Echinacea Dry Extract

For the Treatment of respiratory infections and influenza
CONEFLOWER ROOT EXTRACT

Introduction

EUROMED is a company specialized in making botanical extracts and active principles used as phytomedicines in pharmacy. EUROMED develops and produces therapeutically active raw materials.

The botanical raw materials are subject to strict selection and inspection, and products are manufactured according to methods developed by the EUROMED company. They include inspections to guarantee a standard quality from both analyticochemical and therapeutical points of view and take into consideration the state of art in different fields: research and development, analyses, processes and devices, therapeutic applications on a scientific basis.

EUROMED guarantees the quality of its products by a broad phytochemical know-how.
# CONEFLOWER ROOT EXTRACTION

## Table of Contents

1 Coneflower Extract: General Information .................................................. 5  
1.1 Description ......................................................................................... 5  
1.2 Indications ......................................................................................... 5  
1.3 Extract Specifications ............................................................................. 5  
1.4 Dosage and Methods of Administration .............................................. 5  
1.5 Contraindications and Interactions ....................................................... 6  
1.6 Side-effects .......................................................................................... 6  
2 From Plant to Extract .................................................................................. 8  
2.1 Coneflower root \( (Echinacea angustifolia \, DC \, root) \): Botanical Data ........... 8  
2.1.2 Purple Coneflower root \( (Echinacea purpurea \, root) \): Botanical Data .............. 9  
2.2 Historic Use ........................................................................................ 10  
2.3 Chemistry of Coneflower Extract ......................................................... 11  
2.4 Preparation of the Extract and Quality Control .................................... 14  
2.5 Standardization ..................................................................................... 16  
3 Common Cold ........................................................................................... 17  
3.1 The human immune system .................................................................. 17  
3.2 Epidemiology ....................................................................................... 19  
3.3 Etiology ................................................................................................. 20  
3.4 Symptoms ............................................................................................ 21  
3.5 Stages .................................................................................................. 21  
3.7 Therapy ................................................................................................. 21  
4 Pharmacology ........................................................................................... 22  
4.1 Pharmacodynamic ............................................................................... 22  
4.1.1 Phagocytosis-stimulating action ......................................................... 23  
4.1.2 Effect on immunfunctions ................................................................. 24  
4.1.3 Antibacterial and virustatic action ...................................................... 25  
4.1.4 Antioedema action ............................................................................ 26  
4.1.5 Tumor inhibiting action .................................................................... 27  
4.1.6 Antioxidative actions ....................................................................... 27  
4.2 Pharmacokinetics ............................................................................... 28  
5 Toxicology ............................................................................................... 28  
6 Clinical Pharmacology ............................................................................. 29  
7 Proof of Clinical Efficacy ........................................................................ 30  
7.1 Multi-Center Studies ............................................................................ 35  
7.2 Therapeutic Safety ............................................................................... 35  
8 Bibliography ............................................................................................ 36
1 Coneflower Extract:

General Information

1.1 Description
The coneflower root dry extract is a standardized herbal extract of the roots of *Echinacea angustifolia* DC, *Echinacea pallida* (Nutt.) Nutt. or *Echinacea purpurea* (L.) Moench (all Asteraceae).

The extract of *Echinacea* root is an herbal preventive and therapeutic agent for moderately severe upper respiratory infections, influenza. It is also used for the treatment of slow healing wounds and for inflammatory skin conditions.

1.2 Indications

Prophylaxis and therapy of mild to moderate severe upper respiratory infections, influenza and septic conditions. Locally, Echinacea extracts are used for treatment of slow healing wounds and inflammatory skin conditions.

1.3 Extract Specifications

Coneflower root preparations (as available from Euromed) contain several groups of ingredients like volatile oil, poliacetilenes, alkamides, caffeic acid derivatives and other nitrogenous substances.

1.4 Dosage and Methods of Administration

An oral dose of 20 to 50 drops of extract given twice to three times a day.
1.5 Contraindications and Interactions

Internal administration: not to be used in patients with progressive systemic diseases such as tuberculosis, leukemia, collagenoses, multiple sclerosis, AIDS, HIV or other autoimmune diseases. Also not to be used in patients with allergic tendencies, in particular patients with known allergic reactions to plants of the daisy family and pregnant woman.

