Echinacea and the immune system

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Figure 1: *Echinacea purpurea*

What is Echinacea?

Echinacea, also known as the purple coneflower is a member of the Asteraceae (daisy) family (Figure 1). It is one of the most popular herbal medicines with an estimated 1-4% of the general population using the herb in a given year.

The medicinal properties of *Echinacea were* first recognised in the eighteenth century by Native American tribes (figure 2) who used the plant to treat snake and insect bites, coughs and colds and typhoid fever.

Echinacea has numerous claimed medicinal properties including: anti-viral, anti-bacterial, anti-fungal, anti-oxidant, anti-carcinogenic, anti inflammatory and wound healing properties. Its popularity today is fuelled by claims that it has immune stimulating properties and can reduce the severity of symptoms and duration of the common cold and flu, especially if used in the early stages of infection. Although there are around nine species of *Echinacea,* only three of these have attracted interest regarding their medicinal properties, *E. purpurea*, *E. angustifolia* and *E. pallida.*

Despite the many claims for the health benefits of *Echinacea*, like many other herbal products it lacks government regulation because unlike pharmaceuticals, herbal products do not undergo well established and rigorous testing procedures. The chemical composition of any herb is complex

compared to any drug. Drugs contain a single known active ingredient which can be tested and standardised where as a single herb may contain many active components which are difficult to standardise due to variance between plants and between extraction methods. There is often very little hard science behind the medicinal claims for phytocompounds such as *Echinacea*.

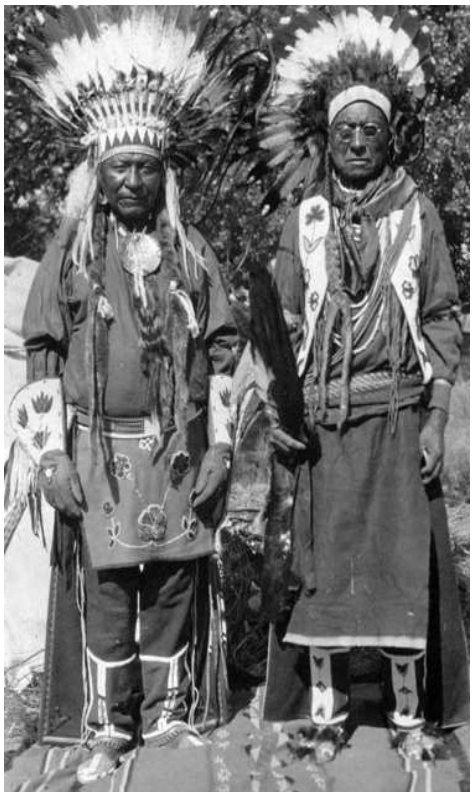


Figure 2: The medicinal properties of *Echinacea* have been recognised for centuries, it was first used by Native American tribes.

Much evidence supplied by the manufacturers of herbal products is often anecdotal or based upon case studies.

It is also a common perception with herbal medications that because they are natural they are safe. However, natural does not necessarily mean safe, what can cure can also kill; it is only the right dose that differentiates a remedy from a poison.

Herbal products such as *Echinacea* can also interfere with the metabolism of prescription drugs, for example, the popular herbal medication "St Johns Wort" is known to interfere with the metabolism of the contraceptive pill and the blood thinning drug "warfarin", such herb-drug interactions could prove to be devastating or even fatal.

Given the popularity of *Echinacea t*he main aims of the review were:

- To determine whether or not claim's for *Echinacea's* medicinal properties are justified.
- To determine how *Echinacea* works by identifying its active components and their interactions with the immune system.
- To determine how effective *Echinacea* is at improving human health.
- To determine whether unregulated use of the herb can cause any adverse effects to health.

What makes Echinacea work?

Several major constituents of *Echinacea* have been identified and reported to be biologically active, they can be divided into the following groups:

Caffeic acid derivatives- these include echinacoside, cynarin and chicoric acid and are thought to contribute to the claimed antioxidant and anti-inflammatory properties of *Echinacea.*

Alkamides- these are predominantly found in the roots of *E. angustifolia* and are thought to have stimulatory effects on the cells of the immune system.

