Echinacea: What’s New

Kevin Spelman, PhD, MCPP
Health, Education & Research

Lecture Map

- The Basics
- Clinical Apps
- Dosing
Echinacea sp.

- Chemistry
- Pharmacology
- Clinical Applications
- Subject Of Over 350 Studies

Echinacea Species

- angustifolia
- pallida
- purpurea
History

- Native Americans
  - Internal use: Infections, Toothache, Joint Pain, Snake Bite
  - External use: Wounds, Burns, Abscesses
- Eclectics Corrects Fluid Deprivation With Tendency To Sepsis And Malignancy

History Continued

- Allopaths-Included in National Formulary Until 1950
Constituents

- Polysaccharides
- Flavonoids
- Caffeic Acid Derivatives
- Essential Oils
- Polyacetylenes
- Alkylamides
- Miscellaneous Chemicals

Immunostimulatory Properties

Activation Of Alternative Complement Pathway:

- Increase Of Properdin
- Promotes Chemotaxis PMNGS
- Solubilization Of Immune Complexes
- Neutralization Of Viruses
- Enhances Bacteriolysis

Med Welt 34: 1463-7, 1983

Echinacea: Myth or Medicine
Immunostimulatory Properties

Enhancement of:
- Serum leukocyte counts
- Granulocyte counts

Z Gastroenterol 1: 19-22, 1975

Immunostimulatory Properties

- Increase Of In Vitro Phagocytosis Of Candida A. By Granulocytes And Monocytes By 30- 40%
- Increase Of Chemotactic Migration Of Granulocytes By 30- 40%

T Lymphocyte Activation:

- Transformation
- Production Of Interferon
- Secretion Of Lymphokines

Effects Of T Cell Activation, Enhanced:

- T Cell Mitogenesis
- Macrophage Phagocytosis
- Ab Binding
- NK Cell Activity
- Increased Numbers Of Circulating PMNs
- Stimulation Of PMN Phagocytosis

Arzneim Forsch 35: 1069-75, 1985
Phytomed 3: 95-102, 1996
Effects of Marcophae Activation

Increased Production Of:
- TNF
- Interferons
- IL-1

Destruction Of Tumor Cells In Tissue Culture

Infection Immunity 46: 845-9, 1984

Antiviral Properties

Viruses Inhibited In Cell Cultures:
- Influenza Virus
- Herpes Simplex Virus
- Vesicular Stomatitis Virus

Plant Medica 33: 89-102, 1978
Antiviral Mechanisms

- Inhibition Of Hyaluronidase
- Enhancement Of Cytotoxic Mediated Killing
- Increase In Interferon Secretion

Arzneim Forsch 2: 467-9, 1952

Antibacterial Properties

- Effective Against:
  - Staphylococcus aureus
  - Corynebacterium diptheria
  - Proteus vulgaris
- 6.3 mg Echinacoside = 10 Oxford Units of Penicillin

Helv Chim Acta 33: 1877-93m 1950
Antineoplastic Activity

- (Z)-1, 8-Pentadecadiene In Vivo Possesses Significant Direct Anticancer Activity


Tissue Regeneration Effects

- Stimulates Fibroblast Growth
- Manufacture of Glycosaminoglycans
- Inhibition of Hyaluronidase

Arzneim Forsch 133-7, 1953
Collagen Protection

- Echinacea Extracts Protect Collagen From Free-Radical-Induced Degradation

Plant Med 61: 510-14, 1995

Anti-Inflammatory Properties

- Mild Cortisone-Like Effect
- Enhances Secretion of Adrenal Cortex Hormones

Riv Ital Essenze Profumi 53: 281-95, 1971
Clinical Applications

- Infections
- Wound Healing
- Arthritis
- Cancer
- Snake Bite
- Ergogenic Effects

Clinical Applications

- Anxiolytic Activity
- Brown Recluse Bites
- Life Extension
- Anti-Anaphylaxis Activity
- AutoImmune Protection
- Dosing
Infections

- **Inhibition Of Candida A. Infection In Rats Infected With Lethal Dose (IV Administration Of 3x10⁵ Candida A. Cells)**