1.6 Side-effects

Well tolerated

Very seldom: Parenteral administration: Rigors, febrile reactions, nausea and vomiting. These side effects are dose-dependent.
**CONEFLOWER ROOT EXTRACT**

**Monopreparations containing Echinacea root extract** (Source: Rote Liste 2000)

<table>
<thead>
<tr>
<th>Preparation name</th>
<th>Total Extract/day [mg]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salus Echinacea Tropfen (E. angustifolia)</td>
<td>120-300</td>
</tr>
<tr>
<td>Echinacea-ratiopharm Tabletten (E.pallida)</td>
<td>24-96</td>
</tr>
<tr>
<td>Pascotox mono Tabletten (E.pallida)</td>
<td>54-108</td>
</tr>
<tr>
<td>SX Echinacea Lösung (E. pallida)</td>
<td>144</td>
</tr>
</tbody>
</table>
2 From Plant to Extract

2.1 Coneflower root (*Echinacea angustifolia DC* root): Botanical Data

*Echinacea angustifolia* DC is perennial plant coming from the US states of Nebraska, Iowa, Minnesota and North Carolina. The plant is 10 – 50 cm tall, branched, glabrous or hairy below; leaves elongate-lanceolate to elliptical, dark green. Flowers pink or purple with relatively short ray florets.\(^1,2\)

The dried roots are cylindrical, mostly 10 – 20 cm in length and 4 – 20 mm in thickness irregularly branched an of gray - brown color. They were collected in autumn.\(^3\)

2.1.1 Pale Coneflower root (*Echinacea pallida* root): Botanical Data

*Echinacea pallida* (Nutt.) Nutt. is a perennial plant growing in the area of the great lakes and southern Canada. The plant is 40-120 cm tall, unbranched with spars hairs below and denser hairs covering above; leaves linear-lanceolate to linear- elliptical, entire dark green. Flowers purple, pink or white with deflexed ray florets 4-9 cm in length, pollen grains white\(^2\).
2.1.2 Purple Coneflower root (*Echinacea purpurea* root): Botanical Data

*Echinacea purpurea* (L.) Moench is a perennial plant native in the North American Central Plateau between the Great Lakes and Southern Canada. The plant is about 60-180 cm tall; stem erect, branched glabrous or with a few rough hairs. Leaves ovate to ovate-lanceolate; flowers purple; pollen grains yellow\(^2\).

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**Fig. 1:** Coneflower (*Echinacea angustifolia* DC)

**Fig. 2:** Pale Coneflower (*Echinacea pallida* (Nutt.) Nutt.)

**Fig. 3:** Purple Coneflower (*Echinacea purpurea* (L.) Moench)
2.2 Historic Use

Medicinal uses for *Echinacea angustifolia* varied. It was used by the Indians of the great Plains since ancient times. It is remarkable to see that the distribution of *Echinacea angustifolia* was in close proximity to the Indian settlements where it was used.

The Omaha-Ponca e.g. placed the whole root on toothaches until the pain subsided.

It was also used for treatment of snakebites, stings and other poisons. The juice of the root was used to bath burns.

In 1868 the Californian Eclectic Medical Journal reported on *Echinacea angustifolia* as a highly recommended Indian remedy against snakebites and stings.

Some years later H.F.C. Meyer, a German physician stated in Pwanee City produced "Meyer’s Blood Purifier" as a remedy against Rheumatism, Headache, Dyspepsia and several other diseases. He began the broad application of *Echinacea angustifolia* root in the US AND it became a very popular herbal preparations.

Often *Echinacea pallida* was used instead of *Echinacea angustifolia*, due to a misidentification of both species.

In Europe *Echinacea purpurea* was already mentioned in 1898 by Dragendorff.