Polysaccharides- these are of two types; a heteroxylan and an arabinogalactan, both have been reported to act on the immune system to boost its effects.

How does Echinacea work?

The active constituents of *Echinacea*may strengthen or stimulate the immune response by interacting with various cells of the immune system. Immune responses can be either innate (non-specific) mediated by macrophages, natural killer cells and polymorphonuclear leukocytes (neutrophils), or adaptive (specific) mediated by B or T lymphocytes.

Activation of the cells of the non specific branch of immunity by *Echinacea* has been demonstrated most convincingly, with activation of the following cell types being the most widely reported of *Echinacea's* immune–stimulating properties:

Macrophages- these are cells of the immune system and are an important first line of defence against a great many infectious agents. Their main role is to remove particulate antigens by phagocytosis (Figure 3)). Their other function is to present antigenic peptides to cells of the acquired system. Once activated macrophages produce a number of cytokines, these are small signalling molecules which include; tumour necrosis factors, interleukins and interferons. Once released cytokines induce resistance against a diversity of viruses and are also important in the activation of other immune cells, such as recruiting cells of the acquired immune system to sites of infection. Once activated macrophages also release nitrous oxide which is the predominant method by which infectious agents are destroyed. Thus, macrophages are important regulators of both innate and acquired immunity. Cell cultures of macrophages have responded to *Echinacea* by increasing their production of cytokines and the rate in which particles are taken up by phagocytosis. Macrophages circulating in a semi-

activated state should be better able to respond quickly to and destroy invading pathogens.

Natural killer cells- these are also cells of the innate immune system. The function of natural killer cells is to recognize and kill target cells, notably virus infected and tumour cells. Thus, any agent that is capable of enhancing the activity of these cells is likely to enhance the overall immune response. Various *Echinacea extracts* and preparations have been shown to enhance natural killer cell activity.

Polymorphonuclear leukocytes- these include; neutrophils, eosinophils, basophils and mast cells. Neutrophils are short lived phagocytic cells whose granules contain powerful bactericidal and antibiotic enzymes. Eosinophils, basophils and mast cells also contain secretory granules and are involved in the inflammatory response. *Echinacea* has been shown to have the ability to enhance the activity of the Polymorphonuclear leukocytes which means they also should be able to respond to and destroy pathogenic agents more quickly.

