Effects of β-glucan on some environmental toxins: An overview

Vaclav Vetvicka

Background. Beta-glucans are naturally occurring polysaccharides and constituents of the cell wall of certain pathogenic bacteria and fungi. They have proven healing and immunostimulating properties, linked to enhanced macrophage and natural killer cell function which likely involves specific interaction with several cell surface receptors, such as lactosylceramide, selected scavenger receptors, and dectin-1 (betaGR). In particular, glucan reduces the immunosuppressive effects of a number of agents including chemo therapy and radiation. More recent studies suggest a positive function for glucan in the immunosuppression caused by toxic agents in the environment.

Aim. An overview of the effects of glucan on the mycotoxin, aflatoxin and other environmental toxins (mercury-thimerosal, depleted uranium).

Conclusion. Glucan is effective as a natural immunomodulator and could be used as an inexpensive solution to reducing the adverse effects of some environmental toxins.

Key words: beta-glucan, aflatoxin, mercury, depleted uranium, detoxification, immunity

INTRODUCTION

Environmental toxins have significant adverse effects on the health of both animals and man. Such toxins increase host susceptibility to infections, compromise the immune system and increase the risk of autoimmune disease. These issues have led to large epidemiological studies that attempt to establish sets of immunologically relevant end points.

Glucans are a major constituent of the cell wall of certain saprophytic and pathogenic fungi. For many years, they have been shown to reduce the immunosuppressive effects of a number of factors, including chemo and radiation treatment. Following discovery of the effects of glucan on bone marrow protection and activation of bone marrow progenitor cells, studies have suggested new functions for glucan. These are based on the well-known fact that glucan strongly stimulates all facets of the immune system, from nonspecific response to both branches of the specific immune system. From this, emerged the hypothesis that glucan might offset or at least reduce immunosuppression caused by toxic agents.

GLUCAN AND MYCOTOXINS

Contamination of the environment from the air to the soil, represents a serious danger not only to commercially farmed animals but also to humans. Some of the most deadly and persistent contaminants of animal feed are aflatoxins. These are naturally occurring mycotoxins that are produced by many species of Aspergillus, predominantly Aspergillus flavus and Aspergillus parasiticus. High-level aflatoxin exposure causes acute hepatic necrosis that may later result in cirrhosis or carcinoma of the liver. Acute hepatic failure manifests as hemorrhage, edema, alteration in digestion and changes to the absorption and metabolism of nutrients. No animal species is immune to the acute toxic effects of aflatoxins and although humans are more resistant, the current data support the danger of hepatocellular cancer in man.

The levels of aflatoxins in agriculture are controlled by a variety of strategies including use of fungicides and pesticides but these treatments have a significant negative impact on the environment and often incur similar health problems to aflatoxins themselves.

The first studies showed that (1-3)-β-D-glucan, particularly with the (1-6)-β-D-glucan side chains, can regulate the presence of aflatoxins. Subsequent research revealed that under physiological conditions, mostly temperature, glucan can absorb up to 50% of zearalenone molecules, most probably via hydrogen bonding between the hydroxyl, lactone, and ketone groups of the zearalenone molecule with the glucan single helix and van der Waals interactions between the phenyl and the β-D-glucopyranose moieties.

Further studies focused on interactions between glucan and aflatoxin B1. These showed that glucan was involved in binding to aflotoxin B1. Using molecular methods, it was revealed that hydroxyl, lactone and ketone groups participated in formation of hydrogen bonds and van der Waals interactions between glucan and aflatoxin B1 (ref.11). The first investigations of glucan as a decontaminant used insoluble glucans isolated from Saccharomyces cerevisiae. A later publication showed that glucan was chemically modified to form crosslinked...
carboxymethyl glucan. The resulting glucan had greatly improved adsorption of the mycotoxin T-2 and zearalenone.

However, to further establish the exact mechanisms of the adsorption of these mycotoxins on glucans, more research will be needed, in particular using a large number of glucan derivates. The exact molecular structure of tetraalkylammonium-modified carboxymethylglucan remains to be determined too.

Another interesting study used the known fact that manno-oligosaccharides can attenuate aflatoxicosis and that glucans protects DNA against oxidative stress-related damage. In testing the mechanisms involved in the aflatoxin-inhibiting effects of *Lentinula edodes* cultures, the authors demonstrated that these cultures act as an external stimulus affecting the anti-oxidant status in the fungal cells, which subsequently inhibits aflatoxin. Glucan present in cultures activates the transcription factors related to the anti-oxidant response. Based on this study, glucan acts not only by absorption of mycotoxins but directly reduces aflatoxin production.

When we understand that mushrooms such as *L. edodes* can grow directly on waste materials such as olive mill wastewaters, it is clear how significant this finding might be. After all, Lentinan isolated from this mushroom has been used for treating gastric cancer for more than 30 years. In addition, *L. edodes*-based glucans have extremely low cellular toxicity. For this reason they can be used directly in animal feed, simultaneously strengthening the immune system of animals and detoxifying their feed.

