

LENTINEX[®]

Build a more resistant immune
system



*Clinically proven to boost
immune system performance
in as little as 6 weeks*

LENTINEX[®] – The Immune System Booster

THE IMMUNE SYSTEM

The immune system is a network of cells, tissues and organs that work together to defend the body against attacks by “foreign” invaders¹. Without an immune system, the body would be exposed to the harmful influences of pathogens and other toxic substances that can compromise the overall wellbeing of an individual.

Types of pathogen



The immune system can be divided into two main parts: the innate (natural) immune system and the adaptive immune system. The main tasks of the body’s immune system are²:

- ✓ Neutralizing and removing pathogens that have entered the body
- ✓ Recognizing and neutralizing harmful substances from the environment
- ✓ Fighting against the body’s own cells that have changed due to an illness, for example cancerous cells

DIFFERENTIATION BETWEEN SELF AND NON-SELF SUBSTANCES²

It is important that the immune system can differentiate between “self” and “non-self” cells, organisms and substances. Typically, the body should not work against its own healthy cells.

The immune system can be activated by many “non-self” substances, called antigens. The proteins on the surfaces of bacteria, fungi and viruses, for example, are all antigens. When the antigens bind to special receptors on the defense cells, a series of cell processes is started. Then the immune system can recall stored “memories” in order to quickly be ready to defend against known pathogens. The body’s own cells have surface proteins as well, but the immune system does not work against them, since it has already learned at an earlier stage to specifically identify these cell proteins as “self.” If the immune system identifies the cells of its own body as “non-self,” it is called an autoimmune reaction.

THE INNATE AND ADAPTIVE IMMUNE SYSTEM

The evolutionary, **innate immune system** is not specific and has no memory. It provides a general defense against pathogens, so it is also called the nonspecific immune system². The innate system is programmed to react to “danger signals” that are characteristic of commonly encountered pathogens or pathogen-infected cells. Phagocytes, natural killer cells, and the complement proteins can attack immediately, because these weapons are already in place. By working together, members of the innate system team provide a fast and effective response to common invaders. The innate system also plays a crucial role in alerting the adaptive immune system to danger.

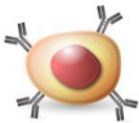
In the **adaptive immune system**, particular agents such as antibodies target very specific pathogens that the body has already had contact with. This is why it is also called learned defense or a specific immune response. By constantly adapting and learning, the body can fight against bacteria or viruses that change over time.² B-cells and T-Cells are important components of the adaptive immune system.

KEY CELLS IN THE IMMUNE SYSTEM



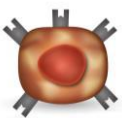
Natural killer

There are two main types of T-cells: helper T-cells and killer T-cells. Helper T-cells stimulate B-cells to make antibodies and help killer cells develop. Killer T-cells directly kill cells that have already been infected by a foreign invader⁴.



B Cell

B-cells fight bacteria and viruses by making Y-shaped proteins called antibodies, which are specific to each pathogen and are able to lock onto the surface of an invading cell and mark it for destruction by other immune cells.⁴



T Cell

NK cells belong to the innate immune system and form a first line of defence against a wide variety of pathological challenges. Particularly, they provide protection against viral and bacterial infections and they help to detect and limit the development of cancer⁵.

LENTINEX®



LENTINEX® is a liquid product obtained from the fermentation of *Lentinula edodes*, which is more commonly known as the Shiitake mushroom. This clear, light brown liquid contains free glucose, protein and the β -glucan polysaccharide Lentinan, which has an extensive history of use as a medical aid in Asia, Europe and North America.

Produced using a proprietary, patented process, LENTINEX® generates completely soluble β -glucans with high molecular weight to aid in absorption while preserving the natural triple helix configuration. Due to its highly efficacious ingredients, only a small daily dose of LENTINEX® is necessary to initiate enhancement of the immune system. Its signature combination of a triple helix structure, high molecular weight, completely soluble β -glucan and 100% natural ingredients all work in concert to product a high immune stimulating effect.

