

Del-Immune V® Profile
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Del-Immune V® is the dry enzymatic lysate powder of a special lactic acid bacteria *Lactobacillus rhamnosus (DV Strain)*. The active ingredients are appropriately sized DNA fragments and cell wall peptidoglycan fragments produced from the above culture.

Active ingredients (capsule)

Finished product: soluble vegetable capsules containing 25 milligrams of active ingredients (appropriately sized DNA fragments and cell wall peptidoglycan fragments of the above culture) and purified cellulose as a filler. The finished formulation contains no live cells!

Product shelf life is two-plus years. The service life is specified on the label. Special storage conditions and refrigeration are not required.

Indications: For immediate immune system support. Reports indicate the alleviation of symptoms of acute and chronic influenza, cold and cough. The product stops the development of diseases or alleviates symptoms, shortens infection duration and prevents complications.

Del-Immune V® is indicated as a supporting medication during antibiotic therapy for: bacterial, viral (especially HCV) and fungal infectious diseases; skin infections; bronchial and pulmonary diseases; allergic conditions of varying degrees; asthma; chronic fatigue and fibromyalgia.

Del-Immune V® is indicated as adjunctive medication in oncological diseases during chemotherapy and radiotherapy.

Effectiveness of Del-Immune V® is predetermined by its ability to affect various components of the innate and adaptive immune systems, both specific and non-specific links, thus controlling coordination of the immune response by Th1 or Th2 pathways, depending on the immune status of the body.

Studies performed at the University of Colorado in Boulder, CO, and Tiburon Laboratories, in Tucson, Ariz., revealed that the effect of **Del-Immune V®** is induced by the mechanisms of the main active ingredients influencing the immune system; specifically, muramylpeptides and nucleoproteins that occur naturally within cell fragments during the probiotic culture phase. These components stimulate the production of the cytokine line (IL-1), tumor necrosis factor (TNF- α), IL-2, IL-6, IL-8, IL-12 and gamma interferon (IFN- γ), which, in turn control production of T-lymphocytes, B-lymphocytes, natural killer (NK) cells and phagocytes that coordinate the immune response, depending on the nature of the aggressive agent by Th1 or Th2 pathways respectively.

Role of the active cytokines: IL-1 is mainly secreted by activated macrophages, as well as other cell types. In monocytes and dendritic cells, IL-1 is secreted by activated macrophages which stimulate production of other cytokines and cytokine receptors by T-cells the same way as they stimulate B- cell proliferation. There are two known types of IL-1; IL-1 alpha and IL-1 beta. Both are equally active, but have different structures. IL-1 alpha is mainly membrane-associated, whereas IL-1 beta can circulate freely. Both bind to the same receptors, two types of which are found in various cells. Examples are T and B-cells, macrophages, neutrophils, bone marrow, fat cells, osteoclasts, brain cells, the cells of the adrenal glands, endothelium cells of the blood vessels and cells of the smooth muscles.

The activity of IL-1 is expressed in pyrogenic action, which produces the main portion of the body's inflammatory response to infection agents. IL-1 also increases the expression of the adhesive factors of the endothelium cells, thus supporting the transmigration of the leucocytes attacking pathogens. IL-1 also takes part in the operation of the thermoregulatory center in hypothalamus, thus increasing body temperature, which helps the immune system fight infection. IL-1, an endogenous pyrogen, increases activity of the natural killer cells (NK cells), increases production of interferon and ensures transmission of signals allowing for the growth and development of B-cells. IL-1 is important for regulation of hematopoietic function, and plays the key role in the evolution of autoimmune diseases.

IL-2 is secreted by T-cells and ensures their proliferation and differentiation. IL-2 is important for T-cell maturation in the thymus while the cells develop into the T-Regs (Regulatory T cells) which protect other T-cells from reacting to their own antigens ("self-antigens"), thus preventing auto-immune reactions. This activity ensures a distinction between the "friendly" and "alien" antigens for the immune system.

IL-2 is responsible for T-cell immunological memory. This cytokine activates macrophages, NK-cells and T-cells and acts as the autocrine factor for components of the Th1 paths of the immune response. It is the most important cytokine in the immunological system. When exposed to antigens, T-cells produce IL-2 and IL-2 receptors. During the first 24 to 48 hours of activation, T-helpers start synthesizing IL-2 and its receptors, exhibiting a high affinity toward membranes. These IL-2 receptors act by an "on-off" action.

The IL-6 cytokine is secreted by macrophages and T and B-cells inherent in the Th2 response, and is expressed in the pyrogenic action of the response. IL-6 intensifies terminal differentiation of B-cells, prolongs the acute phase of the hepatocytic response and it is an anti-inflammatory cytokine. It determines the immune response during trauma, particularly if there are burns or other skin damage causing inflammatory processes. Osteoblasts secrete IL-6 for stimulation of osteoclast formation. IL-6 is one of the most important mediators of the temperature reaction (fever) and the acute phase of this response. In the muscle and fat tissues, IL-6 stimulates energy mobilization, thus causing increased body temperature. **IL-6** is secreted by macrophages in response to penetration pathogen-associated molecular patterns (PAMP) interacting with Toll-like

receptors (TRL) and are represented by the activated macrophages. IL-6 is also a myokine; a cytokine that produces muscle tissue and increased response to muscle contraction.

