

**Echinacea: A review of the literature.**  
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## **The Herb, Occurrence, Harvesting and Preparations Used**

The genus *Echinacea*, a member of the sunflower family (*Compositae* or *Asteraceae*), has nine species (McGregor 1968: 113). The three most common and widespread species, narrow-leaved purple coneflower (*Echinacea angustifolia*), pale purple coneflower (*E. pallida*) and purple coneflower (*E. purpurea*), have a history of medicinal use, both in the United States and Europe.

*E. angustifolia* with a typical height of up to 2 feet is shorter than *E. purpurea* (1.5 to 5 feet) and *E. pallida* (1 to 3 feet). Another key to species identification is that *E. angustifolia*, and *E. purpurea* have yellow pollen while *E. pallida* is noticeably paler and has white pollen. The portions of the plant used for medicinal purposes include the aerial portion, the whole plant including the root, and the root itself (Hobbs 1994:34 – 36).

The eclectics regarded an 80% ethanolic tincture of the root of *E. angustifolia* as being the best preparation (Felter 1898:1). Modern Herbalists tend to extract at 45%.

## **Traditional Use.**

In N. America, both *E. angustifolia* and *E. Purpurea* were widely used in the traditional medicines of the plains Indians for anodynal, anti-inflammatory, and other purposes. The roots were often chewed for treating toothache, sore gums, and sore throats. Their leaves, plant juice, and roots applied to treat painful burns and snakebite, and as an anti-rheumatic. It's value for treating colds was limited to the Crow living in Montana and Eastern Wyoming (Lewis & Elvin-Lewis 2003:102).

*Echinacea* was incorporated into patent medicine in Nebraska in 1870s and promoted by eclectics for wide variety of ailments. After the general acceptance of the germ theory, the view that it was an antiseptic suitable for treating many infectious diseases became widespread (Crellin and Phillipot 1990:278). It was used both internally and topically (Felter 1922:4). In 1915 von Unruh recognised the value of *Echinacea* as an immune stimulant in the treatment of tuberculosis by observing how it increased the phagocytic powers of leukocytes (von Unruh 1915:3). Ellingwood (1919:12) described how *Echinacea* directly influences the 'opsonic index', which was a measure of the ability of the immune system to destroy pathogens by phagocytosis after they are acted on by the an-

tibody opsonin (Hobbs 1994: 36). Among Echinacea's clinical uses Ellingwood enthusiastically listed blood poisoning, boils, carbuncles, abscesses, intestinal antiseptic, typhoid fever, puerperal fever, diphtheria, septic fevers, uremic poisoning, ulcerated sore throat, ulcerated sore mouth, stomatitis materni, post nasal and catarrhal ulcerations, appendicitis, cholera infantum, spinal meningitis, erysipelas, breast cancer, bed sores, tibial ulcers, chronic glandular indurations, scrophulous and syphilitic nodules, snake bite, scorpion bite, haemorrhoids, rabies, tetanus, pyemia, goitre, gangrene, phlebitis, anthrax, urinary tract infections, diabetes mellitus, and diabetic ulcers (Ellingwood 1919:1-15). By 1922, Felter had added measles, small pox, scarlet fever, la grippe (influenza), cholera infantum, rheumatic attacks, eczema and erysipelas (Felter 1922:2-7). With such a massive list of indications it is unsurprising that Felter noted: 'a most excellent medicine been lauded extravagantly and come near to damnation through the extravagant praises of its admirers' (Felter 1922:3). And indeed it fell largely into general disuse after the decline of the eclectics.

### **Modern Uses**

Current use for oral administration of Echinacea preparations include the prophylaxis and treatment of the common cold, bronchitis, influenza, and viral and bacterial infections of the respiratory tract (Mahady et al 2001:199). It is also used orally for fighting urinary tract infections (UTIs), vaginal candidiasis (yeast infections), and genital herpes (I and II) (Natural Medicines Comprehensive Database 2003:490). Modern Herbalists generally prescribe an ethanolic tincture, in the range of 25 - 60% alcohol, or dried forms of the ethanolic extract. Parental use is no longer advised because of potential adverse effects to diabetics and other conditions (Lewis and Elvin-Lewis 2003:102). Echinacea is also used externally for wounds, skin regeneration and skin infections, and for psoriasis, eczema and inflammatory skin conditions. In the parlance of modern western herbalism, Echinacea is also regarded as a stimulating alterative (Priest and Priest 1983:72), promoting suppuration and increasing natural resistance to infections.