Currently there are no other β -glucan products like LENTINEX® on the market that provide the same profound immune stimulating effect due to its triple helix structure

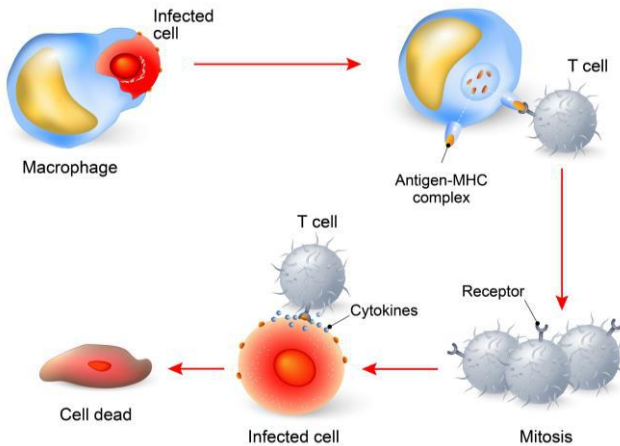
β -GLUCANS

Lentinan, a β -glucan is the main biologically active substance found within medicinal Shiitake mushrooms (*Letinus edodes*). It is characterized as a high molecular weight polysaccharide organized in a triple helix structure. These mushrooms have long traditional uses within Asian cultures for their various medicinal properties, which include its anti-thrombotic activity and its ability to reduce blood cholesterol levels. β -glucans are able to directly activate leukocytes to stimulate phagocytic, cytotoxic and antimicrobial activity as well as the production of pro-Inflammatory mediators, which are necessary to effectively eliminate pathogens from the body.

HOW DOES LENTINEX[®] WORK?

Cellular experimental models and animal studies have demonstrated that the extracts of Shiitake mushroom have anti-viral and anti-tumor properties. These properties occur through the stimulation of immune cell maturation, differentiation or proliferation in host defence mechanisms against cancer or infection.

IMMUNE RESPONSE



Lentinan is able to improve immune cell function through the activation of natural killer cells and the stimulation of helper T-cells. Natural killer cells are a type of white blood cell, which protect against viral infections as well as the formation of tumors within cells.

Helper T cells support the immune activity of other cells by releasing cell signalling proteins that modulate activity between the cell based and humoral immune responses. Additionally, Lentinan inhibits the synthesis of prostaglandins, which are normally responsible for slowing T-cell differentiation, and affects suppressor T cell activity. Lentinan stimulates peripheral blood lymphocytes *in vitro* to increase IL-2-mediated lymphokine-activated killer cell and natural killer cell activity. Increased production of interleukins has also been observed with lentinan supplementation. These cells are responsible for promoting the development and differentiation of T and B-cells. Lentinan is able to act as a T-cell immune adjuvant, to restore and potentiate helper T-cell functions.

CLINICAL TRIAL

STUDY DESIGN

A double-blind, cross-over, placebo-controlled study⁶

PURPOSE

To evaluate the effect and safety of a beta-glucan from *L. edodes* mycelium in LENTINEX[®]

PARTICIPANTS AND METHODS

A total of 42 elderly subjects (both male and female over the age of 65) were randomly allocated to two groups. They were orally given either 2.5mg/day LENTINEX[®] or a placebo (cellulose) for six weeks. After a 4-week washout period, the subjects received the alternate treatment for another six weeks.

At the randomization visit and all following visits, additional 12-hour-fasting blood samples were analyzed for T helper cell (CD4+), T cytotoxic cell (CD8+), total T cell (CD3+), NK cell (CD56+), and B cell (CD19+) counts, and to determine the levels of immunoglobulins IgM, IgG, IgA, and complement C3. Cytokine analyses (IL-8, IL-10, IL-12) and tumor necrosis factor (TNF- α) were also performed⁶.

RESULTS

When a subgroup with pre-treatment values below the group median at entry was analyzed, a high statistical difference in response in B-cells was observed (Figure 1)

Figure 1 shows the increase in B-cells from zero-time (pre-treated) to after 6 weeks of treatment with LENTINEX[®]. The differences between the B-cells in the LENTINEX[®] group compared to those number of B-cells in the control (placebo) group was statistically significant, $p=0.017$.

