M-Gard®

TARGETED IMMUNE ENHANCEMENT

BIOTEC BETAGLUCANS

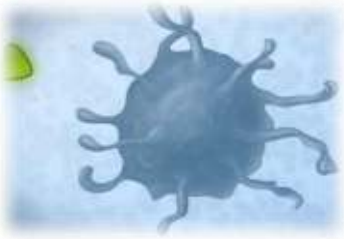
M-Gard® is a purified bioactive beta-1,3/1,6-glucan, a naturally occurring complex polysaccharide found in the cell walls of baker's yeast. M-Gard® enhances your body's vital defense mechanisms against pathogens such as bacteria, virus, fungus etc. Studies have shown that M-Gard® exerts immunomodulatory effects *in vitro* and *in vivo* in experimental animal and human models. M-Gard® represents an excellent immune enhancing compound for human use.

How M-Gard® enhances your immune system

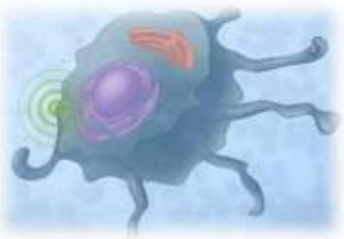
The primary function of the immune system is to protect the body against infections from pathogenic viruses, bacteria, fungi and parasites. It also has a key role in removing dead body cells and repairing damage caused by strong light, irradiation and environmental toxins. The immune system may sometimes over-react or be brought out of balance, resulting in immune disorders like rheumatoid arthritis and certain types of asthma. The immune response may also be suppressed, for many reasons, resulting in reduced overall resistance to infections and impaired ability to counter development of cancer. Thus, a properly functioning immune system is a prerequisite for good health.

M-Gard® interacts with specific receptors on immune cells like monocytes, macrophages, dendritic cells and natural killer cells. These immune cells are present everywhere in the body. On mucous surfaces and underlying mesenchyme tissues, they constitute a powerful defensive force that arrests and destroys infectious microbes - at their port of entry into the body.

The interaction between M-Gard® and its specific receptors on immune cells in epithelia and superficial connective tissues, corresponds to an initial event in a natural infection process and places these cells on highest alert to counter any subsequent infection.



Step 1: The unique molecular structure of the bioactive M-Gard® lets it bind to specific receptors on immune cells. This interaction is known to occur through different cell surface receptors — most notably, the Dectin-1 receptor.



Step 2: Binding of M-Gard® to a receptor triggers cellular signaling cascades, which modulates the immune cell that are part of the innate immune system.

Step 3: The underlying mechanism of M-Gard® is represented by modulation of the innate immune system, leading to enhanced immune responses upon infection (enhanced secretion of cytokines).

White blood cells with beta-1,3/1,6-glucan receptors constitute the backbone of the body's innate immune system, which is the first-line of defense against most infections. The same cells constitute the mastermind of the entire immune system - they control and adjust how the so-called specific immune system responds to infections, vaccines and allergens.

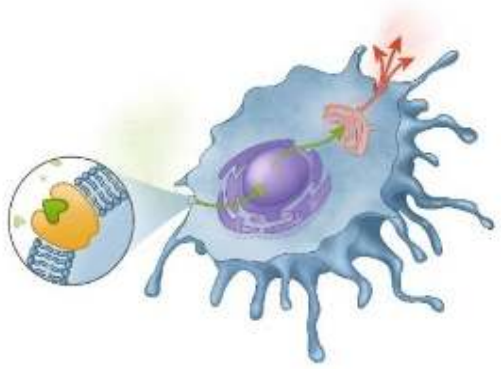
The use of M-Gard® that modulates innate immune mechanisms has therefore becom a promising strategy for controlling and countering immune related disorder. Frequently recurring infections and colds, allergy and asthma, arthritis pain and chronic fatigue are conditions that in some way or another are related to weakened immunity or inadequate immune reactions

