In recent years there has been an explosion of interest in alternative medical therapies. In 1990, a telephone survey of 1539 English–speaking adults conducted by Harvard University showed that one out of three people had used some kind of alternative medical therapy in the past year. Based on this sampling, the researchers determined that Americans made 425 million visits to alternative practitioners in that year (versus 388 million visits to primary care physicians) and that they spent almost fourteen billion dollars on alternative treatments (5). Plant products make up a large portion of this sum, and the plant Echinacea is one alternative treatment–widely used in Europe–which is becoming increasingly popular in the United States and, over the last few decades, has become the target of extensive research.

The echinacea plant is a perennial member of the daisy family (Asteraceae) and is also known as the cone flower or the purple cone flower. It is native to the central United States, where nine species grow, and has stems which can reach up to three feet high and terminate in a single, large, purplish flower. Its flower is characterized by a brown, conically–arched, spiny seed head which prompted the generic name echinacea, derived from the Greek word "rhinos" meaning hedgehog. Three species are mainly used for medicinal purposes–Echinacea augustifolia (narrow–leaved coneflower), Echinacea pallida (Nutt.) Nutt. (pale–flowered echinacea), and Echinacea purpurea (L.) Moench. In today's usage, the three are probably more or less interchangeable, but E. purpurea is the most commonly used because it is the only one which is cultivated. The dried root and rhizome are the major products used for medicinal purposes while the leaves are also sometimes harvested and extracted. (12, 14)

Echinacea is used primarily for its immune–stimulating and anti–inflammatory effects. Research has suggested that its immunostimulatory effects are mediated by: stimulation of phagocytosis, increasing the mobility, number and activity of immune system cells including anti–tumor cells, promoting T–cell activation, and increasing respiratory activity (11, 12, 13). It appears to lessen the symptoms and speeds the recovery from viruses, facilitates wound healing (3), and increases the body's resistance to bacterial activity by increasing the release of proteins such as properdin and interferon (which have both anti–viral and anti–bacterial activity), increasing the activity of the adrenal cortex, and inhibiting the enzyme activity of bacterial hyaluronidase thus preventing bacterial access to healthy cells (11).

Echinacea is historically one of the most important plants used medicinally by the North American Indians. It was first introduced into mainstream medicine by a Nebraskan, Dr. H.C.F. Meyer of Pawnee City. He learned of its therapeutic value from the Indians in 1871 and used it to prepare a "blood purifier" which he claimed was useful in treating almost any condition including: rheumatism, migraine, streptococcus infections, dyspepsia, pain, wounds, sores, eczema, dizziness, sore eyes, poisoning by herbs, rattlesnake bites, tumors, syphilis, gangrene, typhoid, malaria, diptheria, bee stings, hydrophobia, and hemorrhoids. He called the plant to the attention of a pharmaceutical manufacturer, Lloyd Brothers of Cincinnati, and the firm then introduced many echinacea products and marketed them mostly as anti–infective agents. By the 1920s echinacea was the firm's most popular plant drug, but it fell into disuse with the advent of Sulfa drugs in the 1930s. (12, 14) Echinacea was introduced to Europe in the 1930s, extensively researched in the 1950s, and is now well established in mainstream medicine where more than 250 products are available. In 1990 alone there were 2.4 billion dollars worth of counter sales, 65 percent of which were in Germany (14).

Today, echinacea is used internally to treat upper respiratory tract infections, the common cold and its associated symptoms such as sore throat, urinary tract infections, yeast infections, enlarged lymph glands, rheumatoid arthritis (where it reduces inflammation), side effects of radiation therapy, cancer, skin diseases, fungal infections, septicemia, gangrene, slow–healing wounds, abscesses, boils, and venereal diseases such as herpes. Externally is it used in the treatment of hard–to–heal superficial wounds, psoriasis, eczema, inflammatory skin conditions, herpes, acne, and in skin regeneration. Because of echinacea's immune stimulating effects, it has been suggested for the treatment of AIDS or opportunistic infections in AIDS patients, for the treatment of patients suffering from chronic infections with the yeast strain, Candida albicans, and for viruses which replicate in the liver hepatocytes such as viral hepatitis. (1, 3, 8, 11)