Apart from showing this one critical immune marker responding to LENTINEX[®] supplementation, the results from the study indicated that beta-glucans are most effective when the immune system is not optimal. Therefore, the intake of supplements like LENTINEX[®] will probably work like prophylactics, keeping the immune system alert (i.e. "immune surveillance")⁶

Change from Untreated Subgroups (< median), B-cells (CD19⁺)

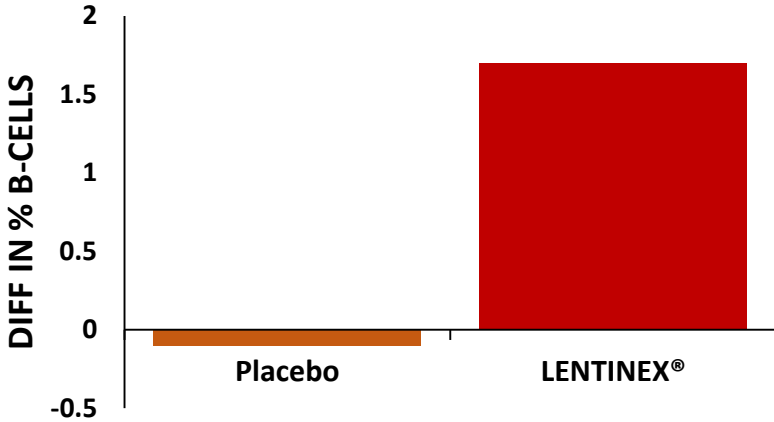


Figure 1: LENTINEX[®] was able to prevent the fall in B-cells observed in an elderly population. The difference between the treatments were significant, $p=0.017$

	LENTINEX [®] pre-treatment mean ± SD	LENTINEX [®] 6 weeks treatment mean ± SD	Placebo pre-treatment mean ± SD	Placebo 6 weeks treatment mean ± SD	Difference (Lent – plac) mean ± SD
T helper cells CD4+(%)	53.07 ± 9.51	51.95 ± 9.59	53.62 ± 9.56	52.14 ± 9.12	0.37 ± 6.65
T cytotoxic cells CD-8+ (%)	24.66 ± 9.81	25.08 ± 8.87	24.22 ± 10.41	24.74 ± 10.73	-0.10 ± 3.22
T-cells CD3+ %	72.77 ± 9.52	71.3 ± 10.12	72.79 ± 9.47	71.86 ± 9.43	-0.48 ± 5.97
B-cells CD19+ %	12.54 ± 4.78	12.98 ± 4.94	13.20 ± 5.12	12.63 ± 5.68	1.14 ± 2.76
NK-cells CD56+ %	11.71 ± 5.92	13.82 ± 7.81	11.33 ± 6.29	13.29 ± 7.59	0.15 ± 7.66

Table 1: Immune cellular responses. A significantly higher number of circulating B-cells was observed during the supplementation with the beta-glucan as compared to placebo

CLINICAL TRIAL – ANIMAL STUDIES

An increase in B-cells was observed in early safety and efficacy studies in mice and rats. B-cells almost doubled in mice from 16% in controls to 25% after an oral intake of LENTINEX®.

The author of the study suggested that the increase in B-cell and monocytic populations could be related to the decrease in the immunosuppressive Interleukin-10 (IL-10). Increases observed in B-cell and monocyte populations as well as increased interferon-gamma (IFN- γ) levels may suggest that LENTINEX® induces an immune-stimulatory response.

The School of Veterinary Medicine at Louisiana State University used a mouse model to determine the effect of oral LENTINEX® treatment on the colonization load of *Helicobacter pylori*. LENTINEX® treatment resulted in a statistically significant increase in antibody response compared to the non-treated mice ($p=0.033$). An average 256-fold increase in antibody production was observed in LENTINEX® treatment animals compared to non-treated (Figure 2). The increase in antibodies is an expression of increased matured B-cells, which in the presence of antigens produce specific antibodies directed against the antigens.

