



จากห้องปฏิบัติการ Glucan #300 (หรือ Beta Glucan #300) สู่มือผู้ บริโภคในนาม Glucan 300® (หรือ beta 1,3D Glucan)


ส่วนหนึ่งของงานวิจัยเชิงเปรียบเทียบที่แสดงให้เห็นว่า Glucan 300®
ดีที่สุด

(ปัจจุบันมีการเปรียบเทียบกันมากกว่า 100 ผลิตภัณฑ์แล้ว)

molecules

Review

Beta Glucan: Supplement or Drug? From Laboratory to Clinical Trials

Vaclav Vetvicka ^{1,*}, Luca Vannucci ², Petr Sima ² and Josef Richter ³

¹ Department of Pathology and Laboratory Medicine, University of Louisville, Louisville, KY 40292, USA

² Department of Immunology, Institute of Microbiology, 142 20 Prague, Czech Republic; vannucci@biomed.cas.cz (L.V.); sima@biomed.cas.cz (P.S.)

³ Zdravotní ústav se sídlem v Ústí nad Labem, 400 01 Ústí nad Labem, Czech Republic; josef.richter@zuusti.cz

* Correspondence: vaclav.vetvicka@louisville.edu; Tel.: +1-502-852-1612; Fax: +1-502-852-1177

Received: 12 March 2019; Accepted: 28 March 2019; Published: 30 March 2019



Another clinical trial studied the mushroom-derived glucan, Maitake, in myelodysplastic syndromes, which can progress to acute myelogenous leukemia [65]. The results showed elevated functions of neutrophils and monocytes, particularly production of reactive oxygen species. For more information about glucans and their application in cancer therapy, see Aleem [66].

In parallel, our own research focused on children with chronic respiratory problems. In the last decade, we conducted a series of clinical, placebo-driven trials evaluating the effects of a short-term supplementation with glucan on the immune parameters in children. For these studies, we used Glucan #300, which is currently the most tested commercially available glucan with established high immunostimulating activity [67]. Randomly selected groups of children were treated with an oral dose with 100 mg of glucan/day for a period of 30 days. The results showed that this short-term supplementation improved the levels of salivary immunoglobulins (sIgM, sIgG, and sIgA) (Figure 5) [22], decreased eNO levels, and improved physical endurance of children [68]. Further,

Comparison of Immunological Effects of Commercially Available β -Glucans: Part III

Abstract

β -Glucans represent the most studied natural immunomodulators. With the well-described structure and function, the use of glucans slowly but steadily progresses from supplements to drug. However, direct comparisons of biological activities of individual glucans are rare. As this study will show, no direct connection between source and immunological activities was found. Based on these results, we can conclude that highly purified and highly active glucans have strong and pleiotropic effects, whereas poorly defined glucans have only medium (if any) biological effects.

Research Article

Volume 2 Issue 4 - 2016

Vaclav Vetvicka* and Jana Vetvickova
Department of Pathology, University of Louisville, USA

*Corresponding author: Department of Pathology, University of Louisville, Louisville, KY, USA. Tel: 502-852-1612; Email: Vaclav.vetvicka@louisville.edu

Received: May 31, 2016 | Published: June 28, 2016

Table 1: Types of glucan used.

Glucan	Source	Manufacturer
Beta Glucan	Oat	Bioimersion, Bellevue, WA, USA
Organic Immuno-build Mushrooms	Mushroom	Rainbow Light Nutritional Systems Santa Cruz, CA, USA
Reishi Mushroom Extract	Mushroom	Mehdi Reishi
Beta Glucan	Yeast	Cape Fear Naturals, Wilmington, NC, USA
Beta 1,3 Glucans	Yeast	The Vitamin Shoppe, North Bergen, NJ, USA
Beta 1,3/1,6-D-Glucan	Yeast	Piping Rock, Ronkonkoma, NY, USA
β -Glucan Ball	Mushroom	Umeken, Cerritos, CA, USA
Beta Glucan	Yeast	Vistra, Thailand
Barley Beta Glucan	Barley	Doctor's Best, Irvine, CA, USA
Beta Glukan	Mushroom	Nef De Sante, Prague, Czech Republic
Yestimun	Yeast	Leiber, Bramsche, Germany
Sangraksu Chaga Mushroom	Mushroom	Betaglucan Korea, Seoul, Korea
Beta 1,3 Glucan	Mushroom	Douglas Laboratories, Pittsburg, PA, USA
Beta Glucan	Yeast	Source Naturals, Santa Cruz, CA, USA
#300	Yeast	Transfer Point, Columbia, SC, USA

described earlier [7].