Infections

- **Reoccurrence of fungal infections**
  - Echinacea in combination with Econazole Nitrate reduced From 60.5% To 5-16.7%

Echinacea: Myth or Medicine

Treatment Of Recurrent Candidiasis With The Fresh-Pressed Juice Of E. Purpurea: Rate At Six Months

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<th>No. Of Patients</th>
<th>Recurrence Rate</th>
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<td>Topical Antimycotic Plus Oral Fresh-pressed Juice Of E. Purpurea</td>
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<td>16.7%</td>
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Influenza

Double-Blind Echinacea Vs. Placebo

3 Groups:
1) Placebo
2) 450 mg E. Purpurea Root
3) 900 mg E. Purpurea Root
   900 mg Significant Reduction In Influenza Sxs (Including Weakness/Low Energy, Chills/Sweating, Sore Throat, Muscle/Joint Aches, Headaches)

Number Of Subjects: 180    Duration: 10 Days

Colds

Double Blind

- Double Blind Echinacea Vs. Placebo
  - Percent of Patients Remaining Healthy: 35.2% Vs. 25.9%
  - Time Between Infections: 40 Days Vs. 25 Days
  - Infections That Occurred Were Less Severe And Resolved Quicker In 78.6% Of Echinacea Group

Number of Subjects: 108         Duration: 8 Weeks
Forum Immunologie 8: 2-12, 1991

Cancer

- Inhibits Growth Of Walker Carcinosarcoma
- Lymphocytic Leukemia Stimulatory Effects On Leukocyte Counts In Radiation Tx Pts

Med Chem 15: 619-23, 1972
Med Klin 64: 1546-7, 1969
**Wound Healing**

- 85% Success In Tx Of:
  - Inflammatory Skin conditions
    (Abscesses, Folliculities, Eczema, Burns, Herpes, Varicose Ulcers Of The Leg)


**Arthritis**

**Reduction In Inflammation**

- Echinacea 21.8%
- Cortisone 42%
- Prednisone 49.2%
- No Side Effects Noted With Echinacea

Z Fur Rheum 16: 231-8, 1957
Snake Bite

- Reputation Among Native Americans As Tx
- Possible Mechanism: Hyaluronidase Inhibition

Arzheim Forsch 2: 467-9, 1952

Toxicology

- 1000x Normal Dose Immunosuppressive
- No Mutagenicity/Carcinogenicity Test Negative
- I.M. Preparations For Short Periods & Longer Term Oral Use (12wk) Completely Safe
- I.V. Preparations May Cause Fever, Shivering, Nausea, & Transienty Lymphopenia (Due To Cytokine Production, INF-Alpha/IL-1)

Continued
Toxicology Continued

- LD-50 (Murine) Of I.V. Echinacin: 50 ml/kg
- LD-50 (Murine) Of Polysaccharides, Peritoneal Administration: 1000-2500 mg/kg
- Chronic Administration Of Echinacin To Rats At Doses Many Times The Human Therapeutic Doses Gave No Evidence Of Any Toxic Effects.

Arzneim Forsch 41: 1076, 1991
Phytomed 3: 95-102, 1996

Meta-Analysis

Number Of Trials: 26
18 Randomized
11 Double-Blind
30 Of 34 Treatment Groups Benefited From Echinacea Compared To Control

Phytomed 1: 245-54, 1994
Immunomodulatory Activity

- Phagocytic Activity of PNGs significantly enhanced by 54.0%

Alcoholic extract of *E. angustifolia* root
Placebo controlled, Human subjects

NK cell activity & ADCC in CFS & AIDS

- Significantly enhanced NK-function
- Significantly increased ADCC of PBMCs in all groups
- *Echinacea pupurea* enhances cellular immune function of PBMC in normal pts. And pts. with depressed cellular immunity

[>0.1 μg/kg], n=60
Antiviral Mechanism

- Enhancement of Cytotoxic Mediated Killing
- Increase in Interferon Secretion

Arzneim Forsch 2:467-9, 1952

Antiviral Mechanism

*E. purpurea* Induced Cytokine Production by Human Macrophages of:

- IL-1
- TNF-α
- IL-6
- IL-10 in vitro [0.012 μg/mL]