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Ancient medicinal plant
## 2.3 Chemistry of Coneflower Extract

Tab. 2: Chemical composition of Echinacea extracts

<table>
<thead>
<tr>
<th>Compounds/Species</th>
<th>Echinacea angustifolia</th>
<th>Echinacea pallida</th>
<th>Echinacea purpurea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volatile Oil</td>
<td>Root of Echinacea angustifolia usually contain less than 0.1 %. Main constituents are compounds of the type of dodeca-2, 4-diene-1-ylisovalerate, palmitic and linolenic acid⁶,⁷.</td>
<td>Root of Echinacea pallida has 0.2 to more than 2.0%⁶,⁷. Main compounds are pentadeca-8Z-ene-2-one and 1-pentadecane⁸.</td>
<td>Overground parts and roots of the plants show only small amounts of volatile oil &lt; 0.1 %⁸.</td>
</tr>
<tr>
<td>Polyacetylenes</td>
<td>About 2% polyacetylenes (calculated in terms of air dried material). The most important are trideca-1-en-3,5,7,9,11-pentaene and ponticaepoxide. Both are very unstable⁸,⁹.</td>
<td>About 2 mg % polyacetylenes (calculated in terms of air dried material). The most important are trideca-1-en-3,5,7,9,11-pentaene and ponticaepoxide. Both are very unstable. Besides these main constituents are several more minor polyacetylenes found⁸.</td>
<td>Several similar polyacetylenes as in the other species were found⁸.</td>
</tr>
</tbody>
</table>
### Coneflower Root Extract

<table>
<thead>
<tr>
<th>Compounds</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alkamides</td>
<td>About 15 alkamides have been identified. The main compounds are the isomeric dodeca-2E, 4E, 8Z, 10E/Z-tetraenic acid isobutylamides. 0.001% of a poly unsaturated alkamide, echinacein (dodeca-2E,6Z,8E,10E/tetraenic acid butylamide). The principal compound from dried herbal material were the isobutylamides of undeca-2E,4Zdiene-8,10-diynic acid and dodeca-2E, 4E, 8Z, 10E/Z-tetraenic acid.</td>
</tr>
<tr>
<td>Caffeic acid derivatives</td>
<td>Echinacoside about 1% in the roots and small amounts of 6-caffeoyl echinacoside. 2,3-O-dicaffeoyl tartic acid (chicoric acid was found up to 1-3% and some other derivatives of caffeic acid in minor concentrations.</td>
</tr>
<tr>
<td>Other nitrogenous compounds</td>
<td>Betain hydrochloride and the pyrrolizidine alkaloids tussilaginine (0.006%) and isolussilaginine. Glycine-betain about 0.2% in fresh leaves.</td>
</tr>
<tr>
<td>Polysaccharides</td>
<td>PSI a 4-O-methyl glucuronorabinoxylan with molecular weight 35,000 D and PSII an acid arabinorhamogalactan (MW 450,000 D). And a pectin-like polysaccharide.</td>
</tr>
</tbody>
</table>
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Fig. 5: Lipophilic constituents of Echinacea species

![Characteristic lipophilic constituents](image)

Fig. 6: Caffeic acid derivatives of Echinacea species

![Caffeic acid derivatives](image)
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2.4 Preparation of the Extract and Quality

**Standard quality assured**
Coneflower roots come from plants grown in Europe and USA. Using these specially identified roots and according to a standard quality, manufactures coneflower root extract.

The quality of coneflower root extract is steadily improved. Permanent professional botanical inspections are part of the growth of the plant.

Adequate size and condition of the plants are of great importance to the quality of the extract of Coneflower root. The roots are collected manually only.

**Inspection of the drug upon its arrival at EUROMED**
When the plant material arrives at EUROMED an exhaustive inspection of the raw material is carried out in order to guarantee the quality of the final product.

Furthermore EUROMED evaluates the possible contamination of the plant material. Only high-quality raw plant material is selected according to strict criteria.

**Strict quality control of the extracts**
EUROMED applies an extraction process in a careful manner, which provides a high yield of valuable constituents and a high-grade extract.
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According to an original process produces a dry extract from the roots of *Echinacea angustifolia* and *Echinacea purpurea*:

- **EXTR. ECHINACEAE, SICCUM**
  **(ECHINACEA DRY EXTRACT)**
  Fine powder brown color, characteristic odor and savor.
  _EUROMED_ coneflower root extract satisfies the highest quality standards. It is produced to meet the requirements for an effective and safe medication.
2.5 Standardization

The consistent batch to batch quality of the **CONEFLOWER ROOT EXTRA** coneflower root extract is guaranteed by the standardized production process.

