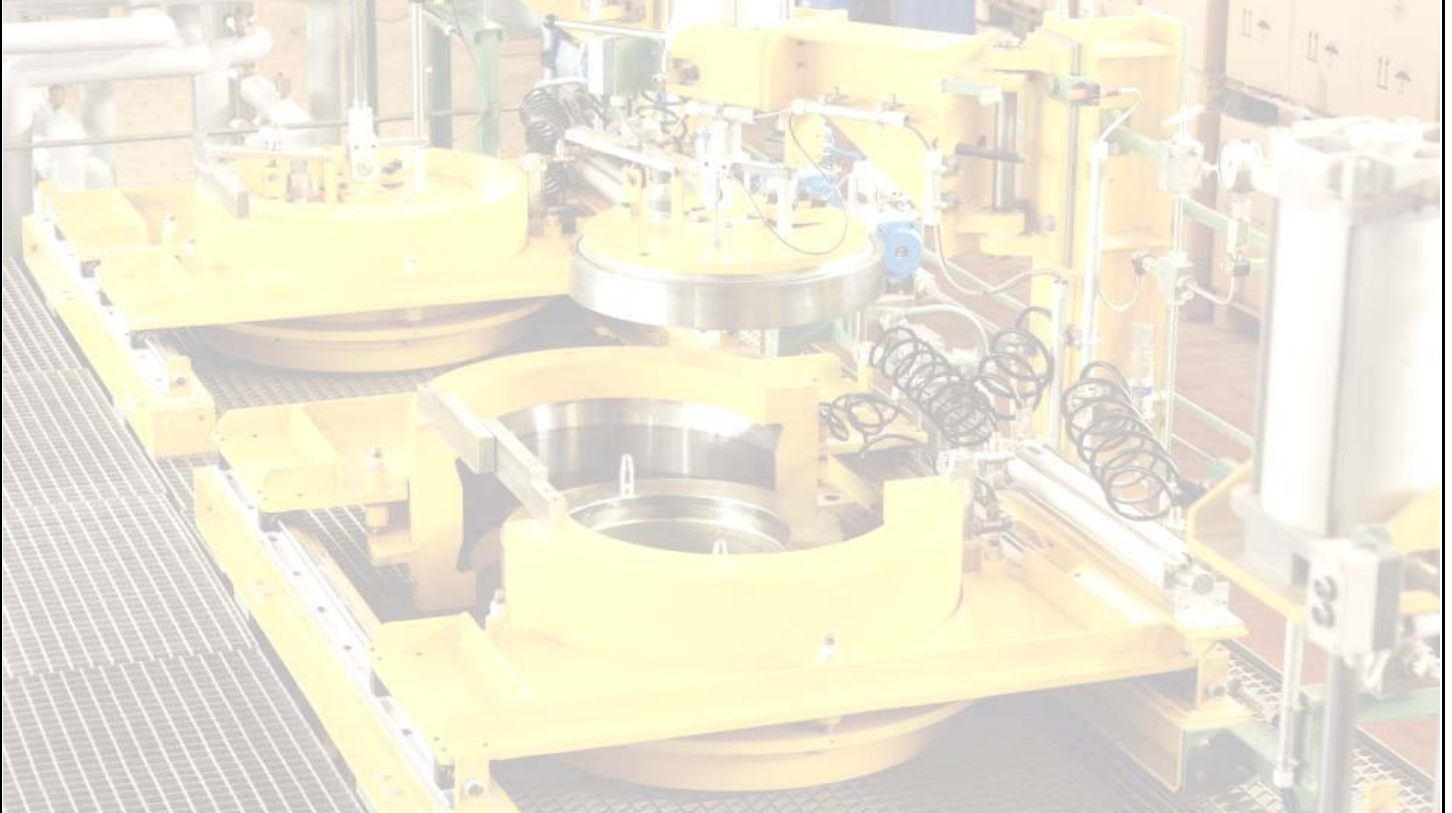


**Rosemary And Sage Antioxidants Can Do More! -  
They Help Combat UV Skin Damage, Premature Skin Aging  
And Have Antimicrobial Efficacy**



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Hochdruckextraktion mit CO<sub>2</sub>

**FLAVEX**<sup>®</sup>  
Naturextrakte GmbH

## **Rosemary and Sage Antioxidants Can Do More! – They Help Combat UV Skin Damage, Premature Skin Aging and Have Antimicrobial Efficacy**

Rosemary and Sage antioxidants are already widely used in cosmetics since they protect products against lipid oxidation.

