The scientific findings of the last few years show that destructive physico-chemical processes through "free" radicals, radical chain reactions and/or through activated oxygen stages are assuming an increasingly important place in the pathogenesis of many acute and especially chronic illnesses, in which, inter alia, arterial and venous angiopathies, allergies, autoagressive diseases and tumorous diseases are to be mentioned. Reactions of "free" radicals and activated oxygen stages (AOS), but also of radicals which arise through ionising radiation in water radiolysis, constantly lead to alterations to and destruction of the biomolecules (DNA, RNA, enzyme- and structure proteins, unsaturated fatty acids and others), and also in all cells and cell organelles via radical reaction phenomena of lipid peroxidation also to membrane damage and membrane destruction. Radical processes are included in the etiology of all diseases; often they are even the cause of these diseases or maintain these through radical chain reactions.

For this reason, humans and animals are protected by particular enzymes acting in an antioxidative manner, such as superoxide dismutases, catalases and peroxidases, which "deactivate" the activated oxygen stages.

It is known (WO 89/00427) that to maintain the functionality of many, perhaps all enzymes of the cell metabolism, to prevent oxidative changes to their catalytic and allosteric centres and to maintain an optimum conformation, the reductive potential of reduced glutathion, i.e. its optimum, high intracellular concentration, is of the most extreme importance and can be increased through doses of reduced glutathion or - in the case of a disturbed cell metabolism - can in any case be produced again.

It is likewise known (WO 89/00427) that it can be more favourable, instead of the reduced glutathion itself, to supply a thiol derivative of glutathion to the body from the

exterior. The thiol derivatives are distinguished by a particularly good bio-availability. Their capability of permeation through biological membranes is high. The SH-group of glutathion which is important for the therapeutic effect is protected on the way through biological compartments up to the desired effective site and they do not cause any inhibition to the enzymes introduced into the endogenous glutathion biosynthesis.

Also, medicaments are already known (DE-OS 27 40 346), which contain as active component an anthocyanidine, e.g. cyanidine, peonidine, delphinidine, petunidine, pelargonidine and/or malvidine. These medicaments are to be administered for the treatment of wounds, ulcers, inflammatory states and pathogenic states of the vascular system or disturbances, which are caused by impairment of the lipoid or glycid metabolism.

Although reduced glutathion as coenzyme (selenium-dependent glutathion peroxidases) and as cofactor (glutathion-S-transferases) and also as non-enzymatic scavenger and nucleophilic substance is able to detoxify directly electrophilic xenobiotics as primary or secondary radicals and also those radicals which have arisen in the cell metabolism through exposure with respect to energy-rich rays, deficiency states can occur with the sole therapeutic use of reduced glutathion - even with sufficient application thereof. These are to be explained by:

- poor genetic provision of antioxidative, i.e. scavenger enzymes (enzymopathies);
- deficient biosynthesis of antioxidative enzymes in various compartments and dependent on particular, unfavourable phases of life (enzymopenia);
- "oxidative wear" of reduced glutathion under particular circumstances, such as intoxications, inflammations, infections, deficiencies of non-enzymatic or enzymatic scavengers, with the extremely unfavourable possibility of

the occurrence of thyil radicals, glutathion disulphide anion radicals or also of glutathion peroxysulphenyl radicals;

- de-novo-biosynthesis disturbances of endogenous reduced glutathion;
- high performance sport, cachexia, dissipating diseases. age.

All these deficiency states, arising differently, lead to changes to the negative redox potential present in all biological areas of living systems and via slips of the "redox displacement system"

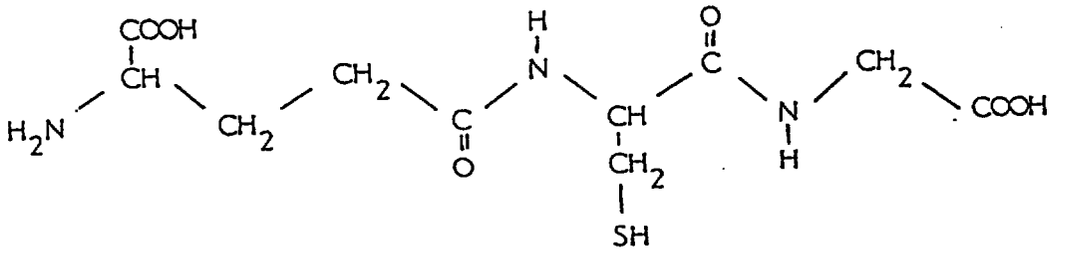
reduced glutathion ⟷ mixed disulphides ⟷ oxidized glutathion

to enzyme disturbances, especially in antioxidative enzymes and repair enzymes, to cell metabolism slips, to mutations, to malignant transformation or also to cell necrosis.