In the United States, echinacea is most readily available in a liquid form, specifically as a hydroalcoholic extract. There has been some suggestion that this preparation is effective because it stimulates lymphatic tissue in the mouth, thereby initiating an immune response (11). Echinacea can also be found as capsules containing the plant in powdered form, as juice from the overground portions, as a coarsely ground preparation which is prepared as a tea (not really recommended because not all of the active ingredients are water soluble), and as creams or gels for external use. (3, 11) Even though the immune stimulating effects of pure plant extracts have been proven in humans (see below, 8), direct conclusions should not be drawn about the effectivity of extracts from echinacea plants sold on the market because the variable composition of components present in these extracts can't be compared with the purified fractions used in most laboratory and clinical studies (8). Consumers should make every effort to obtain the best quality product available and investigate the reputation of the manufacturer before buying an echinacea product (12).

There are many active compounds found in echinacea. High molecular weight polysaccharides are able to stimulate phagocytosis (especially heteroxylan which activates phagocytes and arabingalactan which promotes the release of tumor necrosis factor, or TNF). Their effects are enhanced by the components of the alkamide fraction (mainly the isobutylamides) and by cichoric acid (11, 12). Echinacoside (a caffeic acid derivative) is also of particular interest for its effects (13, 14). (see below)

Until recently, the majority of the scientific and clinical studies of echinacea were carried out in Germany primarily with dosage forms prepared from the fresh overground portion of the plant that are intended to be administered by injection or applied locally. Some of these older studies showed some convincing results about the effects of echinacea. In one, an extract of echinacea significantly increased the resistance to flu and reduced the symptoms of lymph gland swelling, inflamed nasal passages, and headache. Subjects in another study who ingested an extract of echinacea showed an increase of 50–120% in immune function over a five day period. Of the 4500 patients with inflammatory skin conditions in another study, 85% were cured with topical applications of echinacea salve. In a fourth investigation, human white blood cells, when incubated with echinacea extract, showed increased phagocytosis of yeast cells by 20–40% compared to controls. (3)

Some more recent investigations have confirmed many of the results of these older studies. Prior to 1991, it had been shown that, in mice, purified polysaccharides from echinacea were able to stimulate phagocyte activities in vitro and in vivo, stimulate macrophages to secrete mediators like IL–1, IL–6, and TNF–a (immune–stimulating cytokines), produce higher amounts of

reactive oxygen intermediates, display enhanced growth inhibition of Candida albicans in vitro, and increase activities of polymorphonuclear cells (PMN). In vivo, the polysaccharides had been shown to stimulate the mouse macrophages in the spleen and liver to display increased clearance of carbon particles from the blood and to increase recruitment of phagocytes. Both effects resulted in the accelerated elimination of bacteria (Listeria monocytogenes) and yeast cells (C. albicans) from the spleen, liver, and kidneys after systemic infections and protected the mice against acute lethal infections. (8) Because all of these previous studies had been performed in mice, in 1991, Roesler et al. (8) purified polysaccharides of E. purpurea and tested them for the ability to activate human phagocytes in vitro and in vivo using healthy men and non–pregnant women aged 20–45. In vitro, the extracts were able to enhance the spontaneous motility of PMN, increased the ability of these cells to kill staphylococci, and activated monocytes to secrete TNF–a, IL–6, and IL–1. In vivo, intravenous application of the extracts induced an initial fall in the number of PMN in the peripheral blood (indicating enhanced adherence to endothelial cells). The fall was then followed by a proliferation of leukocytes. Increased migration of cells from the bone marrow to the peripheral blood was also noted, and the acute phase C–reactive protein (which binds to the surfaces of bacteria and functions to activate complement and increase phagocytosis) was induced as well. Altogether, these results showed that echinacea polysaccharides could induce acute phase reactions and activate phagocytes in humans as was shown previously in mice.

