

# SAFETY AND EFFICACY OF ECHINACEA (*ECHINACEA AUGUSTAFOLIA*, *E. PURPUREA* AND *E. PALLIDA*) DURING PREGNANCY AND LACTATION

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## ABSTRACT

### Background

There is a lack of basic knowledge on the part of both clinicians and patients as to the indications for use and safety of herbal medicines used in pregnancy and lactation. This is one article in a series that systematically reviews the evidence for commonly used herbs during pregnancy and lactation.

### Objectives

To systematically review the literature for evidence on the use, safety, and pharmacology of echinacea focusing on issues pertaining to pregnancy and lactation.

### Methods

We searched 7 electronic databases and compiled data according to the grade of evidence found.

### Results

There is good scientific evidence from a prospective cohort study that oral consumption of echinacea during the first trimester does not increase the risk for major malformations. Low-level evidence based on expert opinion shows that oral consumption of echinacea in recommended doses is safe for use during pregnancy and lactation.

### Conclusions

Echinacea is non-teratogenic when used during pregnancy. Caution with using Echinacea during lactation until further high quality human studies can determine its safety.

**Keywords:** *Echinacea*, *echinacea augustifolia*, *echinacea purpurea*, *echinacea pallida*, pregnancy, lactation, breastfeeding, systematic review

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**E**chinacea is a perennial herb found in Eastern and Central United States and Southern Canada. While there are nine species of Echinacea, three are most commonly used as medicinal products – *Echinacea augustifolia*, *E. purpurea*, and *E. pallida*.

Historically, Echinacea was the most commonly used herb amongst Native North Americans for a variety of conditions including wounds, insect bites, infections, toothache, joint pain, and as an antidote for rattlesnake bites.

In the early 20<sup>th</sup> century it was established as the remedy of choice for cold and flu and was commonly used as an anti-infective until the advent of modern antibiotics.

Its use in North America declined until the 1980s when consumer interest grew in immune stimulants for conditions such as AIDS, cancer, and chronic fatigue syndrome. Since then, it has made a resurgence as a remedy for viral infections including influenza and the common cold. Over the last decade it has consistently been one of the

top selling herbal products in Canada and for several years has been one of the top three herbal products sold in the United States.<sup>1</sup>

Each year over 6000 telephone calls are made to Motherisk (a teratology information center at the Hospital for Sick Children in Toronto) with regards to the safety of natural health products in pregnancy and lactation.<sup>2</sup> A significant number of those calls pertain to the safety of Echinacea.<sup>3</sup> This is a trend common throughout North America as nearly one-sixth of American women took at least one herbal supplement in the year 2000.<sup>4</sup> Even during pregnancy and lactation a significant number of women continue to use natural products. A recent Norwegian study found that 36% of women had used herbal drugs during pregnancy.<sup>5</sup> The incidence of use increased throughout the first, second, and third trimester. Of those who used herbs, 39% were exposed to products either considered possibly harmful or with no known safety profile. While the use of herbal medicines during pregnancy is not as popular in Canada as it is in other parts of the world, this striking data demonstrates the need for health care personnel to have knowledge about the therapeutic effectiveness and safety of herbal products in pregnancy and lactation. To meet this knowledge void a systematic review of the literature as it pertains to the effectiveness of Echinacea as well as to its safety during pregnancy and lactation was conducted.

## METHODS

The following databases were searched from inception to June 2005: AMED, CINAHL, Cochrane CENTRAL, Cochrane Library, MedLine, Natural Database, and Natural Standard. The common name and Latin name of the herb were used as keywords along with “pregnancy”, “lactation”, and “breastfeeding”.

In the case of a well-known active constituent of the herb, this term was also used in the search for its safety during pregnancy and lactation. In addition, the Complete German Commission E Monographs by the American Botanical Council were also searched. Each relevant journal article was collected and referenced in a database. The nature of the findings and the grade of evidence were then

abstracted and compiled in a final report. The grade of evidence for indications was evaluated as displayed in Table 1. Evidence of harm was rated as displayed in Table 2.

## RESULTS

### Synonyms/ Common Names/ Related Substances<sup>6</sup>

American cone flower, black Sampson, black Susan, *Brauneria angustifolia*, *Brauneria pallida*, comb flower, coneflower, echinaceawurzel, hedgehog, igelkopfwurzel, Indian head, Kansas snakeroot, narrow-leaved purple cone flower, pale coneflower, purple cone flower, purpursonnenhutkraut, purpursonnenhutwurzel, racine d'echinacea, red sunflower, rock-up-hat, roter sonnenhut, schmallblattridge kegelblumenwurzel, schmallblattriger sonnenhut, scurvy root, snakeroot, sonnenhutwurzel

### Indications for Use

	Grade
Upper respiratory tract infection - Treatment <sup>9-11</sup>	A
Upper respiratory tract infection - Prevention <sup>12-14</sup>	B2
Radiation associated leukopenia <sup>15-17</sup>	B2
Cancer survival time <sup>18,19</sup>	C

### Safety of Consumption during Pregnancy

	Level
Not associated with an increased risk for major malformations <sup>20, 21</sup>	1b

A prospective follow-up study on 206 pregnant women, 112 of which had used Echinacea in the first trimester of pregnancy, reported that gestational use of Echinacea during the first trimester (organogenesis) is not associated with an increased risk for major malformations.<sup>20</sup> The German Commission E compendium, produced by an expert panel on botanical medicine, considers oral Echinacea in recommended doses safe for use during pregnancy.<sup>21</sup> Echinacea was not reported in the evidence-based literature as being contraindicated during pregnancy.

