Editorial

Why so many glucans?

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There are various natural sources of β−glucans - it can be isolated from yeast, mushrooms, seaweed, bacteria, various grains and even protozoa. However, there are three main sources: mushrooms, yeast and grain. The reasons are mainly historical-the Western civilization has consumed both bread and beer for centuries, therefore there is a significant surplus of yeast. Similarly, Far East is known for adding mushrooms to the regular diet and various mushrooms are part of the old folk remedies. Grain glucans are the result of a surplus of various grains in Canada and Australia. With so many sources, it is not surprising that any market offers dozens of different glucans. If we calculate the whole world, the number of individual glucan might reach hundreds. Since yeast (usually the common baker's yeast) is the easiest and cheapest source, it is not surprising that glucans are most frequently prepared from fungal cell walls. Baker's yeast (Saccharomyces cerevisiae) is likely the best raw material for glucan isolation. However, it is important to note that it is rather difficult to get the glucan molecule out of the yeast wall structure in a highly active form. Therefore, the high quality glucans cannot be sold for pennies and when a potential buyer sees a bottle of glucan for only few dollars, he should be careful.

The major challenge of the isolation process is to remove the impurities, such as mannoproteins and lipids (attached to the end points of the side branches in the intact cell wall), without the significant loss of desirable biological activity. Often a question about the possible eating of the whole yeasts or mushrooms appears. They surely do not contain glucan, but whole yeasts nor mushroom alone are not the optimal source of active beta glucan. This is due primarily to their content of available glucan not being high enough, so we would have to consume large quantities of raw material. In addition, our gastrointestinal tract is not prepared to digest whole yeast and to extract pure glucan from yeast cell walls. When glucan is not adequately purified, it will contain numerous impurities, often acting against the biological effects of glucan molecules. Some of these impurities can block the specific binding site on the membrane of immunocytes, further inhibiting the binding. In addition, due to their larger size, they are normally not phagocytized by gut cells and, therefore, insufficient amount of glucan can enter our body. The same is true about the glucan versions offering mushroom powder instead of purified glucan.

Until recently, biologically efficient β−glucans were supposed to have similar structures-a main chain of β(1→3) bound D-glucopyranose molecules (for better perspective, imagine beads on the string) to which some D-glucopyranoses are randomly connected by β(1→6) linkages causing a different degree of branching in different glucans. The detailed structure of β−glucans from dissimilar sources differs as well as their biological activity. In native β−glucans, their fibrils are composed from organized parts in which the main chain is coiled to a triple helix. These regions are combined with single or double filaments of β(1→3)-D-glucopyranoses. The triple helix, formed by three hydrogen bonds and stabilized by side chains, is probably present only in high-molecular β−glucans with molecular weight over 90kDa.[1] The hydrogen bonds of triple helices can be interrupted by increased temperature, high pH or certain solvents. On the other hand, numerous studies confirmed that small glucan-based oligosaccharides are as active as large glucans.[2–4]

Diverse data on comparison of structure, molecular size, and biological effects can be found in literature. For example, the antitumor activity of schizophyllan is supposedly conditioned by the triple helix presence and a molecular weight higher than 100kDa. It is more than likely that the triple helix structure is not the sole effective form of β−glucan, because alkalic treatment, used in most isolation procedures, kills this structure. In addition, the most recent opinions do not confirm the established ideas of the necessity of high molecular mass and branching of biologically active β−glucans. Almost forty years ago, Kabat[5] found that, for antigen polysaccharidic determinants, the size of the binding site on an antibody corresponds to six or seven monosaccharide units. The size of the binding site for β−glucan (in this case on a receptor of an immunocompetent cell) also appears to correspond to the number of glucose residues.[5] These findings were recently used in preparation of small, synthetic glucan-based oligosaccharides.[6] So, despite extensive research, we cannot say which physicochemical characteristics will guarantee a highly active glucan and without substantial biological testing.[7–9]

From the information mentioned above, it is clear that our knowledge of glucan chemistry is still far from complete. The same is true about the correlation of size, origin, structure, and biological activities. Clearly, the older assumption that only large, insoluble glucans are biologically active was wrong. This idea most probably originated from the hypothesis that only soluble glucans can bind to the membrane of cells. However, studies performed in recent years show that insoluble glucan is also internalized by cells that are slowly digesting and subsequently releasing it in the form of either soluble glucan or extremely small fragments. The mechanisms of action, therefore, are the same as in the case of soluble glucans.[10] After several cycles, small molecules of soluble glucans bind to their receptors. Another dogma used to say that glucans from sources like grains or seaweed are not good enough or not active at all. This hypothesis was most probably due to the fact that glucans from these resources used to be insufficiently purified, resulting in mediocre biological activities. Grain glucans used to be sold very cheaply as a byproduct from production of flour. However, recent studies using highly purified oat-derived glucan demonstrated that this particular glucan is as active as any high quality glucan. To summarize, information about the molecular size, branching, solubility, three-dimensional structure etc. is often interesting from the scientific point of view, but is most

probably not relevant for the real-world situation. More important are the data about purification and isolation techniques, subsequent characterization, and final purity of the sample. The most important data, however, are data about its biological activities.

One of the problems restricting the use of glucan is the fact that, despite the overwhelming number of scientific papers, far too many individual glucans have been used that differ widely in source, solubility, molecular weight, branching and other physicochemical characteristics. With various routes of administration added to the mix, confusion is clear. The problem with diverse data can be only solved by comparative studies, which are still rare.[11–13] The direct conclusion from these studies is clear-no direct connection between source and immunological activities exists. In addition, highly purified and highly active glucans have strong and pleiotropic biological effects, whereas poorly isolated glucans have only average or minimal biological effects.

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Conflict of interest

The author declares no conflict of interest.

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