Beta Glucan - The Natural Healer
By Man Found Standing, Native American Practitioner

The immune system is used as the body’s natural defense against disease. One of the most important functions is its self/non-self recognition. The immune system will attack and defend against viruses, pathogens (germs) or anything else that might be considered a “foreign invader”. Every cell in the body has a display marker, a genetic locus or alternative DNA for identification. Any cell that does not display this marker is treated as an invader and is attacked. Sometimes, if the immune system is not working properly or weakened, it may start to attack the body. This may lead to such diseases as allergies, asthma, arthritis, chronic fatigue, diabetes, tumors, cancer, and so forth. A wide range of factors may restrict the immune
system response: old age, poor diet, mental or physical stress, radiation, toxins in the environment, and lack of sleep to name a few.

Science has done extensive research for the fight against diseases when the immune system does not work properly and over the years has focused on beta glucan research. Beta glucan, found in high concentrations in Shiaqga, has been determined to be an acceptable immune system modulator that binds and stimulates the macrophages (white blood cells) that attack foreign invaders (disease) and signals to other immune cells to move to the site of the infection or disease to speed up the healing process.

Macrophages are involved with the everyday process of detoxifying the body, performing intestinal flora maintenance, and preventing infection. When taking beta glucan orally (which is acid resistant), it passes through
the stomach unchanged. Macrophages in the intestine absorb the beta glucan that is circulated through the blood and lymph systems and release cytokines that stimulate immune activation. Beta glucan is a diverse group of sugar molecules that are found naturally in oats, barley, mushrooms, fungi, yeast, and bacteria. Some well-known benefits of beta glucan include:

- Production of healthy white blood cells. Stimulates and communicates to the immune system receptors: pattern recognition receptors (PPRs), Toll-like receptors (TLRs), killer activated /inhibitor receptors (KARs & KIRs), complement receptors, Fc receptors, B cell receptors, and T cell receptors.
- Encourages a higher number of macrophages in early inflammatory stages of repair (speeds the healing of wounds and infections). Enhances the
resistance from microbes, bacteria, and viruses. Lowers cholesterol.

- Regulates blood sugar and digestion
- Slows or reverses the aging process
- Prevents infections

A human research review on beta glucan, by Przomysl Spozysczy v. 56, 2002, pp 20-1, states:

“Dietary beta glucan enhances immunity by activation of macrophage cells, doubling their counts in 24 hours. Dietary beta glucan also acts as an antioxidant protecting the body against free radical damage and lowers blood cholesterol levels. Dietary beta glucan can be helpful in treatment of many immunity-related diseases.”

Research and applications:

"Clearly, there are numerous possible uses for an agent such as glucan, which is a potent stimulator of Hemopoietic activity. Currently, we [U.S. Armed Services] are using glucan to enhance Hemopoietic proliferation in conjunction with Hemopoietic injury induced by radiation."

"The soluble phosphorylated glucan are useful for promoting the wound healing process. The soluble phosphorylated glucan are also useful for prophylactic and therapeutic applications against neoplastic, bacteria, viral, fungal and parasitic diseases."


"Previous studies have demonstrated that glucan, a beta-1,3-linked glucopyranose polymer, isolated from the inner cell wall of Saccharomyces cerevisiae, is a potent macrophage stimulant and is beneficial in the therapy of experimental bacterial, viral, and
fungal diseases."

From the University of Toronto (European Journal of Clinical Nutrition. 56, 2002, pp. 622-8) beta glucan was given to humans.

“Addition of beta glucan predictable reduces the glycemic index while maintaining palatability..........making it a useful functional food component for reducing postprandial (after meals) Glycemia”. (In other words beta glucan helps normalize blood sugar levels and keeps them from rising.)

These excerpts are just a few that prove the wonders of beta glucan as a natural healer. The science and medical world have known about the benefits of beta glucan for over 30 years! Shiaqga with its therapeutic levels of beta glucan is a natural defense against disease that everyone should take,
whether it be to heal the body or as a preventative measure for good health.

Below is a more extensive description of beta glucan research.

Extant Research on Beta 1-3 glucans

Introduction
This article is from the Townsend Letter for Doctors and Patients Copyright© 1998 All Rights Reserved (...). Beta-1,3-D-Glucan: An Adjuvant Concept by Leonid Ber, MD

According to the Webster Medical Dictionary, adjuvant (from Latin ad-juvo, to give aid to) is a substance added to a drug product formulation which affects the action of the active ingredient in a predictable way. This term has been widely utilized in immunology, where it means a vehicle used to enhance antigenicity of vaccines (for example, Freund’s adjuvant). Much broader utilization of this term can be applied today to some naturally derived substances. This adjuvant concept closely relates to what is today referred to as a complementary/alternative modality.

Poly-branched beta-1,3-D-glucan is a naturally occurring polysaccharide that can be found in a variety
of fungal cells including cell walls of yeast, such as Saccharomyces cerevisiae, basidiomycetes, such as Lentinuluis edodes and Fometopsis pinicola, and to a very small degree from the hull of many grass seeds. As any other glucan (or polyglucose), it consists of glucose units linked together. For example, most starches are alpha-glucans. Out of different glucans, the beta-1,3-D-glucan configuration has been shown to act as a non-specific immune-activator.

Goldman, and later Czop, identified a specific receptor on the cells of macrophage origin that binds to the beta-1,3-D-glucan molecule. This receptor is a protein complex that appears to be present throughout the whole differentiation cycle of macrophages, starting in the bone marrow. Mature macrophages are found in virtually all the tissues including the central nervous system. When a macrophage encounters beta-1,3-D-glucan, it becomes activated. All the functions, including phagocytosis (ability to engulf foreign cells and particles), release of certain cytokines (intercellular hormones), and the processing of antigens are improved and brought up-to-date. Macrophages are extensively involved in everyday detoxifying processes, intestinal flora maintenance, anti-infective and anti-tumor protection and maintenance of overall health integrity. Although most of the research with this substance has been done in vitro and parenterally, later research at Baylor College of Medicine, sponsored by ImmuDyne, indicates the oral effectiveness of purified
beta-1,3-D-glucan (Wyde, 1989).

The integrity of beta-1,3-D-glucan taken orally differs from other food substances. This type of glucan is acid resistant so it passes the stomach virtually unchanged. Further, in the intestine there is a lack of a specific enzyme (beta-1,3-glucanase) that would break it down to glucose or di-glucose so as to be absorbed through the intestinal wall. On the other hand, there are macrophages that inhabit the intestinal wall and are able to pick up beta-1,3-D-glucan particles through beta-glucan receptors. Immediate activation of these cells follows and later, they are able to travel back to the local lymph nodes (Payers Patches) as a part of their natural antigen-presenting function, to release cytokines (IL-1, IL-6, GM-CSF, Interferons) and induce systemic immune activation.

The mechanism described above is called phagocytic transport and it is common for certain microorganisms. Studies conducted with oral application of C13 labeled glucan also support existence of phagocytic transport for beta-1,3-D-glucan.

An adjuvant concept of pharmacological application for beta-1,3-D-glucan was suggested by DiLuzio in the 70s. This article is an attempt to overview this concept from today's perspectives utilizing modern knowledge of oral effectiveness, and a specific transport mechanism of beta-1,3-D-glucan.
There is now enough data to support the use of beta-1,3-D-glucan as an adjuvant in several important medicinal applications.