**Dosage:** eclectics measured dosage in drops, ranging from 5-60 drops of the specific tincture every half to one hour in acute cases, every 3-4 hours in chronic (Felter 1922:6). Mills and Bone

(2000:355) recommend 1-3g per day (or equivalent) of *E. angustifolia* or *E. pallida* root, and 1.5-4.5 g per day of *E. purpurea* root for preventative doses or doses for chronic conditions. For acute conditions these doses may be substantially increased in the short term, for example, 10-15g per day of *E. angustifolia* root.

## **Modern Pharmacology and Clinical Trials**

### **Pharmacology**

The chemistry, pharmacology and clinical applications of *Echinacea* spp. have been the subject of over 350 scientific studies in the past 50 years (Lewis and Elvin-Lewis 2003:100). In vitro and in vivo studies have reported on various immune system responses, including the activation of phagocytosis and stimulation of fibroblasts; increased respiratory activity; and increased motility of leucocytes; (Bauer and Wagner 1991) (Buneton 1999:174). Other areas of inquiry include tissue regeneration and anti-inflammatory properties; anti-viral and anti-cancer properties; and bacteriostatic properties. The lipophilic alkylamides, polar caffeic acid derivatives, and polysaccharides have been suggested as the potential bioactive constituents of *Echinacea* spp. (Goel et al 2002:488) (Bone 1998:4).

### **Caffeic acid derivatives:**

These polyphenols include echinacoside, which accumulates in the roots of *E. angustifolia* and *E. pallida*, but is also found in smaller concentrations in the flowers (Bauer and Remiger 1989). *E. angustifolia* root additionally contains cynarin, whereas chicoric acid and some derivatives are the predominant caffeic acid based compounds in *E. purpurea*. These compounds are also present but in much lower concentrations in *E. angustifolia* and *E. pallida* (Hobbs 1989:43). It is interesting to note from the Herbalist's point of view that, as Bauer has pointed out, enzymatic activity tends to catalyse the breakdown of chicoric acid in fresh plant preparations, and that chicoric acid is far more stable in preparations made from the dried plant, thus the dried plant tincture preparation might be preferable if chicoric acid is, indeed, an essential active component (Bauer 1996). A

study has demonstrated that increasing the drying temperature in fact increases the level of chicoric acid in *E. purpurea* and *E. pallida* (Li and Wardle 2001:22). Chicoric acid or echinacoside are often used as marker compounds for standardised extracts of Echinacea.

#### Alkylamides:

Many alkylamides, particularly isobutylamides, have been isolated from *E. angustifolia* and *E. purpurea* roots and aerial parts, but they are largely absent from *E. pallida* (Bauer and Wagner 1991) (Laasonen et al 2002:574). The alkylamides are composed of a highly unsaturated carboxylic acid, often with triple carbon bonds, and an amine compound. It has been suggested by Bone that this bond between the acid and the amine will be broken during digestion, and the true active entity in these compounds is the carboxylic acid (Bone 1998:4). The alkylamides cause the characteristic tingling sensation on the tongue, and are prone to oxidation, thus Echinacea roots in powdered form should not be stored for prolonged periods (Bone 1998:4).

#### Polysaccharides:

Echinacea, like all plants, contains a number of polysaccharides. Most notable are inulin, which was found in a high percentage (5.9%) in *E. angustifolia* root, and the high molecular weight polysaccharides found in the aerial part of *E. purpurea*, as these components are claimed to possess significant immune-enhancing properties (Bauer and Wagner 1991).

#### Flavonoids

The leaves and stems of *E. angustifolia* and *E. purpurea* have been shown to contain numerous flavonoids with rutoside being the most abundant.

#### Phagocytic activity

A host of different preparations, including chemically standardised extracts, ethanolic extracts, and fresh pressed and dried plant juice from various parts the three main Echinacea species have been assessed for their phagocytic potential. Furthermore, many different techniques have been

employed to assess phagocytic activity. For example, the carbon clearance test, where the rate of disappearance of carbon granules from the blood at varying intervals following oral administration of the test substance is measured, to demonstrate systemic macrophage activation (Bauer and Wagner 1991)(Wacker and Hilbig1978)(Bauer 1988) appears to be a standard method.