The analytical specifications of the **CONEFLOWER ROOT EXTRA** coneflower root extract are

<table>
<thead>
<tr>
<th></th>
<th>E. angustifolia root</th>
<th>E. purpurea root</th>
</tr>
</thead>
<tbody>
<tr>
<td>* Aspect</td>
<td>Fine powder, brown color, characteristic savor and odor</td>
<td>Fine powder, brown color, characteristic savor and odor</td>
</tr>
<tr>
<td>* Identification</td>
<td>HPLC Fingerprint</td>
<td>HPLC Fingerprint</td>
</tr>
<tr>
<td>* Loss on drying</td>
<td>---</td>
<td>Max. 5%</td>
</tr>
<tr>
<td>* Water</td>
<td>Max. 5.0 %(KF)</td>
<td>---</td>
</tr>
<tr>
<td>* Assay</td>
<td>Echinacoside min. 4.0% (HPLC)</td>
<td>Total phenols as sum of caftaric acid, chicoric acid, chlorogenic acid and echinacoside min. 4% (HPLC)</td>
</tr>
</tbody>
</table>
3 Common Cold

3.1 The human immune system

The human body is in communication with its environment not only through the nutrients which it takes in and the metabolic products which it discharges. The environment also contains potentially harmful toxins and pathogenic microorganisms. With the aid of the immune system the human body can defend itself against the harmful agents in the environment that cause disease.

Several organs of the human body are involved in the defense mechanisms

Fig. 7: The organs of the human immune defense
The immune system recognizes these agents as foreign and distinguishes them from the intrinsic substances, cells and tissues of the body. An immunologist would say that the immune system distinguishes between "self" and "not self".

The intact immune system mounts defenses against toxic substances, viruses, bacteria, pathogenic fungi and parasites that have gained entry into the body, and also against its own infected cells, tumor cells and foreign tissue; it recognizes them as foreign and in most cases successfully repels them. Together with its capability for recognizing "not self", the immune system has a kind of memory which endows it with the capacity of responding better and faster in the event of a renewed threat from a toxic substance or pathogenic microorganism which it has previously encountered.
3.2 Epidemiology

The importance of the interactions between these complex defense mechanisms is illustrated by patients who have to be treated with cytostatics or antibiotics. During the period of treatment many of these drugs suppress the defense mechanisms of the immune system, e.g., those which deal with invading pathogens or virus-infected cells. Consequently, patients become more susceptible to infections and suffer from more frequent recurrences \(^{27,28}\).

Infections of the upper respiratory system are very common. Averaging two infections each year and only one day of unfitness per year, about 72 million of lost working days result each year in Germany (population 70 million). This represents loss of about 20 Billion DM calculated on basis of the German GNP 1997.

For these reasons adequate treatment or prophylaxis with immunemodulating agents like *Echinacea angustifolia* root extract can save 10 billion DM annually\(^ {29}\).
3.3 Etiology

Causes of a weakened immune system
Because the structure of the human immune system is so complex, there is a wide range of adverse factors that can impair its working.

*Inborn immune deficiency*

Non-specific
Genetic defects which impair the numbers and functioning of active phagocytes. Genetic defects of the complement system.

Specific
T cell defects (numbers and functions).
B cell defects (numbers and functions).
Combined defects
Acquired immune deficiency

*Behavioral disorders*
Faulty nutrition; Excessive alcohol consumption;
Heavy smoking; Lack of sleep; Physical exhaustion/stress

*Infection-induced disorders*
Acute viral infections often weaken the immune defenses against superadded infections.

*Immune deficiencies due to metabolic disorders, therapeutic measures or ageing*
Diabetes mellitus, Hepatic cirrhosis, Uraemia
Operations, Radiotherapy,Cytostatic therapy
Immunosuppressive antibiotic therapy
Advanced age (the immune defences weaken as age advances)
3.4 Symptoms

Physical exhaustion / stress
Fever
Cough, hoarseness, irritable cough
Shortness of breath
Stuffed nose and sinuses
Perspiring

3.5 Stages

Colds develop normally within a few days. They begin with soreness in the throat, stuffed nose and nocturnal perspiring. Later cough or bronchitis may follow.