Why choose M-Gard®

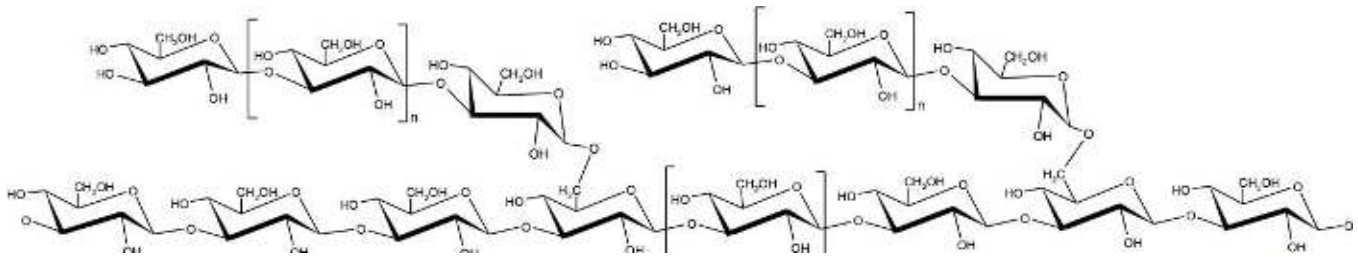
The molecular structure and branching between the glucose molecules is essential for immune enhancing activity of be- ta-1,3/1,6-glucans, and this is what makes M-Gard® so potent compared to other types of glucan.

Biotec Pharmacon ASA has developed and patented processes for extracting the beta-1,3/1,6-glucan present in baker's yeast without damaging the branching points or side chains, ensuring that the purified M-Gard® molecule remain it's crucial bioactivity.

The common feature of glucans which have the ability to activate the immune system, is a chain of glucose molecules linked together in so-called beta-1,3-linkages. However, to exert high bioactivity there must also be "branches" of glucose molecules attached (by beta-1,6-linkage) to this beta-1,3-glucan chain. The branched beta-glucans, called beta-1,3/1,6-glucans are very potent immunemodulators.



The unique molecular structure of the bioactive M-Gard® lets it bind to specific receptors on immune cells. Binding of M-Gard® to a receptor triggers cellular signaling cascades, which modulates the immune cell leading to enhanced immune responses upon infection. The unique structure of M-Gard® is what makes M-Gard® so much more potent compared to other types of glucan.



The unique structure of M-Gard®

Other glucans, such as beta-glucans from barley, oats and other grains have completely different chemical structure than M-Gard®. Such plant beta-glucans contain a large proportion of beta-1,4-linakages and they are not very effective with regard to immune modulation.

Benefits

Every day your immune system is under attack from virtually millions of pathogens, like bacteria, virus, fungus etc. A strong immune system is what keeps you healthy and the pathogen invaders away. Any slight change, be it increased pollution, stress, overwork or poor diet, can lower your resistance and tip the scales in favor of the pathogens. M-Gard® keeps you healthy by boosting your immune system and significantly raising your level of resistance, M-Gard® is your insurance against pathogens.

M-Gard® helps support healthy immune function, in a large variety of different situations. Studies have demonstrated the M-Gard® can:

- Strengthen the immune system
- Enhance the protection against pathogens
- Protect in periods of exceeded stress
- Promote healthy inflammatory responses
- Support respiratory health

Quality

M-Gard® is produced in the most northern beta-glucan production facility on the globe. The product is the outcome of first class scientific efforts combined with the extremely high Norwegian quality standards.

- Approved as Novel food in EU
- Naturally-derived
- Non-GMO
- Allergen-free
- ISO 13485:2012
- GMP
- Halal & Kosher certified
- GRAS
- Informed Sport certified (M-Gard® Sport)

Research

The company has closely collaborated with leading research groups in Norway, Europe and the United States, executing projects that have revealed novel
insights for the mode of action and potential uses of beta-glucans. Since the early 1990's, beta-1,3/1,6-glucan has been introduced as a feed additive to improve the health and performance of farmed shrimp, fish, pigs, chicken, laying hens, calves, ,horses and pets.

Building upon the foundations it laid in animal health and consumer products, Biotec BetaGlucans has invested major resources in R&D to better understand how beta-1,3/1,6-glucan's modulation of immune mechanisms can be used to treat or prevent immune-related disorders and diseases. As a result, the company has developed beta-1,3/1,6-glucan products for human consumption and advanced wound healing.

M-Gard® is supported by numerous animal and human trials and in various applications including safety and mechanism-of-action studies. The vast majority of our studies and trials have been published in peer-reviewed science or medical journals.