Prevention of URTIs

- 13% Relative risk reduction for *E. angustifolia*
- 20% Relative risk reduction for *E. purpurea*
- Prophylactic effect could not be shown
- Dose 50 gtts. bid (tincture 1:11, 30% EtOH)

Photo by Kelly Kindscher
Kansas Biological Survey
Ergogenic Effects

Performance enhancement

The Effect of 4 Wk of Oral Echinacea Supplementation on Serum Erythropoietin and Indices of Erythropoietic Status

Malcolm T. Whitehead, Tyler D. Martin, Timothy P. Schewitz, and Michael J. Webster

The purpose of this investigation was to determine whether echinacea supplementation results in alterations of erythropoietin levels and erythropoietic status. Twenty-eight age-matched (26±2 ± 2, height 1.8 ± 0.0 m, weight 70 ± 4 ± 4 kg, and 13±5 ± 5.5 body fat) men were grouped using a double-blind design and received either echinacea (Echinacea purpurea L.) extract (50 mg/kg body weight) or an equivalent volume of placebo per day for 4 weeks. Blood samples were collected and analyzed for red blood cell (RBC), hemoglobin (Hb), hematocrit (Hct), mean corpuscular volume, mean corpuscular hemoglobin concentration, platelet counts, and erythrocyte indices and indices of erythropoietic activity. No significant differences were noted in RBC, Hb, Hct, and indices of erythropoietic activity in response to echinacea supplementation in this study. The data indicate that echinacea supplementation results in no significant alterations in RBC, Hb, or Hct.

Key Words: erythropoietin, red blood cells, 0-1-3, erythropoietic growth factors, nutrition, exercise physiology.

Echinacea is a herbal supplement that is derived from the North American purple coneflower plant and is traditionally considered a constitutional and anti-inflammatory. Evidence from animal models (16, 20) and cell cultures (6, 25, 33) indicates that echinacea supplementation might also stimulate the production of erythropoietic growth factors, induce erythropoiesis, and increase the oxygen transport capacity of the blood. Echinacea supplementation in humans (250 mg/kg for 9 days) resulted in no significant changes in RBC, Hb, and Hct. However, increased erythropoiesis and increased oxygen consumption were observed in rats. While these results suggest a potential role for echinacea in human erythropoiesis, additional studies are needed to fully understand the effects of echinacea on erythropoiesis and oxygen transport.

Whitehead is with the Dept. of Health and Human Performance, Northwestern State University, Natchitoches, LA 71494. Martin and Schewitz are with the Dept. of Kinesiology, University of Mississippi, University, MS 38677. Schewitz is with the Dept. of Physical Education and Health, College of Education, Dayton, OH 45469.
Design

- Randomized double-blind placebo controlled, n = 24
  - 8000 mg/d of *Echinacea purpurea*, Puritan’s Pride, Oakdale, NY + multivitamin
  - Placebo + multivitamin

Photo by Martin Wall
Echinacea supplementation increased the hemoglobin and packed cell volume.

Echinacea supplementation also increased the lymphocyte count and stimulated neutrophil migration into tissues and phagocytic ability.
Design

- Randomized, placebo controlled crossover, n = 8, *E. angustifolia* root standardized to 4% echinacoside 1:3 powdered root extract, 30 mL of syrup BID for 4 days, equivalent of 2000 mg/day
Protection in Athletes

- *E. purpurea* is effective in the prophylaxis, as well as the treatment, of the common cold in athletes
Protection in Athletes

- Investigators (97.5%) rated the treatment as having "very good" or "good" tolerability
  - 75% of patients and investigators rated its efficacy during a common cold as "very good" or "good,"
  - 71% of subjects were free of cold episodes

This study is the first to suggest that
Design

- open, multicenter study, n = 80
- tablet formulation of Echinacea purpurea extract (Echinaforce Forte; A. Vogel, Bioforce AG, Roggwil, Switzerland)

Anxiolytic activity

Chill...
Why Anxiety???