3.7 Therapy

*Early prophylaxis is important in Cough*

It is important to treat of common colds with immunmodulating substances as early as possible, preferably as soon as the first soreness in the throat is noticed.
4 Pharmacology

4.1 Pharmacodynamic

Most of the pharmacological effects of *Echinacea* root extract preparations involve the human immune system. Its action results from synergistic effects of multiple chemical components in the herb.
4.1.1 Phagocytosis-stimulating action

In vitro a solution of dried residue from an ethanol extract (1:10) of *Echinacea angustifolia* in a concentration of $10^{-3}\%$ raises the phagocytosis index of human granulocytes for yeast by 17%. A dose depending action could be shown, as below concentration of $10^{-5}\%$ this effect was no longer detectable. Also a the dried residue from a chloroform extract at a concentration of $10^{-1}\%$ produced a stimulation up to $34\%^{32,33}$.

In vivo the application of a solution of 0.5 ml of the ethanol extract in 30 ml physiological saline given orally to mice over two days the phagocytosis rate showed a significant increase (factor 1.7) of carbon particle injected intravenously on day 3 (as compared with controls) Under same test conditions the lipophilic alkamide fraction given in doses of 0.33 mg/kg bodyweight/day increased the carbon elimination a factor of 1.5 on day 3.

The ethanol extract (1:10) from *Echinacea pallida* root, in a concentration of $10^{-2}\%$, raised phagocytosis rate of human granulocytes by 23%.

The in vivo carbon clearance test in mice showed, in a two days treatment with a solution of 0.5 ml of the ethanol extract in 30 ml of isotonic saline, given p.o. in a dose of 10 ml/Kg bodyweight three times daily, a raised elimination rate of the carbon particle by factor of 2.2 as compared to the control group.
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A lyophilisate of pressed juice from *Echinacea purpurea* used in a concentration of 0,5 mg/ml, significantly increased the phagocytosis rate 79% to 95% 34.

Stimulation of phagocytosis has also been demonstrated in vitro and in vivo for the ethanolic extract (1:10) in the carbon clearance test. There was shown, that by p.o. application of 10 ml/ Kg bodyweight (0,5 ml of extract in30 ml isotonic saline), three time daily for 2 days raise the carbon excretion by factor 4 in comparison to controls.

4.1.2 Effect on immunfunctions

New Results 35 indicate that extracts from *Echinacea angustifolia* root enhance immune function by increasing antigen-specific immunoglobulin production. These results were measured in rats that were injected with the antigen keyhole limpet hemocyanin (KLH) and treated over a 6 weeks period with *Echinacea angustifolia* root extract. Immunoglobulin production was monitored by ELISA over a period of 6 weeks. The Echinacea treated group showed a significant rise of their primary and secondary IgG response to the antigen.

The polysaccharides isolated from *Echinacea purpurea* herb, mainly 4-O-methy-glucurono-arabinoxylan and Arabino-rhamo-galactan exhibit a stimulation of cytokine liberation of TNF-α, IL-I and IL-6 from peritoneal macrophages 36, 37.
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4.1.3 Antibacterial and virustatic action

Echinacea angustifolia as well as Echinacea pallida and Echinacea purpurea\textsuperscript{38} show antibacterial and virustatic action.

Echinacoside has been found to have a weak inhibitory action against Staphylococcus aureus. The effect of 6.3 mg echinacoside in 8 x 10\textsuperscript{3} molar solution was equivalent to that of about 10 Oxford units of penicillin.

At a concentration of 50 µg/ml inhibited the growth of Escherichia coli totally. With Pseudomonas aeruginosa the same effect was reached at a concentration of 1000 µg/ml\textsuperscript{39}.