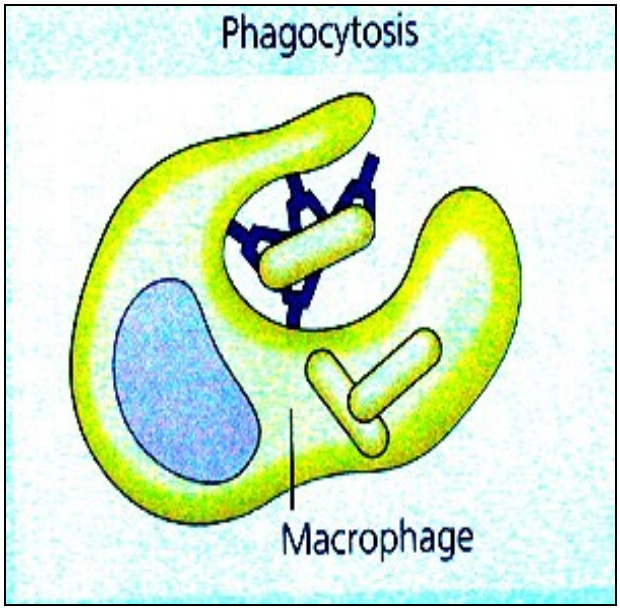
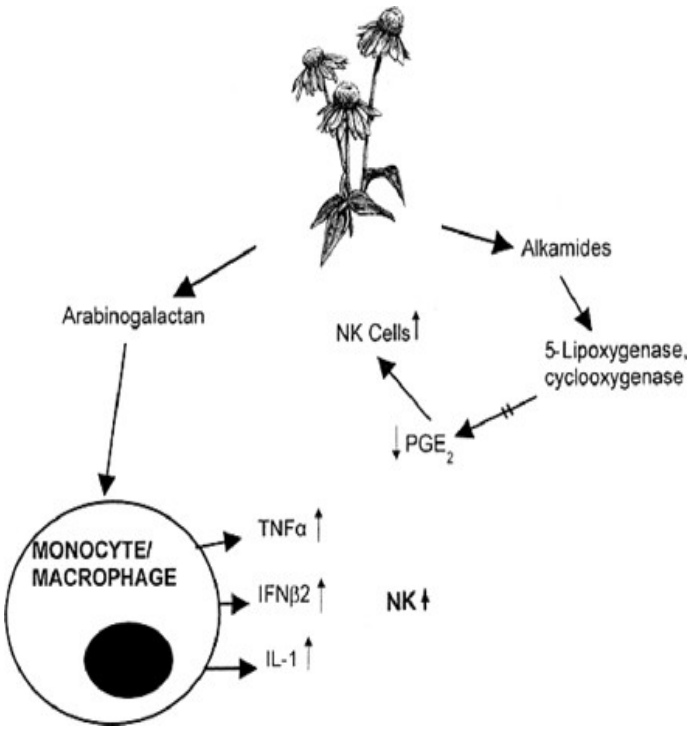


Figure 3: *Echinacea* stimulates macrophages and other cells of the innate immune system, causing them to become activated and release cytokines. Increases in phagocytic activity and the uptake of foreign particles also result following exposure of the immune cells to *Echinacea*.

Which part of *Echinacea* is the most effective immune-stimulant?

Besides there being three different species of pharmacologically active *Echinacea*, there are also many types of preparation available. Some of these contain whole plant parts of *Echinacea* whilst others may contain individual active constituents which have been isolated and purified. Whereas preparations containing the whole plant ingredients have been shown to be efficacious immune stimulating agents, extracts that have been standardized to contain a particular active ingredient have not produced such convincing results. This is because the combined action and balance of active constituents produces a more powerful effect together than would be expected from the addition of the individual components. The active constituents of *Echinacea* work as a team, enhancing each others effects- this phenomenon is known as "synergy".



Source of diagram: Miller, S. C., (2005), *Echinacea*: A miracle herb against ageing and cancer? Evidence *in vivo*, *Evidence based complementary and alternative medicine*, **3**: 304-314.

Figure 4: Synergy: the active constituents present in *Echinacea* complement each others actions. The polysaccharide Arabinogalactan stimulates macrophages to release a number of cytokines (TNF_{α}, IFNβ2 and IL-1) which in turn stimulate the function of natural killer cells (NK). On the other hand the Alkamides present in *Echinacea* release natural killer cells from their endogenous inhibitors, the prostaglandins (PGE_2). The combined effect results in *Echinacea* being a powerful natural killer cell stimulant.

Whole *Echinacea* preparations can enhance the activity of the natural killer cells considerably. However, *Echinacea* preparations standardized to contain only polysaccharides or only alkamides have no such effect. The alkamides found within *Echinacea* root extracts are thought to release natural killer cells from their natural endogenous inhibitors the "prostaglandins", whereas a complex group of polysaccharides known as the arabinogalactans release a host of natural killer cell stimulants. The combined effects of these two active components result in *Echinacea* being a powerful natural killer cell stimulant (figure 4). However, the effects of either constituent alone may not be sufficient enough to cause significant activation of natural killer cells. In summary, whole *Echinacea* may be more beneficial than standardized extracts.

How effective is Echinacea at improving human health?

Echinacea does indeed exhibit immune stimulating properties as shown by its effects on the cells of the innate immune system. However, despite this cellular evidence of immune stimulation, whether these effects translate into better human health is less well understood.