Cannabinoid activity

The Anxiolytic Potential and Psychotropic Side Effects of an Echinacea Preparation in Laboratory Animals and Healthy Volunteers

INTRODUCTION

Echinacea is a plant species that has been documented to have several potential therapeutic effects, including anxiolytic activity. However, there is limited research on the role of echinacea in anxiety management. In a recent study, the authors investigated the anxiolytic potential of a specific echinacea preparation in laboratory animals and healthy volunteers.

We investigated the anxiolytic and psychotropic effects of a commercial echinacea preparation in laboratory animals and healthy volunteers. Our findings suggest that echinacea may have potential therapeutic effects in managing anxiety and improving overall well-being.

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Echinacea: Myth or Medicine
The study consisted of three phases:

(i) a preliminary phase of 3 days when two baseline anxiety scores were recorded
(ii) a 1-week treatment phase when subjects were treated as described below
(iii) a 2-week washout period when no treatment was administered, but anxiety scores were recorded on days 11 and 24
Design

- Data were collected using a structured self-assessment diary technique

- Healthy volunteers scoring high on the State-Trait Anxiety Inventory

- Subjects n = 33, randomly assigned to 1 or 2 tablets per day for 1 week, *E. angustifolia* extract 20mg (ExtractumPharma Zrt, Budapest, Hungary)
Echinacea: Myth or Medicine

Undeca-2E-ene-8,10-diynoic acid isobutylamide
Echinacea: Myth or Medicine
Implications of PPAR-γ Activation

- Enhanced insulin sensitivity
  - Metabolic syndrome
  - Type 2 Diabetes
- Immunomodulatory Activity
  - Broad spectrum cytokine modulation
  - Profound shift in inflammatory milieu
Peroxisome proliferator-activated receptor pathway

Somoza M. October 8, 2006

http://www.cas.psu.edu/docs/CASDEPT/VET/paw/ppar/PPARinformation.html

PPARγ pathways

http://www.cas.psu.edu/docs/CASDEPT/VET/paw/ppar/PPARinformation.html
Brown recluse bites

Saving Tissue

A Clinical Observation

- In combination with turmeric (*Curcuma longa*), both internally and topically, *E. purpurea* root has been useful for the particularly difficult-to-heal bites of brown recluse spiders (*Loxosceles reclusa*)
A Clinical Observation

- The bite had progressed into severe dermonecrotic lesions migrating up the left arm and down the right arm.
- The lesions were resolved over about 16 weeks’ time with topical and internal use of *E. purpurea radix* and *Curcuma longa rhizoma*.

Possible Modes of Activity

- Stimulation of fibroblast activity
- Hyaluronidase inhibition
- Wound healing properties
Anti-Anaphylaxis Activity?

Clinical Observations

Kevin Spelman

Case 1: 37 yrs Ø

Primary Complaint: Patient started to sneeze and was diagnosed with a common cold. She was treated with an over-the-counter cold medication.

Within hours of taking the third dose, she became very nervous and then started to have a sense of impending doom and turned to break out into a rash that the described as her skin crawling. She became increasingly drowsy as we were on the phone.

Pulse: 90, BP 160/90, JVP normal, respiration normal, temp: 38.2ºC.

She was given Prednisone 50 mg PO qd x2, diphenhydramine 25 mg PO qid, and acetaminophen 650 mg PO qid. She was hospitalized in the ICU.

Case 2: 52 yrs Ø

Primary Complaint: Patient started to cough and then developed a rash. She was diagnosed with a common cold.

Within hours of taking the third dose, she started to feel very nervous and turned to have a sense of impending doom and turned to break out into a rash that the described as her skin crawling. She became increasingly drowsy as we were on the phone.

Pulse: 80, BP 160/90, JVP normal, respiration normal, temp: 38.2ºC.

She was given Prednisone 50 mg PO qd x2, diphenhydramine 25 mg PO qid, and acetaminophen 650 mg PO qid. She was hospitalized in the ICU.

Echinacea purpurea radix and Echinacea officinalis radix: ethnomedicinal extracts ameliorate acute allergic reactions

Kevin Spelman

Clin. Exp. Allergy

Echinacea purpurea radix and Echinacea officinalis radix: ethnomedicinal extracts ameliorate acute allergic reactions. Kevin Spelman

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Echinacea: Myth or Medicine

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Echinacea: Myth or Medicine
Case Study

- Case 1: 37 y/o ♀,
- Primary Complaint: Former patient whom had gone to an acupuncturist who “diagnosed” parasites. She was treated with an unknown Chinese herbal formula.

