



ImmunExtra®

A dietary supplement containing the patented, active ingredient **PROLIGNA®** isolated from pinecones

Scientifically proven to enhance immune system activity

Manufactured to high standards using Good Manufacturing Practices—only by Allera Health Products

Extensive research shows that a healthy immune system helps prevent common illnesses. It is also well known that stress, poor diet, lack of sleep and even some medications can reduce your immune system's ability to work at its best.

Immunextra® is a nutritional supplement that optimizes immune cell activity. Its active ingredient, **PROLIGNA®**, contains two of the most important natural compounds on earth, **lignin** and **polysaccharides**¹.

The scientific name for **PROLIGNA®** is Polyphenylpropenoid-Polysaccharide Complex, or PPC. More than 30 peer-reviewed scientific studies have been published describing the properties of PPC.

The **PROLIGNA®** Story

The health benefits of pinecone extract were first documented in 500 A.D by Greek physicians. Since that time, the extract has been used in modern day Japan to treat illness ranging from the common cold to cancer (Sakagami et al, 1991). Ingestion of pinecones (matsu) or the drinking of teas brewed from pinecones has long been associated with an increase in health and longevity in Japan.

Closer to home, there has been more than 20 years of positive human experience in the United States with pinecone extract. **PROLIGNA®**, the active ingredient in Immunextra™ should not be confused with **pycnogenol**, or any other pinecone extract that may be available. ImmunExtra is the only product that contains **PROLIGNA®**, which has been shown to scavenge free radicals and to act as a potent antioxidant (Satoh and Sakagami, 1996).

¹ In fact, Lignin is the most abundant natural phenolic polymer on earth, and is a component of dietary fiber.

How is PROLIGNA® made?

Fresh, renewable pinecones harvested from the forests of Wisconsin are the starting material for a patented method that extracts the active molecules. The liquid extract is tested extensively to ensure that it does not contain any contaminants, such as herbicides, pesticides or heavy metals. The liquid is then gently dried to a powder and used to make vegetarian ImmunExtra® capsules. Allera Health Products follows Good Manufacturing Practices when making ImmunExtra® and all testing is performed by independent laboratories that comply with FDA standards and practices.²

The Science behind PROLIGNA®

There are now more than 30 peer-reviewed scientific studies describing research with PROLIGNA® (PPC). In these studies, PPC exhibits **antibacterial, antiviral, and antitumor properties** (Fukuchi et al., 1989a, Harada et al., 1991; Kurakata et al., 1989; Nagata et al., 1990; O-Hara et al., 1990; Sakagami et al., 1991). Moreover, extensive experimentation shows that PPC has a positive and lasting effect on human immune cell activity at the dosage contained in ImmunExtra® capsules (Bradley *et al.*, 2003).

PROLIGNA® effects on Immune Cells

PROLIGNA® (PPC) promotes immune cell development in human cells and animal models. In 2003, Dr. Guy Bradley demonstrated that PPC is capable of promoting the rapid differentiation of human peripheral blood mononuclear cells (PBMC) into mature **dendritic cells**.

This is important because **dendritic cells are recognized as the most potent antigen presenting cells of the immune system**. Their ability to uptake, process, and present antigen to T cells is central to the development of immune responses against bacterial- and viral-infected cells, cancer cells and vaccine antigens.

In an earlier study, Lai et al. (1990) purified the active components of pinecone extract and identified fractions that induced the production of **macrophages**, a white blood cell that surrounds and kills microorganisms, removes dead cells, and stimulates the action of other immune system cells. Importantly, PROLIGNA® is otherwise nontoxic to cells and effective at low doses.

² <http://www.cfsan.fda.gov/~dms/gmp-toc.html>

PROLIGNA[®] effects on bacteria and viruses

Dr. Satoh's laboratory (Satoh et al., 1999) showed that PPC inhibits HIV induced effects on cells in cell culture. Moreover, pretreatment of mice with PPC by injection protects them from a lethal infection with E. coli bacteria. These results support the potential benefits of PPC.

PROLIGNA[®] effects on tumor response to chemotherapy⁴

Dr. Mark Jaroszeski's laboratory at the University of South Florida investigated the potential beneficial effects of PROLIGNA[®] (PPC) when used in conjunction with a procedure called electrochemotherapy (ECT) for the treatment of tumors.