It has now been found that the therapeutic failures, which occur with the sole use of reduced glutathion from the said pathobiochemical disturbances, can be prevented by a combination of reduced glutathion with anthocyans, in which instead of the reduced glutathion or in addition thereto also the thiol derivatives of glutathion are able to be advantageously used.

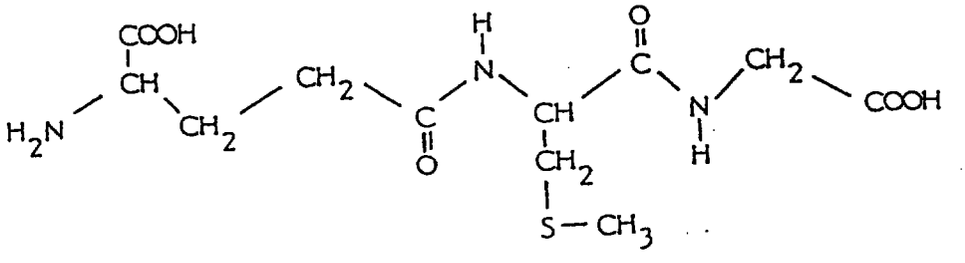
Therefore, the invention makes available a mixture for the therapeutic treatment of the human or animal body, which mixture contains reduced glutathion and at least one anthocyan compound from the group pelargonidine, peonidine, cyanidine, malvidine, petunidine, delphinidine, in which the reduced glutathion can be replaced in whole or in part by at least one thiol-derivative of glutathion from the group methyl-glutathionyl-(thio)-ether, ethyl-glutathionyl-(thio)-ether,mono-acetyl-glutathionyl-(thio)-ester, mono-phosphoric acid-glutathionyl-(thio)-ester.

Reduced glutathion is a tripeptide occurring in its reduced form (G-SH) in most cells of humans and mammals, which consists of the three amino acids glutamine acid, cysteine and glycine and has the following structural formula:

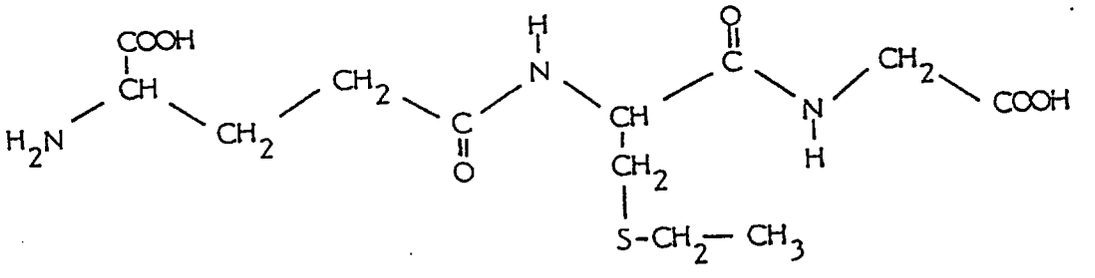


reduced glutathion (gamma-glutamyl-cysteinyl-glycine).

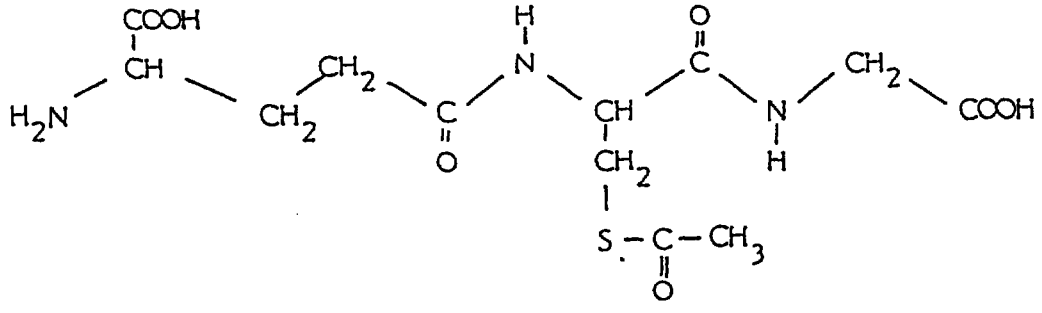
The thiol derivatives of glutathion which are able to be used in accordance with the invention have the structural formula:



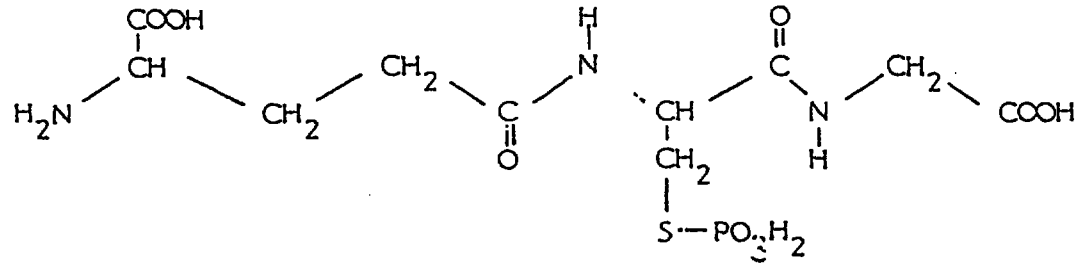
methyl-glutathionyl-(thio)-ether or monomethyl-thioester



ethyl-glutathionyl-(thio)-ether or monoethyl-thioester

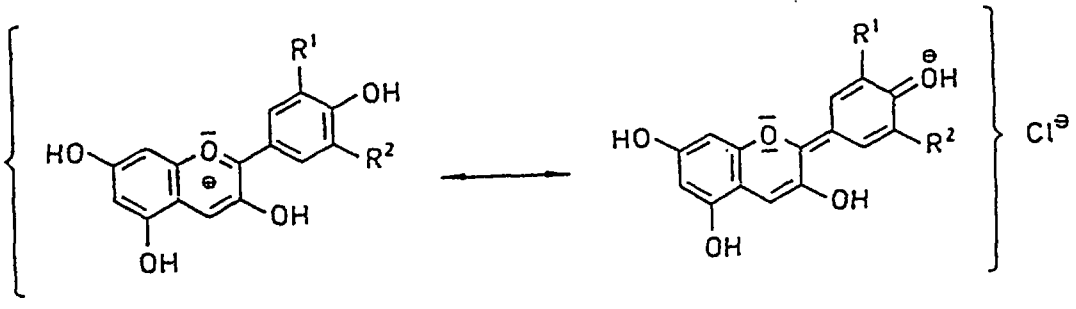


mono-acetyl-glutathionyl-(thio)-ester or
monoacetyl-thioester



mono-phosphoric acid-glutathionyl-(thio)-ester or
monophosphoric acid-thioester

Anthocyans occur in many higher plants and are responsible there for the red, violet, blue or blue-black colour of flowers and fruits. These are heterocyclic 2-phenylchromenol multi-ring systems with different hydroxylation patterns and different absorption spectra in visible light. The sugar-free aglycon components of the anthocyans are designated as anthocyanidines. They can be easily obtained by hydrolysis of the glycosides contained in common fruits (cf. DE-OS 27 40 346) and have the following structural formula:



R^1	R^2	Trivial name	λmax (nm) (colour)
H	H	pelargonidine	520 (red orange)
H	OCH_3	peonidine	532 (red violet)
H	OH	cyanidine	535 (red violet)
OCH_3	OCH_3	malvidine	542 (violet red)
OH	OCH_3	petunidine	543 (violet red)
OH	OH	delphinidine	544 (blue violet)

Anthocyans can function as good scavengers for the superoxide anion radical ($O_2^{\cdot}$), for hydrogen peroxide (H_2O_2), for the hydroxyl radical (OH•), for alkoxyl radicals (LO•), peroxyl radicals (L O O•), for singlet oxygen ($O_2(^1\Delta g)$) and many other radicals. Anthocyans can, however, also act as photobiological inhibitors in a regulating and detoxifying manner in sensitised photoreactions occurring via oxygen and can thus prevent radical- and radical chain reactions damaging cells and molecules, irrespective of the way in which these have arisen.

