

# Echinacea: When Should it be Used?

*Editorial Note: This article is the second in a two-part series on Echinacea. In the earlier article (Alt Med Rev 1997;2(2):87-93), Mr. Bone discussed the activities of the lipophilic, polysaccharide and caffeic acid components of various Echinacea species, detailing their differences and corresponding clinical implications. In that article, he advanced the theory that many of the activities often attributed to Echinacea (stimulation of interferon, interleukin 1, and tumor necrosis factor  $\alpha$ ) are actually due to specific polysaccharides found in Echinacea juice, but not in ethanol-containing Echinacea extracts, and that basing the clinical use of ethanol-containing Echinacea extracts on these properties is therefore inappropriate. Readers interested in more detailed information regarding this aspect of Echinacea use should consult the previous article.*

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## Abstract

Limitations on the use of Echinacea preparations have recently been proposed by some, based on misconceptions of the herb's action on the immune system. These suggestions have included restrictions on the length of time that Echinacea should be given, as well as prohibitions on the use of Echinacea in autoimmune disorders. These recommendations, however, are based on a limited understanding of immune system function and misinterpretations of the Echinacea research, but above all they ignore the strong traditional basis for the use of Echinacea. It will be argued that the best way to overcome this conceptual dilemma is to view Echinacea as an immunomodulator, rather than as an immunostimulant.

(*Alt Med Rev* 1997;2(6):451-458)

## Introduction

Recently, various sources have proposed limitations to the scope and duration of the therapeutic use of Echinacea preparations. These limitations are essentially derived from the concept that Echinacea stimulates the immune system. The assumptions are then made that:

- since it is not healthy to stimulate the immune system all of the time, Echinacea should only be used as a short-term treatment.
- stimulation of the immune system will be detrimental in autoimmune disorders (such as multiple sclerosis) or in disorders where a heightened immune response may be counterproductive (such as AIDS, asthma, leukemia and tuberculosis); hence, Echinacea is contraindicated in their treatment.

However, the way in which Echinacea acts on the immune system is not fully understood. The importance of polysaccharides to the activity of most Echinacea preparations has been misinterpreted and over-emphasized. It is the polysaccharides in Echinacea which have demonstrated T-cell activation; stimulation of tumor necrosis factor  $\alpha$ , interleukin 1 and interferon B3; and activation of the alternate complement pathway. However, traditional ethanolic extracts

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Table 1. Eclectic Uses of Echinacea.<sup>3,4</sup>

Abscesses	Mastitis, acute and chronic
Alopaecia	Measles
Anthrax	Meningitis
Appendicitis	Nasal catarrh
Bed Sores	Psoriasis
Bee sting	Puerperal infection
Boils	Pulmonary gangrene
Cancer	Purulent salpingitis
Carbuncles	Quinsy
Chicken-pox	Rabies
Cholera	Renal hemorrhage
Chronic bronchitis	Respiratory catarrh
Chronic glandular indurations	Scarlet fever
Chronic malaria	Scorpion sting
Chronic ulcerations	Septic injuries
Diabetes mellitus	Septicemia
Diphtheria	Small pox
Dysentery	Snake bite
Eczema	Spider bite
Empyema	Syphilis and syphilitic nodules
Epidemic influenza	Tetanus
Erysipelas	Tonsillitis
Exophthalmic Goitre	Tubercular abscesses
Fevers	Tubercular phthisis
Gangrene	Typhoid fever
Gonorrhoea	Typhoid pneumonia
Impetigo	Ulcerative stomatitis
Impotence	Urethral infection
Intestinal indigestion	Vulvitis
Leg ulcers	Wasp sting
Leucorrhoea	Wounds

### Traditional Use Does Not Support Limitations

The concept of traditional use is very misunderstood. For example, conventional medical scientists often confuse traditional use information with that from folk use or anecdotal accounts. It is important that the concept of traditional use is elevated to the high status it deserves.

Traditional use occurs in the context of a traditional medical system. This healing system may have evolved over thousands of years, and be part of a great culture, or it may be part of a smaller or more primitive system. The important point is that traditional use is the refined

of Echinacea do not rely on polysaccharides for their activity (in fact, these extracts probably contain insignificant amounts of polysaccharides). Therefore, conclusions regarding the appropriate use of such extracts should not be based on arguably incorrect interpretations of the polysaccharide research.<sup>1</sup> What useful evidence there is suggests that Echinacea mainly stimulates phagocytosis.<sup>1,2</sup> In other words, it acts mainly on the non-specific immune response. Hence, the assumed limitations on its use may not be supportable. In fact, there is no conclusive evidence that it is detrimental to use Echinacea for long periods, or that Echinacea is contraindicated in disorders such as autoimmune disease and asthma.

knowledge of many generations, carefully evaluated and re-evaluated by many of the practitioners of the craft. It is not just anecdotal accounts of a few practitioners.