Ethanollic extracts, containing the lipophilic alkylamides and polar caffeic acid derivatives have demonstrated immunostimulant activity by stimulating phagocytosis of neutrophils (Melchart 1994:245-254) (Bauer and Wagner 1991:253-321). A study by Jurcic et al (1989) ( cited by Lewis and Elvin-Lewis 2003:101) where oral administration to 24 humans of alcoholic root extract, 4.5 ml per day, of *E purpurea* showed the enhancement of chemotaxis and the rate of phagocytosis of granulocytes and monocytes. The use of a placebo group in this trial adds weight to the findings, although no mention was made of the total number of participants in the trial.

The significance of these different avenues of inquiry is that the overall immunostimulant or immunomodulatory activity of the alcoholic and aqueous extracts of *Echinacea* spp. appears to depend on the combined effects of several constituents (Bauer and Wagner 1991:253-321).

#### Immunomodulatory effects

An ethanolic extract of *E angustifolia* root fed orally to rats demonstrated immunomodulatory effects by enhancing the production of specific immunoglobulins. Following primary and secondary exposure to the novel antigen KLH, a sustained IgG response was recorded (Rehman et al 1999:395). The increase in antibody production appeared to be restricted to specific time points during the treatment period. Other studies have identified other potential targets for the immunomodulatory effects of *Echinacea* (Melchart 1995:145-160).

#### Tissue regeneration and anti-inflammatory properties

Polysaccharide components have been shown to promote tissue regeneration and reduce inflammation in experimental studies (Tubaro et al 1987). It is likely that this is due to anti-hyaluronidase

activity (Mendoza 2002), which may help increase the resistance of tissue to the spread of certain infections and, in conjunction with the increased presence of fibroblasts, facilitate connective tissue regeneration (Mills and Bone 2000:357). Echinacoside appears to be responsible for the anti-hyaluronidase activity (Speroni et al 2002:265)

Polyunsaturated alkylamides isolated from *Echinacea purpurea* have been shown, in vitro, to have anti-inflammatory effects by inhibiting both free arachidonic acid inflammatory pathways – ie. Lipoxigenase and cyclo-oxygenase. Cyclooxygenase (sheep seminal microsomes) and 5-lipoxygenase (porcine leukocytes) assays were inhibited, the activity appearing to depend on the particular structure of the alkylamides (Muller-Jakic et al 1994:37). Wagner et al (1988:567) demonstrated how an alkylamide fraction from *Echinacea purpurea* roots markedly inhibited activity in the 5-lipoxygenase model (porcine leucocytes).

#### Anti-viral activity

The fresh-pressed juice of the aerial portion of *E. purpurea* along with alcoholic and aqueous extracts of the roots have been shown to possess antiviral activity. Some of the viruses inhibited in cell cultures include: influenza, herpes and vesicular stomatitis viruses (Wacker & Hilbig 1978:89). Whilst certain *Echinacea* components (e.g. echinacoside, other caffeic acid derivatives, polysaccharides, etc.) may block virus receptors on the cell surface and stimulate interferon production in host cells, the antiviral effects may also be due to inhibition of hyaluronidase, as the viral inhibiting action of *Echinacea* is significantly diminished when hyaluronidase is added to the cell cultures (Mills and Bone:357).

#### Anti-cancer activity

The stimulation of macrophages to greater cytotoxic activity against tumour cells has been demonstrated using plant cell cultures from *E. purpurea* (Luettig et al 1989:675). Polysaccharides Isolated

from *E. purpurea* cell cultures have been demonstrated to counteract undesired effects of chemotherapy (Melchart et al 2002:142).

