



REVIEW ARTICLE

PHARMACOLOGY

PHARMACOLOGICAL IMPORTANCE OF *ECHINACEA PURPUREA***K.M.Kumar and Sudha Ramaiah***

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India**ABSTRACT**

Echinacea (E.) purpurea is a medicinal herb commonly known as the purple coneflower, red sunflower and rudbeckia. *Echinacea purpurea*, a plant is mostly used to treat respiratory infections. This paper reviews the history, chemistry and pharmacological action of *Echinacea* species. The *Echinacea* species, *Echinacea angustifolia*, *Echinacea pallida* and *Echinacea purpurea* have a long history of medicinal use particularly infections, and today *Echinacea* preparations are the best herbal medicine used in several countries like America, Germany, Australia, Thailand and some other European countries. Mainly *Echinacea* is focused on its immunomodulatory effects, anti inflammatory and antioxidant effects, anti viral effects, particularly in the prevention and treatment of upper respiratory tract infections. The chemistry and pharmacology action of *Echinacea* species is well documented and several groups of bioactive constituents, including alkaloids and lipophilic alkaloids, water-soluble phenolic compounds (mainly caffeic acid derivatives) and polysaccharides, benzalkonium chloride are considered important for its activity. The efficacy of *Echinacea* is not yet revealed completely. From the available data it is reported *Echinacea* appears to be well tolerated. However, further investigation and surveillance are necessary to establish the safety profiles of different *Echinacea* preparations. Safety issues include the possibility of allergic reaction, dose dependent adverse effects and overdose. In this article we have reviewed the role of bioactive compounds and the pharmacological properties of *Echinacea purpurea*.



KEY WORDS

Immunomodulatory, anti-inflammatory, anti oxidant, Phenolic compounds and alkamides

INTRODUCTION

Echinacea is the composite family of Asteraceae, which is commonly known as purple cone flower. *Echinacea* is perennial, herbaceous plant mostly found in eastern North America. Mc Gregor (1968) and Binns et al (2002) presented the detailed morphological classification as well as the numerical and statistical method of the *Echinacea*^{1,2}. According to Mc Gregor and Binns there are 11 Taxa and 2 subgenera and four species with two botanical varieties were recognized.

Echinacea is an herbal medicine, which is used by native Americans for enhancing the human immune system^{3,4}, the herbal product which is found in the *Echinacea* was isolated for the roots of *Echinacea angustifolia* Dc and from the nut of *Echinacea Pallida* which has consistently one of the top species in the U.S herb market⁵. In Europe and North America they widely used the *Echinacea purpurea* (L) Moench as the herbal medicine for most of the remedies. Due to the increased market demand, economic value and its potential benefits to human health make increased cultivation of *Echinacea*. As well as, a little effort has been directed in the field of genetic improvement of *Echinacea* for medicinal use. Beside this, *Echinacea purpurea* is used for both ornamental use and phytochemical use has been conducted in Europe^{6,7}, United States⁸ and Australia⁹.

Three groups of phytochemicals are determined such as caffeic acid derivatives, polysaccharides and lipophilic alkamides, which are responsible for the genus medicinal properties¹⁰. Both immunological and pharmacological studies showed that the importance of caffeic derivatives and cichoric acid¹¹⁻¹³, more over the result demonstrated

immunological activity of alkamides both invitro and invivo^{14,15}. Most recent studies of placebo-controlled clinical studies¹⁵ identified that the liquid extraction of freshly harvested flowering top of *Echinacea purpurea* contains alkamides(0.25mg), cichoric acid(2.5mg) and polysaccharides(25.5 mg.ml-1) respectively, which is used to treat common cold in adults thus *Echinacea purpurea* is widely utilized and cultivated species, accounting for 80% of commercial production¹⁶.

Due to the human health benefits of *Echinacea*, it is vital to increase the bioactive compounds of the plant by doing breeding and selection for extract preparation, the roots and above ground parts are used, which is potentially useful to evaluate the relationship between the roots and above ground parts to know the production of phytochemicals as well as variation among individual plants. The significant variations were found in caffeic acid and alkamides in different plants and its developmental stages were reported by Li, Binns et al and Stuart et al¹⁷⁻¹⁹.