Tab. 2: Minimal inhibitory concentrations of Trideca-1-ene-3,5,7,9,11-pentaine against bacteria, yeasts and fungi\textsuperscript{40}

<table>
<thead>
<tr>
<th>Organism</th>
<th>MIC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspergillus niger</td>
<td>0.1 %</td>
</tr>
<tr>
<td>Candida albicans</td>
<td>0.2 %</td>
</tr>
<tr>
<td>Epidermophyton floccosum</td>
<td>0.01 %</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>0.1 %</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>0.01 %</td>
</tr>
<tr>
<td>Trichphyton mentagrophytes</td>
<td>0.01 %</td>
</tr>
<tr>
<td>Trichphyton rubrum</td>
<td>0.01 %</td>
</tr>
<tr>
<td>Trichphyton schoenleinii</td>
<td>0.01 %</td>
</tr>
</tbody>
</table>
CONEFLOWER ROOT EXTRACT

Some publications report that echinacoside and chicoric acid have some inhibitory action against VSV (vesicular stomatitis virus) in L-929 mouse cells. Chicoric acid (concentration 125 µg/ml) reduced the VSV infection after 4 hours of incubation by more than 50%. For comparison caffeic acid had the same effect in a concentration of 62.5 µg/ml. Other results indicate that flavonoids isolated from *Echinacea angustifolia* root extract may act as an interferon like action against VSV infection when the cells were pre-incubated with active principle 41.

4.1.4 Antioedema action

In some animal models extracts of *Echinacea angustifolia* root produced inhibition of about 65% in the carrageenan-rat’s paw model at a dose of 0.1 mg/kg bodyweight. Topical application in the croton oil mouse ear oedema test gave an ID$_{50}$ value of 100.8 µg/ear (indometacin 41.6 µg/ear) 42.

An n-hexane extract from *Echinacea angustifolia* root inhibited in vitro the formation of prostaglandin E$_1$ (cyclooxygenase from sheep seminal vesicles) and also 5-lipoxygenase from pig leucocytes. Among the akamide group from *Echinacea angustifolia* root extract there are compounds proven to be potent inhibitors of 5-lipoxygenase 43, 44.
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4.1.5 Tumour inhibiting action

The pentane-soluble volatile oil obtained by distillation from *Echinacea angustifolia* roots reduced tumor weight in rats with Walker carcinosarcoma at about 69%. In mice with lymphocytic leukemia survival was lengthened by 100%.

In vitro experiences with expressed juice of *Echinacea purpurea* have shown that activated macrophage (activation by pressed juice) have cytotoxic effects on tumor cells.

An expressed juice of *Echinacea purpurea* showed in vivo after oral application a remarkable antitumor action.

4.1.6 Antioxidative actions

Root extracts of *Echinacea angustifolia*, *Echinacea pallida* and *Echinacea purpurea* containing different amounts of echinacoside exhibited in vitro antioxidant activity, depending on the method used to evaluate peroxidation reactions.

The methanolic extract derived from *Echinacea pallida* root exhibited the greatest relative antioxidant activity of the three species.

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27
4.2 Pharmacokinetics

The extract of coneflower root is a complex compound. Therefore pharmacokinetic experiments are difficult, and data is not yet available.

5 Toxicology

The toxicity of coneflower root extract and their preparations is generally very low. The pyrrolizidin alkaloids tussilagine and isotussilagin do not contain the 1,2-unsaturated necine structure and therefore do not have any hepatotoxic action\(^\text{48}\).

Acute Toxicity

There is no published information available.

Chronic Toxicity

There is no published information available.

Reproduction Toxicology

There is no published information available.

Genotoxicity/Carcinogenicity

There is no published information available\(^\text{49}\).
6 Clinical Pharmacology

A double blind placebo controlled randomized clinical trial was conducted to investigate the safety and efficacy of Echinacea extracts for preventing upper respiratory tract infections.

Three hundred healthy volunteers were included in this study. The main outcome measure was time until first upper respiratory tract infection.

Ethanolic extracts of *Echinacea angustifolia* root and *Echinacea purpurea* root or placebo were given for 12 weeks.

Results indicate that the time until first occurrence of the first upper respiratory tract infection was 66 days in the *Echinacea angustifolia* group and 69 days in the Echinacea purpurea group and 65 days in the placebo group (all at CI 95%).

In the placebo group 36.7% had an infection in the *Echinacea angustifolia* group 32% and in the *Echinacea purpurea* group 29.3%.

The benefit of medication was a slightly shorter duration of infection and the subjective feeling of symptomatic was better in the treatment groups.
7. Proof of Clinical Efficacy

Similar results were reported by using different combinations of *Echinacea angustifolia* and other medicinal plants like Baptisia or Thuja. There were five different placebo controlled randomized clinical studies with healthy volunteers discussed.