Case Study

- Case 2: 42 y/o ♀,
- Primary Complaint: Patient had gone to see an acupuncturist and again in this case, and was diagnosed with parasites. Patient was treated with an unknown Chinese formula.
Classroom Observation

- 25 y/o ♀
- Sampling herbs in classroom and had an anaphylactic reaction

Possible Modes of Activity

- Cannabinoid Activity
- Antioxidant Activity
- Hypothesis – direct down regulation of leukotriene and histamine secretion from mast cells
Echinacea purpurea and Melatonin Augment Natural-Killer Cells in Leukemic Mice and Prolong Life Span

NATHAN L. CURRIER, B.SC., and SANDRA C. MILLER, P.H.D.

ABSTRACT

Objective: We recently showed that daily dietary administration of Echinacea purpurea root extract to normal mice for as long as 1 week resulted in significant elevations of natural-killer (NK) cells immune cells that are cytotoxic to virus-containing cells and many tumor cells. Such boosting of this fundamental immune cell population suggests a prophylactic role for this herb in normal animals. Based on this evidence, our goal in the present work was to assess the role of dietary administration of this herbal extract to mice bearing leukemia, a type of tumor well known to be a target for NK cells.

Design. A commercially available root extract of E. purpurea, which we have already shown to be highly effective in mice, was administered daily for 50 days from the onset of leukemia (day 0). Control leukemia mice received no extract. Other leukemia mice received the NK-enhancing neurohormone, melatonin, administered precisely as above.

In all treatment and control categories, some mice were sampled in 9 days after tumor onset; others were sampled at 3 months, and well others were left to assess treatment effects on leukemic mice. None of the treatment groups showed any appreciable tumor size changes at 3 months. Experiments of 3 months after leukemia onset, untreated mice had a 2.5-fold increase in the absolute numbers of NK cells in their spleens. By 3 months after leukemia onset, E. purpurea-treated mice still had 2.5 times the normal numbers of NK cells in their spleens. No leukemia, untreated (control) mice remained alive at 3 months, hence the comparison with normal animals. Moreover, at 3 months post-tumor onset, all the major hematopoietic and immune cell lineages in their bone marrow cell lines, were recorded at normal numbers, in E. purpurea-consuming, leukemia mice. The survival advantage provided by administrating these leukemic mice with E. purpurea was highly significant versus untreated, leukemic mice when analyzed by Kaplan-Meier survival analysis.

Conclusion: The present study has provided the first systematic analyses, under controlled laboratory conditions, of the effects of the botanical, E. purpurea, in vivo, in leukemic hosts. The profoundly positive effects of this herb in disease abatement observed in this study suggest the therapeutic potential of E. purpurea at least with respect to leukemia, if not other tumors as well.
Design

- **Mice** (Male DBA/2) of 15–16 months, (mice in the last 1/3 to 1/4 of their lives)

- **E. purpurea** (Phyto Adrien Gagnon, Sante´ Naturelle (A.G.) Lt´e, LaPrairie, QC, Canada) given in diet for 9 d or 50 d
Echinacea: Myth or Medicine
Design

- Mice (Male DBA/2) of 15–16 months, (mice in the last 1/3 to 1/4 of their lives)
- *E. purpurea* (Phyto Adrien Gagnon, Sante´ Naturelle (A.G.) Lté´e, LaPrairie, QC, Canada) given in diet for 14 d
Echinacea: Myth or Medicine
Autoimmune?

Immunomodulation

Autoimmune Protection

- THEORITICAL!!!!!
- Cannabinoid Activity
**Endocannabinoids**

2-arachidonoylglycerol

anandamide

**Endocannabinoids**

Dodeca-$2E,4E,8Z,10Z$-tetraenoic acid isobutylamide

anandamide
**Endocannabinoids**

Dodeca-2\textit{E}, 4\textit{E}-ene-dienoic acid isobutylamide

anandamide

**Endocannabinoids**

Dodeca-2\textit{E}, 4\textit{E}, 8\textit{Z}-trienoic acid isobutylamide

anandamide
Cannabinoids & Autoimmune

- Cannabinoids are currently used to treat autoimmune diseases...
- PPAR-γ activity also shows preliminary research that suggest autoimmune protection
Posology

The Question

- How long does it take for a shift in WBC parameters after a single oral dose of either ethanolic extract or capsule?