Echinacea's benefits to human health are largely backed up by anecdotal evidence, as many thousands of people over the centuries have reported numerous health benefits. However, controlled clinical trials involving humans have failed to produce convincing results. Although several human clinical trials have reported health benefits, much of this evidence is contradictory and the trials are limited in both size and methodological quality. Therefore, effectiveness in humans from a scientific point of view has not yet been proven beyond reasonable doubt.

One factor affecting the validity of studies is the quality of the *Echinacea* material used in both clinical trials. *Echinacea's* immune stimulating properties are dependent on the presence of certain active constituents. Recent research into the quality of herbal products revealed that only 28% of *Echinacea* products tested contained the same amounts and types of constituents as listed on the label. This could explain why *Echinacea* is effective in some trials but not in others. In summary, before definitive conclusions can be made on the efficacy of *Echinacea* at improving human health, efforts should be made to ensure that the quality of the *Echinacea* material being tested is up to standard.

How safe is Echinacea?

Echinacea appears to be well tolerated. It has been estimated that 1-4% of the general population uses *Echinacea* in a given year. No deaths and few significant adverse reactions have been reported, so the overall risk ratio appears favourable. Investigations into the toxic effects of *Echinacea* have failed to find a lethal dose.

Those with a known allergy to the Asteraceae (daisy) family should avoid *Echinacea* as a few cases of *Echinacea* induced anaphylaxis, asthma attack; urticaria and contact dermatitis have been reported.

Echinacea can interfere with drugs metabolized by an enzyme family known as the cytochrome p450 system and thus prolong their action. These include common drugs and other substances such as warfarin, alchohol, caffeine, ibuprofen and several drugs used to treat HIV. Hence patients on prescription medication known to be metabolized by this enzyme system should avoid *Echinacea* or seek medical advice before doing so.

Conclusion

Echinacea is a relatively well studied medicinal plant that certainly does have the potential to act a non-specific immune stimulatory agent, as well as exhibiting some antioxidant, anti-inflammatory, antibacterial and antifungal properties. Several active constituents have been identified that may contribute to *Echinacea's* immune stimulatory activity, these include: alkamides, caffeic acid derivatives and polysaccharides. The alkamides and a group of polysaccharides known as the arabinogalactans appear to contribute to the activation of the immune cells, where-as the caffeic acid derivatives appear to contribute to the antioxidant, anti-inflammatory and anti-bacterial properties of *Echinacea*. It seems likely that the combined or "synergistic" effects of each of the active components may contribute to the overall reported ability of *Echinacea* to lead to alleviation of symptoms and faster resolution of the cold and flu viruses. This means that "Whole" *Echinacea* preparations are probably the most efficacious type of medicinal preparation as opposed to standardized extracts.

Despite the convincing cellular evidence for the immunological activities of *Echinacea*, whether these effects translate into better human health is less well understood. Several human clinical trials have reported health benefits, however much of this evidence is contradictory and the trials are limited in both size and methodological quality. Inconsistency of results may be

explained by the lack of use of quality herbal material. Therefore, whilst there is a large amount of scientific data regarding *Echinacea*, effectiveness in humans has not yet been proven beyond reasonable doubt.

With regard to safety *Echinacea* appears to be well tolerated, no deaths and few adverse reactions have been reported.

Finally, could *Echinacea* be a potentially lifesaving medicine that is being largely ignored by the government? Cancer and HIV cases are on the increase and relatively few trials have investigated the therapeutic value of *Echinacea* in these conditions, although the effect of *Echinacea* on the immune system may have therapeutic potential. Chemotherapy patients often die from overwhelming infection due to suppressed immune function, *Echinacea* could possibly help to boost their immune function at this critical time, and futher act as an antioxidant .

Further reading

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Author profile:

Juliet is 22 years old, studied in the school of Biosciences at the University of Nottingham graduating in 2006 with a first class BSc degree in Animal Science. Juliet was particularly interested in alternative medicines and would eventually like to work within the pharmaceutical industry.