Nitrite production

For nitrite (NO₂⁻) formation we employed a technique described in Green & Nacy [13] with LPS as triggering agent.

IFN γ production

eliminating false positivity [14]. Our results are summarized in Table 2 and show that some glucans are not active even in massive 800 μ g dose, whereas other glucans (such as Reishi Mushroom Extract, Beta 1,3/1,6-D-Glucan, Yestimun, or Beta Glucan) showed clear dose-dependency. In general, **Glucan #300** was again the most active glucan showing significant effects even at the lowest 25 μ g dose.

Conclusion

The third part of our ongoing investigation of commercially available glucans clearly demonstrated that several differences among samples exist, which might be an explanation for sometimes confusing results found in the literature. Similarly to our previous two comparisons [7,12], we tested 15 different glucans differing in source (mushroom, yeast, barley and oat). Again, **Glucan #300** served as a benchmark. Our study confirmed that where there is

no basal level (IL-2 or IFN- γ), all or at least most glucans showed significant activity. However, in other biological activities, most of the glucans showed very limited if any activity, which was most clear in case of cancer growth. Clearly, individual glucans differ in biological effects based on tested characteristics. No clear relevance between the source used for isolation and biological effects has been found. **From all samples, the Glucan #300 was the most active sample.**

Glucans and Cancer: Comparison of Commercially Available β -glucans – Part IV

VACLAV VETVICKA and JANA VETVICKOVA

Department of Pathology, University of Louisville, Louisville, KY, U.S.A.

Table I. List of glucans used in this study.

	Glucan	Source	Solubility	Manufacture
1	Beta Glucan 500 mg	Yeast	Insoluble	Priority One Vitamins
2	Beta Glucan (1,3/1,6) -Hypoallergenic	Yeast	Insoluble	Kirkman
3	Supreme Beta Glucan 95% 500 mg	Yeast	Insoluble	Hippo Herbs
4	Beta 1,3 Glucan #710	Yeast	Insoluble	Dee Cee Lab
5	ImmunotiX 500	Yeast	Insoluble	Xymogen
6	Beta Glucan,	Yeast	Insoluble	Wonder Laboratories
7	ImmunoMed 3-6	Yeast	Insoluble	NuMedica
8	Super Pure Beta 1,3 Glucan Algae Extract	Algae	Insoluble	The Synergy Company
9	Beta 1,3 Glucans	Yeast	Semi-Soluble	Puritan's Pride
10	Immune Support with β Glucan	Yeast, Mushrooms	Insoluble	Lindberg
11	Glucan Elite	Yeast	Semi-Soluble	Pro Formulations MD
12	Beta Glucan	Yeast	Semi-Soluble	Professional Formulas
13	Avena Sativa (Oat) Powder	Oat	Semi-Soluble	Maple Lifesciences
14	Beta Glucan 1,3-1,6	Yeast	Soluble	Bulk Supplements.com
15	Beta 1,3 Glucan	Yeast	Insoluble	AFI (America's Finest)
16	Glucan #300	Yeast	Insoluble	Transfer Point

we can conclude that on one hand, glucans can have substantial effects on all branches of the immune system, but on the other hand, not all glucans are created equal. Similar to our older comparative studies, we used glucans isolated from yeast, mushroom, algae, and oat. However, no clear correlation between function and other characteristics, such as source or solubility, could be reached. The differences between activities of our commercially available glucans might be an explanation for the sometimes confusing results found in the literature. In all tests employed in our study, Glucan #300 was the most active.

Conflicts of Interest

No conflicts of interests exist for the Authors.

2013.