HISTORY

The *Echinacea* plant have been used since 1600 by native Americans, the *Echinacea* used for a variety of medical problems like sore gums, coughs to bowel trouble and snake bites²⁰. *Echinacea purpurea* is one of the most popular herbal plants cultivated in North America. Other name of *Echinacea* is 'Echinos' (the word comes from Greek)²¹ and also named as perennial herbs, Indianhead, comb flower and hedgehog²⁰⁻²³. *Echinacea* have close relationship with Asteracea family members like sunflowers, ragweed and daisies. The general



treatment of *Echinacea* did not occur until 1800's. The root extract used as a blood purifier^{21,22}, also marketing as anti-infective agents²⁰. *Echinacea purpurea* is very popular in beginning of this century and starts from 1916 to 1950. Recent studies have been focused on *Echinacea* to treat upper respiratory problems, urinary tract infections, chronic wounds, and snake and mosquito bites²⁴.

CHEMISTRY

The active substances of *Echinacea* are polysaccharides, flavonoids, chicoric acid, alkyl amides, polyacetylenes and essential oils^{20,23}. Polysaccharides and chicoric acid glycosides have immunostimulatory activity in *Echinacea*. Based on the composition, extraction method and time of harvest the *Echinacea purpurea* is differ from other *Echinacea* species. Part of the plant using can mainly affect the amount of active substance²¹.

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The number of polysaccharide have been isolated and analysed its pharmacological effects on the immune system. The high molecular weight polysaccharide heteroxylan has potential to activate phagocytosis. Other polysaccharide arabinogalactan induces the release of tumour necrosis factor (TNF) that increases the level of macrophage interleukin-1 and interferon beta-2. Alkylamide and chicoric acid glycosides also stimulate phagocytosis. Isobutylamide is one of the alkylamides which gives pungent smell and distinct taste for *Echinacea*²⁵. *Echinacea* have an antibacterial or antiviral activity through the immune system modulation, thus indirectly it acts on infection. Several studies on pharmacology of *Echinacea* used the parenteral formulation, because it is unclear activity of orally administered preparations^{21,26}.

MEDICINAL USES

Echinacea angustifolia, *Echinacea Pallida* and *Echinacea purpurea* are used medicinally.

The constituents of each species of herb are similar with slight variations but they varied each other according to the active compounds present in roots, leaves and whole plant. Most of American Indians have been used medicinal preparation of *Echinacea purpurea* for the treatment of many diseases, including colds, toothaches, snake bites, headache and wound infections²⁷. It is the most effective antioxidant and it has immunoenhancing effects²⁸. The roots of *Echinacea* are used to treat blood poisoning, snake poisoning, skin disease, syphilis and rabbits. *Echinacea purpurea* herb is also used to treat chronic infections of respiratory tract and lower urinary tract (viral and bacterial origin). The polysaccharide from *Echinacea purpurea* used to kill bacteria such as staphylococci. Arabinogalactan, a high molecular weight purified polysaccharide from plant cell cultures of *Echinacea purpurea* has potent to activate macrophage cytotoxicity actions against tumor cells and micro organisms²⁷.

BIOACTIVE COMPONENTS OF ECHINACEA PURPUREA

Earlier studies reported that many bioactive components have been identified in *Echinacea*.

Above ground parts of *Echinacea* plant have less oils and pyrrolizidine alkaloids, such as tussilagine and isotussilagine than the root parts. The active components of the upper plant are thought to be caffeic and ferulic acid derivatives (such as chicoric acid and echinacoside) and complex polysaccharides (such as acidic arabinogalactan, rhamnourabinogalactans, and 4-O-methylglucuronylarabinoxylans).

Alkylamides and alkylamide-rich alcohol extracts of *Echinacea* inhibit production of inflammatory mediators^{29,30}. Lipophilic alkylamides, water-soluble phenolic compounds (mainly caffeic acid derivatives) and polysaccharides are the most recognized for their immunomodulatory properties³¹.



Glycerin extract of *E. purpurea* increases in immunoglobulin (Ig) M response against sheep red blood cells (sRBC) in the mice³². Polysaccharides were considered critical for stimulation of nonspecific immune responses^{33, 34}.

E. purpurea found an increase in CD4+ T-lymphocytes in mouse peripheral blood but implied it is a secondary effect in association with macrophage activation³⁵. Alkamides and Caffeic acid derivatives are good antioxidants in cell-free free radical generation systems³⁶⁻³⁸.