New clinical trials with Sage antioxidant standardized to 5 % ursolic/oleanolic acids demonstrate similar efficacy in the UV erythema test as the gold standard hydrocortisone. Recent research reveals also good antibacterial activity of Rosemary & Sage antioxidant extracts against a broad spectrum of germs with dermatological relevance. They are recommended for topical treatment of acne vulgaris, seborrheic eczema and atopic dermatitis.

Rosemary & Sage extracts are produced from high-grade leaf material. First the essential oil is removed by supercritical CO<sub>2</sub>-extraction. Afterwards the di- and triterpene phenols are extracted with CO<sub>2</sub> and ethanol as entrainer to give high-grade antioxidants under gentle conditions which are practically free of volatiles. They contain the active diterpene phenols (DTPs), mainly carnosolic acid as well as the triterpenes ursolic/oleanolic acids in high concentration. The standardized products can easily be blended into the lipophilic phase of cosmetic preparations.

Skin aging is caused by oxidation of cell membranes. Rosemary and Sage antioxidants act as natural anti-aging ingredients, since they inhibit the oxidation of polyunsaturated fatty acids in cell membranes (1).

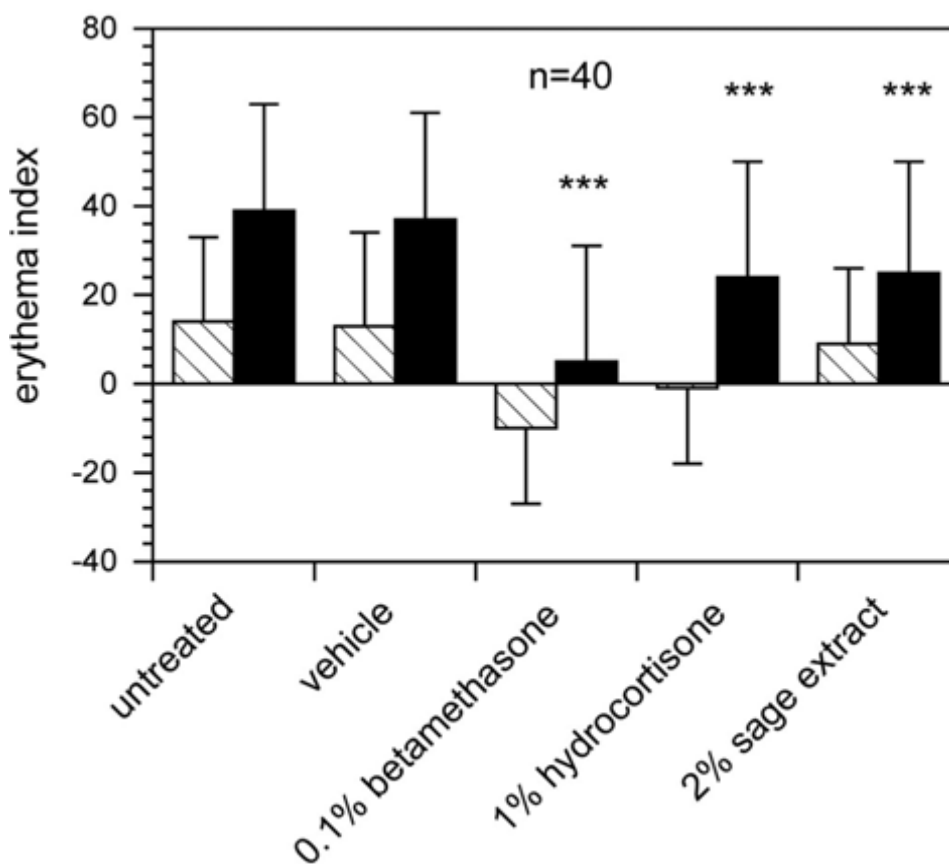
The antioxidative activity correlates with the inhibition of non-enzymatic glycosilation of proteins. Cumulation of glycosilated proteins influences skin aging processes negatively. The bioactivity of Rosemary in dermatological applications is higher than the activity of ascorbic acid or alpha-tocopherol (2,3).