- Vetvicka V and Vetvickova J: Immunostimulating properties of two different β -glucans isolated from maitake mushroom (*grifola frondosa*). JANA 8: 33-39, 2005.
- Vetvicka V and Vetvickova J: An evaluation of the immunological activities of commercially available beta 1, 3 glucans. JANA 10(1): 9-15, 2007.
- Vetvicka V and Vetvickova J: Physiological effects of different types of beta-glucan. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub 151(2): 225-231, 2007.
- Vetvicka V and Vetvickova J: A comparison of injected and orally administered beta glucans. JANA 11(1): 42-49, 2008.
- Vetvicka V and Vetvickova J: Comparison of immunological effects of commercially available β -glucans Appl Sci Rep 1: 1-7, 2014.
- Vetvicka V, Fornusek L, Kopecek J, Kaminkova J, Kasperek L

$\beta(1-3)$ -D-glucan affects adipogenesis, wound healing and inflammation

Vaclav Větvicka · Jana Větvicková

lesterolemic animals and patients (Tietyen et al. 1990). Our later study is not only made a direct comparison of the cholesterol-lowering activity of two different yeast-derived $\beta(1-3)$ -D-glucans, but also is the first to compare normal animals and mice with experimentally-induced cholesterolemia (Větvicka and Větvicková 2009). In addition, we showed that the type of branching is probably not responsible for these effects.

In addition to the effects mentioned above, $\beta(1-3)$ -D-glucan has been shown to have other numerous biological effects. An interesting study used $\beta(1-3)$ -D-

$\beta(1-3)$ -D-glucans

Yeast-derived insoluble $\beta(1-3)$ -D-glucan #300 were purchased from Transfer Point (Columbia, SC), yeast-derived Now BETA $\beta(1-3)$ -D-glucan from Now Foods (Bloomington, IL), grain-derived Glucagel T from GraceLinc (Christchurch, New Zealand), mushroom-derived Krestin from (Kureha Chemical Industries, Tokyo, Japan), and Epicor from Embria Health Sciences, Ankeny, IA. Using the *Limulus* lysate test, we determined the LPS contamination to be below 0.005 U/ml.

(Větvicka and Větvicková 2010). We used the most effective $\beta(1-3)$ -D-glucans and focused on their less studied biological activities.

To allow investigation of the effect of $\beta(1-3)$ -D-glucan on the wound healing process, simple scratch-wound model was used. The effect of exogenously added $\beta(1-3)$ -D-glucans has been tested on the regeneration of monolayer. We have seen the remarkable influence of the presence of three types of $\beta(1-3)$ -D-glucan on the regeneration of monolayer. Since the $\beta(1-3)$ -D-glucans do not influence the proliferation of keratinocytes, we hypothesize that $\beta(1-3)$ -D-glucan enhances the regeneration process of wound healing both by paracrine stimulation of the cytokines. Whereas wound healing effects of $\beta(1-3)$ -D-glucan are usually considered to be result of enhanced macrophage functions (Browder et al. 1988), our experimental design using a single cell monolayer suggests either the stimulation of collagen synthesis (Wei et al. 2002) or increased production of cytokines (Větvicka et al. 2007).

Data presented in this study clearly demonstrated significant differences in activities among individual types of $\beta(1-3)$ -D-glucans. In addition, it is clear that individual $\beta(1-3)$ -D-glucans can be highly active in one particular part of immune reaction and mediocre in other parts of immune reaction. The only $\beta(1-3)$ -D-glucan consistently showing the highest activity in all tested reactions was Glucan #300, which corresponded with the previous studies (Větvicka and Větvicková 2008, 2009, 2010). In addition, we showed that besides the well-established effects of $\beta(1-3)$ -D-glucans on immune reactions, this natural immunomodulator has multiple pleiotropic functions such as inhibition of adipogenic differentiation and inhibition of acute inflammation. Studies seeking detailed information on the mechanisms of these actions are currently in progress.

Conflict of interest There is no conflict of interest.

β 1,3-Glucan: Silver Bullet or Hot Air?