Where traditional use is part of a great system and culture, that information should be regarded highly because it has evolved over many years in large numbers of people. It represents a cumulative wisdom which should cancel out aberrations from so-called placebo effects and observer bias.

In the case of Echinacea, information about its use first came from American Native tribes. Their use of Echinacea was subsequently adopted by the Eclectics, a group of practitioners who were prominent around the late 19th and early 20th centuries in the United

States. By 1921, Echinacea (specifically the root of *E. angustifolia*) was by far the most popular treatment prescribed by Eclectic physicians.<sup>2</sup> The Eclectics used Echinacea for about 50 years, which is a relatively short time in the context of traditional use. However, given that the Eclectic use of Echinacea was based on tribal knowledge and that they accumulated extensive clinical experience in its use, their traditional use data is of a high quality. The best sources of this data are King's American Dispensatory<sup>3</sup> and Ellingwood.<sup>4</sup> The extensive range of conditions for which Echinacea was prescribed are listed in these texts and are summarized in Table 1.

It is clear from this table that the limitations on Echinacea use suggested by modern writers are not supported. The conditions in the table are mainly infections and envenomations of various kinds (which clearly attest to Echinacea's influence on the immune system). However, the inclusion of tuberculosis and disorders related to autoimmunity such as diabetes, exophthalmic goitre, psoriasis and renal hemorrhage contrasts with the contraindications suggested by some modern writers.

The Eclectics were also not averse to using Echinacea long-term. For example, according to Ellingwood, Echinacea was recommended for the following chronic conditions: cancer, chronic mastitis, chronic ulceration, tubercular abscesses, chronic glandular indurations, and syphilis. He cites a dramatic case history of vaccination reaction where Echinacea was taken every two hours for up to six weeks. In other examples, Ellingwood describes cases where Echinacea was used for periods as long as nine months with positive effects.

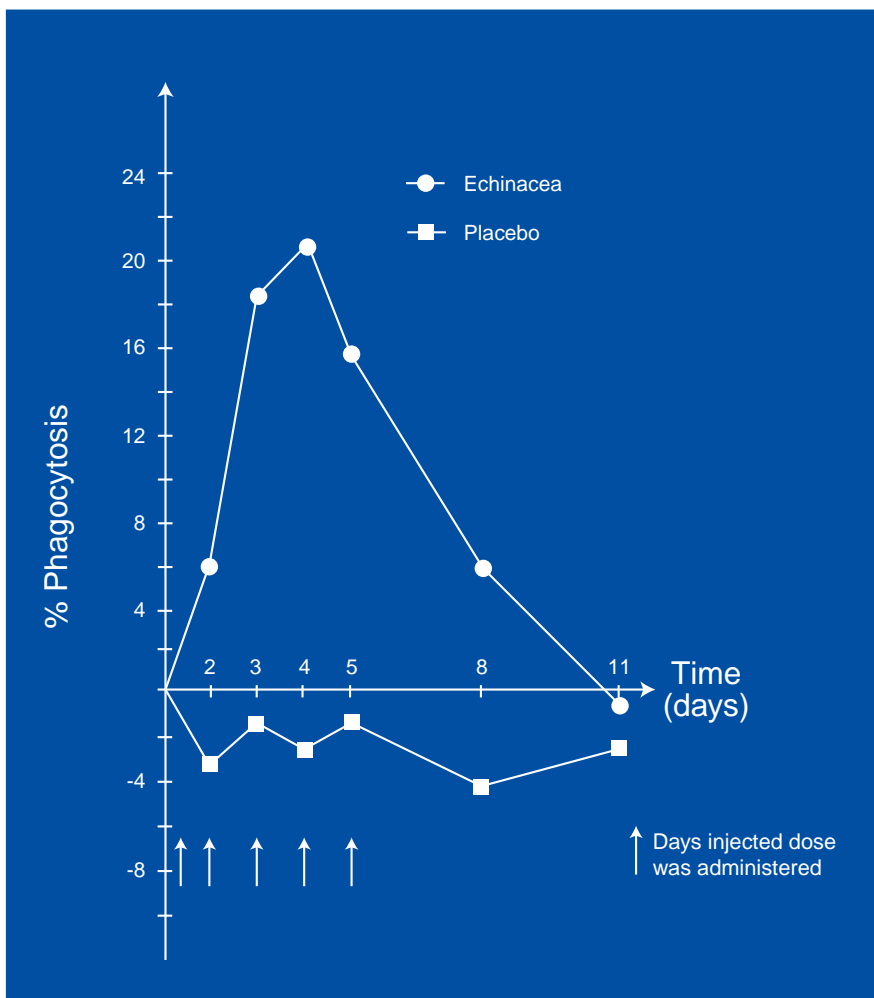
## Modern Research Does Not Support Limitations