- What is the change in WBC parameters between ethanolic extract and capsule?
Setting & Recruitment

- Clinic of Collaborative Medicine in Albuquerque, NM
- Students of Ayurvedic medical training program
- Students of a massage training program
- Volunteer basis

EPE Group 1 Participants

- 2.5 ml of *Echinacea purpurea* ethanolic
- Ages 20-45; Means = 31.2
- Mean Weight = 53.6 kg
- 5 Participants
EPC Group 2 Participants

- 2750 mg (5x550 mg) *Echinacea purpurea* capsule
- Ages 20-45; Means = 33.3
- Mean Weight = 62.7 kg
- 4 Participants; 1 dropped

Exclusion Criteria

- Any herb use 48 hours prior to study
- Acute respiratory tract infection or other infections within the last 7 days
- Serious progressive disease such as tuberculosis, multiple sclerosis, or AIDS
Exclusion Criteria Continued

- Systemic intake of corticosteroid
- Antibiotics or immunostimulants
- Allergy to Asteraceae family
- Pregnancy

Effects of *Echinacea purpurea*

2.5 ml Ethanolic Extract

EPE, Change in WBCs

Baseline 30m 60m 120m 180m
Effects of Echinacea purpurea

2.5 ml Ethanolic Extract

EPE, Change in WBCs

Effects of Echinacea purpurea

2750 mg, Capsule

EPC, WBC Changes
Effects of *Echinacea purpurea*  
*2500 mg Capsule*

**EPC, WBC Changes**

---

Effects of *Echinacea purpurea*  
*2.5 ml Ethanolic Extract*

**EPE, Neutrophil Change**
**Effects of Echinacea purpurea**

*2.5 ml Ethanolic Extract*

**EPE, Neutrophil Change**

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**Effects of Echinacea purpurea**

*2500 mg Capsule*

**EPC, Neutrophil Change**

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Effects of Echinacea purpurea

2.5 ml Ethanolic Extract

EPE, Lymphocyte Change

Baseline 30m 60m 120m 180m

Echinacea: Myth or Medicine
Effects of Echinacea purpurea 2750 mg Capsule

EPC, Lymphocyte Change

Baseline 30m 60m 120m 180m

Effects of Echinacea purpurea 2750 mg Capsule

EPC, Lymphocyte Change

Baseline 30m 60m 120m 180m
**Echinacea** Lack of Efficacy Over Time?

adapted from *Zeitschrift Fur Phytotherapie* 1989 10:67-70

Oral Dosing: Echinacea vs Placebo

Dose (tid)
The Dogma

- Dried Root (or tea): 0.5-1.0g
- Freeze Dried Plant: 325-650mg.
- Juice (Aerial Portion of E. Purpurea 22% EtOH) 1-2mg
- Fluid Extract (1:1) 1-2 mL
- Tincture (1:5) 30-90 gtts.
- Solid Ext. (6.5:1 or 3.5% Echinacoside) 100-250mg.
Efficacious Dose (tid)

- Dried Root (or tea): 0.1 - 2.0g
- Freeze Dried Plant: 650 - 1300mg.
- Juice (Aerial Portion of E. Purpurea 22% EtOH) 2 - 4mg
- Fluid Extract (1:1) 2 - 4mL.
- Tincture (1:5) 5 - 10mL.
- Solid Ext. (6.5:1 or 3.5% Echinacoside) 250 - 500mg.

Acute Dosing Strategy
At First Signs of Infection

Loading Dose:
- Dried Root (Tea or Capsule) 1000mg.
- Tincture 5mL.
- Solid Extract 250mg.

Followed by:
- Dried Root 400 - 500mg.qh
- Tincture 2 - 3mL. qh
- Solid Extract 100mg. qh