

Archived at the Flinders Academic Commons:

<http://dspace.flinders.edu.au/dspace/>

This is the publisher's copyrighted version of this article.

The original can be found at: <http://www.medicinetoday.com.au/>

© 2005 Medicine Today

Published version of the paper reproduced here in accordance with the copyright policy of the publisher. Personal use of this material is permitted. However, permission to reprint/republish this material for advertising or promotional purposes or for creating new collective works for resale or redistribution to servers or lists, or to reuse any copyrighted component of this work in other works must be obtained from the publisher.

Echinacea in the prevention and treatment of infections

RAYMOND J. MULLINS MB BS, PhD, FRACP, FRCPA

ROBERT HEDDLE MB BS, PhD, FRACP, FRCPA

Echinacea is a traditional medicine commonly used to prevent or treat infections. An estimated 200 million doses are consumed yearly in Australia.

What is echinacea?

Echinacea (coneflower) is a flowering genus of the Compositae (Asteraceae) family. Other members of the family include weeds like ragweed, decorative species like chrysanthemums, sunflowers and daisies, and edible species like lettuce and artichoke.¹ Other plants in the family used in complementary medicine include dandelion, chamomile, feverfew, milk thistle and wormwood.²

Physiological actions

Echinacea preparations have been shown to activate lymphocytes and stimulate proinflammatory cytokines *in vitro* and in animal studies, actions that have been attributed to plant-derived polysaccharides and perhaps minor constituents such as inulin, alkaloids and caffeic acid esters (reviewed in reference 3). Echinacea products licensed for sale in Australia are labelled with an AUST L number (indicating registration with the TGA), but commercial preparations are not standardised according to individual ingredients and some have been found to contain no echinacea.⁴

Dr Mullins is a Consultant Physician in Clinical Immunology and Allergy, Canberra, with a special interest in food allergy and anaphylaxis. He holds teaching appointments at The University of Sydney, Australian National University Medical School, and The University of Canberra. He also chairs the Education Committee of the Australasian Society for Clinical Immunology and Allergy.

Dr Heddle is a Consultant Physician in Clinical Immunology and Allergy, Adelaide, with a special research interest in venom-induced anaphylaxis. He is Director of Allergy, Division of Medicine, Cardiac and Critical Services, Flinders Medical Centre, and Senior Lecturer, Flinders University of South Australia, SA.

This image is unavailable due to copyright restrictions

Clinical use

The traditional use of echinacea as an antiseptic and for treating wounds and infections by native Americans is reflected in its contemporary use in enhancing resistance to infection as a prophylactic or therapeutic agent.³ Some practitioners advocate echinacea for treating other conditions, such as allergy, without evidence of efficacy.⁵

Evidence for effectiveness

A Cochrane review published in 2000 concluded that some extracts of echinacea are more effective than placebo for treating or preventing upper respiratory tract infections.⁶ The reviewers also commented that extrapolation of the literature to clinical practice is difficult because studies used extracts of different plant species and parts (sometimes in combination with other plants), used different extraction methods, were not standardised in terms of 'active ingredients', and used differing treatment regimens. Of 11 double-blind, placebo-controlled studies published since that time (of over 2300 children and adults), six have described clinical benefit for treating or preventing upper respiratory tract infections.⁷⁻¹⁸

Adverse events

An estimated 200 million doses of echinacea are consumed in Australia each year. Adverse events are relatively rare but

Important points about using echinacea

- The evidence for the effectiveness of echinacea in treatment and prophylaxis of upper respiratory tract infections is conflicting.
- Adverse events are uncommon – the most common are nausea, burning mouth and rash. Rare cases of hepatitis and severe allergic reactions have been reported.
- Echinacea is normally taken orally, three or four times per day with food.
- The potential for drug interactions related to hepatic P450 metabolism has been demonstrated, but no cases have been reported.
- No specific monitoring is recommended unless adverse events or drug interactions are suspected.
- Precautions for use of echinacea include atopy, pregnancy, HIV infection, autoimmune disease, transplantation and other surgery.

occasionally serious (these are reviewed in reference 19). Gastro-intestinal upset and nonspecified rash are the most common events reported to ADRAC. Rare (but serious) cases of hepatitis and severe allergic reactions (asthma, anaphylaxis) have been documented; the latter are more common in atopic subjects.²⁰ Erythema nodosum, contact allergic dermatitis, arthralgia and myalgia have also been noted, and transient burning or stinging of the tongue is considered an intrinsic property, not a side effect.¹⁹

Dosage and administration

Echinacea is normally taken three or four times daily with food to reduce the risk of stomach upset, with the recommended dosage varying according to brand. Extracts of the flower, root or whole plant are available as capsules, tablets or liquid, or in dried form for infusion. No prescription is required in Australia, and no specific monitoring is recommended unless adverse events or drug interactions are suspected.