Cytokine IL-8 is a peptide produced by various cells activated and recruited by polymorphonuclear leucocytes in inflammatory processes. These process possibly occur during birth. IL-8 is also the chemotaxis factor for many immune system cells by being a chemokine, or a messenger of inflammatory response, specifically the Neutrophil Chemotactic Factor.

Cytokine IL-12 is produced by macrophages and lymphoblastoid B-cells in response to antigen stimulation. IL-12 is involved in differentiation of new I-cells in the Th1 cell system, ensuring pathogen stability. IL-12 is known as a T-cell stimulant, promoting T-cell growth and development. This cytokine stimulates IFN- γ and TNF- α production in T and NK-cells. IL-12 reduces IL-4 production, inhibiting IFN- γ production. IL-12 plays an important role in activation of NK-cells and T-lymphocytes, stimulating cytotoxic lymphocyte activity. It provides a connection for IL-2 and IL-12 transduction signals in NK-cells. IL-2 stimulates expression of the two IL-12 receptors; beta1 and beta2. IL-12 is anti-angiogenic, thus blocking origination of new blood vessels. It can be used as an anti-cancer drug. IL-12 stimulates autoimmune reactions and also determines the Th1 immune response direction.

IFN- γ is produced by Th1 cells, CD4+ and CD8 and activated NK-cells. It participates in activation of macrophages, neutrophils, NK-cells and lymphocytes, enhancing anti-microbial and anti-tumor effects. IFN- γ increases cell-mediated response and inhibits humoral immune response, acknowledging B-cell activity via production of IgG2a. It activates macrophages, stimulates a slowed hypersensitivity response and has anti-viral activity. IFN- γ increases the expression of the major Histocompatibility Complex II. It also increases IL-1 and IL-2 production and reduces IgE, G1, G2 G3 synthesis (its action is contrary to IL 4).

TNF- α factor is produced by macrophages and NK-cells. It regulates the immune response by the Th1 path, expressed in pyrogenic action, and activates the endothelial cells. TNF- α increases polymorphonuclear neutrophils activity and macrophages and increases activity of the Major Histocompatibility Complex-I. It regulates necrosis and apoptosis of cancer cells. TNF- α activity is similar to IL-1. They both induce systemic inflammation, either jointly or separately. The lipopolysacharides of gram-negative bacteria (LPS) stimulate TNF production. It is believed that TNF- α upregulates VIH replication and participates in increasing fat cell fat consumption, increasing muscle cell metabolism. TNF- α is responsible symptoms associated with bacterial infections, such as septic shock, fever, muscle pain, lethargy, headache and inflammation.

When Del-ImmuneV® is administered, multiple positive effects in a wide range of diseases are accounted for by the ratio of cytokines involved in the immune response of the organism.

For example, IL-1 ensures a response to infectious pathogens because it stimulates the inflammatory process and capture of the pathogen by macrophages, followed by elimination of the pathogenic cells. In the case of viral diseases, the effect is accounted for by the IL-1 stimulation of interferon production.

Del-Immune V® increases the activity of the NK-cells, which accounts for its effectiveness in oncology disease. In addition, the presence of IL-1 contributes to hematopoiesis regulation, or blood cell production needed by an organism exposed to chemotherapy and radiation agents.

At the same time, the presence of IL-2 in the body's immune response after administration of Del-Immune V® guarantees no autoimmune effects, particularly in patients with expressed autoimmune pathologies. IL-2 helps produce antibodies for infection pathogens guaranteeing long-lasting protection of the organism. This cytokine acts as the main "coordinator" between humeral and cell immunity reactions, is an excellent adjuvant substance for vaccination, ensures active origination of antibodies and the possibility of reducing the dosage and aggressiveness of a vaccine. Effectiveness of Del-Immune V® as an adjuvant has been noted by physicians who have administered vaccinations with the Del-Immune V®.

The presence of IL-6 harmonizes the immune system's response to tissue damage in traumas, burns and surgical wounds, accelerating recovery. IL-6 also stimulates bone tissue growth, accelerating fracture consolidation and the healing of other bone injuries.

The presence of this interleukin ensures the activation of energy processes. This activation is expressed in a significant increase of vitality. This has been confirmed as the first observable effect with all kinds of diseases by those who have administered Del-Immune V®, most noticeably in Chronic Fatigue Syndrome patients.

IL-8 supports the efficiency of many cells of the immune system.

The main activity of IL-12 is fighting tumor cells by gamma interferon stimulation, tumor necrosis factor (IFN- γ and TFN- α) and the ability to block the origination of new blood vessels in tumor tissues. IL-12 actively participates in cell and humoral immunity coordination, reducing high production of IL-4 which blocks the activity of IFN- γ .

The presence of IFN- γ ensures effectiveness of Del-Immune V® in infectious diseases, viral lesions and oncological diseases.

TFN- α is an active element an organism's anti-tumor defense and takes an active part in metabolic processes, increasing consumption of fat by fat cells and increasing production of protein components.