### **Clinical Trials**

Barrett et al reviewed 7 German studies published between 1984 and 1997 (Barrett et al 1999). The studies were classified as double blind, randomized clinical trials with a total of 910 subjects. All seven demonstrated beneficial effects for Echinacea in flu-like and upper respiratory tract symptoms, showing both a decrease in symptoms and duration of illness. Recent controlled clinical trials have suggested that Echinacea spp. might not be effective for the prophylaxis of upper respiratory tract infections, but may be useful in decreasing the symptoms and duration of the illness (Mahady et al 2001:200)

Barrett himself led a trial on 148 students with common colds of recent onset. Compared with the placebo, unrefined echinacea provided no detectable benefit or harm (Barrett et al 2002:939). However, the authors themselves pointed out that they used an encapsulated mixture of unrefined *E. angustifolia* root and whole-plant *E. purpurea*, which had not been tested previously and which may be ineffective because of bioavailability or phytochemical constituents. Furthermore, the type of people included in the study, healthy undergraduate college students, may not gain much benefit from echinacea. This example demonstrates how the constellation of variables in a trial can affect validity of the outcome.

In another systematic review of controlled clinical trials, a total of 26 controlled clinical trials were identified from the literature, with a total of 34 test treatment groups; 18 of the trials were randomized, 11 double-blind; six of the trials tested extracts of Echinacea alone, and 20 tested preparations containing Echinacea in combination with other ingredients. Each study was concerned with investigating in a controlled clinical setting the prophylactic or therapeutic effect of Echinacea (Melchart et al 1994: 245-254). The results, predictably were mixed, owing to variations in both the

methodological quality of the research, and the appropriateness of the interventions being studied. The authors, however, concluded by stating that some of the trial provide strong evidence that " medicines containing Echinacea can be efficacious immunomodulators. (Melchart et al 1994: 252)

### **Contraindications and Safety Issues**

Following available scientific evidence, Echinacea appears to be a relatively safe herbal medicine. There have been reports of allergic reactions to Echinacea in people hypersensitive to asteroaceous allergens (Bielory 2002:7-9), including two cases of anaphylaxis (Mullins and Heddle 2002: 42-51). Within this context, simply using it repeatedly can result in hypersensitisation (Lewis and Elvin-Lewis 2003:101). As Barrett has pointed out, perhaps the most convincing rationale for the reasonable safety of Echinacea comes from epidemiological evidence. The ratio of reported serious adverse effects (less than 100) to the estimated number of courses of treatment (more than 10 million) yields a risk estimate of less than 1:100,000 (Barrett 2003:37).

It has been postulated that autoimmune diseases such as rheumatoid arthritis, SLE, or multiple sclerosis could be triggered or activated as a result of the immunostimulating properties (Blumenthal et al 1998:122), and that common problems such as asthma, allergic rhinitis, or skin allergies could be worsened. Although, as Treasure has stated, the contraindication of Echinacea spp. with autoimmune conditions has no published basis in the medical literature nor in databases of pharmacovigilance or in adverse reaction reports (Treasure 1999:5). Barrett is more cautious and advises that these possibilities should not be ruled out (Barrett 2003:39).

Extracts of Echinacea have shown to inhibit the activity of cytochrome P<sub>450</sub> and, therefore, may have the potential to influence drug metabolism (Mahady et al 2001:208). Gorski suggests Caution should be used when echinacea is coadministered with drugs dependent on CYP3A or CYP1A2 for their elimination (Gorski et al 2004:100).

According to Bergner, the most serious adverse effect of echinacea on health is that its habitual

use can mask the symptoms of general immune weakness due to diet or lifestyle factors, and thus enable progressive deterioration of the health or exhaustion of the system (Bergner 1997:2)

## **Evaluation and Discussion**

It is an immense task to link modern research methods to the literature on traditional use and the empirical experience of Medical Herbalists down the ages. The variables associated with assessing the efficacy of *Echinacea* spp. in the modern time include:

- the species used:

It is interesting to note that the vast majority of research has focused on *Echinacea purpurea*, and yet the eclectics, as Ellingwood (1919:1) pointed out, regarded *E. purpurea* as 'universally disappointing' when compared to *E. angustifolia*. This is likely to be due to the fact that the cultivation of *E. angustifolia* has proved to be problematic in Europe compared to the relative ease with which *E. purpurea* can be grown, and thus most European commercial preparations are of the latter species. Within the species of *E. angustifolia*, as Lloyd observed, The best quality of root comes from the prairie lands of Nebraska (J. U. Lloyd in *E. M. J.*, 1897, p. 427, quoted in Felter 1898:1). In the present day the major producers of *E. angustifolia* are far to the east of Nebraska (The Herbal Apothecary 2004), and whether they are farming from original Nebraskan stock is an interesting question. Modern research concurs that variables such as geographic location where the herb is grown, and the time of year it is harvested, may impact the final chemical composition (Shalaby et al 1997: 34-35) (Binns et al 2002:837-854), but nevertheless, this is very rarely taken into account.