1. Combination "glucan + anti-infective agent"
Beta-1,3-D-glucan itself can elicit broad anti-infective effects. The nature of macrophage activation induced by this compound is non-specific. Staphylococcus aureus, Eschericia coli, Candida albicans, Pneumocytis carinii, Listeria monococytogenosis, Leishmania donovani, Herpes simplex, Ascaris suum - this is an incomplete list of microorganisms, against which a protective effect of glucan has been established. This list, as you can see, includes bacteria, fungi, viruses and parasites. None of the anti-infective agents possess such a broad spectrum of activity. Unlike an antibiotic compound interfering with metabolism of a pathogen, beta-1,3-D-glucan is a substance that modifies host response to cells genetically different from the host.

Numerous studies support the theory that an antibiotic and a macrophage activator work synergistically.

Experimental peritonitis in rats was used to show synergy between widely used antibiotic ampicillin and glucan. A 100% survival was the result of the combination treatment, while glucan alone gave 30% survival, and ampicillin in the given dose elicited 65% survival (20% survival in the control group). All the
results were statistically significant (Lahnborg 1982).

A 56% survival was achieved when subtherapeutic doses of gentamycin was combined with intraperitoneally delivered glucan at just 0.1 mg/mice challenged with Escherichia coli. This was a very significant increase of survival rate, considering that either no treatment or this low dose of antibiotic alone, gave no protection from peritonitis (0% survival), while glucan alone gave 9% increase in survival. The difference between controls and the combination treatment was highly statistically significant (Browder, 1987).

Anti-fungal effect of beta-1,3-D-glucan from yeast cell wall is particularly interesting. It is known that glucan configuration in Saccharomyces cerevisiae resembles the one in Candida albicans. Glucan administered orally in mice with chronic generalized Candida infection, resulted in significant increase in the candidacidal activity of alveolar and spleen macrophages. The resistance not only to systemic infection with Candida albicans, but also Staphylococcus aureus increased, significantly reducing the growth of microorganisms in the kidneys of infected animals. Glucan also worked synergistically with the anti-fungal drug Amphotericin B (Nicoletti, 1992).

Although there is not enough data collected with regard to the anti-viral effect of glucan, there is now work in
progress regarding its adjuvant anti-HIV effect.

Mortality, associated with Herpes simplex in mice was shown to be profoundly modified in early works and later, it was supported by oral studies (Wyde, 1990).

Mice treated with glucan both before and after the lethal viral hepatitis challenge, exhibited only limited liver pathology, minimal plasma enzyme alterations, and greatly enhanced survival versus a group receiving no treatment (DiLuzio, 1980). Macrophage phagocytizing function, significantly impaired by hepatitis, was maintained by glucan application.

Another study shows that virally challenged mice have a limited wound-healing capacity that was corrected by systemic glucan application (Kenyon, 1983).

2. Combination "glucan + anti-neoplastic agent"
Glucan anti-tumor effect can be local or systemic. A local injection of beta-1,3-D-glucan suspension into melanoma lesions has been shown to successfully resolve the tumor locally (Mansell, 1978). In these human experiments, the site of injection revealed no previously established tumor, but plenty of macrophages filled with pigments. Obviously, macrophages were drawn to the site where they phagocytized and destroyed pigment-bearing tumor cells. These intralesional injections in some cases were able to control further growth of remote metastasis of
the same tumor which resumed growth after glucan treatment withdrawal.

Unfortunately, no clinical applications were developed out of these results until recently (Carrow, 1996). The latest data contains very promising information, not only in regard to human melanoma, but also to basal cell carcinoma.

Experimental animal data on systemic applications of beta-1,3-D-glucan anti-tumor effects is abundant. Significant reduction in tumor growth and prolonged survival was observed in mice with transplanted melanoma. In mice with adenocarcinoma, there was an 85% reduction of tumor mass accompanied by prolonged survival. An anaplastic mammary carcinoma study showed results of 70% tumor regression and 80% survival versus 100% in the group with no glucan treatment. Chronic administration of glucan to aging mice with lymphocytic leukemia significantly improved their survival (DiLuzio, 1980).

In these and other experimental models, systemic macrophage activation and certain cytokine releases, seem to be critical for clearing tissues from the tumor cells (Proctor, 1980) and inhibiting metastasis (Sakurai, 1991).

A combination of beta-1,3-D-glucan and an antineoplastic agent(s) might have a significant
potential considering its a) direct anti-tumor effect, and b) ability to counteract chemotherapy-induced immunosuppression resulting in higher mortality from opportunistic infections.

The efficacy of glucan in combination with BCNU chemotherapy was measured using the disseminated transplantable leukemia; the combination yielded a high level (56%) of cures compared to no survival for either agent alone (Stewart, 1978).

Glucan application can also protect a patient from leukocytopenia (decrease in the number of peripheral leukocytes) associated with a chemotherapeutic agent, which is one of the major obstacles in the chemotherapy of cancer. A decrease in the number of peripheral leukocytes by 5-fluorouracil was prevented by the oral application of glucan in mice. Proliferative responses of bone marrow cells to granulocyte/macrophage colony stimulating factor (GM-CSF) or granulocyte colony stimulating factor (G-CSF) were suppressed by 5-fluorouracil treatment, and their recoveries were enhanced by glucan and serum level of cytokines such as IL-1 and IL-6 were increased (Miyazaki, 1992).

Interestingly, that use of corticosteroid hormones, also having immunosuppressive effect, and widely used as a part of chemotherapy programs or in autoimmune situations, might be another indication for use of beta-1,3-D-glucan in combination with this class of
drugs. Goldman showed that the amount of beta-1,3-D-glucan binding capacity of macrophages increases when they are exposed to hydrocortisone. She states that this might be a result of enhanced expression of beta-glucan receptor. A logical interpretation of that can be that it's an attempt to compensate the diminished phagocytic ability of macrophages exposed to this class of hormones.

3. Combination "glucan + radiotherapy"
This combination seems to be very logical in the light of the data mentioned above. Radioprotective (bone marrow protective effect) of yeast glucan is well-established and documented with the mechanism of enhancing hemopoietic recovery and hence, by regenerating the host's ability to resist life-threatening opportunistic infections. However, it also has been demonstrated that host resistance to opportunistic infection in glucan-treated irradiated animals is enhanced even prior to the detection of significant hemopoietic regeneration. This early enhanced resistance to microbial invasion could be correlated with enhanced and/or prolonged macrophage (but not granulocyte) function.

These results suggest that early post-irradiation glucan may mediate its radioprotection by enhancing resistance to microbial invasion mechanisms not necessarily predicated on hemopoietic recovery.
Experimental data suggest that glucan can also function as an effective free-radical scavenger (primarily toward hydroxyl radical).

Because macrophages have been shown to selectively phagocytize and sequester glucan, it is possible that these specific cells may be protected by virtue of glucan's free-radical scavenging ability (Patchen, 1987).

Oral application of yeast beta-1,3-D-glucan for 20 consecutive days after a single, near lethal, dose of radiation resulted in 70-90% survival versus 30% in the control group.

4. Combination "glucan + topical agent"  
Glucan is an excellent wound healer. In experiments glucan-treated wounds showed a higher number of macrophages in the early, inflammatory stage of repair, with fewer polymorphonuclear neutrophilic leukocytes than did control wounds. Both re-epithelization and the onset of fibroplasia commenced at an earlier stage in glucan-treated wounds than in control wounds. Five days following the incision, glucan-treated wounds were generally completely re-epithelialized, while control wounds were not. The organization of fibroblasts in glucan-treated wounds was more advanced at 5 and 7 days following injury, and the extent of fibroplasia was also greater. By 10 days following injury, glucan-treated wounds were completely re-epithelialized and no formation of granulomas was observed up to one month.
following wounding (Leibovich, 1980).

In humans, topical glucan treatment resulted in 73% improvement in chronic decubitus ulcers with complete closure and epitalization in 27% of treated ulcers. All wounds remained clean with no infections occurring during this treatment (DiLuzio, 1984).

