Comparison of immunological effects of commercially important beta-glucans

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The history of beta-glucan began over 50 years ago with two different starting points, one originated in Europe and the United States and the second in Japan. Research on beta-glucans in the Euro-American milieu was based on the immunomodulatory effects of zymosan (mixture of polysaccharides isolated from the cell walls of *Saccharomyces cerevisiae*). On the other hand, the Japanese research was based on Asian medicine, where consuming medicinal mushrooms has been a long tradition.

The biological effects of beta-glucans are already well established and reach from stimulation of anti-infectious immunity to potentiation of cancer defense, from stress reduction to reduction of cholesterol. In addition to various animal studies, where beta-glucans were found to be active in wide range of species, basically from bees to monkeys, the effects of beta-glucans have also been also successfully examined in human models. Recently, beta-glucan was successfully used as part of a vaccine for high risk neuroblastoma. In addition, a series of clinical studies showed strong effects on the treatment of children with chronic respiratory problems. In addition, in Japan, beta-glucan has been widely used, since 1983, in the treatment of gastrointestinal cancer.

Over 10, 000 publications describing various biological effects of beta-glucans can be found in scientific literature. One of the problems resulting in rather low acceptance of beta-glucans in current medicine is the fact that, despite the overwhelming number of scientific reports, far too many individual beta-glucans have been used that differ widely in source, solubility, molecular weight, branching and other physicochemical characteristics. Diverse data on the comparison of structure, molecular size, and biological effects can be found in the literature.

In addition, various concentrations and routes of administration (oral, intraperitoneal, intravenous, subcutaneous) have been tested. All this leads to severe confusion, with numerous manufacturers claiming that their beta-glucan possesses the highest biological activities. The problem of diverse data can be solved only by

comparative studies. However, scientific reports directly comparing individual beta-glucans are extremely limited. This led us to the current comparative review of several different commercially available and well-established beta-glucans. To evaluate them better, we used four different, yeast-derived β-beta-glucans. Two of them were available in two different purities.

All beta-glucans were either donated or purchased from the manufacturers or distributors. Beta-glucan T85 was from USA and with 85% purity, beta-glucan K75 was 75% purity. Beta-glucans B80 and B70 were from Brasil with 80% and 70% purity, resp. Beta-glucan L75 was from Germany with 75% purity and beta-glucan Z80 was from China and 80% pure. In all cases, we measured the immunological effects after 14 days of oral food supplementation with 100 μg of beta-glucan/day.

For evaluation of biological activities, we decided to use five different tests able to evaluate the effects. We tested the effects on phagocytosis of peripheral blood neutrophils and on superoxide production by the same type of cells, evaluating the cellular part of the immune reactions. Testing the effects on production of IL-2 and on specific antibody formation we evaluated the effects on humoral part of the immunity. The final tests involved the effects on cancer growth and progression.

Beta-glucans are manufactured, tested and used in almost every country of the world. For our study, we decided to use several samples originating from the same source (*Saccharomyces cerevisiae*), but differing in purity and in manufacturer. All of these beta-glucans are commercially available, often in several countries.

The effects of beta-glucans on cellular immunity are well established. Usually, the test of choice are the effects on phagocytosis, as if the beta-glucan does not stimulate phagocytosis, it might have little effects on additional facets of the defense reactions. As in our previous comparative study, we employed synthetic hydroxyethyl methacrylate particles known for minimal nonspecific adhesion to the membrane of phagocytosing cells.

Figure 1 summarizes the effects on phagocytic activity. Whereas all tested beta-glucans significantly increased phagocytosis, it is clear that two beta-glucans clearly showed the strongest activity – beta-glucan T85 and B80.