- the part of the plant used

Again, this has largely been dictated by the availability and use of commercial products.

- the method of extraction

ditto. It appears that, in many instances, medical and pharmaceutical researchers are often quite proud of their scientific protocol and yet pay little attention to their test materials. Much

research has focused on the actions of polysaccharides (eg. Burger et al 1997), but as Mills and Bone have pointed out (2000:357), following oral administration, 'gastrointestinal breakdown, poor absorption and poor tissue motility' may all act to decrease the quantity of polysaccharides available for action. The same authors also point out that 'polysaccharides are probably not present in pharmacologically significant quantities and are not absorbed in levels sufficient to achieve the concentrations used in the in vitro studies. Moreover, the quantities of polysaccharides present in preparations containing 50% alcohol or more will be negligible.' Both the lipophilic fraction and the hydrophilic fraction have been shown separately to enhance phagocytic activity, but the activity seems to be less than with the whole plant extract (Barrett 2003:83) (Goel et al 2002:492). This tallies with the fact that, whilst many commercial products might be standardised according to marker compounds in order to differentiate themselves within the market place, full spectrum preparations using traditional extraction techniques are still preferred by professional Herbalists.

- the experimental design

- in vitro or in vivo?

If in vitro, which tissue cultures and why? The results of in vitro pharmacological studies do not always correspond accurately to the physiological and pharmacological responses occurring within the body of a living being.

- what animals

- Mice?
    - Rats?
    - Humans?
      - If humans, were they healthy?
      - Age? Sex?

- the method of administration.

Furthermore, one has to question the provenance of any research that is carried out. Who is funding it, and why? The pharmaceutical industry, in its relentless pursuit of a single compound magic bullet, which it can patent and reap large rewards as a result, is not particularly interested in the concept of synergy between different components of the same plant. Aside from being hugely difficult to prove in the context of the established hierarchy of evidence, it is highly likely that there would be no magic bullet at the end of the process anyway.

In addition to these considerations, a major use of *Echinacea* spp. is as an immunomodulator, or immunostimulator. The immune system itself is highly complex, and whilst cellular evidence of immunostimulation and pathways leading to resistance to infectious disease have not been described adequately, most researchers now accept that clinical success with *Echinacea* spp. must be down to a combination of effects from a combination of compounds. In terms of clinical trials, it is notoriously difficult to substantiate claims for the prevention of disease, since very large studies are needed for statistical validity and these are difficult and expensive to perform (Heinrich et al 2004:232). The most robust data that there is to date comes from trials testing *E.purpurea* extracts in the treatment of upper respiratory tract infection, but these trials are limited in both size and methodological quality (Barrett 2003:86)

Whilst interpretation of existing literature suggests that *echinacea* should be used as a treatment for illness, not as a means for prevention of illness (Percival 2000:155), modern Herbalists continue to rely on clinical experience, and also use *Echinacea* spp. prophylactically, alongside its use as an anti-inflammatory, anti-viral, and immunomodulator.