Considering the data above, a topical combination of an antibiotic and beta-1,3-D-glucan as an adjuvant for wound healing applications, seems to be appropriate.

An interesting effect of topical application of glucan was observed in regard to non-wounded aged skin. Revitalizing, such as reducing the number, depth and length of wrinkles, thickening, reducing roughness and dryness of the skin was shown in a group of female volunteers (Smith, 1991).

Applied topically, glucan activates epidermal macrophages (Langerhans cells). This mechanism plus its free-radical scavenging effect makes it a photoprotective agent. Glucan application resulted in the reduction of after-UV erythema and preservation of the amount of Langerhans cells in the epidermis (Elmets, 1992). A combination of a sunscreen + glucan is suggested.

Anti-irritant effect of beta-1,3-D-glucan was also shown in combination with otherwise severe irritation causing
levels of lactic acid (Smith, 1991). Glucan also has a synergistic effect with another anti-aging topical ingredient: retinoic acid (Retin-A). Similar to corticosteroids, Retin-A significantly increases the number of beta-glucan receptor-sites on phagocytic cells.

5. Combination "glucan + nutrients"
Very recent discoveries have been made on combined use of glucan and vitamin C derivatives.

Intracellular ascorbate content in phagocytizing cells reaches 40 times the level of plasma ascorbates. Macrophages activated with beta-1,3-D-glucan exhibit a significant drop in the intracellular ascorbate content. This might lead to the exhaustion of free-radical scavenging capacity of these cells, as well as to impaired motility and certain enzyme production by macrophages.

There are products on the market now that combine beta-1,3-D-glucan and vitamin C derivatives to replenish ascorbate levels in the glucan-activated macrophages. This is not only physiological from the standpoint of glucan pharmacological effects, but it also seems to have a great impact on results of Vitamin C treatments.

Commercial application of yeast derived purified beta-1,3-D-glucan, available in a dietary supplement form
and in a pure form for compounding, started in 1995. There is obviously a lack of recent double-blind human studies but plenty of anecdotal clinical data ranging from tumor mass rejection to healing of chronic wounds. Hopefully, we will see more studies with beta-1,3-D-glucan in the near future as this substance gains acceptance within the medical community.

Clinical directions presented in this paper are not by any means a complete list of all possible applications and combinations with this substance. A good physician can find more ways to utilize this material in practice. Now, when we have a better understanding of its mode of action, we can prognose and prove in practice the benefits of using beta-1,3-D-Glucan by itself or by adding it to either conventional or alternative types of therapies that would affect such therapies in a predictable way.

Bibliography


Leibovich, S.J. and Danon, D. Promotion of wound repair in mice by


Czop, J.K., Valiante, N.M. and Janusz, M.J. Phagocytosis of particulate


Carrow, D. Beta-1,3-D-glucan as a primary immune activator. Townsend letter June: 86, 1996.


Overview of the Research
Alphabetical Listing
**Note:** Beta 1-3 glucan research is on the main focused on yeast-source glucans. Quantitative analysis has determined that the polypore and other basidiomycetes contain significantly more beta glucans than yeast-based products. Notwithstanding the research has to do with yeast-type fungi, the data is viable and transferable to the basidiomycete-based glucans. The importance of this finding cannot be overlooked, because the amount of yeast-based B1-3 glucan that can be naturally absorbed from the ingestion of brewer’s or dietary yeast is vastly smaller than from the ingesting of basidiomycete-based glucan. For this reason, yeast-based glucan must be highly processed and concentrated. Basidiomycete-based glucan is rendered bio-available with minimal processing.

"...the presence of a particulate activator can rapidly initiate assembly and amplification of a host defense system involving humoral and cellular interactions with B-glucans. ...Animals pretreated with purified glucan particles are subsequently more resistant to bacterial, viral, fungal, and protozoan challenge, reject antigenically incompatible grafts more rapidly and produce higher titers of serum antibodies to specific antigens. Administration of glucan particles ...stimulates...proliferation of macrophages and increases in phagocytic and secretory
activities of macrophages. ...A cascade of interactions and reactions initiated by macrophage regulatory factors can be envisioned to occur and to eventuate in conversion of the glucan-treated host to an arsenal of defense."


**Adjuvant - Antibiotics:** Tzianabos AO, Cisnerol RL, et al; "Protection against intraabdominal sepsis by two polysaccharide immunomodulators (Beta 1,3/1,6 glucan), J Infect Dis, 178:1,200-6. 1998.
"These data demonstrate the usefulness of [Beta 1,3/1,6 glucan]... in preventing experimental intraabdominal sepsis...and may represent a new adjunct to antibiotic regimens currently used to prevent clinical cases of this disease"
**Adjuvant:** Tzianabos AO, Cisneros RL; "Prophylaxis with the immunomodulator PGG glucan enhances antibiotic efficacy in rats infected with antibiotic-resistant bacteria," Ann NY Acad Sci 797: 285-287; Oct 1996.* Quote: "Results of these studies demonstrated that prophylaxis with PGG glucan in combination with antibiotics provided enhanced protection against lethal challenge with Escherichia coli or Staphylococcus aureus as compared with the use of antibiotics alone."

**Adjuvant-Anti-infective Agents:** Wyde, P., "Beta-1,3-glucan activity in mice: intraperitoneal and oral applications." Baylor College of Medicine Research Report. 1989. "This demonstration of bactericidal enhancement via oral dosing suggests an application for beta-1,3-glucan as a component in a combined modality with conventional anti-infective agents. Beta glucan, through the stimulation of host defense systems, creates a more supportive environment within the body to assist the primary killing action of the conventional agent."


**Adjuvant:** Benach J.L., et al., "Glucan as an adjuvant for a murine Babesia microti immunization trial," Infection and Immunity, 35(3):947-951. 1982. Quote: "These observations demonstrate that glucan is an effective adjuvant in
enhancing immunity to murine babesiosis.


"It is concluded that glucan, in combination with ampicillin, has a significant effect on the survival rate of rats with induced peritonitis, probably by enhancing the activities of the reticuloendothelial system, an important part of the total host resistance."


"The efficacy of glucan in combination with BCNU chemotherapy was measured using the disseminated AKR transplantable leukemia; the combination yielded a high level of cures compared to no survival for either agent alone."


"immuno-pharmacologic agents [glucan] that enhance macrophage function may be an important adjunct to surgical therapy requiring bowel anastomosis."

Aging: Carrow, D.J. MD.; "Beta-1,3-glucan as a Primary Immune Activator," Townsend Letter; June 1996.
"...beta 1,3-glucan may well be the first and only true anti-aging supplement available to all of us."


**Antibiotics:** Tzianabos AO, Cisneros RL; "Prophylaxis with the immunomodulator PGG glucan enhances antibiotic efficacy in rats infected with antibiotic-resistant bacteria,"Ann NY Acad Sci 797: 285-287; Oct 1996.*

"Results of these studies demonstrated that prophylaxis with PGG glucan in combination with antibiotics provided enhanced protection against lethal challenge with Escherichia coli or Staphylococcus aureus as compared with the use of antibiotics alone."


**Antimicrobial Activity:** Hunter K, Washburn R, "Efficacy of topical antimicrobial acid and immunostimulatory B-Glucan
"...the B-glucans have been shown to activate macrophages to enhance their antimicrobial activity. Our laboratory has developed preliminary evidence that B-1,3/1,6 glucans possesses immunostimulatory activity for macrophages in vitro, leading to secretion of the Th-1 cytokines IL-1 B, IL-12, and TNF-B."

