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Severe Differences in Immunological Activities Among Our Selected Group of Glucans

Mark Twain [1*], Acton [1]

KAWUN Institute of Higher Education, Afghanistan.

***Corresponding Author:** Mark Twain, KAWUN Institute of Higher Education, Afghanistan.

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Abstract

Biological and most of all immunological effects of natural immunomodulator glucan are already well established. However, since hundreds of individual glucans, isolated from various sources, used at different concentrations and having different physicochemical characteristics are being used, the current scientific knowledge is not complete. In addition, direct comparisons of individual glucans are quite rare. In the present paper, we tested fifteen varieties of glucans differing in source and solubility. Whereas no direct connection between source and immunological effects was found, we can conclude that the best glucans have pleiotropic effects stimulating all facets of immunological reactions, whereas other glucans have low effects or none at all.

Keywords: Glucan; phagocytosis; IL-2; antibodies; breast cancer; superoxide anion

Introduction

The biological effects of 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 (for review see [1,2]). In addition to various animal studies, where glucans were found to be active in wide range of species, basically from shrimp to horses, the effects of glucans have also been also examined in human models. Soluble glucan was found to decrease the infection incidence and need for antibiotics [3]. Recently, glucan was successfully used as part of a vaccine for high risk neuroblastoma [4]. In addition, a series of clinical studies showed strong effects on the treatment of children with chronic respiratory problems [5,6]. In Japan, glucan has been widely used, since 1983, in the treatment of gastrointestinal cancer [7].

Over 7,000 publications describing various biological effects of glucans can be found in scientific literature. One of the problems resulting in low acceptance of glucans in current medicine is the fact that, despite the overwhelming number of scientific reports, far too many individual 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 [2]. Some studies suggest that the effects are dependent on the helical conformation. However, the triple helix structure most likely is not a solely effective form of glucan, because alkaline treatment, used in most isolation procedures, destroys this structure [8].

Methods

Animals

Female, 8 week old BALB/c mice were purchased from the Jackson Laboratory (Bar Harbor, ME). All animal work was done according to the University of Louisville IACUC protocol. Animals were sacrificed by CO_2 asphyxiation followed by cervical dislocation.

Material

All glucans were either donated or purchased from the manufacturers or distributors.

Cell lines

Human myeloblastic cell line HL-60 was obtained from the ATCC (Manassas, VA). The BALB/c mouse-derived mammary tumor cell line Ptas 64 was generously provided by Dr. Wei-Zen Wei of the Michigan Cancer Foundation, Wayne State University, Detroit, MI. The cells were maintained in RPMI 1640 (Sigma Chemical Co., St. Louis, MO) medium containing HEPES (Sigma) buffer supplemented with 10% heat-inactivated FCS (Hyclone Lab., Logan, UT), without antibiotics, in plastic disposable tissue culture flasks at 37°C in a 5% CO_2/95% air incubator.

Results

Glucans are manufactured, tested and used in almost every country of the world. For our study, we decided to use several samples differing in the source (yeast, mushroom, oat and barley), solubility (both soluble and insoluble), and origin (United States, Germany, Denmark, South Korea and Czech Republic). All of these glucans are commercially available, often in several countries. Almost none of the manufacturers provide any information about solubility. We tested the solubility by solubilization of three different concentrations of glucan in water at 22°C under constant shaking for 30 minutes. Based on the amount of sugar measurable in the solution after filtration (data not shown), we called the sample soluble (over 90% of glucan), semisoluble (20-89%) or insoluble (below 20%).

In the next step, 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 glucan injections caused significant reduction of cancer growth (measured as tumor weight) in five cases–Glucan #300, Immunox 3-6, GlucanReal, Beta Glucan (Germany) and Reishi.

In the last part of our study, we evaluated the less known area of glucan effects-antibody response. We used an immunization of mice with ovalbumin, where glucans were applied together with two separate intraperitoneal injections of antigen. As positive control, ovalbumin was used with Freund's adjuvant.

Discussion

Glucans are carbohydrates consisting of linked glucose molecules, which are major structural components of the cell walls of yeast, fungi and some bacteria. In addition, cereals such as barley and oat contain glucans as a part of their endosperm. Glucans are the most studied natural immunomodulators 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 glucan differing in source, isolation techniques, solubility and other physicochemical characteristics such as branching or molecular weight. These comparisons are possible only when individual glucans are compared in one study using identical experimental design. Despite thousands of scientific papers, often describing new and new types of glucan, comprehensive reviews comparing individual biological or immunological activities are rare. Most of them are focused more on the relation between biological activities and chemical properties, which does not fully help to answer the question which glucan is better. Other comparative studies focused on comparison of glucans extracted from oat, wheat or barley, but the studied effects were focused on effects on liver and glucose regulation. However, there are no similar comparative studies on glucan and immune reactions.

Conclusion

Our study clearly demonstrated that there are severe differences in immunological activities among our selected group of glucans. Several glucans consistently showed higher biological activities, most of all Immunox 3-6, Glucan Real, Beta-Glucan (Germany) or Reishi, but in every tested reaction, the Glucan #300 was the most active sample. The differences between individual glucans found in this report might explain the sometimes-confusing results published in the literature. It is clear that the immunological and biological effects of individual glucan are not connected to their source or solubility.

Competing Interests

The authors declare that they have no competing interests.

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