## References

- Barrett B, Kiefer D, Rabago D (1999) Assessing the Risks and Benefits of Herbal Medicine: An Overview of Scientific Evidence. *Alternative Therapies* 5:pp40-49
- Barrett B (2003) Echinacea: A Safety review. *Herbalgram*. 57:pp36-39
- Barrett B (2003) Medicinal Properties of Echinacea: a critical review. *Phytomedicine*. 10:(1):pp 66-86.
- Barrett B, Brown R, Locken K, Maberry R, Bobula J, D'Alessio D (2002) Treatment of the common cold with unrefined echinacea. A randomized, double-blind, placebo-controlled trial. *Annals of Internal Medicine* 137:(12): pp939-46
- Bauer R (1996) Lecture presented at plants for foods and medicines conference. Quoted in Bone K (1998) Echinacea: What Makes It Work? *British Journal of Phytotherapy* Vol 5:(1). pp 3-8
- Bauer R, Wagner H. (1991) Echinacea Species as Potential Immunostimulatory Drugs. In: Wagner H., Farnsworth NR, eds. *Economic and Medicinal Plant Research*. Vol. 5. London: Academic Press Limited; 253-321.
- Bauer R, Remiger P (1989) Der Einsatz der HPLC bei der standardisierung von echinacea-drogen *Arch Pharm* 322:324. Cited in Hobbs C (1994) Echinacea: A Literature Review. *HerbalGram* No. 30: 33-49.
- Bauer R (1988) Immunological in vivo and in vitro examinations of Echinacea extracts. *Arzneim Forsch* 38:pp 276-81.
- Bergner P (1997) Cautions with echinacea in auto immune disease? <http://www.herbological.com/bookworm.html> accessed 1/4/04
- Bielory L (2002) Adverse Reactions to Complementary and Alternative Medicine: Ragweed's Cousin, The Coneflower (Echinacea), is a Problem More Than a Sneeze. *Annals of Allergy, Asthma, Immunology*. 88:pp7-9
- Binns S, Arnason J, Baum B (2002) Phytochemical variation within populations of *Echinacea angustifolia* (Asteraceae) *Biochemical Systematics and Ecology*. Vol 30: (9) pp 837-854
- Blumenthal M (Ed) (1998) *The Complete German Commission E Monographs*. Austin. American Botanical Council
- Bone K (1997) Echinacea: When Should It Be Used? *European Journal of Herbal Medicine* Vol 3(3) pp 13-17
- Bone K (1998) Echinacea: What Makes It Work? *British Journal of Phytotherapy* Vol 5:(1) pp 3-8
- Bruneton J (1999) *Pharmacognosy* 2<sup>nd</sup> Edition. Paris. Intercept.
- Burger RA, Torres AR, Warren RP, Caldwell VD, Hughes BG (1997) Echinacea-induced cytokine production by human macrophages. *International Journal of Immunopharmacology*. 19:(7): pp371-9
- Crellin J, Philpott J (1990) *A Reference Guide to Medicinal Plants*. London. Duke University Press

- Ellingwood F (1919) American Materia Medica, Therapeutics and Pharmacognosy. Accessed 11/2/04 at <http://www.swsbn.com/homepage/>
- Felter HW, Lloyd JU (1898) King's American Dispensary. Accessed 9/02/04 at: <http://www.ibiblio.org/herbmed/eclectic/kings/main.html>
- Felter HW (1922) The Eclectic Materia Medica, Pharmacology and Therapeutics. Accessed 11/2/04 at <http://www.swsbn.com/Felter/Felters.html>
- Goel v, Chang C, Slagma J, Barton R, Bauer R, Gahler R, Basu T (2002) Echinacea stimulates macrophage function in the lung and spleen of normal rats. The Journal of Nutritional Biochemistry Vol13: (8) pp487-492
- Gorski J, Huang S-M, Pinto A, Mitchell A, Hamman B, Janna K (2004) The effect of echinacea (*Echinacea purpurea* root) on cytochrome P450 activity in vivo. Clinical Pharmacology & Therapeutics Vol 75:(1:) pp 89-100
- Heinrich M, Barnes J, Gibbons S, Williamson E (2004) Fundamentals of Pharmacognosy and Phytotherapy. London. Churchill Livingstone.
- Hobbs C (1989) The Echinacea handbook. Portland. Electic Medical Publications
- Hobbs C (1994) Echinacea: A Literature Review. HerbalGram No. 30: pp 33-49.
- Laasonen M, Wennberg T, Harmia-Pulkinnen T, Vuorela H (2002) Simultaneous analysis of alkaloids and caffeic acid derivatives for the identification of *Echinacea purpurea*, *Echinacea angustifolia*, *Echinacea pallida* and *Parthenium integrifolium* roots. Planta Med Vol 68:(6): pp 572-574
- Lewis W, Elvin-Lewis M (2003) Medical Botany, Plants Affecting Human Health 2<sup>nd</sup> Edition. Hobokan. John Wiley and Sons.
- Li T, Wardle D (2001) Effects of root drying temperature and moisture content on the levels of active ingredients in *Echinacea* roots. Journal of Herbs, Spices, and Medicinal Plants Vol 8(1) pp15-22
- Luettig B, Steinmuller C, Gifford G, Wagner H, Lohmann-Matthes M (1989) Macrophage activation by the polysaccharide arabinogalactan isolated from plant cell cultures of *Echinacea purpurea*. Journal of the National Cancer Institute 81(9) pp 669-75
- Mahady G, Qato D, Gyllenhaal C, Chadwick L, Fong H (2001) Echinacea: Recommendations for its use in Prophylaxis and Treatment of Respiratory Tract Infections. Nutrition IN Clinical Care. Vol. 4(4) pp 199-208
- McGregor, R. L. (1968). The Taxonomy of the Genus *Echinacea* (Compositae). Univ. of Kansas Science Bulletin 48 pp 113-142.
- Melchart D, Clemm C, Weber B, Draczynski T, Worku F, Linde K, Weidenhammer W, Wagner H, Sellar R (2002) Polysaccharides Isolated from *Echinacea purpurea* herba Cell Cultures to Counteract Undesired Effects of Chemotherapy—a Pilot Study. Phytotherapy Research 16 pp138–142
- Melchart D (1994) Immunomodulation with Echinacea: A Systematic Review of Controlled Clinical Trials. Phytomedicine. 1 pp 245-254
- Melchart D, Linde K, Worku F, Sarkady L, Holzmann M, Jurcic K, Wagner H (1995) Results of five randomized studies on the immunomodulatory activity of preparations of *Echinacea*. Journal of Alternative and Complementary Medicine. 1 pp145–160