## Safety of Consumption during Lactation

	Level
Safe in recommended doses <sup>21</sup>	4

The German Commission E compendium, produced by an expert panel on botanical medicine, considers oral Echinacea in recommended doses safe for use during lactation.<sup>21</sup> Echinacea was not reported in the evidence-based medicine literature as being either safe or contraindicated during lactation.

### Parts Used<sup>8</sup>

Roots, stems and leaves.

### Constituents<sup>7</sup>

- Caffeic acid derivatives (echinocoside, cichoric acid, cynarin)
- polysaccharides
- glycoproteins
- alkamides.

### Toxicity

The LD<sub>50</sub> in mice is over 2500 mg/kg<sup>22</sup> and the LD<sub>50</sub> of intravenous Echinacea juice is 50 mL/kg.<sup>23</sup>

### Pharmacology

The immune-stimulating properties of Echinacea have not been attributed to any single compound.<sup>24</sup> Echinacea increases the proliferation of phagocytes in spleen and bone marrow, stimulates monocytes to produce cytokines (IL-1, IL-6, TNF), increases the number of PMN, activates macrophages, and promotes the adherence of PMN to endothelial cells.<sup>25-28</sup>

Echinacea has anti-viral, anti-bacterial, and anti-fungal properties.<sup>7,29-31</sup> Echinacea was shown to inhibit the influenza virus and the herpes simplex virus (I and II).<sup>30,31</sup> Topically, Echinacea has anti-inflammatory properties where it inhibits edema.<sup>32,33</sup> Echinacea may interfere with cytochrome P450 (CYP) 3A4 (CYP3A4) enzyme.<sup>34</sup>

### Drug Interactions

- Immunosuppressant drugs<sup>35</sup>
- Drugs metabolized by the cytochrome P450 (CYP) 3A4 (CYP3A4) enzyme<sup>34</sup>.

## DISCUSSION

There is very strong scientific evidence for the use of Echinacea in the treatment of upper respiratory tract infections. There is good scientific evidence for the use of Echinacea for the prevention of upper respiratory tract infections and for radiation-associated leukopenia. There is also fair scientific evidence of Echinacea use in cancer survival time.

During pregnancy, good scientific evidence via a prospective follow-up study found that oral consumption of Echinacea during the first trimester was not associated with an increased risk for major malformations. Further theoretical evidence via an expert panel on botanical medicine reported that oral consumption of Echinacea in recommended doses is safe for use during pregnancy.

Although an expert panel on botanical medicine reported that oral consumption of Echinacea in recommended doses is safe for use during lactation, Echinacea should be used with caution until there is stronger evidence of its safety.

While traditional and common use has not indicated any substantive risks of taking this herb during pregnancy and lactation, clearly more rigorous and well-controlled research is needed in this area. Clinicians and patients should also be concerned about the potential for interactions that may occur between Echinacea and immunosuppressant drugs.

**TABLE 1** Grades for evidence for efficacy

<b>GRADE</b>	<b>EVIDENCE</b>
A	<b>VERY STRONG SCIENTIFIC EVIDENCE</b> Statistically significant evidence of benefit from one or more systematic reviews/ meta-analysis.
B1	<b>STRONG SCIENTIFIC EVIDENCE</b> Statistically significant evidence of benefit from one or more properly conducted random control trials (RCTs).
B2	<b>GOOD SCIENTIFIC EVIDENCE</b> Statistically significant evidence of benefit from one or more RCTs. The RCTs, however, are either of small sample size OR have discrepancies in their methodologies.
C	<b>FAIR SCIENTIFIC EVIDENCE</b> Statistically significant evidence of benefit from one or more cohort studies OR outcome studies.
D	<b>WEAK SCIENTIFIC EVIDENCE</b> Evidence from case series.
E	<b>INDIRECT AND/OR CLINICAL EVIDENCE</b> Evidence from case reports OR expert opinion OR laboratory studies.
F	<b>HISTORICAL OR TRADITIONAL EVIDENCE</b> Historical or traditional use by medical professionals, herbalists, scientists, or aboriginal groups.

**TABLE 2** Levels for evidence for harm

<b>LEVEL</b>	<b>EVIDENCE</b>
1a	<b>STRONG SCIENTIFIC EVIDENCE</b> Statistically significant evidence from one or more systematic reviews or RCTs.
1b	<b>GOOD SCIENTIFIC EVIDENCE</b> Statistically significant evidence from one or more cohort studies OR control study.
1c	<b>WEAK SCIENTIFIC EVIDENCE</b> Evidence from one or more case series.
2	<b>VERY WEAK SCIENTIFIC EVIDENCE</b> Evidence based on case reports.
3	<b>IN VITRO SCIENTIFIC EVIDENCE</b> Evidence based on scientific studies conducted on animals, insects or microorganisms OR laboratory studies on human cells.
4	<b>INDIRECT EVIDENCE</b> Evidence based on scientific theory OR expert opinion.
5	<b>UNKNOWN</b> No available information.

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