V. Vetvicka* and J. Vetvickova

University of Louisville, Department of Pathology, Louisville, USA

Table 1. Types of Glucan Used in this Study

Glucan	Source	Solubility	Manufacturer	Reference
Maitake Gold	Mushroom	Soluble	NutraGenesis, Brattleboro, VT	[6]
Krestin	Mushroom	Soluble	Kureha Corp, Japan	[5]
Aktival	Yeast	Insoluble	Farmal, Croatia	
Immutol	Yeast	Insoluble	Biotec ASA, Norway	[7]
Now Glucan	Yeast Mushroom	Insoluble Soluble	Now Foods, Bloomingdale, IL	[7]
Sweet Beta Glucan	Yeast	Soluble	K2 Global, Las Vegas, NV	
Beta Right 101	Yeast	Insoluble	Biothera, Eagan, MN	[26]
Epicor	Yeast	Insoluble	Vitamin Research Products, Carson City, NV	
NSC	Yeast	Insoluble	Nutritional Scientific Corp., Liberty, TX	[27]
Glucagel	Barley	Soluble	PolyCell Technologies, Crookston, MN	[7]
Better Immunity	Yeast	Insoluble	Young Again Nutrients, Magnolia, TX	
Macroforce	Yeast	Insoluble	ImmuneDyne, Houston, TX	[28]
Solgar	Yeast	Insoluble	Solgar, Leonia, NJ	
Wellmune	Yeast	Insoluble	Biothera, Eagan, MN	[26]
Swanson	Yeast	Insoluble	Swanson Health Products, Fargo, ND	
Glucan #300	Yeast	Insoluble	Transfer Point, Columbia, SC	[7]

parts of immune reaction. **Glucan #300 showed the highest activity in all tested reactions (with the exception of the antibody formation where it was close second). Some of the**

immunology, CRC Press, Boca Raton 2000.
[12] Green SJ, Nacy CA. Antimicrobial and immunopathological effects of cytokine-induced nitric oxide synthesis. *Curr Opin Infect Dis* 1993; 6: 284-396.



Comparison of immunological effects of commercially available β -glucans

Vaclav Vetvicka* and Jana Vetvickova

*Correspondence: Vaclav.vetvicka@louisville.edu



CrossMark

← Click for updates

Department of Pathology, University of Louisville, Louisville, KY, USA.

Table 1. Types of glucan used.

Glucan	Source	Solubility	Manufacturer
Beat Max	Yeast	Insoluble	Chisolm Biological Laboratories, Aiken, SC
Oat Beta Glucan	Oat	Insoluble	Health Breakthroughs, Lake Oswego, OR
Bio-Glucan	Yeast	Insoluble	Pharma Nord, Vojens, Denmark
Qore defense	Mushroom	Insoluble	Quivana, Provo, UT
Immunox 3-6	Yeast	Insoluble	Xymogen, Orlando, FL
Betacan 500	Yeast	Insoluble	Arrowhead Healthworks, Cedarpine Park, CA
Glucan Real	Mushroom	Soluble	QueGen Biotech, South Korea
MC-Glucan	Mushroom	Soluble	Macrocare Tech, South Korea
Beta Glucan (Germany)	Yeast	Insoluble	Biotikon, Germany
Barley Glucan	Barley	Insoluble	Sigma, St. Louis, MO
Beta Glucan	Mushroom/yeast	Partly soluble	Vitabase, Monroe, GA
Reishi	Mushroom	Soluble	Hostdefence, Olympia, WA
Beta Glucan	Yeast	Insoluble	Greenpath, Wrightsville Beach, NC
Hliva ustricna	Mushroom	Insoluble	Walmart, Trinec, Czech Republic
Glucan #300	Yeast	Insoluble	Transfer Point, Columbia, SC

Vetvicka et al. *Applied Scientific Reports* 2014,
<http://www.hoajonline.com/journals/pdf/2054-9903-1-2.pdf>

doi: 10.7243/2054-9903-1-2

demonstrate the effects of various doses of tested glucan on phagocytosis of peripheral blood neutrophils. Several trends can be observed—clear dose-dependency, several glucans showed no activity even at the highest doses, and the most active glucan (Glucan #300) reached the plateau at a dose of 100 μ g, with the level of stimulation not achieved by other glucans even at a dose of 800 μ g. The glucans with

IL-2 by splenocytes (*in vitro*). The secretion of IL-2 by untreated murine splenocytes is zero, therefore all glucans significantly increased the IL-2 production (Table 4). It is clear, that the Concanavalin A elicited the highest response, with Glucan #300 being close. Several other glucans showed high activity—Bio-Glucan, Immunox 3-6, Glucan Real and MC-Glucan. Similar effects were seen in stimulation of IFN- γ secretion.