"Beta-Glucans with 1,3-and 1,6 glycosidic linkages are the major structural components of yeast and fungal cell walls and are active pharmacologic agents in host defense systems of plants and animals....The administration of particulate glucans from S. cerevisiae to laboratory animals induces host resistance to a variety of lethal pathogens by mechanisms involving macrophage stimulation.

In vitro studies reveal that bone marrow-derived mouse macrophages and human peripheral blood monocytes possess Beta-glucan receptors that mediate phagocytosis of glucan particles and induce release of proinflammatory mediators..."

Issued Dec 4, 1990.
"Beta 1,3 glucan has proven to both stimulate and activate the macrophage cells,...People with high risk of atherosclerosis should definitely add beta 1,3 glucan to their diet in addition to any cholesterol-reducing drugs."

Auto-Immune Disorders - See Diabetes: Rheumatoid arthritis, fibromyalgia, systemic lupus erythrematosus, glomerulonephritis, scleroderma, multiple sclerosis and diabetes mellitus sufferers should consult their physician before using any immune response potentiator and then use only in accord with physician instruction.


"Beta-1,3-D-polyglucose derivatives protect mice against otherwise lethal bacterial infections."

Bacterial Infections: Kokoshis PL, DiLuzio NR et al, "Increased resistance to Staphylococcus aureus infection and enhancement in serum lysozyme activity by glucan." Science, 199(4335);1340-1342; 1978:
"Prior treatment of mice with glucan significantly enhanced their survival when they were challenged systemically with Staphylococcus aureus. These studies indicate glucan confers an enhanced state of host defense against bacterial infections."

"This demonstration of bactericidal enhancement via oral dosing suggests an application for beta-1,3-glucan as a component in a combined modality with conventional anti-infective agents. Beta glucan, through the stimulation of host
defense systems, creates a more supportive environment within the body to assist the primary killing action of the conventional agent."


"The initial 9 patients studied had malignant carcinoma of the breast. Control and experimental lesions were injected; subsequently biopsies were performed at varying intervals for histologic evaluation. Always when glucan or glucan and RF fraction were administered intra-lesionally, the size of the lesion was strikingly reduced in as short a period as 5 days. ...In small lesions, resolution was complete, whereas in large lesions, resolutions was partial."


"Intravenous administration of soluble or particulate glucan resulted in significant reduction in the growth of a syngeneic anaplastic mammary carcinoma and melanoma B16 and enhanced survival."

"Intravenously administered DiLuzio glucan...caused dose dependent increases in the tumor cell loss from the lungs of ...mice challenged respectively with intravenous 125IuDR labelled B16 or T 1699 mammary carcinoma cells."

"Intravenous administration of soluble or particulate glucan
resulted in significant reduction in the growth of a syngeneic anaplastic mammary carcinoma and melanoma B16 and enhanced survival."


Cancer - Sarcoma: Seljelid R, et al, "Evidence that tumor necrosis induced by an irradiated beta 1-3D polyglucose is mediated by a concerted action of local and systemic cytokines," Scand J Immuno 30(6): 687-694. Dec 1989.* "Aminated beta 1-3D polyglucose (AG) causes regression of Meth A sarcoma in syngeneic mice when injected systemically on day 7 after tumour inoculation. AG does not concentrate in the tumour, but distributes throughout the body. AG treatment causes release of large amounts of interleukin 1 (IL-1) both in vivo [in the body] and in macrophage cultures in vitro [out of body]."

Cancer : Carrow, D.J.; "Beta-1,3-glucan as a Primary Immune Activator," Townsend Letter; June 1996. "Over the past 11 months I have been able to convince five out of eight breast cancer patients who were undergoing radiation therapy, to consume one capsule of beta 1,3/1,6
glucan (NSC-24 3 mg) three times per day. To date, I have observed that none of the patients using NSC-24 have suffered from any type of radiation injury to the skin, while the three patients who chose not to use NSC-24 all show signs of extensive radiation damage to the skin."

"Macrophages stimulated by an insoluble beta 1-3-D-glucan from yeast cell walls were able to destroy tumour cells as measured by the release of radioactive label from prelabelled 14C-thymidine cells. Target cells were B-16 melanoma, P-815 mastocytoma, and the L-929 cell line. A significant target cell killing by macrophages stimulated by glucan was observed after 72-96 h."


Cancer: Niskanen E.O., Burgaleta C., Cline M.J., Goide D.W.; Effect of glucan, a macrophage activator, on murine hemopoietic cell proliferation in diffusion chambers in mice; Cancer Res 38: 1406-1409, 1978.


"The soluble phosphorylated glucans are also useful for stimulating macrophage cells, either in vivo or in vitro, to produce a cytotoxic/cytostatic factor effective against cancer cells." [cytotoxic: toxic to cell - prevents reproduction or growth]

"When stimulated with interferon-gamma and soluble beta 1,3-D-glucan, macrophages exerted cytotoxicity towards syngeneic Meth A [sarcoma] tumor cells."


"Protection against C. albicans was observed in the glucan-treated groups. ...These observations suggest that Biologic Response Modifiers such as glucan may be effectively employed in patients who are at risk for post-operative infections."*


contains a \( \beta(1-3) \text{glucan}-1,3/1,6 \)-glucoside bond). Issued June 13, 1995.


"...Ginkgo biloba/carboxymethyl-beta-1,3-glucan formulation can mitigate against allergic contact dermatitis."

Diabetes: Carrow, D.J.; "Beta-1,3-glucan as a Primary Immune Activator," Townsend Letter; June 1996.
"The following list includes benefits from the use of Beta 1,3-glucan supplementation: ...people with chronic degenerative disorders such as diabetes or chronic inflammation. ...

"The preventive effect of an immunopotentiator, beta-1,6;1,3 D-glucan, on the development of diabetes and insulitis was studied in BB rats....[and] decreased the cumulative incidence of diabetes from 43.3% to 6.7% and also the incidence of insulitis from 82.4% to 26.3%....These data indicate that immunopotentiators could modulate the autoimmune mechanisms directed to pancreatic islets and
inhibit the development of diabetes in BB rats.


"These data denote that the intraperitoneal administration of glucan significantly modifies the course of E. coli-induced peritonitis and bacteremia due, in part, to glucan-induced enhancement of macrophage function."


"Mice challenged with Escherichia coli or Staphylococcus aureus were protected against lethal peritonitis by the intravenous administration of 10 micrograms of poly-beta 1-6-glucotriosyl-beta 1-3-glucopyranose (PGG) glucan per animal 4 to 6 h prior to bacterial challenge."
"Pretreatment with beta-1,3-D-glucan-drivatized plastic beads conferred strong protection against Escherichia coli infection in mice."

"Results of these studies demonstrated that prophylaxis with PGG glucan in combination with antibiotics provided enhanced protection against lethal challenge with Escherichia coli or Staphylococcus aureus as compared with the use of antibiotics alone."


Free Radical Scavenger: Carrow, D.J.; "Beta-1,3-glucan as a Primary Immune Activator," Townsend Letter; June 1996. "Free radical scavenging assays were repeated in different
models, which then confirmed the antioxidant effect of beta 1,3-glucan. In light of what is presently known about the potential of free radicals to accelerate aging, cause cancer and other degenerative diseases, this particular effect of beta 1,3-glucan is especially important."

"...evidence suggest that glucan can also function as an effective free radical scavenger."

"Previous studies have demonstrated that glucan, a beta-1,3-linked glucopyranose polymer, isolated from the inner cell wall of Saccharomyces cerevisiae, is a potent macrophage stimulant and is beneficial in the therapy of experimental bacterial, viral, and fungal diseases."

(p347) "The broad spectrum of immunopharmacological activities of glucan includes not only the modification of
certain bacterial, fungal, viral and parasitic infections, but also inhibition of tumor growth."