One published clinical study has been subjected to considerable misinterpretation or overinterpretation, which has led some writers to suggest that Echinacea depletes the immune system when used continuously for periods longer than several days. This is the study by Jurcic and coworkers which tested the effect of an *Echinacea purpurea* tincture on the phagocytic activity of human granulocytes following intravenous or oral administration.<sup>5</sup> The results from this study are adapted in Figures 1 and 2, respectively. A cursory examination of the figures might lead to the conclusion that use of Echinacea for more than a few days does deplete the phagocytic response. However, this would be a misinterpretation of the results. The arrows at the bottom of the figures indicate the application of the test dose, which was administered for only the first five days. While the Echinacea was given, phagocytic activity remained high. Only when the Echinacea was stopped does the phagocytic activity decline to normal levels, a typical washout effect. The study, in fact, demonstrates the following:

- phagocytic activity remains higher than normal while Echinacea is given.
- oral doses of Echinacea stimulate phagocytic activity more than injected doses.
- when Echinacea is stopped, phagocytic activity remains well above normal for a few days, indicating that far from causing depletion, there is a residual stimulating effect when Echinacea is stopped.
- phagocytic activity only returns to normal, that is, there is no depleting effect where activity drops less than normal.

Returning to Figure 1, although emphasis has been placed on the slight decline in phagocytic activity between days 4 and 5 of the administered dose, this decline is probably within experimental variation. And although the authors' comment that, "The observation

Figure 1. Single-blind study with injectable Echinacea versus placebo



that a consistent decrease in activity occurred after the last injection may indicate the operation of a tiring or exhaustive effect after a short period of stimulation,” the simpler explanation (suggested above) that the decline is due to a normal washout effect has far greater credibility. Moreover, the authors do not make the same suggestion for the oral results depicted in Figure 2, nor do they mention this hypothesis in their conclusion. Why should a passing comment on an atypical use of Echinacea (injection), based on an unlikely premise, influence the use of Echinacea by a whole generation of phytotherapists?

A number of published clinical studies on Echinacea do not support the suggestion that long-term use is detrimental. For example, a review of published Echinacea studies by Parnham found that adverse events on oral administration for up to 12 weeks are infrequent and consist mainly of digestive symptoms.<sup>6</sup> Parnham concluded that Echinacea is well-tolerated on long-term oral administration. Another study found immune reactivity after 10 weeks of continuous oral doses of Echinacea was considerably greater than after two weeks, which in turn was significantly greater than before therapy.<sup>7</sup>

### Echinacea in Autoimmunity Leukemia and Asthma

The German Commission E monograph (B Anz no. 162, dated 29 August 1992) states that in principle, Echinacea should not be used in “progressive conditions” such as tuberculosis, leukemia, collagen disorders, multiple sclerosis, AIDS, HIV infection, and other autoimmune disease.<sup>8</sup> However, the key words here are “in principle.” There are no clinical studies which document an adverse effect resulting from Echinacea use in any of these conditions.