### **Sage Leaf Extract with 5 % Ursolic/Oleanolic Acids Inhibit Ultraviolet-Induced Erythema in Vivo**

Plant extracts containing ursolic and oleanolic acids are active both topically and internally. The anti-inflammatory, anti-tumor and antimicrobial properties make them useful in cosmetic applications (4).

Interesting to know are the proven regenerative properties of ursolic and oleanolic acids in case of aging and sun damaged skin (5,6). The collagen fibre bundle structure which has been damaged by UV-B irradiation can be restored by topical application of these triterpene acids. This leads to the improvement of skin elasticity and the reduction of wrinkles.

The anti-inflammatory effect of Sage leaf extract was analysed in a randomised double-blind placebo-controlled in vivo study (7). Test areas on the backs of 40 healthy volunteers were irradiated with ultraviolet light and treated with different agents. The study was performed according to Good Clinical Practice criteria. The results are demonstrated in form of a bar chart.



Mean values  $\pm$  standard deviation are shown  
 \*\*\*  $p < 0.001$  compared to vehicle

The hatched bars refer to test sites without irradiation; the black bars display the irradiated skin areas. The Sage leaf extract significantly reduces UV-B induced erythema to a similar extent as 1 % hydrocortisone, but is less effective than the more potent betamethasone. The vehicle alone as placebo showed the same result as the untreated area. No irritant effect of the Sage CO<sub>2</sub>-extract is observed on the non-irradiated site. In contrast, the corticosteroids

show a typical blanching effect. This study demonstrates that the Sage CO<sub>2</sub>-extract is useful in the topical treatment of inflammatory skin conditions.

A frequent stressor to healthy skin is the so-called oxidative stress, i.e. Reactive Oxygen Species (ROS) created by UV radiation, ozone or toxic substances interacting with skin lipids and proteins. Oxidative stress plays a key role in premature skin aging. Here, the described Sage CO<sub>2</sub>-extract offers considerable benefits. On the one hand the diterpene phenols represent potent antioxidants and radical scavengers, on the other hand the regenerative and anti-inflammatory triterpenes, ursolic and oleanolic acids exhibit effective repair properties.

This is the first clinical trial that demonstrates equivalence of a plant extract to the gold standard hydrocortisone in the UV erythema test (7). Other studies demonstrate that topically applied ursolic acid derived from Rosemary extract inhibits TPA-induced tumor initiation and promotion as well as inflammation and ornithine decarboxylase activity in mouse skin (8). Ursolic acid has no primary irritating and no sensitizing potential and therefore it is an ideal cosmetic ingredient. The overall chronic and acute toxicity is low (9).

### **Antimicrobial Activity of Rosemary and Sage Extracts Against Bacteria with Dermatological Relevance**

Today there is a growing interest to use natural compounds against bacteria and germs, which are associated with common skin disorders. The reason is that widely applied synthetics like benzoyl peroxide and retinoids are skin irritating while antibiotics such as macrolides or tetracyclines may cause resistance against bacteria. The use of these compounds in less severe infections should therefore be reduced.

Scientific literature provides sparse information on antimicrobial activity of Rosemary and Sage extracts. Most of the published work refers to the essential oil (10,11). In contrast the Rosemary & Sage CO<sub>2</sub>-extracts tested in a recent study contain standardized concentrations of diterpene phenols with carnosolic acid as major component but only traces (<2 %) of essential oils (12).

Rosemary and Sage CO<sub>2</sub>-extracts and carnosolic acid are tested in the agar dilution test against 29 aerobic and anaerobic bacteria and yeasts, which are associated to infection of the skin, causing disorders like acne, rosacea, seborrheic eczema and dandruff:

Effects of Rosemary and Sage antioxidants and carnosolic acid on **aerobic** bacteria and *Candida* species