Anthocyans protect from aldehydes which are toxic to cells and carcinogenic (4-hydroxy-hexenal, 4-hydroxy-octenal, 4-hydroxy-nonenal, propanal, butanal, pentanal, hexanal, 2,4-heptadienal, malondialdehyde, and others). They even prevent their formation within lipid peroxidative chain reactions. They also detoxify the acetaldehyde occurring in the breakdown of ethanol and the formaldehyde occurring in

the breakdown of methanol or incorporated in other methods.

The anthocyan compounds and reduced glutathion and/or its thiol derivatives complement each other dependent on dose in therapeutic use optimally in many cell destructions and many cell and enzyme regulation disturbances. Alongside the qualitative therapeutic aspect, with the combined use of reduced glutathion and/or its thiol derivatives together with anthocyan compounds, especially the quantum yield is substantially more effective with regard to the scavenger function. Thyil radicals (GS•), glutathion-disulphide-anion-radicals (G-S-S-G•) and also glutathion-peroxysulphenyl radicals (G-S O O•) are either prevented in their formation or detoxified.

In addition, not only do a reduction of oxidized glutathion (G-S-S-G) and a prevention and/or detoxification of glutathion radicals occur, but even in an oscillating reaction cycle between the two substances or substance groups (glutathion and anthocyans) a permanent regeneration of the radical-detoxifying functions occurs.

The reciprocal complementing of the two substance groups in the mixture according to the invention is so optimal that the reduced glutathion can again fully comply with its vital regulating functions on a genetic and on an enzyme level and finally on all levels.

Reduced glutathion (G-SH) reacts inter alia with quinones with the formation of glutathionyl-hydroquinone conjugates, which can auto-oxidize to the corresponding hydroquinones. The G-SH-conjugation reduces the radical, electrophilic character of quinones with an improvement of their hydrophily. Such conjugate formations, which are of great toxicological interest, are, however, limited intracellularly both by the quinone concentration and also by the G-SH-concentration. This is a further therapeutic

starting point for many phenomenologically thus differently occurring diseases. Above all, the combination of reduced glutathion or its thiol derivatives with anthocyan compounds, alongside the reinstatement of a physiological regulating cycle behaviour on all biological levels and in all compartments of living systems, also shows therapeutic effects in radical and radical chain reactions initiated in various ways (thermal, chemical, mechanical, infectious-toxic, caused by radiation and others) and in the so important phenomenon pathobiochemically of lipid peroxidation.

The mixture according to the invention largely prevents cross links of biomolecules (connective tissue, proteins, DNA and others) in diabetes mellitus and particularly also in diabetic late onset syndrome (prevention of amadori bodies). It additionally prevents polyneuropathic degenerations occurring lipid peroxidatively and caused pathogenetically on the peripheral and central nervous system in the sense of the prevention of lipofuscine formation or lipofuscine groups. In addition, through the combination of glutathion- and anthocyan compounds, the prevention of protein denaturisations occurs on bradytrophic tissue, such as, for example, on the cornea, lens of the eye and vitreous humour of the eye.

A further increase in effectiveness is produced through the addition of vitamin E (alpha-tocopherolacetate) and/or vitamin A and/or beta carotene and/or selenium and/or L-cysteine into the mixture according to the invention.

An oral administration of the mixture according to the invention is particularly suitable, in which the therapeutic dose lies in the range of 50 mg to 2400 mg per day.

The mixture according to the invention accordingly has a broad pharmacological and therapeutic field of application.