The main caffeic acid derivative (caftaric acid, chlorogenic acid and echinacoside) in EA and EPA, has been functionally linked to anti-inflammatory and wound healing properties of *Echinacea* when applied topically^{41,42}.

Caffeic acid derivatives are effective antioxidants in free radical generation systems³⁸. Groups of phenolic compounds and alkamides, which have demonstrated antiviral and antifungal properties, respectively^{41,42}. Benzalkonium chloride and phytochemicals derived from *Echinacea purpurea* was reported to have antiviral activity against herpes virus in a human cell model⁴³.

PHARMACOLOGICAL ACTION

ANTI-INFLAMMATION ACTIVITY

Echinacea purpurea is one of the main medicinal *Echinacea* species and have long been used to treat infections, to aid in wound healing and to enhance the immune system⁴⁴. Alkamides and caffeic acid derivatives are potent anti-inflammatory agents present in *Echinacea*^{39,40}. *Echinacea*-derived alkamides have immunomodulatory and anti-inflammatory activity⁴⁵. *E. purpurea* (EP) have been used for wound healing, pain relief and alleviation of cold symptoms³³. Alcohol extracts of *Echinacea* offers anti-inflammatory effects through inhibition of production of inflammatory mediators tumor necrosis factor-alpha (TNF- α) and nitric oxide (NO)^{29,30}. Prostaglandin E2 (PGE2) is a critical

inflammatory mediator that is produced through the arachidonic acid cascade. The anti-inflammatory role of *Echinacea* is also mediated through own regulation of cyclooxygenase-1 and cyclooxygenase-2 through suppression of Prostaglandin E2 activation. COX-1 and COX-2 catalyze the reaction converting arachidonic acid, released by phospholipase A, to Prostaglandin E2^{46,47}. Wagner has reported lipoxygenase-inhibiting anti-inflammatory activity attributable to one of *E. purpurea*'s isobutylamides, dodecatetraenoic acid⁴⁸.

Alcohol extracts of *Echinacea* are composed of two classes of natural chemicals lipophilic alkamides and water-soluble caffeic acid derivatives. Caffeic acid derivatives have an antihyaluronidase activity⁴⁹. An inhibition of hyaluronidase leads to accumulation of enough hyaluronan in the extracellular matrix for wound repair⁴⁰. In rats, excision wounds treated with a caffeic acid derivative, showed a healing process characterized by reduced inflammatory response and higher hyaluronan content³⁹. These data indicate that *Echinacea* presents a clear anti-inflammatory activity that may promote wound tissue recovery. However, there are no studies that have tested the efficacy of oral administration of *Echinacea* or its chemical constituents in wound healing.

ANTI-OXIDANT ACTIVITY

Echinacea was found to be a very potent antioxidant³⁸. Arachidonic acid metabolism and prostaglandin E2 production were reduced by several *E. purpurea*. Alcohol extracts of *Echinacea* are typically composed of two classes of natural chemicals, lipophilic alkamides and water-soluble caffeic acid derivatives. Caffeic acid derivatives are effective antioxidants in free radical generation systems³⁸ and have an anti hyaluronidase activity⁴⁹. Enhancement of free-radical scavenging activity has been shown by laboratories in the U.S. and Canada^{36,50}. Hu and Kitts investigated anti-oxidant and free-radical



scavenging activity, including suppression of oxidation of human low-density lipoprotein³⁶.

ANTI IMMUNOSUPPRESSANT

Echinacea products are the most popular herbal immunostimulants in North America and Europe. In 1997 *Echinacea* may be best known as an immunostimulant⁵¹. There have been numerous reports of immunomodulatory properties in various preparations derived from different parts of several species of *Echinacea*^{52,31,53,54}. A series of studies in mice using purified polysaccharides from *Echinacea* plant cell cultures showed a stimulatory effect when applied to immune cells in culture or injected intraperitoneally into mice⁵⁵. Mice with suppressed immunity due to treatment with cyclophosphamide or cyclosporin also had an increase in these immune functions when given purified polysaccharides from *Echinacea*⁵⁶. These studies suggest that *Echinacea* stimulates immune functions in healthy or in immunosuppressed animals. These immunologically active polysaccharides did not stimulate all immune cells. B cells were not activated, nor did the B cells produce more antibodies to sheep red blood cells⁵⁷. Apparently, Luettig et al purified polysaccharides from *E. purpurea* act on the nonspecific branch of immunity. Recent studies have been shown that rhinoviruses could stimulate the transcription of various immuneresponse genes in different types of cells^{58,59,60}. Furthermore the expression of cytokine genes and some of their secreted products in bronchial epithelial cells could be reversed by *Echinacea* preparations^{60,61}. Several animal and human studies have suggested that *Echinacea* stimulates neutrophil and macrophage phagocytic function^{62,63,57}. Other scientific studies suggests that the *Echinacea purpurea* possesses nonspecific, short-term immune system stimulant properties^{20,64}.