Heart Disease: Carrow, D.J.; "Beta-1,3-glucan as a Primary Immune Activator," Townsend Letter; June 1996. "...immunosuppression is observed in people with stress-related disease such as coronary heart disease. Under such influences the number of macrophages [white immune cells] available are reduced and unable to participate in the immune cascade, which caused an even greater immunosuppression.

Beta 1,3 glucan has proven to both stimulate and activate the macrophage cells, which will counter these negative effects. ...People with high risk of atherosclerosis should definitely add beta 1,3 glucan to their diet in addition to any cholesterol-reducing drugs. Macrophage activation helps draw extra cholesterol from the blood, prevent further plaque formation on the arterial walls and phagocytes [eats] existing plaque which is recognized as a foreign body."

"Clearly, there are numerous possible uses for an agent such as glucan, which is a potent stimulator of hemopoietic activity. Currently, we [U.S. Armed Services] are using glucan to enhance hemopoietic proliferation in conjunction with hemopoietic injury induced by radiation."


"Thus glucan is capable of increasing survival, inhibiting hepatic necrosis, and maintaining an activated state of phagocytic activity in mice challenged with [mouse hepatitis virus strain] MHV-A59."


IL 1 and TNF-α Production: Hunter K, Washburn R, "Efficacy of topical antimicrobial acid and immunostimulatory B-Glucan in Animal Models of Cutaneous Infection," U Nevada Medical School-Applied Res Grant, Aug 1998. "Our laboratory has developed preliminary evidence that B-1,3/1,6 glucans possesses immunostimulatory activity for macrophages in vitro, leading to secretion of the Th-1 cytokines IL-1 B, IL-12, and TNF-B."


IL-1 Enhancement: Poutsiaka D.D., et al, "Cross-linking of the beta-glucan receptor on human monocytes results in interleukin-1 receptor antagonist but not interleukin-1 production," Blood 82: 3695-3700; Dept of Med, New England Med Ctr, Boston, MA. 1993. "Because of their differential effects on cytokine production, beta-glucans may be used to therapeutic advantage in the diseases in which IL-1 is implicated."*

and are active pharmacologic agents in host defense systems of plants and animals....The administration of particulate glucans from S. cerevisiae to laboratory animals induces host resistance to a variety of lethal pathogens by mechanisms involving macrophage stimulation.

Immune response - Activation of White Blood Cells: Czop, Joyce K., "The Role of .beta.-Glucan Receptors on Blood and tissue Leukocytes in Phagocytosis and metabolic Activation".


Immune Response - Increased Survival: Todd, R.F.; "The Continuing Saga of Complement Receptor Type 3 (CR3)," J. Clin Invest.: Vol 98, 1-2. 1996. Div of Hematology/Oncology Dept of Int. Med, U of Michigan Med Ctr.* (p2) "In certain controlled clinical trials, the increased survival of patients receiving these immunostimulatory Beta-glucans has been reported."
Immune Response - Macrophage Cell Production Increase:

Immune Response - Macrophage Cell Production Increase:
"These studies indicate that glucan administration results in increased granulocyte and macrophage production....glucan as an immunotherapeutic agent can result in an increased number of available effector cells."


Animal studies indicate that beta-glucans with 1,3- and/or 1,6-linkages are active pharmacologic agents that rapidly confer protection to a normal host against a variety of biological insults. The beta-glucan receptors provide a mechanism by which a heightened state of host responsiveness is initiated.


Immune Response - Small Particle Effectiveness: Donzis B. A.; Sustantially purified beta (1,3) finely ground yeast cell wall glucan composition with dermatological and nutritional uses; U.S. Patent 5705184; 1998.

Immune Response - Small Particle Effectiveness: Donzis B. A.; Sustantially purified beta (1,3) finely ground yeast cell wall glucan composition with dermatological and nutritional uses; U.S. Patent 5702719; 1997. "The preferred particle size of the find grind glucan product is about 1.0 micron or less and more preferably, .20 microns or less."

Immune Response - Small Particle Effectiveness: Donzis B. A.; Sustantially purified beta (1,3) finely ground yeast cell wall glucan composition with dermatological and nutritional
uses; U.S. Patent 5576015; 1996. "Upon oral administration, the smaller or finer particle sized glucan is more quickly dissolved in the gastrointestinal tract and consequently, more readily absorbed."


Immune Response Enhancement: Spiros J.; Method for immune system activation by administration of a \( \beta(1-3) \) glucan which is produced by Saccharomyces cerevisiae strain R4; U.S. Patent 5504079; 1996.

Immune Response Enhancement Jordan, F.; "An Effective Immune System Enhancer - Beta-1,3/1,6-glucan Derived from Yeast," Carmel Research Quarterly; Vol II,1; 1997. "Leading the list of effective immune enhancers, according to extensive research, is undiluted, unaltered, unradiated Beta-1,3/1,6-glucan (...)."


Immune Response Enhancement Vetvicka V., Thornton B.P., Ross G.D.; "Soluble Beta-glucan Polysaccharide Binding to the Lectin Site of Neutrophil or Natural Killer Cell Complement Receptor Type 3 (CD11b/CD18) Generates a Primed State of the Receptor Capable of Mediating Cytotoxicity of iC3b-Opsonized Target Cells,". Journal Clin Invest 98: 50-61. Div of Experimental Immuno and Immunopath, Dept Path, U of Louisville, KY.* 1996. "This investigation showed that soluble CR3-specific polysaccharides such as beta-glucan induced a primed state of CR3 that could trigger killing of iC3b-target cells that were otherwise resistant to cytotoxicity."
"This demonstration of bactericidal enhancement via oral dosing suggests an application for beta-1,3-glucan as a component in a combined modality with conventional anti-infective agents. Beta glucan, through the stimulation of host defense systems, creates a more supportive environment within the body to assist the primary killing action of the conventional agent."


"...glucan enhances the immune response through stimulation of macrophages by increasing their number, size, and function, stimulates secretion of lysozyme and TNF by activated macrophages, increases the phagocytosis of antigens, activates the formation of granulocyte and monocyte colonies, and factors increased activity of T and B lymphocytes, as well as complement activation."

Dept of Med, New England Med Ctr, Boston, MA. "Because of their differential effects on cytokine production, beta-glucans may be used to therapeutic advantage in the diseases in which IL-1 is implicated."


Immune Response: Bodenbach B.; NSC-24(tm): An Extraordinary New Immune Enhancing Supplement; Health Perspectives, vol 2, no 2; 1996.

"...PSAT and scleroglucan favorably affect the non-specific host defense and cellular immune response in mice."


"The following list includes benefits from the use of Beta 1,3-glucan supplementation: People who have impaired immunity from any cause including, but not limited to HIV infection; have a high occurrence of infectious diseases; have tumors and/or those undergoing chemotherapy or radiation therapy; are over forty who are concerned about the natural aging process or might have noticed a slowing down of
immune reactivity; who are geriatric patients; and other with compromised immune disorders.
In vitro studies reveal that bone marrow-derived mouse macrophages and human peripheral blood monocytes possess Beta-glucan receptors that mediate phagocytosis of glucan particles and induce release of proinflammatory mediators...


"Beta 1,3-glucan is a potent stimulator of macrophage functions and has a protective effect against a range of infections in rodent models."


"Mice challenged with Escherichia coli or Staphylococcus aureus were protected against lethal peritonitis by the
intravenous administration of 10 micrograms of poly-beta 1-6-glucotriosyl-beta 1-3-glucopyranose (PGG) glucan per animal 4 to 6 h prior to bacterial challenge."