Precautions and interactions

Atopic patients

Sensitisation to Asteraceae is common, with Asteraceae-derived pollens triggering allergic rhinitis and asthma in patients in many countries.²¹⁻²³ The potential for cross reactivity between members of this family suggests that patients who are allergic to any of these should avoid echinacea.²⁴

Pregnancy

Despite frequent use by pregnant patients in some surveys,²⁵⁻²⁷ the safety of echinacea in pregnancy has been examined in only

one small study of 206 Canadian women.²⁸ Although no significant increase in the type or incidence of malformations or pregnancy related complications was found, this study had only sufficient power to detect a major teratogen. The proabortion activity of other Asteraceae, together with the absence of evidence of safety from large studies, suggest that the use of echinacea during pregnancy may be imprudent.^{3,29}

Children

Australian studies have shown use of one or more complementary medicines (including echinacea) during the preceding year in up to 87% of paediatric hospital patients.^{30,31} Of the studies of echinacea conducted in children, one has shown a greater risk of rash.¹⁶

Drug interactions

The presence of pyrrolizidine alkaloids in echinacea, together with reports of hepatitis, have led to advice to avoid combining potentially hepatotoxic medication such as anabolic steroids, methotrexate, ketoconazole or amiodarone with echinacea.^{32,33} Echinacea inhibits CYP3A4, a cytochrome P450 enzyme involved in drug metabolism.³⁴⁻³⁷ Human studies have demonstrated conflicting evidence of altered metabolism of medications such as midazolam, dextromethorphan and tolbutamide.^{37,38} Although no reports of significant interactions have yet been reported, it may be prudent to use echinacea with caution in patients taking drugs metabolised by these pathways – particularly those with narrow therapeutic windows like amiodarone, carbamazepine, cyclosporin, some cancer chemotherapy drugs or antiretroviral agents.³⁹

Autoimmune disease

Reports of exacerbation of pemphigus vulgaris and dermatomyositis support recommendations that echinacea is best avoided in patients with autoimmune disease because of the risk of exacerbation.⁴⁰

Chronic infection, surgery and transplantation

Authorities recommend that echinacea be avoided in patients with HIV infection and those undergoing transplantation surgery because of its immunostimulatory properties.^{3,32,41,42} These properties may lead to increased risk of rejection. Indeed, one study of 290 liver transplant patients treated for graft rejection showed that half were taking complementary medications, and of those taking echinacea, abnormal transaminase levels normalised with cessation.³³

Conclusions

Echinacea is a relatively safe medication commonly used by Australians to prevent or ameliorate the symptoms of upper

respiratory tract infections. Evidence of efficacy is conflicting, and interpretation of published studies is confounded by the lack of standardisation of compounds in studies and in commercially available products. Adverse events are rare but occasionally serious, and the potential for drug interactions has been demonstrated in humans. **MT**

Suggested reading

Budzinski JW, Foster BC, Vandenhoeck S, Arnason JT. An *in vitro* evaluation of human cytochrome P450 3A4 inhibition by selected commercial herbal extracts and tinctures. *Phytomedicine* 2000; 7: 273-282.

Chavez ML, Chavez PI. Echinacea. *Hospital Pharm* 1998; 33: 180-188.

Flockhart D, and Division of Clinical Pharmacology, School of Medicine, University of Indiana. Cytochrome P-450 drug interaction table [<http://medicine.iupui.edu/flockhart>]; 2001.

Gallo M, Sarkar M, Au W, et al. Pregnancy outcome following gestational exposure to echinacea: a prospective controlled study. *Arch Intern Med* 2000; 160: 3141-3143.

Gilroy CM, Steiner JF, Byers T, Shapiro H, Georgian W. Echinacea and truth in labeling. *Arch Intern Med* 2003; 163: 699-704.

MacLennan AH, Wilson DH, Taylor AW. The escalating cost and prevalence of alternative medicine. *Prev Med* 2002; 35: 166-173.

McKinnon R, Evans A. Cytochrome P450. Clinically important drug interactions. *Aust J Hosp Pharm* 2000; 30: 146-149.

Melchart D, Linde K, Fischer P, Kaesmayr J. Echinacea for preventing and treating the common cold. *Cochrane Database Syst Rev* 2000; 2.

Mullins RJ, Heddle R. Adverse reactions associated with echinacea and other Asteraceae. In: Miller SC, Yu H, eds. *Echinacea: The genus Echinacea* [a volume in the series entitled 'Medicinal and Aromatic plants – Industrial profiles']. London: Harwood Academic Publishing; 2004.

Pastore L. Home remedies used during pregnancy. *Cochrane Library* 2000; 3: 911-924.

A full list of references is available on request to the editorial office.

DECLARATION OF INTEREST: None.