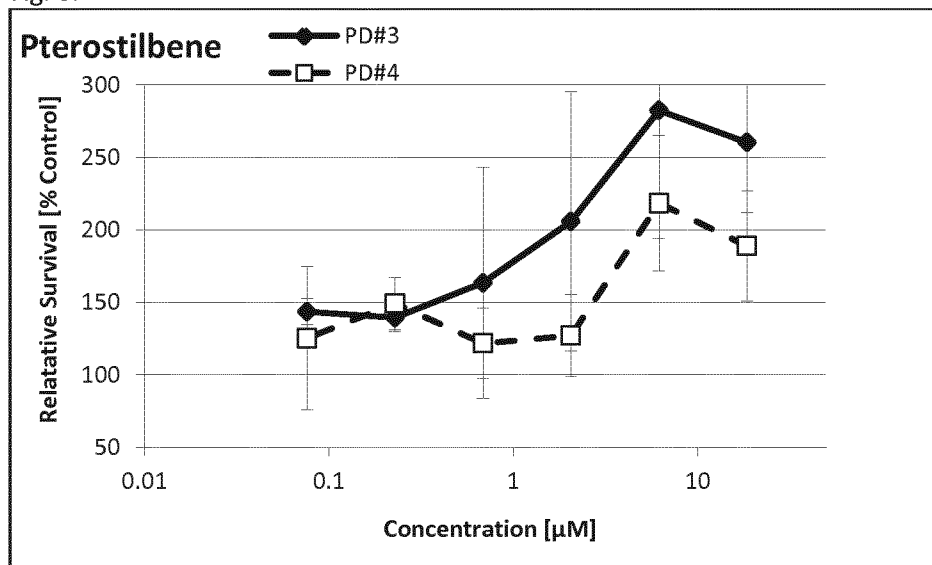


Fig. 9a:

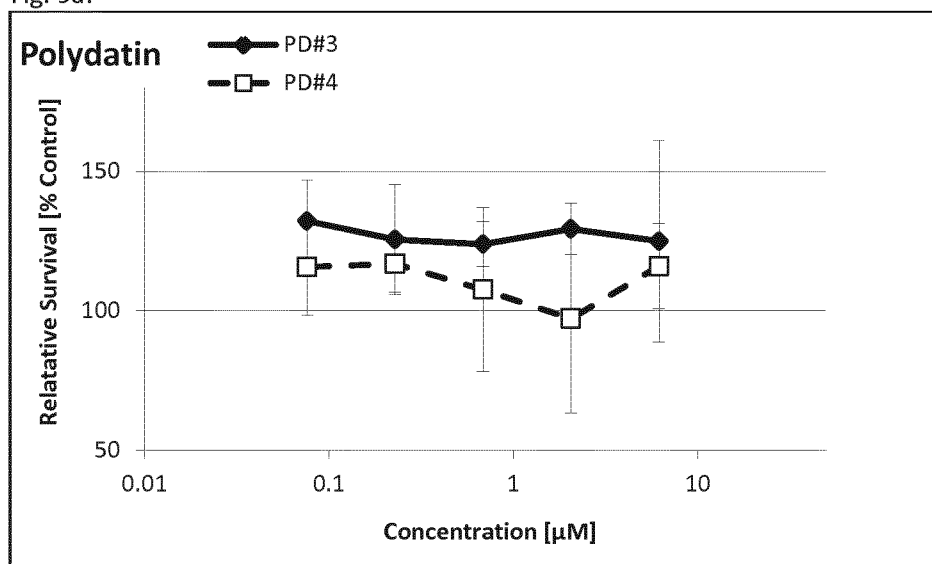


Fig. 9b:

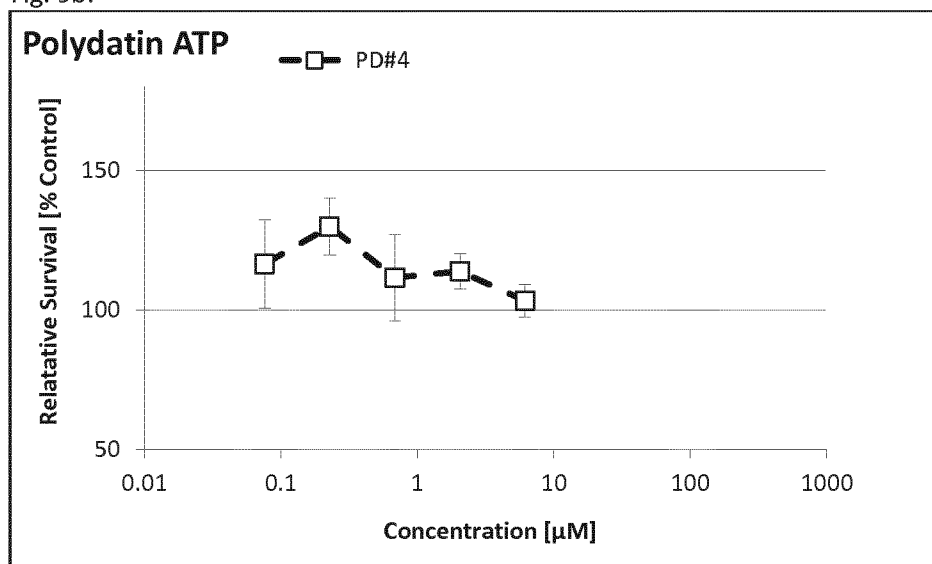


Fig. 10:

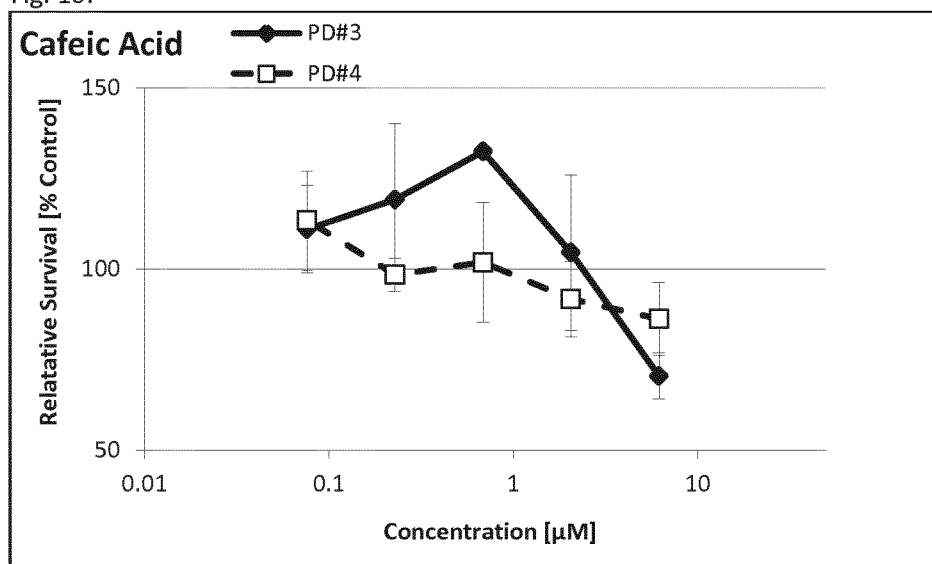


Fig. 11:

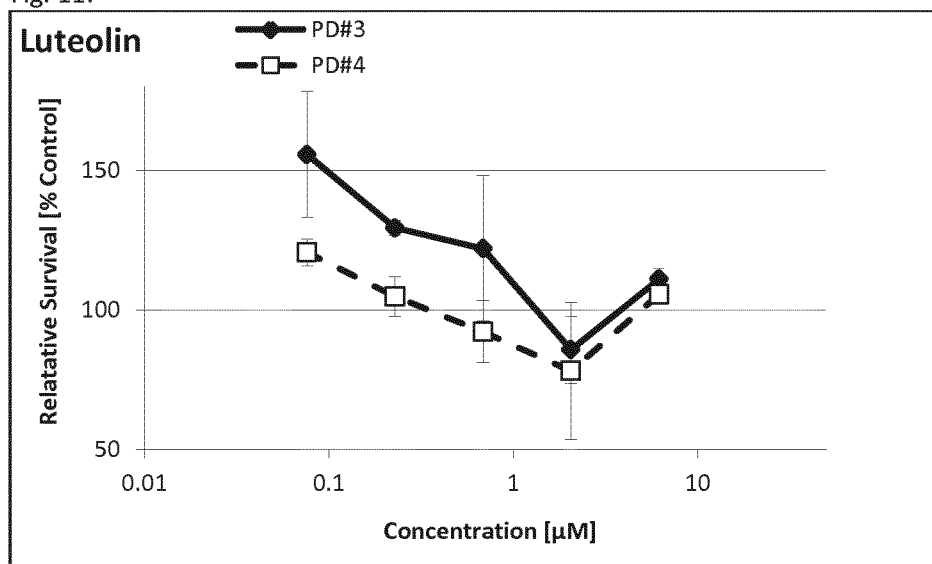
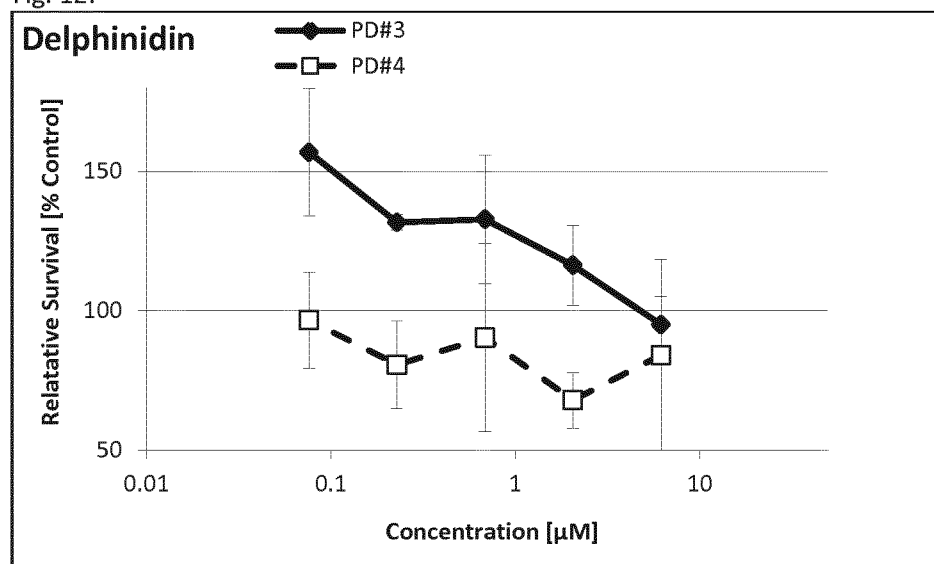


Fig. 12:



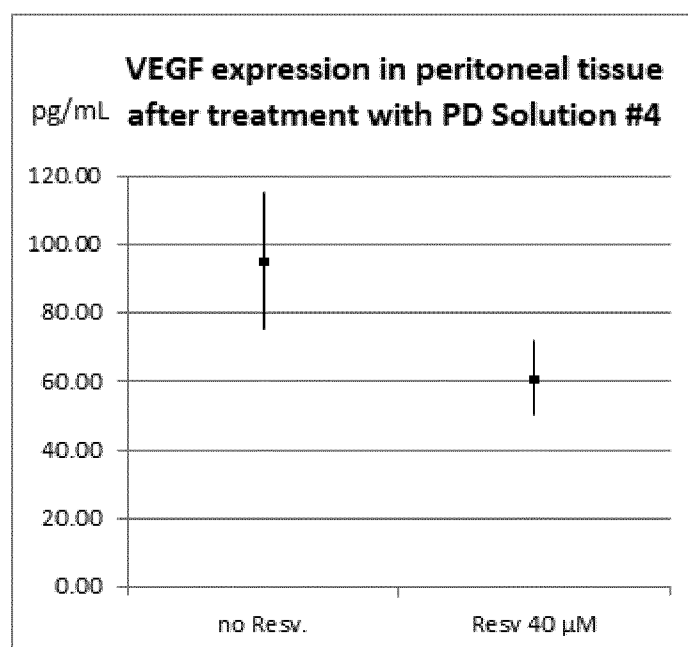


Fig. 13