- Mendoza M (2002) Course Notes, BSc Herbal Medicine. University of Westminster
- Mills S, Bone K (2000) Principles and Practice of Phytotherapy. London. Churchill Livingstone
- Muller-Jakic B, Breu W, Probstle A (1994) In vitro inhibition of cyclooxygenase and 5-lipoxygenase by alkaloids from Echinacea and Achillea species. *Planta Med* 60 pp37-40.
- Mullins R, Heddle R (2002) Adverse Reactions Associated With Echinacea: The Australian Experience. *Annals of Allergy, Asthma, Immunology*. 88(1) pp42-51
- Natural Medicines Comprehensive Database (2003). Echinacea. pp 490-492
- Percival S (2000) Use of Echinacea in Medicine. *Biochemical Pharmacology* Vol.6(2) pp 155-158
- Priest A, Priest L (1983) Herbal Medication a Clinical and Dispensary Handbook. Saffron Walden. CW Daniel Company
- Rehman J, Dillow J, Carter S, Chou J, Le B, Maisel A (1999) immunoglobulins G and M following in vivo treatment with the medicinal plants *Echinacea angustifolia* and *Hydrastis Canadensis*. *Immunology Letters* Vol 68 (2-3) pp 391-395
- Shalaby A, Angina E, El-Gengaihi A (1997) Response of Echinacea To Some Agricultural Practices. *Journal of Herbs, Spices, and Medicinal Plants* 6 pp 34-35
- Speroni E, Govoni P, Guizzardi S, Renzulli C, Guerra MC (2002) Anti-inflammatory and cicatrizing activity of Echinacea pallida Nutt. root extract. *J Ethnopharmacol*. 7(2) pp265-72.
- The Herbal Apothecary (2004) Personal Communication 26/2/04
- Treasure J (2001) Making Sense of the Commission E Monographs. <http://www.herbological.com/bookworm.html> accessed 1/4/04
- Tubaro A, Tragni E, Del Negro P (1987) Anti-inflammatory activity of a polysaccharide fraction of Echinacea angustifolia. *J Pharm Pharmacol* 39:567-569. Quoted in Lewis and Elvin-Lewis (2003)
- Von Unruh V (1915) Echinacea angustifolia and Inula helenium in the treatment of tuberculosis. *The National Medical Association Quarterly*. Vol 7:(1) accessed 11/2/04 at <http://www.swsbm.com/quarterlies/quarterly.html>
- Wacker A and Hilbig W (1978): Virus-inhibition by Echinacea purpurea. *Planta Medica* 33 pp 89-102
- Wagner H et al. (1988) In vitro inhibition of acetylcholinesterase metabolism by some alkaloids and prenylated phenols. *Planta Medica* 55:566-567). Quoted in WHO Monograph on Radix Echinaceae. <http://www.herbmed.org/Herbs/Herb6.htm#Category22Herb6>. Accessed 5/3/04