This study reports the use of glucan, a beta-1,3-polyglucose, as a nonspecific immunostimulant for postsplenectomy pneumococcal sepsis. Nonspecific immunostimulation appears to have significant potential as a treatment strategy against postsplenectomy infection.

The incidence of hospital pneumonia of 55% and sepsis of 35% confirms results of previous studies of patients with multitrauma. Glucan decreased pneumonia and sepsis to a significantly lower level of 9.5%. The mortality rate related to infection decreased from 30.0 to 4.8%. The lower number of instances of pneumonia and sepsis decreased the period of time in the intensive care and the hospital, with a global reduction of 40% on hospital cost.

The administration of glucan significantly prolonged survival of S. Aureus infected control and chronic ethanol mice.


"...these studies demonstrate that a soluble glucan preparation exhibits significant anti-tumor and anti-staphylococcal activity."

"...glucan reduces the risk of staphylococcal abscess formation. Neutrophil-activating agents [glucan] are a novel means of prophylaxis against surgical infection and may be less likely than antibiotics to be affected adversely by the
increasing antibiotic resistance of nosocomial pathogens.


Infection-Post Surgery: Babineau, et al., "Randomized Phase I/II Trial of a Macrophage-Specific Immunomodulator (PGG-Glucan) in High Risk Surgical Patients", Annals of Surgery; 220:(5):601-609. 1994. Dept of Surgery, Deaconess Hospital, Harvard Medical Sch, Boston MA.* Quote: "PGG-glucan is safe and appears to be effective in further
reduction of the morbidity and cost of major surgery.*

"These studies indicate that glucan confers an enhanced state of host defense against bacterial infections."

"Beta-1,3-D-polyglucose derivatives protect mice against otherwise lethal bacterial infections."


"Glucan administration is associated with the modification of a variety of experimentally induced infectious disease states as well as the inhibition of growth of implantable and spontaneous tumors."
"In a prospective, randomized double-blind study, [Babineau, et.al.] demonstrate that the perioperative administration of PGG-glucan, a substance derived from yeast that increases the microbial killing activity of leukocytes, can decrease infectious complications in patients undergoing major surgical procedures...the preliminary results are positive and should be interpreted as good news."


These data denote that glucan enhances nonspecific resistance to S. aureus sepsis, promotes survival during leukemic episodes, and increases survival time of leukemic mice with experimentally induced staphylococcal infection.

"The efficacy of glucan in combination with BCNU chemotherapy was measured using the disseminated AKR transplantable leukemia; the combination yielded a high level of cures compared to no survival for either agent alone."

"...A post-treatment regimen of glucan significantly enhanced survival of AKR/J mice with lymphocytic leukemia as well as leukemic mice with experimentally induced systemic staphylococcal infection."


Melanoma: Williams DL, et al, "Therapeutic efficacy of glucan
"...coincubation of particulate glucan with diverse populations of normal or tumor cells in vitro indicated that glucan exerted a direct cytostatic effect on sarcoma and melanoma cells and, in contrast, had a proliferative effect on normal spleen and bone marrow cells."

"Mindful of the extremely high rate of atherosclerotic complications and the extraordinary requirements for antioxidants in diabetic patients, the use of beta-1,3 glucan becomes an obvious adjunct for improved lifestyle under these conditions."


Modulation: Rasmussen LT, Seljelid R, "The modulatory effect of lipoproteins on the release of interleukin 1 by human peritoneal macrophages stimulated with beta-1,3-D-
polyglucose derivatives." Apr 1989.*


Murine hemopoietic cell proliferation: Niskanen E.O., Burgaleta C., Cline M.J., Goide D.W.; Effect of glucan, a macrophage activator, on murine hemopoietic cell proliferation in diffusion chambers in mice; Cancer Res 38:1406-1409, 1978.


"...glucan enhances the immune response through stimulation of macrophages by increasing their number, size, and function, stimulates secretion of lysozyme and TNF by activated macrophages, increases the phagocytosis of antigens, activates the formation of granulocyte and monocyte colonies, and factors increased activity of T and B lymphocytes, as well as complement activation."


promoting the wound healing process. The soluble phosphorylated glucans are also useful for prophylactic and therapeutic applications against neoplastic, bacteria, viral, fungal and parasitic diseases.

Parasitic Infection: DiLuzio N.R., "Immunopharmacology of glucan: a broad spectrum enhancer of host defense mechanisms," Trends in Pharmacol. SCI., 4:344-347. Dept of Physiology, Tulane U, New Orleans, LA.* 1983. (p347) "The broad spectrum of immunopharmacological activities of glucan includes not only the modification of certain bacterial, fungal, viral and parasitic infections, but also inhibition of tumor growth."

Particle Size - Smaller more Effective: Donzis B. A.; Sustantially purified beta (1,3) finely ground yeast cell wall glucan composition with dermatological and nutritional uses; U.S. Patent 5702719; 1997. "The preferred particle size of the find grind glucan product is about 1.0 micron or less and more preferably, .20 microns or less."

Particle Size - Smaller more Effective: Donzis B. A.; Sustantially purified beta (1,3) finely ground yeast cell wall glucan composition with dermatological and nutritional uses; U.S. Patent 5576015; 1996. "Upon oral administration, the smaller or finer particle sized glucan is more quickly dissolved in the gastrointestinal tract and consequently, more readily absorbed."
"PGG glucan-treated animals had significantly less infection-stimulated periapical bone resorption than control animals..."

"It is concluded that glucan, in combination with ampicillin, has a significant effect on the survival rate of rats with induced peritonitis, probably by enhancing the activities of the reticuloendothelial system, an important part of the total host resistance."

"Mice challenged with Escherichia coli or Staphylococcus aureus were protected against lethal peritonitis by the intravenous administration of 10 micrograms of poly-beta 1-6-glucotriosyl-beta 1-3-glucopyranose (PGG) glucan per animal 4 to 6 h prior to bacterial challenge."


Platelet Production: Spiros J.; Use of neutral soluble glucan preparations to stimulate platelet production; U.S. Patent 5488040; 1996.

Platelet Recovery: Pachen ML, MacVittie TJ, "Comparative effects of soluble and particulate glucans on survival in irradiated mice," J Biol Response Mod 5(1):45-60. Experimental Hematology Dept, Armed Forces Radiobiology Research Inst, Bethesda, MD. Feb 1986. "Both glucan-P and glucan-F enhanced the recovery of peripheral blood white cell numbers, platelet numbers, and hematocrit values. In addition, both agents increased endogenous pluripotent hemopoietic stem cell numbers in sublethally irradiated mice."
Pneumonia: Maurici da Rocha e Silva et al; "Infection Prevention in Patients with Severe Multiple Trauma with the Immunomodulater Beta 1-3 Polyglucose (glucan);" Surgery, Gynecology & Obstetrics; 177:383-388. 1993. "The incidence of hospital pneumonia of 55% and sepsis of 35% confirms results of previous studies of patients with multitrauma. Glucan decreased pneumonia and sepsis to a significantly lower level of 9.5%....The mortality rate related to infection decreased from 30.0 to 4.8%. The lower number of instances of pneumonia and sepsis....decreased the period of time in the intensive care and the hospital, with a global reduction of 40% on hospital cost."


glucan purified from the cell walls of Saccharomyces cerevisiae, has been shown to synergize the myeloid growth factors in vitro and to enhance hematopoietic recovery in myelosuppressed mice and primates.


"Likewise, although both glucan and granulocyte colony-
stimulating factor (G-CSF) alone enhanced survival following an 8-Gy radiation exposure, greatest survival was observed in mice treated with both agents. These studies suggest that glucan, a macrophage activator, can synergize the G-CSF to further accelerate hemopoietic regeneration and increase survival following radiation-induced myelosuppression.