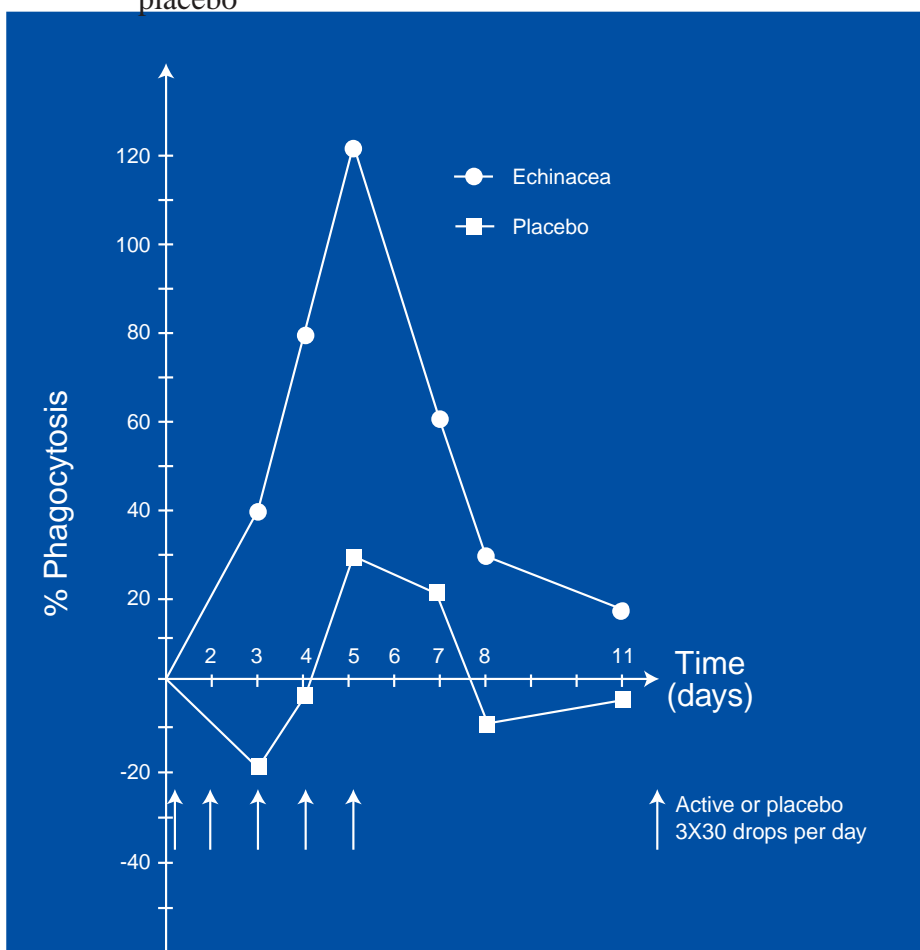
The suggestion that Echinacea is contraindicated in autoimmune disease assumes that any enhancement of any aspect of immune function is detrimental. However, immune function is extraordinarily complex, and a substance which acts largely on phagocytic activity may be safe or even

beneficial in autoimmunity. Many theories have been proposed as to the causative factors in autoimmune disease. However, there is growing evidence that an inappropriate response to infectious micro-organisms, through phenomena such as molecular mimicry, may be at work.<sup>9,10</sup> If this is the case, Echinacea may be beneficial in these disorders because it might decrease the chronic presence of micro-organisms. There is now a large body of clinical observations, including those of the author, that long-term Echinacea use is at least not harmful in autoimmunity, and is probably beneficial. Similarly, there is one published case study of long-term Echinacea use in chronic lymphocytic leukemia which did not reveal adverse effects.<sup>11</sup>

Recently, an article in the *Australian Medical Observer* has cautioned that Echinacea is a danger to asthmatics.<sup>12</sup> This caution is apparently based on the concern that Echinacea increases the cytokine known as Tumour Necrosis Factor alpha (TNF-alpha) which increases the inflammatory process in asthma. However, the information for TNF-alpha comes from *in vitro* tests on Echinacea polysaccharides. For a number of reasons discussed in a previous article, such studies are likely to have little

relevance to normal oral use of Echinacea.<sup>1</sup> This has been recently confirmed in a clinical study which found that oral therapy with Echinacea had no detectable effect on cytokine production by lymphocytes. Specifically, levels of TNF-alpha release were not changed

Figure 2 Oral double-blind study with *Echinacea purpurea* versus placebo



by Echinacea.<sup>13</sup> The *Australian Medical Observer* article also quotes a clinical immunologist who found a significant number of stored serum samples from allergy patients reacted to Echinacea on RAS testing. However, these results can have little credibility because

it is unlikely these patients had ever been exposed to Echinacea, and the tests more likely showed a high degree of meaningless cross-reactivity. Moreover, the part of the Echinacea plant tested was not specified.

The clinical experience of many phytotherapists is that long-term Echinacea is beneficial for asthmatics in particular, because its use reduces the frequency of respiratory viral infections which are well known exacerbating factors in asthma.

However, there is concern in some circles that Echinacea may cause an allergic reaction in susceptible patients which may be severe or even life-threatening. The Commission E monograph cautions that Echinacea should not be used by people who have a tendency to allergic reactions, especially against Asteraceae (Compositae: daisy family). This fear was highlighted in television and print media journalism in Germany in 1996, which attributed three deaths to Echinacea over a six-year period.