test germs	Sage CO <sub>2</sub> -extract, 35 % DTPs		Rosemary CO <sub>2</sub> -extract, 14 % DTPs		Carnosolic acid	
	MIC	MBC	MIC	MBC	MIC	MBC
<i>Staphylococcus aureus</i>	100	100	10	10	64	64
<i>Staphylococcus aureus, Pen.res</i>	100	100	10	10	128	128
<i>Staphylococcus aureus, MRSA</i>	100	100	10	10	-	-
<i>Staphylococcus epidermidis</i>	20	100	10	10	64	128
<i>Staphylococcus lugdunensis</i>	20	100	10	10	128	128
<i>Streptococcus pyogenes gr. A</i>	10	100	10	10	64	128
<i>Streptococcus agalactiae gr. B</i>	20	100	10	10	64	n.e.
<i>Enterococcus faecalis</i>	100	100	20	20	-	-
<i>Escherichia coli</i>	-	-	100	100	-	-
<i>Morganella morganii</i>	100	100	10	20	-	-
<i>Klebsiella pneumoniae</i>	-	-	-	-	-	-
<i>Pseudomonas aeruginosa</i>	100	100	20	20	-	-
<i>Serratia marcescenes</i>	-	-	100	100	-	-
<i>Pseudomonas maltophilia</i>	100	100	10	10	-	-
<i>Bacillus subtilis</i>	20	20	10	10	64	128
<i>Micrococcus luteus</i>	100	100	10	10	-	-
<i>Corynebacterium amycolatum</i>	20	100	2	10	64	128
<i>Corynebacterium pseudodiphthericum</i>	10	20	2	2	32	128
<i>Candida albicans</i>	-	-	20	100	-	-
<i>Candida krusei</i>	-	-	20	100	-	-

Effects of Rosemary and Sage antioxidants and carnosolic acid on **anaerobic** bacteria

test germs	Sage CO <sub>2</sub> -extract, 35 % DTPs		Rosemary CO <sub>2</sub> -extract, 14 % DTPs		Carnosolic Acid	
	MIC	MBC	MIC	MBC	MIC	MBC
<i>Clostridium perfringens</i>	10	10	1	1	16	16
<i>Propionibacterium acnes</i>	10	100	10	100	16	32
<i>Fusobacterium nucleatum</i>	-	-	10	10	128	128
<i>Bacteroides fragilis</i>	10	20	10	10	64	64
<i>Bacteroides vulgatus</i>	10	10	2	10	32	32
<i>Prevotella intermedia</i>	20	20	10	10	64	64
<i>Veillonella parvula</i>	100	-	10	20	-	-
<i>Porphyromonas gingivalis</i>	2	10	1	1	16	32
<i>Peptococcus magnus</i>	100	100	10	20	32	64

Minimal Inhibitory Concentration (MIC) and Minimal Bactericidal Concentration (MBC) are indicated in µg/ml. -, no inhibition; n.e., not evaluated

The screening demonstrates that these products have a broad spectrum of activity against 29 germs, different gram-positive *Staphylococcae* and *Streptococcae* involved in atopic dermatitis, gram-negative *Pseudomonas* species which are frequent pathogens of wound infections, as well as against *Bacillus subtilis*, *Micrococcus luteus* and *candida* species. Antibacterial effects are also approved against *Propionibacterium acnes*, which plays an important role as causative agent in acne vulgaris and which is associated with pathogenesis of seborrheic eczema and dandruff.

The efficacy against gram positive bacteria was superior to gram negative bacteria and fungi.

Rosemary CO<sub>2</sub>-extract inhibits the growth of all tested aerobic bacteria, with the exception of *Klebsiella pneumoniae* and is effective in all of the anaerobic bacteria. It is most effective against *Clostridium perfringens* and *Porphyromonas gingivalis* (MIC and MBC 1mg/ml). Sage extract shows similar inhibition spectrum as Rosemary, but with higher MIC and MBC values and some gaps in the gram-negative range. Carnosolic acid is effective in all anaerobic bacteria except *Veillonella parvula*.

Remarkably Rosemary is the only extract that inhibits the growth of the *Candida* strains. *Candida albicans* may occur in low frequency on skin and mucous membranes without causing symptoms. As opportunistic pathogen it can however overgrow the normal skin flora and cause diseases like intertrigo and candidiasis in diabetic, adipose and immunodeficient subjects.

Accordingly Rosemary and Sage CO<sub>2</sub>-extracts is recommended for the topical treatment of skin disorders like acne vulgaris, seborrheic eczema and atopic dermatitis. They protect skin against UV damage, inflammation and oxidative stress.

Flavex Natureextrakte GmbH offers a complete range of highly concentrated CO<sub>2</sub>-extracts with antioxidative, anti-inflammatory, antibacterial and anti-aging activity. All CO<sub>2</sub>-extracts fulfill the strict criteria of certified organic and natural cosmetics established by BDIH, Ecocert and Natrue for example.

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