A 1993 study by Steinmuller et al. (10), investigated the influence of polysaccharides isolated from E. purpurea on the nonspecific immunity in immunodeficient mice which had been immunosuppressed by injection with either cyclophosphamide (which has a strong antiproliferative effect in vivo, blocking primarily the proliferation of precursors of polymorphonuclear lymphocytes) or cyclosporin A (which mainly affects the specific responses of the immune system as it blocks the stimulating function of CD4–positive lymphocytes during an antigen–specific immune response). In vitro, polysaccharides were able to activate macrophages isolated from animals after treatment with either CP or CsA to function as cytotoxic effector cells against tumor targets and microorganisms. After injection with CP, the polysaccharide treatment resulted in an earlier return of the number of peripheral granulocytes to normal in vivo. Protection against infections with L. monocytogenes or C. albicans in the immunosuppressed animals was also shown, and the polysaccharides were able to support the individual to defend against infections with lethal doses that killed control animals.

Also in 1993, Muller et al. (7), showed in vitro inhibition by alkamides of 5–lipoxygenase and cyclooxygenase which are the key enzymes of the two major pathways of arachidonic acid metabolism, responsible for the formation of leukotrienes–mediators of allergic responses and inflammation which produce bronchoconstriction, constrict arterioles, increase vascular permeability, and attract neutrophils and eosinophils to inflammatory sites (6)–and prostaglandins which are released from inflamed tissues, respectively. The inhibitory properties of the alkamides on arachidonic acid metabolism are in accordance with the traditional use of echinacea in the therapy of inflammatory diseases. It is likely that the alkamides act as arachidonic acid analogues via competitive inhibition of the enzymes.

A 1995 study by Facino et al. (4) investigated the protective effects on UV–exposed skin of the echinacea constituents echinacoside, chlorogenic acid, chicoric acid, cynarine, and caffeic acid. Their study was performed in a model which was as close as possible to real skin: the oxygen

radical–induced degradation of collagen which mimics free radical mediated skin damage by UV radiation. Acid–soluble Type III collagen (mainly present in skin) was the substrate and the xanthine/xanthine oxidase system was used as the promoter of oxygen free radicals. Both caffeic acid and its listed derivatives, especially echinacoside, which is the most representative constituent of the echinacea species, strongly protected collagen from free radical attack. The conclusion from the study was that extracts from echinacea could be used for the prevention of skin photodamage.

Last year See et al. (9) evaluated extracts from E. purpurea for their capacity to stimulate cellular immune function by peripheral blood mononuclear cells from normal individuals and patients with either the chronic fatigue syndrome (CFS) or AIDS. Subjects were treated with increasing concentrations of the extracts, and it was shown that increasing concentrations progressively increased both the antibody–dependent cellular cytotoxicity and natural killer cell function. Previous studies have shown that immune enhancement may be of clinical benefit for CFS patients but, although immune suppression is the hallmark of HIV infections, the utility of immune stimulation in arresting HIV progression has not been clearly demonstrated. If clinical efficacy of immune stimulation in CFS and/or HIV patients were eventually demonstrated, the use of this low–cost, non–toxic immune modulator might be an attractive treatment alternative for these patients.

Side effects are always a concern when proposing the use of a new substance as a drug, but the long history of echinacea use and recent investigations have found no significant side effects in mice, rats, or humans even when administered intravenously at high doses, though allergies are always a possibility particularly with plants in this family (9,12). Those people suffering from severe systemic illnesses such as tuberculosis, leukosis, collagen diseases, multiple sclerosis, and the like should not use echinacea (11). It should also be avoided in malignant or premalignant disorders with danger of exacerbation by colony stimulating factors (such as dysplasia of bone marrow causing neutropenia) (8). In addition, internal and external usage should not exceed a consecutive usage period of 8 weeks because the immunostimulating effects seem to decrease after that time period (11).

The current research on the effects of echinacea on the human immune system holds great promise for its use in mainstream medicine in the future. The number of ways that this non–toxic, low–cost drug could be used are virtually immeasurable. Its long history of successful use both in the United States. and in Europe along with the research which is now coming to light prove that the purple cone flower with the hedgehog top is highly deserving of continued attention by scientists and especially by clinicians seeking alternative ways to help their patients.

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