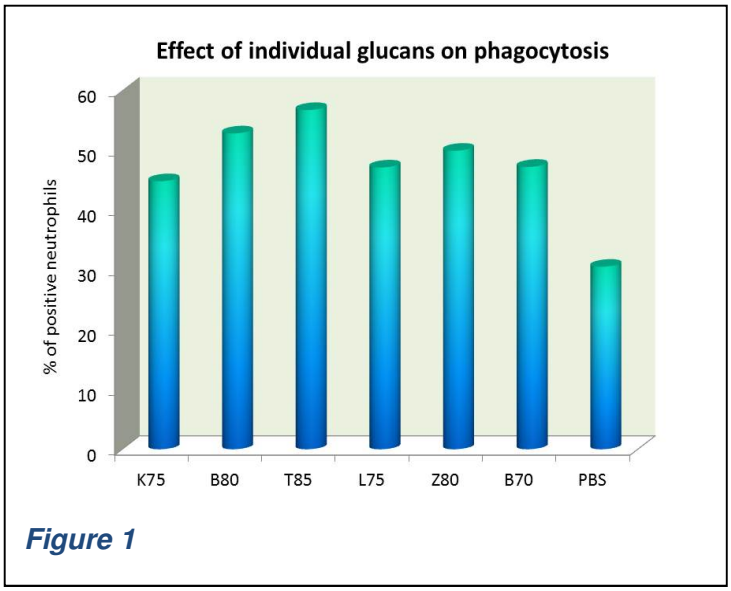

Figure 1

Phagocytosis results in internalization of the prey, but represents only one of the several subsequent steps, leading to burst of metabolic activity and final killing and/or destruction of the ingested material. Therefore, we evaluated the effects of our beta-glucans on production of superoxide anion using a model of mouse neutrophils. Data shown in Figure 2 confirmed that again, all tested beta-glucans significantly increased the formation of superoxide anion, with beta-glucan T85 and B80 being again the most active samples.

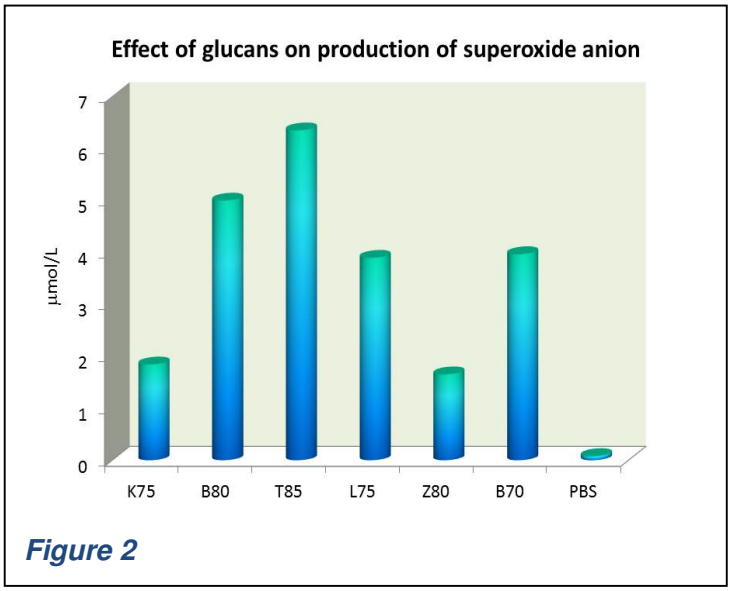

Figure 2

Besides effect on cellular branch of the immune reactions, beta-glucan were also shown to affect humoral branch of immunity. Among these effects, beta-glucans have significant effects on various cytokines with a wide range from IL-1, IL-2, and IL-6 to TNFα, and IFNγ. To compare the effects of our group of beta-glucans, we measured the production of IL-2 by splenocytes (*in vitro*). The secretion of IL-2 by untreated murine splenocytes is zero, therefore all beta-glucans significantly increased the IL-2 production (Figure 3).

Next, we evaluated the less known area of beta-glucan biological effects - antibody response. Recent observation suggested that the best beta-glucan also support antibody production, leading to suggestions that beta-glucan can be part of vaccination. In farmed animals such as fish or chicken, beta-glucan inclusion in vaccine is already being intensively studied. We used an immunization of mice with ovalbumin, where orally applied beta-glucans were used together with two separate intraperitoneal injections of antigen. As positive control, ovalbumin was used with Freund's adjuvant. The results summarized in Figure 4 are expressed as a percentage of control immunization with antigen only. It is clear that all beta-glucans significantly increased the formation of specific antibodies, but again, activities of beta-glucan T85 and B80 were the highest.

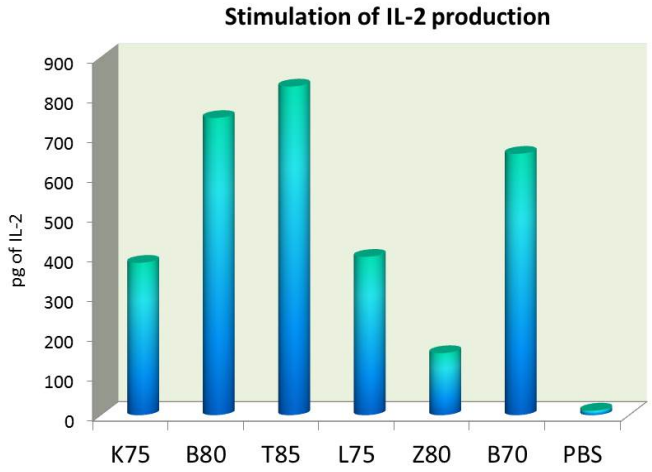

Figure 3

In the last part of our study, we focused on the role of tested substances in cancer development. As an experimental model, we used mice challenged with Ptas64 mammary tumors. Two weeks of beta-glucan supplementation caused significant reduction of cancer growth (measured as tumor weight), with beta-glucan T85 and B80 showing the highest reduction of breast cancer growth (Figure 5).