**GLUCAN AND OTHER TOXINS-MERCURY, PERLUOROCTANIC ACID, DEPLETED URANIUM**

Glucan has been found to protect bone marrow against the toxic effects of both chemotherapy and irradiation, most probably via direct stimulation of bone marrow progenitor cells. It is not surprising that glucan is attracting interest as a supplement for reducing the side-effects of cancer treatments. Additional effects of glucan were found using a model of 2.45 Ghz electromagnetic radiation and oxidative injury of the skin. This experiment showed that the prophylactic use of glucan reversed the radiation-caused changes in MDA levels and SOD activities. The authors hypothesized that glucan can offer protection against oxidative injury induced by electromagnetic radiation, most likely through its known anti-oxidant abilities.

Our laboratory focused on the ability of yeast-derived insoluble glucan #300 to decrease the immunosuppressive actions of various immunotoxins including mercury and perfluorooctanoic acid. The presence of mercury salts in the environment represents a serious problem, resulting in accumulation of mercury in fish and despite the fact that organic ethylmercury present in limited amounts in vaccines was apparently officially cleared from causing autism, it can still have strong immunosuppressive properties including lowering of cellular and humoral reactions such as phagocytosis, IL-6 and IL-12 secretion and NK cell activity. Similarly, perfluorooctanesulfonates were found to decrease humoral immunity, IL-6 and IL-10 secretion and natural killer cell activity.

Our studies showed that two-week oral administration of glucan greatly ameliorated the immunosuppressive action of mercury, including IL-6 and IL-12 production,
Glucan was also tested in the case of depleted uranium toxicity. The toxic effects of this compound manifests mostly via mitochondrial dysfunction, with the most relevant toxic mechanisms believed to be oxidative stress and reactive oxygen species. A detailed study showed that glucan attenuated the formation of depleted uranium-induced mitochondrial reactive oxygen species, lipid peroxidation and glutathione oxidation. In addition, further mitochondrial dysfunction including outer membrane damage and release of cytochrome c was prevented. The mechanisms by which glucan supplementation blocks or at least lowers immunosuppression are currently unclear. One option is simple stimulation of immune reactions which supplements the lowering of immunity caused by exposure to toxins. A second option might be upregulation or down-regulation of some important genes, such as ERCC5, CASP9, CYPIAI, CDC42, OKC, BCl-2 or NF-κB. Clearly, more research is needed before glucan can be fully established in the treatment immunotoxic disorders. The relevant activity of glucan in vitro and in vivo is summarized in Table 1.

### Table 1. Antitoxic activity of glucan in vitro and in vivo.

<table>
<thead>
<tr>
<th>Type of glucan</th>
<th>Source</th>
<th>Effects on</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insoluble</td>
<td><em>Saccharomyces cerevisiae</em></td>
<td>Adsorption, animal protection</td>
<td>10</td>
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<tr>
<td>Insoluble</td>
<td><em>Saccharomyces cerevisiae</em></td>
<td>Myxotoxin complexation</td>
<td>11</td>
</tr>
<tr>
<td>Alkali-soluble</td>
<td><em>Saccharomyces cerevisiae</em></td>
<td>Myxotoxin complexation</td>
<td>11</td>
</tr>
<tr>
<td>Insoluble</td>
<td><em>Saccharomyces cerevisiae</em></td>
<td>Adsorption of aflatoxin</td>
<td>12</td>
</tr>
<tr>
<td>Soluble</td>
<td><em>Saccharomyces cerevisiae</em></td>
<td>Adsorption of zearalenone and T-2 toxin</td>
<td>13</td>
</tr>
<tr>
<td>Insoluble</td>
<td><em>Saccharomyces cerevisiae</em></td>
<td>Oxidative DNA damage</td>
<td>15</td>
</tr>
<tr>
<td>Soluble</td>
<td><em>Lentinula edodes</em></td>
<td>Antioxidant enzymes stimulation</td>
<td>16</td>
</tr>
<tr>
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<td><em>Saccharomyces cerevisiae</em></td>
<td>Antioxidant enzymes</td>
<td>22</td>
</tr>
<tr>
<td>Insoluble</td>
<td><em>Saccharomyces cerevisiae</em></td>
<td>IL-6, IL-12, phagocytosis, antibodies</td>
<td>30</td>
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<tr>
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<td><em>Saccharomyces cerevisiae</em></td>
<td>Proliferation, NK cell activity</td>
<td>31</td>
</tr>
<tr>
<td>Insoluble</td>
<td><em>Saccharomyces cerevisiae</em></td>
<td>Cellularity, proliferation, antibodies</td>
<td>32</td>
</tr>
<tr>
<td>Insoluble</td>
<td><em>Saccharomyces cerevisiae</em></td>
<td>Amikain-caused ototoxicity</td>
<td>33</td>
</tr>
<tr>
<td>Insoluble</td>
<td><em>Saccharomyces cerevisiae</em></td>
<td>ROS formation, GSH oxidation</td>
<td>35</td>
</tr>
</tbody>
</table>

There are additional reports describing the protective effects of glucan against toxicity. One is a report evaluating the effect of glucan on hearing loss caused by amikacin. Amikacin treatment showed significant ototoxicity by causing serious deterioration of hearing at most tested frequencies. Oral administration of glucan together with amikacin limited the hearing loss. In addition, glucan also showed some hearing improvement when used alone. The exact mechanisms are not known but the authors speculate that inhibition of free radical formation might be involved.

### CONFLICT OF INTEREST STATEMENT

The author stated that there are no conflicts of interest regarding the publication of this article.

### REFERENCES

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