ECT involves applying electrical pulses to living cells, which cause the rapid appearance and disappearance of tiny holes in the cell membrane. This procedure allows chemotherapy drugs to enter the cells more efficiently. ECT has been exploited to deliver chemotherapeutic agents to tumor cells in clinical trials in the US and Europe.

The current study tested ECT plus PROLIGNA[®] (PPC) in an animal model for melanoma, a particularly aggressive cancer type.

Treatment "success" was defined as the complete absence of tumor at the end of 50 days. Remarkably, 50 to 64% of the animals that received oral PPC plus ECT had a complete absence of tumor versus 31% for animals that received ECT alone. **It was concluded that treatment of animals with PPC caused a doubling of the number of animals that were tumor free, or "cured", during the course of the experiment.**

Additional studies will need to be done to sort out the precise basis for these interesting results.

⁴ Dr. Mark J. Jaroszeski et al, (2006) Abstract to the American Institute of Chemical Engineers Annual meeting. This work was supported by Grant Number R21AT001259 from the National Institutes of Health (NIH), National Center for Complimentary and Alternative Medicine (NCCAM).

The Safety of PROLIGNA®

Toxicology experiments have proved that Proligna® is non-toxic when taken orally for 30 days at a range of dose levels (5 mg/kg up to 405 mg/kg)⁵. Studies performed in mice further support these results. Moreover, more than a million doses of pinecone extract have been distributed to people with no apparent side effects.

In summary, all of these study results suggest that pinecone extract could be useful for maintaining health without associated side effects.

Immunextra® PRODUCT INFORMATION

Immunextra® is available in vegetarian capsules- 30 or 60-day supply per bottle.

Immunextra® contains no artificial flavors, colors, preservatives, known allergens, or animal products.

Immunextra® can be stored at room temperature and is stable for two years or more.

Inert Ingredients:

Microcrystalline cellulose, hydroxypropylmethyl cellulose, stearic acid, pectin, glycerin. Contains Patented ProLigna™.

Supplement Facts
Serving Size 1 Capsule
Amount Per Serving
Powdered Scotch Pinecone Extract (Proligna) 16mg*
* Daily Value not established.

⁵ Performed in a rat model

Scientific Publications Addressing the Efficacy of Alkaline Pinecone Extracts

Antimicrobial effects

1. Harada *et al.*, (1988) Induction of antimicrobial activity by antitumor substances from pinecone extract of *Pinus parviflora* Sieb. et Zucc. *Anticancer Research*. 8:581-588.
2. Oh-hara *et al.*, (1990) Antimicrobial spectrum of lignin-related pinecone extracts of *Pinus parviflora* Sieb. et Zucc. (1990) *In vivo*. 4: 7-12.

Antiparasitic effects

1. Abe *et al.*, (1989) Induction of antiparasitic activity by pinecone lignin-related substances. *In vivo*. 3:359-362.

Antitumor/antiviral effects

1. Mark J. Jaroszeski¹, Richard Heller², Anna Claire Johnson³, Kathleen Merkler², Akiko Tanaka⁴, and William Guy Bradley⁵. (2006) Extract of Pinecones Augments Tumor Response to Electrochemotherapy. Abstract. 2006 AIChE Annual Meeting.
2. Kikuchi *et al.*, (1991) Stimulation of mouse peritoneal macrophages by lignin-related substances. *Anticancer Research*. 11:841-846.
3. Nagasawa *et al.*, (1992) Inhibitory effect of lignin-related pinecone extract on cell proliferating enzyme activity of spontaneous mammary tumors in mice. *Anticancer Research*. 12: 501-504.
4. Nagasawa *et al.*, (1992) Suppression by a pinecone extract of *Pinus parviflora* Sieb. et Zucc of mammary tumor virus in milk of mice. *Anticancer Research*. 12: 845-848.
5. Unten *et al.* (1989) Stimulation of granulocyte cell iodination by pinecone antitumor substances. *Journal of Leukocyte Biology*. 45: 168-175.