Analysis of the molecular mechanism of Del-Immune V® function explains its curative and prophylactic effects in diseases of various origins as well as autoimmune and allergic reactions. Del-Immune V® is representative of a new generation of biological

immunotherapeutic substances whose main action is coordination of the activity of individual links of the immune system in accordance with the natural mechanisms created by evolution.

Contraindications : Multiple Sclerosis (MS) and Lupus.

Cytokines (the anti-inflammatory protein) associated with the MS process are not bound to cytokines activated by Del-Immune V®.

Compatibility with medicines and nutrient substances: There is no known incompatibility of Del-Immune V® with any medicinal product, food supplement or food. Del-Immune V® is compatible with chemotherapy and radiation therapy.

Safety: No adverse effects have been detected while using Del-Immune V®. It can be used for long time periods with antibiotics, chemotherapy, radiotherapy and probiotics. Like all medications and supplements, keep Del-Immune V® away from children under six months.

Those sensitive to the active ingredients in Del-Immune V® might develop diarrhea. If so, Del-Immune V® should be taken with food.

Dosages:

For Support of the immune system: Two capsules in the morning and in the evening for four days, then two capsules every day for five days.

Viral infections: Three capsules three times a day for two days. After two days, reduce the dosage to two capsules twice a day until the symptoms disappear; one capsule a day thereafter.

Supporting dose: One or two capsules daily.

Effectiveness: usually within six to eight hours. In case of respiratory diseases, earlier administration of Del-Immune V® produces a faster response.

The rate of the immune response is accounted for by the fact that DNA fragments and cell wall peptidoglycan fragments (the active ingredients of **Del-Immune V®**) act as pathogen-associated molecular patterns (PAMP), interacting with innate immunity receptors (**PRR** – Pattern Recognition Receptors). This interaction is characterized by an immediate reaction without generation of an immunity memory.

Clinical observations in the United States, Russia and the Ukraine confirm the disappearance of cold and influenza symptoms as well as significant reduction of the disease's duration after administration of the product in the above dosages.

Del-Immune V® combined with antibiotic therapy contributes to a reduction of dosages and quicker recovery without dysbacteriosis.

Del-Immune V® reduces the complications and adverse effects of chemotherapy and radiation. This formula can be used as an adjunct in oncology, enabling patients to tolerate full courses of chemo and radio therapy. Del-Immune V® minimizes the usual adverse effects of cancer therapies. Addition benefits include stabilized hemopoetic factors, particularly leukocytes; increases energy levels and dysbacterioses prevention. Del-Immune V® maintains the activity of the digestive tract, particularly when combined with probiotic medicines.

These unique characteristics of Del-Immune V® come from the unique culture of the *Lactobacillus rhamnosus (DVstrain) bacteria*. The specific traits of the culture relate to cell wall structure fragments enhanced by technically advanced culturing conditions. The DNA fragments possess an ability to affect vital components of immune system cells, contributing to a restoration of the balance of the cytokines, which originate by the Th1 or Th2 paths, i.e. regulating disorders associated with prevalence of either path.

It is currently known that a majority of probiotic cultures primarily increase Th1 response and subsequent cytokine synthesis. Some probiotics have demonstrated a regulation the Th2 pathway. Discovery of probiotics cultures capable of coordinating the balance of both paths is quite rare.

There are individual cases known to date regarding the immunological activity of DNA fragments of probiotic cultures, which are preconditioned by the mandatory presence of a specific sequence of nucleotides.

The latest research with the NK-cell quantitative and qualitative content determination method (Natural Killer and Cytotoxic T cell Flow Cytometric Profile, Becton Dicenson Dual Laser FACS Calibur, TIBURON Diagnostic Laboratories of Tucson, Ariz.) has demonstrated that Del-Immune V® causes induction of quantitative increase of the natural killer cell synthesis and multiple increase of their cytotoxicity against cancer cells.

The product was registered July 15, 2002 by the U.S. Food and Drug Administration (21 U.S.C. 350b (a)(2)) as a food supplement for immediate immune system support with the brand name of Del-Immune V® (United States Patent and Trademark Office, Reg.No. 3,023,625. Registered Dec.6, 2005), and is manufactured by Pure Research Products, LLC (Boulder, Colorado, USA , www.del-immune.com).

Innate immunity	Adaptive immunity
Pathogens are recognized by receptors inherent to the species	Pathogens are recognized by receptors originating incidentally (non-incidentally)
Receptors have a broad specificity and recognize many general molecules, for example, PAMP, or pathogen associated molecular patterns are not capable of fast evolution	Receptors have a narrow specificity, recognizing epitopes,
PAMPs are polysaccharides and	Majority of pathogens differ in

polynucleotides which are different in different species of pathogens, yet are NEVER present in the host	polypeptides (proteins)
	In the vertebrates, those receptors are produced by B cells (BCR) and T cells (TCR)
<i>Response of the immune system – IMMEDIATE</i>	<i>Response is generated slowly– within 3-5 days</i>
The immune memory is not generated	The immune memory is generated in the previous interaction

This table will be used as a supplement to the mechanism of action.