"These results suggest that early after irradiation glucan may mediate its
radioprotection by enhancing resistance to microbial invasion via mechanisms not necessarily predicated on hemopoietic recovery. ...glucan can also function as an effective free radical scavenger. Because macrophages have been shown to selectively phagocytize and sequester glucan, the possibility that these specific cells may be protected by virtue of glucan's scavenging ability is also suggested.

Radiation: Pachen ML, MacVittie TJ, "Comparative effects of soluble and particulate glucans on survival in irradiated mice," J Biol Response Mod 5(1):45-60. Experimental Hematology Dept, Armed Forces Radiobiology Research Inst, Bethesda, MD. Feb 1986. "Both glucan-P and glucan-F enhanced the recovery of peripheral blood white cell numbers, platelet numbers, and hematocrit values. In addition, both agents increased endogenous pluripotent hemopoietic stem cell numbers in sublethally irradiated mice."


Radiation: Patchen M.L, MacVittie T.J.,"Dose-dependent responses of murine pluripotent stem cells and myeloid and erythroid progenitor cells following administration of immunomodulating agent glucan." Immunopharmacology, 5(4):303-13, Apr 1983. "The hemopoietic effects produced by six different doses of a commercially available glucan preparation were investigated....bone marrow pluripotent stem cells (CFU-s) content increased...In the spleen, all aspects of hemopoiesis increased after glucan administration."

Radiation: Patchen M.L., McVittie T.J.; Temporal Response of Murine Pluripotent Stem Cells and Myeloid and Erythroid Progenitor Cells to Low-dose Glucan Treatment. Acta Hemat; 70:281-288. Experimental Hematology Dept, Armed Forces Radiobiology Research Insti, Bethesda, MD. 1983. "Clearly, there are numerous possible uses for an agent such as glucan, which is a potent stimulator of hemopoietic activity. Currently, we [U.S. Armed Services] are using glucan to enhance hemopoietic proliferation in conjunction with
hemopoietic injury induced by radiation."


"Both glucan-P and glucan-F enhanced the recovery of peripheral blood white cell numbers, platelet numbers, and hematocrit values. In addition, both agents increased endogenous pluripotent hemopoietic stem cell numbers in sublethally irradiated mice."


Safety - FDA Classification: Carrow, D.J. MD; "Beta-1,3-glucan as a Primary Immune Activator," Townsend Letter; June 1996.
"Beta 1,3-glucan is a safe and potent nutritional supplement with a profound systemic effect that can be described as nonspecific immune stimulation combined with its free radical scavenging activity. Remember, beta 1,3-glucan is generally recognized as safe (category GRAS, according to FDA) and has no known toxicity or side effects."


"Soluble glucan, a beta-1,3-linked glucopyranose biological response modifier, is effective in the therapy of experimental neoplasia, infectious diseases and immune suppression."

"Aminated beta 1-3D polyglucose (AG) causes regression of Meth A sarcoma in syngeneic mice when injected systemically on day 7 after tumour inoculation. AG does not concentrate in the tumour, but distributes throughout the body. AG treatment causes release of large amounts of interleukin 1 (IL-1) both in vivo [in the body] and in macrophage cultures in vitro [out of body]."

"...coincubation of particulate glucan with diverse populations of normal or tumor cells in vitro indicated that glucan exerted a direct cytostatic effect on sarcoma and melanoma cells and, in contrast, had a proliferative effect on normal spleen and bone marrow cells."

Sepsis-Intraabdominal: Tzianabos AO, Cisnerol RL, et al; "Protection against intraabdominal sepsis by two polysaccharide immnomodulators (Beta 1,3/1,6 glucan), J Infect Dis, 178:1,200-6. 1998."
"These data demonstrate the usefulness of [Beta 1,3/1,6
glucan in preventing experimental intraabdominal sepsis...and may represent a new adjunct to antibiotic regimens currently used to prevent clinical cases of this disease


Skin Revitalization: Donzis B.A.; Sustantially purified beta (1,3) finely ground yeast cell wall glucan composition with dermatological and nutritional uses; U.S. Patent 5702719; 1997.

Skin Revitalization: Donzis B.A.; Method of revitalizing skin by applying topically water insoluble glucan; U.S. Patent 5223491; 1993.


Skin: Murphy G, Messadi D, Fonterko E, Hancock W; "Phenotypic Transformation of Macrophages to Langerhans

Staphylococcus aureus: Kokoshis PL, DiLuzio NR et al, "Increased resistance to Staphylococcus aureus infection and enhancement in serum lysozyme activity by glucan." Science, 199(4335):1340-1342; 1978: "Prior treatment of mice with glucan significantly enhanced their survival when they were challenged systemically with Staphylococcus aureus. These studies indicate glucan confers an enhanced state of host defense against bacterial infections."

Staphylococcus aureus: Onderdonk, A.B., et al., "Anti-Infective Effect of Poly-.beta.1-6-Glucotrisyl-.beta.1-3-Glucopyranose Glucan In Vivo," Infe. Immun.; 60:1642-1647. 1992. Dept of Pathology, Channing Lab, Brigham and Women's Hospital, Boston, MA.* "Mice challenged with Escherichia coli or Staphylococcus aureus were protected against lethal peritonitis by the intravenous administration of 10 micrograms of poly-beta 1-6-glucotriosyl-beta 1-3-glucopyranose (PGG) glucan per animal 4 to 6 h prior to bacterial challenge."

Stress - Physical or Emotional: Carrow, D.J.; "Beta-1,3-glucan as a Primary Immune Activator," Townsend Letter; June 1996. "The following list includes benefits from the use of Beta 1,3-glucan supplementation: Professional and amateur athletes as well as people who work outdoors intensively. People under physical or emotional stress"

(p1): "Beta-Glucans with 1,3 and/or 1,6 linkages are the major structural components of yeasts and fungi and are pharmacologic agents in animals...The cell wall glucans of S. cerevisiae consist of two structurally distinct Beta-glucans: major components comprised of consecutively, 1,3-linked glucopyranosyl residues with small numbers of 1,6-linked branches, and minor components with consecutive 1,6-linkages and 1,3-branches."


Structure: Donzis B.A.; Solubilized yeast glucan; U.S. Patent 5519009; 1996.


"Previous studies have demonstrated that glucan, a beta-1,3-linked glucopyranose polymer, isolated from the inner cell wall of Saccharomyces cerevisiae, is a potent macrophage
stimulant and is beneficial in the therapy of experimental bacterial, viral, and fungal diseases. Use of glucan in a murine model of hind-limb crush injury decreased macrophage PGE2 release while stimulating bone marrow proliferation."


"The incidence of hospital pneumonia of 55% and sepsis of 35% confirms results of previous studies of patients with multitrauma. Glucan decreased pneumonia and sepsis to a significantly lower level of 9.5%. The mortality rate related to infection decreased from 30.0 to 4.8%. The lower number of instances of pneumonia and sepsis decreased the period of time in the intensive care and the hospital, with a global reduction of 40% on hospital cost."


"Differential augmentation by recombinant human tumor


"When water-soluble aminated beta 1,D-glucan (AG) was injected intravenously or intraperitoneally on day 7 of tumor growth, the tumors underwent complete regression."

"Aminated beta 1-3D polyglucose (AG) causes regression of Meth A sarcoma in syngeneic mice when injected systemically on day 7 after tumour inoculation. AG does not concentrate in the tumour, but distributes throughout the body."

from yeast cell walls were able to destroy tumour cells as measured by the release of radioactive label from prelabelled 14C-thymidine cells. Target cells were B-16 melanoma, P-815 mastocytoma, and the L-929 cell line. A significant target cell killing by macrophages stimulated by glucan was observed after 72-96 h.