Its use comes into consideration inter alia

- for the treatment of cancerous diseases of every genesis, also for malignant diseases of the blood cells and their prior stages,
- for substitution and metabolism regulation in carrying out other cancer therapies, chemotherapies, radiotherapies and/or naturopathic therapies,
- for the prophylaxis and treatment of metastases in malignant tumorous diseases,
- for the treatment of hepatopathy, in particular acute and chronic diseases in hepatitis such as chemo-toxic and infectious-toxic hepatitis, hepatitis caused by virus, rickettsia, bacteria or protozoa and also chronic-aggressive hepatitis, fatty liver, fat cirrhosis and liver cirrhoses of every genesis,
- for the treatment of disturbances to the immunological defence function in the range of natural killer cells, monocytes, macrophages, granulocytes, T- and B-lymphocytes, plasma cells, and also disturbances to the complement factors and antibody synthesis,
- for the treatment of complex disturbances to the lymphocon biosynthesis in T-helper cells, macrophages and other cells,
- for the treatment of cardiomyopathy of every genesis, also in connection with other therapies, all forms of coronary disease, angina pectoris, myocardial infarction prophylaxis and also emergency therapy of cardiac infarction in connection with other emergency medicaments,
- for the treatment of acquired and also congenital forms of skeletal muscle disturbances,
- for the treatment of neurological diseases of inflammatory, allergic or degenerative genesis,
- for the treatment of all forms of blood cell diseases, anaemia, leucopenia, lymphopenia and thrombocytophenia,
- for the prophylaxis of damage to the lens of the eye, toxic disturbances to the retina and to the vitreous humour, and also for cataract prophylaxis,
- for the treatment of all forms of peroxidation or of

oxidative stress, for example within the scope of the application of oxygen therapies or therapies with activated oxygen stages (oxygen radicals) and also for protection in the use of hyperbaric oxygen therapy, oxygen multiple step therapy, in ozone therapies and HOT therapies,

- for intoxications, which in the human organism lead via radical chain reactions to biomolecule and tissue damage,
- for accompanying therapy in radiation treatment, cytostatic treatment and also to decrease or prevent sickness, nausea and others,
- after narcoses, in particula after full narcoses in patients with damaged heart and liver,
- for intoxications with xenobiotics, in particular with toxic trace elements and with heavy metals,
- for the treatment of proliferation disturbances and differentiation disturbances of epithelial, endothelial and mucous membrane tissue,
- for the treatment of pathophysiological and variously occurring arterioscleroses,
- for the basic treatment and adjuvant treatment of allergies,
- for the treatment of impotentia coeundie and impotentia generandi, and also fertility disturbances and potency disturbances of every genesis,
- in premature ageing, in the wear of all tissues due to ageing, also of skin and skin connective tissue and for prophylaxis in activities and habits which lead to premature ageing or to premature wear of organs and tissue.

CLAIMS

1. A mixture containing

reduced glutathion

and at least one anthocyan compound from the group

pelargonidine
peonidine
cyanidine
malvidine
petunidine
delphinidine

for the therapeutic treatment of the human or animal body.

2. A mixture containing

at least one thiol-derivative of glutathion from the group

methyl-glutathionyl-(thio)-ether
ethyl-glutathionyl-(thio)-ether
mono-acetyl-glutathionyl-(thio)-ester
mono-phosphoric acid-glutathionyl-(thio)-ester

and at least one anthocyan compound from the group

pelargonidine
peonidine
cyanidine
malvidine
petunidine
delphinidine

for the therapeutic treatment of the human or animal body.

3. A mixture containing

reduced glutathion

and at least one thiol-derivative of glutathion from the group

methyl-glutathionyl-(thio)-ether
ethyl-glutathionyl-(thio)-ether
mono-acetyl-glutathionyl-(thio)-ester

mono-phosphoric acid-glutathionyl-(thio)-ester

and at least one anthocyan compound from the group

pelargonidine
peonidine
cyanidine
malvidine
petunidine
delphinidine

for the therapeutic treatment of the human or animal body.

4. A mixture according to claim 1, 2 or 3, which additionally contains vitamin E and/or vitamin A.

5. A mixture according to claim 1, 2, 3 or 4, which additionally contains beta carotene.

6. A mixture according to claim 1, 2, 3, 4 or 5, which additionally contains selenium.

7. A mixture according to claim 1, 2, 3, 4, 5 or 6, which additionally contains L-cysteine.

8. A mixture according to one of claims 1 to 7 as radical catcher (non-enzymatic scavenger) and radical chain terminator for the treatment of illnesses which develop with hyperradicalism, with the phenomenon of "oxidative stresses" (peroxidation) and/or with enzymopathy and enzymopenia of enzymes having an antioxidant effect.