A critique of these claims has been written by Professor Bauer, from the Institute for Pharmaceutical Biology at Heinrich Heine University, considered to be an expert on Echinacea.<sup>14</sup> Bauer asserts the health authorities saw no cause to take action on the reported cases, since a causal relationship between the deaths and the taking of Echinacea preparations could not be proven. For example, in the first case, which presented with allergic vasculitis with the patient dying of acute renal failure, Dr Peter Schönöfer attributed this to an allergic reaction to the plant, but he also noted that influenza can trigger a vasculitis of that type. Bauer argues that for the second case, in which thrombocytopenia was connected with another Echinacea product, independent investigations could not establish causality.

Bauer points out that since over 10 million units of Echinacea products are sold annually in Germany, if the risk of allergic reaction was substantial then more cases would

have been reported. Finally, Bauer draws on his extensive research on the chemistry of Echinacea products, stating that any proteins they may contain are denatured by alcohol and are unlikely to cause allergic cross-reactivity.

The previously cited review by Parnham concluded that the stabilized juice from *Echinacea purpurea* tops (the most common form of Echinacea sold in Germany and the product most likely to cause allergic reaction since it includes the flowers) is well-tolerated.<sup>6</sup> All available published and unpublished articles in which the presence or absence of adverse events were reported were considered, provided the dose and route of administration as well as the patient population were defined. Results for several thousand patients over more than 40 years were analyzed by Parnham.

### **Authoritative Sources Do Not Support Limitations**

Although the Commission E recommends limitations on Echinacea use (including a contraindication in pregnancy) several writers and other authoritative sources do not support these restrictions. For example, the *British Herbal Pharmacopoeia* 1983<sup>15</sup> and the *British Herbal Compendium*<sup>16</sup> offer no contraindications for Echinacea. In fact, the indications in the Compendium for prophylaxis of colds and influenza, and chronic viral and bacterial infections suggest long-term usage. Weiss suggests Echinacea does no harm and has no side effects,<sup>17</sup> and Leung and Foster suggest no contraindications nor only short-term use.<sup>18</sup>

### **Echinacea as an Immunomodulator**

When the clinical and *in vivo* studies of Echinacea are carefully examined, the only significant conclusion which can be reached is that the herb increases phagocytic activity. Even the controversial polysaccharides only enhance macrophage activity and killing.<sup>1</sup>

Phagocytic cells are part of non-specific immunity. What is often not appreciated is that the activities of phagocytic cells, especially macrophages, are a key element of immune surveillance. The macrophage processes antigenic material and then presents this to the helper T-cell. Helper T-cells can only effectively respond to antigen presented in this way. Hence, if a herb such as Echinacea significantly increases phagocytic activity, the end result will be enhanced immune surveillance. For infections in general, the fact that Echinacea increases phagocytic activity emphasizes that it works best as a preventative, or in the very early stages of an infection. This is because enhanced phagocytosis means:

- better direct clearance and inactivation of pathogenic organisms by phagocytes, which is one of the first lines of immune defence;
- better immune surveillance which accelerates the response of the immune system to the new pathogen, or to other opportunistic pathogens.

That Echinacea works best as a preventative is consistent with the clinical experience of many phytotherapists.

In fact, it may be more accurate to describe Echinacea as an immunomodulator. While it stimulates phagocytic activity, this may have the end effect of modulating immune function overall. For example, the chronic presence of a micro-organism may cause a state of immune dysregulation which results in autoimmune disease or a chronic inflammatory condition such as asthma. Such theories have been proposed in mainstream scientific literature. A substance which enhances immune surveillance may help the body to eliminate the organism or neutralize its imbalancing effect on the immune system, thereby “toning down” an inappropriate immune response. Similarly, the body’s response to an allergen may be reduced if a more appropriate response results from enhanced phagocytic activity and immune recognition.

## Conclusions

Limitations on the use of Echinacea have resulted from preconceived and simplistic concepts of the immune system and Echinacea’s influence on it. Misinterpretations or overinterpretations in the scientific literature have compounded the problem, and it is obvious additional scientific research should be conducted to address these issues. However, the weight of existing evidence, including traditional, observational, and scientific, is that limitations on the use of Echinacea are ill-advised.

Perhaps if the understanding of Echinacea’s activity was shifted towards the concept of an immunomodulator rather than an immunostimulant, fears about its use would subside. Echinacea is undoubtedly one of the most valuable herbs in use in the world today. Misconceptions about its use can only devalue its role in modern health care and needlessly restrict the efficacy of phytotherapy.

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