(p347) "The broad spectrum of immunopharmacological activities of glucan includes not only the modification of
certain bacterial, fungal, viral and parasitic infections, but also inhibition of tumor growth."


Tumors: Glovsky MM, et al.; "Effects of particulate beta-1,3 glucan on human, rat, and guinea pig complement activity," J. Reticuloendothel Soc. 33:401-413. 1983.* "Glucan administration is associated with the modification of a variety of experimentally induced infectious disease states as well as the inhibition of growth of implantable and spontaneous tumors."


Tumors: Morikawa K., Takeda M., Yamazaki, M., and Mizuno D., "Induction of tumoricidal activity of polymorphonuclear leukocytes by a linear B-1,3-D-glucan and other immunomodulators in murine cells". Cancer Res., 45: 1496-

"Intravenously administered DiLuzio glucan...caused dose dependent increases in the tumor cell loss from the lungs of...mice challenged respectively with intravenous 125IuDR labelled B16 or T 1699 mammary carcinoma cells."


"In the established tumor model, beta glucan + Bispecific antibody (BsAb) reduced the incidence of s.c. tumors as compared with control...It also prolonged survival of tumor-bearing mice compared with control. We conclude that T cells can be activated in vivo by beta glucan..."


Previous studies have demonstrated that glucan, a beta-1,3-linked glucopyranose polymer, isolated from the inner cell wall of Saccharomyces cerevisiae, is a potent macrophage stimulant and is beneficial in the therapy of experimental bacterial, viral, and fungal diseases.

"The broad spectrum of immunopharmacological activities of glucan includes not only the modification of certain bacterial, fungal, viral and parasitic infections, but also inhibition of tumor growth."


"Both glucan-P and glucan-F enhanced the recovery of peripheral blood white cell numbers, platelet numbers, and hematocrit values. In addition, both agents increased endogenous pluripotent hemopoietic stem cell numbers in sublethally irradiated mice."


"Of all the substances tested, glucan was the only substance to exhibit a particularly marked enhancement of the proliferative phase of wound healing. It appears, from these experiments, that the effect observed by others in terms of the activation of reticuloendothelial function by glucan and the activation of macrophages, both locally and systematically, also apply to activation of macrophages in healing wounds."

"...macrophage modulation with glucan phosphate will increase tensile strength in experimental colon and skin wounds. In addition, we have observed a positive correlation between glucan phosphate treatment, wound tensile
strength, and collagen biosynthesis."


Yeast Infections - See Candida Albicans (Note: While derived from yeast cell wall, Beta 1,3/1,6 glucan is purified in extraction and contains no yeast proteins and thus in no way causes or aggravates Candida Albicans.

References and quotes contained herein should not be construed as express or implied representations, endorsements or warranties of Carmel Research, Inc.
Fungal beta-glucan interacts with vitronectin and stimulates tumor necrosis factor alpha release from macrophages

EJ Olson, JE Standing, N Griego-Harper, OA Hoffman and AH Limper
Department of Medicine, Mayo Clinic, Rochester, Minnesota 55905, USA.

beta-Glucans are polymers of D-glucose which represent major structural components of fungal cell walls. It was shown previously that fungi interact with macrophages through beta-glucan receptors, thereby inducing release of tumor necrosis factor alpha (TNF-alpha). Additional studies demonstrated that vitronectin, a host adhesive glycoprotein, binds to fungi and enhances macrophage recognition of these organisms. Since vitronectin contains a carbohydrate-binding region, we postulated that vitronectin binds fungal beta-glucans and subsequently augments macrophage TNF-alpha release in response to this fungal component. To study this, we first determined the release of TNF-alpha from alveolar macrophages stimulated with fungal beta-glucan. Maximal TNF-alpha release occurred with moderate concentrations of beta-glucan (100 to 200 micrograms/ml), whereas higher concentrations of beta-glucan (> or = 500 micrograms/ml) caused apparent suppression of the TNF-alpha activity released. This suppression of TNF-alpha activity by high concentrations of beta-glucan was mediated by the particulate beta-glucan binding soluble TNF-alpha, through the lectin-binding domain of the cytokine, rendering the TNF-alpha less available for measurement. Next, we
assessed the interaction of vitronectin with beta-glucan. Binding of 125I-vitronectin to particulate fungal beta-glucan was dose dependent and specifically inhibitable by unlabeled vitronectin. Furthermore, treatment of beta-glucan with vitronectin substantially augmented macrophage TNF-alpha release in response to this fungal component. These findings demonstrate that fungal beta-glucan can directly modulate TNF-alpha release from macrophages. Further, these studies indicate that the host adhesive glycoprotein vitronectin specifically binds beta-glucan and augments macrophage cytokine release in response to this fungal element.

This article has been cited by other articles:


The influence of glucan polymer structure and solution conformation on binding to (13)-ß-D-glucan receptors in a human monocyte-like cell line Antje Mueller2,6, John Raptis2,6, Peter J. Rice3,6, John H. Kalbfleisch4,6,
Glucans are (1–3)-β-D-linked polymers of glucose that are produced as fungal cell wall constituents and are also released into the extracellular milieu. Glucans modulate immune function via macrophage participation. The first step in macrophage activation by (1–3)-β-D-glucans is thought to be the binding of the polymer to specific macrophage receptors. We examined the binding/uptake of a variety of water soluble (1–3)-β-D-glucans and control polymers with different physicochemical properties to investigate the relationship between polymer structure and receptor binding in the CR3- human promonocytic cell line, U937. We observed that the U937 receptors were specific for (13)-β-D-glucan binding, since mannan, dextran, or barley glucan did not bind. Scleroglucan exhibited the highest binding affinity with an IC50 of 23 nM, three orders of magnitude greater than the other (13)-β-D-glucan polymers examined. The rank order competitive binding affinities for the glucan polymers were scleroglucan>>>schizophyllan > laminarin > glucan phosphate > glucan sulfate. Scleroglucan also exhibited a triple helical solution structure (Ω = 1.82, β = 0.8). There were two different binding/uptake sites on U937
cells. Glucan phosphate and schizophyllan interacted nonselectively with the two sites. Scleroglucan and glucan sulfate interacted preferentially with one site, while laminarin interacted preferentially with the other site. These data indicate that U937 cells have at least two non-CR3 receptor(s) which specifically interact with (13)-β-D-glucans and that the triple helical solution conformation, molecular weight and charge of the glucan polymer may be important determinants in receptor ligand interaction.

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'Dectin-1 and its role in the recognition of beta-glucans in macrophages' Gordon D. Brown. Sir William Dunn School of Pathology, University of Oxford. gbrown@molbiol.ox.ac.uk

The innate cellular recognition of pathogens is dependent on germ line encoded receptors which recognise conserved microbial structures. Using a novel method to isolate these receptors, we identified Dectin-1 as the
macrophage b-glucan receptor. Dectin-1 acted as a classical pattern recognition receptor, recognising a variety of b-1,3 and/or b-1,6 linked glucans, as well as intact yeasts, and is the primary receptor for these carbohydrates in macrophages. Dectin-1 also mediates the phagocytosis of particulate glucans, an activity which is dependent of the cytoplasmic tail of this molecule. In addition to these exogenous ligands, the receptor recognised an endogenous ligand on T-cells, but through a binding site which was distinct from that which recognised b-glucans. We found Dectin-1 to be expressed in many tissues and highly expressed on the surface of immune cells, especially those of the monocyte / macrophage and neutrophil lineages. We have also identified the human homologue of Dectin-1 and have shown that it is structurally and functionally similar to the mouse receptor.