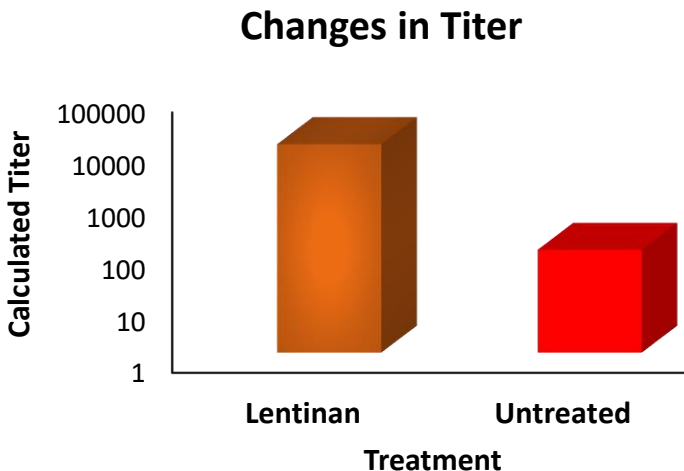


Figure 2: Difference in antibody titer after treatment with LENTINEX® compared to controls.

SUPPLEMENT INFORMATION

Recommended Use:

Supports immune health.

Medicinal Ingredients (per mL):

Beta Glucan1 mg

Directions for use:

Take half a teaspoon (2.5 mL) with meal once daily.

Duration of use:

For use beyond 6 weeks, consult a healthcare practitioner.

Storage:

Store at room temperature.

Safety & Drug Interactions:

Keep out of reach of children. Consult a healthcare professional prior to use if you are pregnant or breastfeeding or if you suffer from an immune system disorder or if you are taking immunosuppressants.

LENTINEX® has been registered with Health Canada; the Health Canada NPN number is: 80049210.

FAQs

- 1. How should LENTINEX® be taken?**
2.5 mL (half a teaspoon) with a meal once daily. LENTINEX® should only be taken by individuals 18 years of age or older.
- 2. Who should take LENTINEX®?**
Individuals who are looking to improve their overall immune function, optimize immune cell performance to build a more resistant immune system or improve overall wellness can benefit from taking LENTINEX®.
- 3. Are there any known side effects of taking LENTINEX®?**
No, LENTINEX® exerts no side effects on the individual.
- 4. Has LENTINEX® been clinically tested?**
Yes, there are several trials that evaluated the efficacy of LENTINEX® and have shown to greatly improve immune responses within 6 weeks.
- 5. What benefits can my patient expect from LENTINEX®?**
B-glucan in Shiitake mushrooms has been documented to stimulate the function of macrophages and directly activate leukocytes to stimulate phagocytic, cytotoxic and antimicrobial activity as well as the production of pro-inflammatory mediators. These are necessary to effectively eliminate pathogens from the body and boost immune system performance while providing energy and improving overall wellness.
- 6. Where is LENTINEX® available?**
LENTINEX® is available in stores and online at www.xediton.com/product/lentinex or by calling 1-905-286-9111, email: customerservice@xediton.com

CONTACT US

For more information, please visit www.xediton.com/product/lentinex or call +1 905 286 9111



Xediton
Pharmaceuticals Inc.

XEDITON PHARMACEUTICALS INC
2000 Argentia Road
Mississauga, ON
L5N 1W1
Email: customerservice@xediton.com

REFERENCES

¹ Understanding the immune system: how it works (Vol. 3). (2003).² How does the immune system work? (2016, September 21). Retrieved from <https://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0072548/> ³ Sompayrac, L. (2016). *How the immune system works* (Vol. 4). Chichester: Wiley Blackwell. ⁴ Tan, M. A. (2017, May 30). What's the Difference? B-cells and T-cells | CTCA. Retrieved from <http://www.cancercenter.com/discussions/blog/whats-the-difference-b-cells-and-t-cells/> ⁵ Natural Killer Cells. (n.d.). Retrieved from <https://www.immunology.org/public-information/bitesized-immunology/cells/natural-killer-cells> ⁶ Gaullier, J. et al. Supplementation with a Soluble Beta-Glucan Exported from Shiitake Medicinal Mushroom, *Lentinus edodes* (Berk.) Singer Mycelium: a Crossover, Placebo-Controlled Study in Healthy Elderly. *International Journal of Medicinal Mushrooms*, 13(4), 319-326.



LTDB01

LENTINEX® – The Immune System Booster