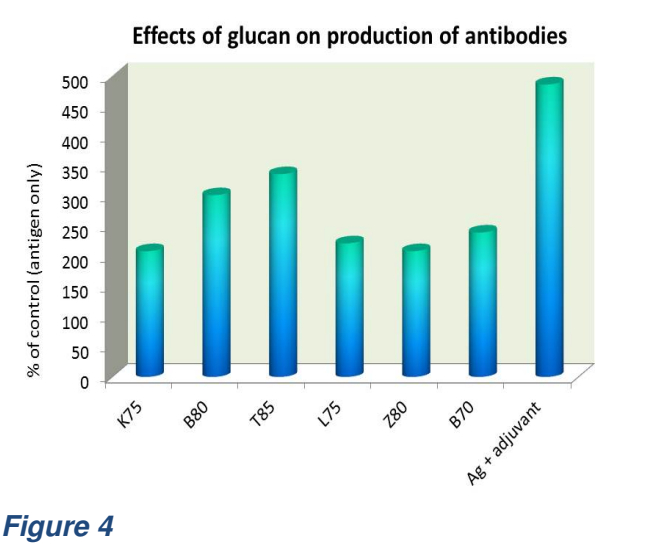

Figure 4

Beta-glucans are the most studied natural imunomodulators which, due to the numerous ongoing human clinical trials, have the strongest chance to become an approved drug even in Western medicine. However, it is often difficult to compare the effects of beta-glucan differing in source, isolation techniques, solubility and other physicochemical characteristics such as branching or molecular weight. These comparisons are possible only when individual beta-glucans are compared in one study using identical experimental design.

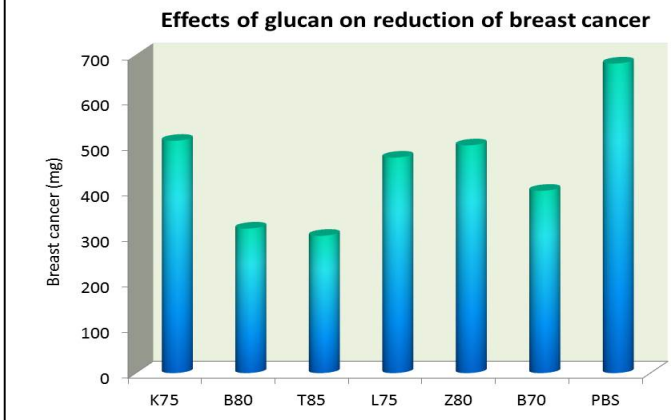

Figure 5

From our study we can conclude that we clearly demonstrated that there are severe differences in immunological activities among our selected group of beta-glucans. Despite the fact that all beta-glucans were isolated from the same source, we showed that not all beta-glucans are created equal. Beta-glucans T85 and B80 were in every experiment the most active beta-glucans and the differences between these two beta-glucans were insignificant. On the other hand, the Z80 beta-glucan (despite its quite high purity) repeatedly showed only average effects.

Regardless of the country, there are dozens and most probably hundreds of different beta-glucans available, differing in quality, source, purity, and price. All offer the best effects under the sun. Which one should we buy? Beta-glucans can be isolated from numerous sources, including yeast, mushrooms, and grain. In fact, beta-glucans can and have been isolated from almost every species of mushroom and yeast. In addition, several additional, more exotic sources of beta-glucan have been described, including plants such as lilies or even protists. There is a lack of comprehensive reviews comparing the biological effects of beta-glucans isolated from various sources, and despite extensive investigations, no final conclusion has been reached with respect to structure and function. Therefore, there is not a single research paper willing to state that one source of beta-glucan is better than another.

This takes us back to the original question: which, out of hundreds of individual beta-glucans on the current market, is the best one? Which one has superior biological and/or immunological properties?

From our study and from careful comparison of other studies, it is evident that individual beta-glucans widely differ in their biological effects. Yes, Bentley and Dacia are cars and both will get us to our destination eventually, but the level of comfort and pleasure will be substantially different. The same is true about beta-glucans. The real importance in deciding which beta-glucan to buy and to consume lies in finding a respectable company. It might not be surprising that every retailer claims that his beta-glucan is the best, and the competitors are selling inferior products, and the question arises once again. The most important aspect is to either manufacture or purchase beta-glucan from a solid source and control the quantity, purity, and the biological activity.

To summarize the facts mentioned above, it is extremely important to choose a manufacturer or distributor closely connected to the manufacturer, who invested not only in careful isolation and purification, but also in research. In doing just this, one can be certain that the beta-glucan purchased will be doing its part in helping the immune system to fight intruders.