Cytotoxic/mitogenic effects

1. Kawazoe *et al.*, (1993) Mechanism of splenocyte-mitogenesis induced in mice by water-extract of coniferous slash pine. *Anticancer Research*. 13: 1223-1230.
2. Kurakata *et al.*, (1989) Mitogenic activity of pinecone extracts against cultured splenocytes from normal and tumor-bearing animals. *Anticancer Research*. 9: 961-966.
3. Sakagami *et al.*, (1990) Induction of cytotoxic factor in mice by lignified materials combined with OK-42 (Picibanil). *In vivo*. 4: 371-376.

Immune modulating effects

1. Bradley *et al.*, (2003) The novel differentiation of human blood mononuclear cells into CD 1a negative dendritic cells is stimulated in the absence of exogenous cytokines by an extract prepared from pinecones. *International Immunopharmacology*. 3: 209-223.

2. Eberhardt and Young (1996) Assessment of anti-viral activity of a pinecone isolate. *Planta Medica*. 62: 63-65.
3. Fukuchi *et al.*, (1989) Inhibition of *Herpes simplex* virus infection by pinecone antitumor substances. *Anticancer Research*. 9: 313-318
4. Kunisada *et al.*, (1992) Effect of lignins on HIV-induced cytopathogenicity and myeloperoxidase activity in human myelogenous leukemic cell lines. *Anticancer Research*. 12: 2225-2228.
5. Lai *et al.*, (1990) Modification of HIV replication by pinecone extracts. *AIDS Research and Human Retroviruses*. 6(2): 205-217.
6. Lai *et al.*, (1992) Polymeric phenylpropenoids are the active components in the pinecone extract that inhibit the replication of type-1 HIV *in vitro*. *Journal of General and Applied Microbiology*. 38: 303-312.
7. Sakagami *et al.*, (1986) Partial purification of novel differentiation-inducing substances from hot water extract of Japanese pinecone. *Japanese Journal of Cancer Research*. 77: 59-64.
8. Sakagami *et al.*, (1990) Anti-Influenza virus activity of synthetically polymerized phenylpropenoids. *Biochemical and Biophysical Research Communications*. 172 (3): 1267-1272.
9. Sakagami *et al.*, (1992) Multiple immunological functions of extracts from the cone of Japanese white pine, *Pinus parviflora* Sieb. et Zucc. *Microbial Infections*. Ed. H. Friedman *et al.*, 331-335.
10. Satoh *et al.*, (1999) Radical modulation activity of pinecone extracts of *Pinus elliottii* var. *Elliottii*. *Anticancer Research*. 19: 357-364.
11. Takayama *et al.*, (1991) Inhibition of HIV forward and reverse transcription by PC6, a natural product from cones of pine trees. *AIDS Research and Human Retroviruses*. 7(3): 349-357.
12. Tamura *et al.*, (1991) A soluble factor induced by an extract from *Pinus parviflora* Sieb. et Zucc can inhibit the replication of HIV *in vitro*. *Proceedings of the National Academy of Science*. 88: 2249-2253.

ASK THE PHYSICIAN (FAQ)

How can I help my immune system?

Various factors can stress your immune system. Smoking, poor eating habits, unhealthy diets, excessive alcohol, lack of exercise, lack of sleep and anxiety all affect how your body will fight off invaders and recover from illness.

All of us come in contact with harmful bacteria, viruses and other pathogens at some point during our life, if not on a daily basis. Fortifying and maintaining your immune system by leading a healthy lifestyle and making healthy choices will reduce susceptibility to infection and other diseases while augmenting your body's ability to protect itself.

Try these 4 simple tasks to help your body protect and heal itself:

1. Regular exercise will help reduce daily stress while physically strengthening your body and improving general well being.
2. Getting enough rest so your body has time to defend itself will also reinforce the health of your immune system.
3. To further optimize immune system function, minimize your intake of sugar, saturated fat and alcohol and exchange it for minerals and nutrients that are in fresh fruits, vegetables and whole grain foods and drink plenty of water and pure fruit juice.
4. Finally, supplementing your diet with vitamins and antioxidants such as vitamin C and beta-carotene as well as ImmunExtra™ can positively impact the response and performance of your immune system.

How is Immunextra® different from other immune system boosting products?