Over a period of 32 years (1961 to 1993) more than 26 controlled clinical trials have been conducted. A critical review demonstrates the value of Echinacea root extracts in the treatment of common cold.

One of the studies, a single blind study, has been conducted with *Echinacea angustifolia* homeopathic complex (D1 and D4). In both studies phagocytic activity of PNG (polymorphonuclear neutrophil granulocytes) was significantly enhanced in comparison to placebo.
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In a placebo-controlled unicentric study with an *Echinacea pallida* root preparation comprising 160 patients, an alcohol-water tincture (1:5) given in a dose of 90 drops (ca. 900 mg of the herbal product) / day achieved considerably more rapid improvement in patients of the upper respiratory tract than a placebo group. The duration of illness was shortened from 13 to 9.8 days in patients with bacterial infections and from 12.9 to 9.1 in patients with viral infections53.

Several clinical studies have been conducted with the pressed juice from *Echinacea purpurea*. A placebo-controlled double blind study with patients particularly susceptible to infection was conducted in order to find whether a treatment with pressed juice from *Echinacea purpurea* could reduce the recurrence rate of infection.

108 patients, who in the winter half-year preceding the study had suffered at least three attacks of respiratory infection of coryzal type; received a dose of 2 x 4 ml *Echinacea purpurea* pressed juice or placebo juice over a 8 week treatment period.

The time elapsed before the first infection was longer in the treatment group (40 days) than in the placebo group (25 days)54.
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Fig. 9: Recurrence rate of infections

These results were recently confirmed in a GCP conform study with 120 patients suffering of an infection of the upper respiratory tract in a monocentric double-blind study. Pressed juice of *Echinacea purpurea* (20 drops every two hours at the first day and 3 x 20 drops in the following days) showed a significant shortening of time for the reduction of the symptoms of infection in comparison to the placebo group.\(^{35}\)

Fig. 10: Time until disappearance of symptoms (days)
- Placebo – upper line
- Echinacea pressed juice – lower line
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In the treatment of skin conditions such as wounds, eczema, herpes simplex or burns *Echinacea purpurea* pressed juice ( ointment) showed in a study with 4598 patients healing within one week in about 85%. This is explained in terms of fibroblast activation and hyaluronidase inhibition56.

A 55% ethanolic extract from *Echinacea purpurea* roots was investigated in patients with influenza infections in a single center placebo-controlled double-blind study. The dose was 180 drops of extract (= 90 mg herbal product) daily. There was a definitive improvement in the symptomatic picture of the influenza infection (overall score of various symptoms) as compared with the placebo group. In patients given half the daily dose no significant effects were seen57.
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Fig. 10 Overall score of various symptoms as a mean value dependent on time and the extract.

- Placebo
+ Dose 1 ( = 450 mg extract) , * Dose 2 ( = 900 mg extract)

K0 = starting point
K1 = 3-4 days after treatment
K2 = 8-10 days after treatment
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7.1 Multi-Center Studies

Not available

7.2 Therapeutic Safety

*High level of therapeutic safety* No subjective side effects were reported
8 Bibliography

3. American Pharmaceutical Association, National Formulary VI (1936)
5. Dragendorff G, Die Heilpflanzen der verschiedenen Völker und Zeiten, F. Enke Verlag, Stuttgart (1898)
CONEFLOWER ROOT EXTRACT

28 Little PS, Williamson I, Are Antibiotics appropriate for sore throats?- Costs outweigh the benefits, BMJ 309, 1010-1012 (1994)
38 Thompson KD, Antiviral activity of Viracea® against aacyclovir susceptible and acyclovir resistant strains of herpes simplex virus, Antiviral Research 39, 55-61 (1998)
CONEFLOWER ROOT EXTRACT

46 Mantovani A, Int J Cancer 27,221-228 (1981)
53 Bräunig B, Knick E, Therapeutische Erfahrungen mit Echinacea pallidae bei grippalen Infekten, Naturheilpraxis 1, 72-75 (1993)
CONEFLOWER ROOT EXTRACT

58 Werning C, Medizin für Apotheker, Stuttgart (1997), 213-214