The technology behind M-Gard® has been successfully developed for several alternative indications and applications including nutraceuticals (enhanced resistance against infections), wound care (improved healing of chronic wounds; product Woulgan®), as well as treatment of oral mucositis, certain bowel diseases and cancer treatment (immunotherapy).

In cancer treatment, our Soluble Beta-Glucan (SBG®) is given peroral to increase tumor-killing activity of white blood cells. Phase I part (safety) of study (15 patients) finalised in 2013. Phase II part (efficacy) of study ongoing aiming to recruit 130 patients (145 in total), currently 99 patients treated, expected to recruit the remaining patients during 2018. For more information, please consult: https://biotec.no/beta-glucans/ and https://woulgan.com.

Abstract of clinical and preclinical studies done with beta-glucan from Biotec BetaGlucans AS

"Proof-of-concept", double blind, parallel group study comparing the immune modulating effect of M-Gard® with that of placebo (cellulose)

Comparing the immune modulating effect of M-Gard® with that of placebo (cellulose). This study was carried out with 140 healthy individuals who according to standards in Norway could be defined as having mild to moderate hypercholesterolemia, but in some other countries were regarded as not healthy and subject to any cholesterol lowering treatment. The primary objective was to record eventual effects on blood CRP levels, since there is a likely link between elevated blood cholesterol and inflammations that may result in increased CRP. In accordance with this hypothesis, the average CRP-level in the study group went down compared to placebo after daily intake of M-Gard® for 8 weeks. But since the majority in the study groups were healthy, most of the analytical figures for CRP were within the healthy range, whereas high values of CRP dropped off in the study group compared to placebo.

M-Gard® reduced sick leave by 44.2% in a one-year study

One-year study of healthy Norwegian ski athletes taking/not taking M-Gard® dietary supplement daily. The number of sick leave days were related to symptoms like cold, flu and fever. The group taking M-Gard® daily reduced sick leave with 44.2% compared to the control group. The result from this study indicates that a daily intake of M-Gard® enhances your protection against bacterial and viral infections.

Oral administration of a new soluble branched beta-1,3-D-glucan is well tolerated and can lead to increased salivary concentrations of immunoglobulin A in healthy volunteers

In this study oral administration of our clinical grade, soluble β-glucan, SBG® was investigated primarily for assessment of safety and tolerability in an early phase human pharmacological study (phase I). Eighteen healthy volunteers were included among non-smoking individuals. Groups of six individuals received SBG® 100 mg/day, 200 mg/day or 400 mg/day, respectively, for four consecutive days.

A statistically significant increase in the saliva Immunoglobulin A (IgA) concentration was observed in the high dose-level group. IgA is an antibody that plays a critical role in the immune function of mucous membranes. IgA is the major class of antibody present in the mucosal secretions of most mammals, represents a key first line of defense against invasion by ingested and inhaled pathogens at the mucosal surfaces.

Oral Administered Particulate Yeast Derived Glucan Promotes Hepatitis B Virus Clearance

This study demonstrate that M-Gard® exhibits potent antiviral and immunostimulatory effects in viral infection. Importantly, M-Gard® boosted HBV-specific T-cell immune responses in liver and promoted HBV clearance without causing liver damage. This study strongly indicates that M-Gard® might be a promising immunotherapeutic agent for the treatment of chronic HBV infection.

Dectin-1 plays a redundant role in the immunomodulatory activities of β-glucan-rich ligands in vivo

In this study they show that pre-treatment of mice with SBG®, our clinical grade, soluble β-glucan prior to infection with *S. aureus*, significantly increased the ability of mice to resist the infection, which corresponded to reduced weight loss and reduced pathology in the kidneys. The results from this study indicate that pre-treatment of mice with our clinical grade, soluble β-glucan, can provide better protection against systemic S. aureus infections.

Some clinical and preclinical studies done with beta-gulcan from Biotec BetaGlucans

Clinical research

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7. Oriental Yeast Company, *Survey on allergy symptoms in humans*. Internal information, 2004.
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Preclinical research

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5. Harnack U, et al., *Comparison of the effect of orally administered soluble beta-(1-3),(1-6)-D-glucan and of G-CSF on the recovery of murine hematopoiesis.* In Vivo.2010;24(1):59-63.
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