Immunextra® is the only dietary supplement based on the patented PROLIGNA™ compound. Many immune health products on the market claim to prevent disease and illnesses by using a combination of ingredients, such as echinacea and vitamin C. By contrast, Immunextra® contains a single active ingredient.

PROLIGNA™ (also termed PPC in the scientific literature) has been studied by scientists for more than 20 years. PROLIGNA™ has been shown to have a positive and lasting effect on human immune cell activity at the dose contained in Immunextra® capsules.

Does Immunextra® cause any side effects?

There has been more than 20 years of human experience with PROLIGNA™ pinecone extract in the U.S. To date, there have been no known associated or

reported side effects or adverse reactions. In addition, pinecone extract has been used for medicinal purposes for centuries.

What is in Immunextra®?

Each capsule of Immunextra® contains the active ingredient PROLIGNA™. The other ingredients called excipients, are used to ensure proper flow of materials during production. There is a small amount of potassium chloride salt, in addition to some vegetable-based material required for making a capsule. Immunextra® does not contain any animal products, yeast, dairy, eggs, gluten, soy, wheat, peanuts, tree nuts, fish, shellfish, or any artificial ingredients. The pinecones from which the botanical compound is extracted are considered to be GRAS (Generally Recognized as Safe) by the FDA as a supplement ingredient.

Allera Health Products, Inc. adheres to Food GMPs and the regulations of the Dietary Supplement Health Education Act of 1994 (DSHEA) for the product. The provisions of DSHEA define dietary supplements and dietary ingredients; establish a new framework for assuring safety; outline guidelines for literature displayed where supplements are sold; provide for use of claims and nutritional support statements; require ingredient and nutrition labeling; and grant the FDA the authority to establish Good Manufacturing Practice regulations. Any advertising claims made about Immunextra® are subject to regulation by the U.S. Federal Trade Commission (FTC).

What are some of the conditions for which Immunextra® may help?

Whereas clinical trials are currently being planned to evaluate specific medical conditions, people who have taken Immunextra® have anecdotally reported that they have had fewer and more mild episodes of cold and flu. The anti-inflammatory effects of ImmunExtra may also help with arthritis, allergies, and similar inflammatory conditions.

How many capsules of Immunextra® should I take and how often?

The recommended effective dose is one or two capsules every day. It does not matter if you take the capsule in the morning, afternoon or evening.

Should I take Immunextra® with food?

The food you eat or the dietary supplements you take could cause a medication you are taking to work incorrectly. When supplements or drugs and certain foods are taken together they can interact in ways that can diminish or intensify the

effectiveness of the drug or reduce the absorption of food nutrients. In addition, vitamin and herbal supplements taken with certain medications can result in adverse effects. For example, food can speed up or slow down the action of a medication or supplement, while certain drugs can change how nutrients are used or decrease the absorption of vitamins and minerals in the body, or stimulate or suppress the appetite, and certain herbs can interact with anesthesia, beta-blockers, and anticoagulants.

The impact of food-drug and food-supplement interactions can depend on a variety of factors such as the dose, age, weight and health of the person, and the timing of when food is eaten and when a medication or supplement is taken.

Avoiding interactions does not necessarily mean not taking supplements or drugs and not eating foods. In the case of tetracycline and dairy products, each should simply be taken at a different time rather than eliminating one or the other.

There are no known interactions of Immunextra® and food. Immunextra® can be taken with food and liquids or without.

Can I take Immunextra® with other medications and/or dietary supplements?

There have been no reported contraindications for Immunextra® when taken together with other medicines or dietary supplements including vitamins.

Can children take Immunextra®?

Yes, children can take Immunextra® at a recommended dose of one capsule a day.

Can I take Immunextra® if I'm pregnant?

There have been no formal clinical studies conducted with women who are pregnant. If you are pregnant or trying to become pregnant, you should not take Immunextra® since there is no information regarding any effects it may have on an unborn baby. It is always best to consult with your doctor before taking a new supplement, medicine, or product especially if you are pregnant.

What happens if I take too many capsules of Immunextra®?

There is no information on the effects of overdose or taking too many capsules of Immunextra®. No safety concerns have been reported over the many years Immunextra® and pinecone extract have been used. Formal clinical trials with Immunextra® are being planned to evaluate product safety and efficacy in a standard manner. Consult with your doctor if you have any concerns.