ANTI FUNGAL ACTIVITY

The Extract of *E. purpurea* has been shown to have antifungal activities in a series of *in vitro* experiments testing activity against various *Candida* species, and various *Saccharomyces cerevisiae*, *Candida albicans* the most common fungal cause of human skin disease⁶⁵. Antimicrobial actions were observed in various *E. purpurea* root and herb extracts. Other laboratories have also reported anti-*Candida* activity of extract of *Echinacea purpurea*^{66,67}. Phagocytosis of *Candida* by *ex vivo* human macrophages and natural killer cells was found to be enhanced following exposure to extracts of both *E. purpurea* and Gingseng⁶⁸. Mouse macrophage activity against *Candida* has also been observed to be stimulated by *E. purpurea* polysaccharide exposure^{69,48}. The polysaccharide rich *Echinacea purpurea* extract was found to decrease the infection and death rates of immunosuppressed mice infected with *Candida*⁵⁶. Coeugnet and Kuhnast demonstrated a human clinical trial testing an expressed juice of *E. purpurea* (Echinacin®) for ability to effect recurrent vaginal yeast infections. They found Echinacin®-treated groups demonstrated increased skin reactivity and decreased recurrence of vaginal candidiasis over the 6-month monitoring period while 60% of controls got new infections, only 5–17% of women in the treatment groups were diagnosed with recurrent vaginal infections ($P < 0.05$)⁷⁰.

ANTI VIRAL ACTIVITY

Biological activity of the chemical Components of *E. purpurea* have been characterized⁷¹, Eichler and Kruger reported *Echinacea* has antiviral and anti bacterial activity and they have found that cultured cells infected with virus and exposed to *E. purpurea* juice demonstrated an increased rate of presentation of viral antigen⁷². Benzalkonium chloride and phytochemicals derived from *Echinacea purpurea* was found to have antiviral activity against herpes virus in a human cell model⁴³. *Echinacea purpurea* was also very effective



against influenza virus⁷³. Skwarek et al revealed that the extract of *E. purpurea* has been found to inhibit viral replication in animal cell viral culture models⁷⁴. Eilmes demonstrated that complex hydrophilic and lipophilic extracts of *Echinacea* has more viral-infection- inhibitory activity fractions⁷⁵. Polysaccharide derived from *Echinacea purpurea* has been shown to stimulate macrophage activity and several functions related to cytokine production^{76,77,50,78} and groups of phenolic compounds and alkaloids, which have demonstrated antiviral and antifungal properties, respectively^{2,79}. These activities could be related to the reports that some *E. purpurea* preparations were able to prevent or control upper respiratory infections (URIs)⁸⁰. Turner and colleagues have recently described a human trial testing the efficacy of *Echinacea* in preventing colds induced by a cultured rhinovirus⁸¹. There are no reports on *E. Purpurea* in relation to HIV.

CONCLUSION

Extensive literature survey revealed that *Echinacea* has a long history of traditional use for a wide range of diseases. Much of the traditional uses have been validated by scientific research. It is the most important species that has more herbal medicinal value. The plant is used in common cold, coughs, bronchitis, upper respiratory infections, urinary tract infections and some inflammatory conditions. Studies suggest in this article that *Echinacea* possessed anti-inflammatory activity, antiviral activity, anti fungal activity, anti oxidant activity and anti immunosuppressant activity. Although many of the active compounds of *Echinacea* have been identified, the mechanism of action is not known, nor is the bioavailability, relative potency, or synergistic effects of the active compounds known. Existing literature suggests that *Echinacea* should be used as a treatment for illness, not as a means for prevention of illness. The studies reported in the present review confirm the medicinal value and pharmacological action of *Echinacea purpurea*. Future work needs to be carried out to identify the species of *Echinacea* and efficacy of the different plant parts (roots versus upper plant parts).

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