ตัวอย่างงานวิจัยที่ใช้ Glucan 300® จาก Transfer Point, USA

American Journal of Immunology 9 (2): 43-47, 2013

ISSN: 1553-619X

©2013 Science Publication

doi:10.3844/ajisp.2013.43.47 Published Online 9 (2) 2013 (<http://www.thescipub.com/aji.toc>)

PLACEBO-DRIVEN CLINICAL TRIALS OF TRANSFER POINT GLUCAN #300 IN CHILDREN WITH CHRONIC RESPIRATORY PROBLEMS: ANTIBODY PRODUCTION

¹Vetvicka Vaclav, ²Richter Josef, ³Svozil Vladimír, ²Rajnohova Dobiasova Lucie and ²Kral Vlastimil

¹Department of Pathology, School of Medicine, University of Louisville, Louisville, KY, USA

²Zdravotní ústav se sídlem v Ústí nad Labem, Czech Republic, Europe

³Sanatorium Edel, Zlaté Hory, Czech Republic, Europe

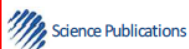
immunomodulator β -glucan as a possible solution.

β -Glucans are well-known natural Biological Response Modifiers (BRM). Thus far, glucans are classified as "non-specific" because their biological effects are pleiotropic. On the other hand, for the past 30 years,

body's defense against pathogens (Auinger *et al.*, 2013).

For our clinical trial, we used the best characterized insoluble, yeast-derived glucan #300, which was repeatedly confirmed to be the most active commercially available glucan (Vetvicka and Vetvickova, 2007; 2010).

Correspondence Author: Vaclav Vetvicka, Department of Pathology, University of Louisville, 511 S. Floyd, Louisville, KY 40202, USA



2.2. Glucan

Yeast-derived insoluble glucan #300 (>85% dry w/w basis) was purchased from Transfer Point (Columbia, SC, USA). This glucan contains 96% carbohydrates and 2.1% proteins. Neutral sugar analysis confirmed 91.3% glucose and 8% mannose.

and 3). The highest increase was found in sIgA (183%).

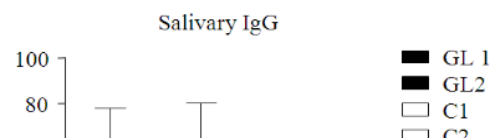


Table 1. Mean concentration of IgA, IgG and IgM saliva of children at baseline (day 1) and after completion of oral administration of glucan (day 30)

	GL1	GL2	C1	C2
IgG (mg/l)	44.3 (33.6)	47.4 (32.3)	33.9 (2.9)	15.5 (2.4)
	p<0.0001		p<0.0001	
IgA (mg/l)	288.4 (30.8)	502.9 (26.0)	295.1 (23)	123.0 (24)

increased the quality of results (Topkas *et al.*, 2012).

For our study we choose glucan #300, which is currently not only highly studied glucan, but also a glucan with the highest and most pleiotropic activities (Vetvicka and Vetvickova, 2010; 2012) regardless the route of administration (Vetvicka and Vetvickova, 2010). This study is a follow-up of our original finding of the



Effects of **Transfer Point Glucan #300** Supplementation on Children exposed to Passive Smoking - Placebo-driven Double-blind Clinical Trials

Richter Josef¹, Král Vlastimil¹, Svozil Vladimír², Rajnohova Dobiasova Lucie¹, Pohorska Jitka¹, Stiborova Ivana¹, Vetvicka Vaclav^{4,3}

¹Zdravotní ústav se sídlem v Ústí nad Labem, Czech Republic

²Sanatorium Edel, Zlaté Hory, Czech Republic

³University of Louisville, Department of Pathology, Louisville, KY, USA

*Corresponding author: Dr. Vetvicka Vaclav, University of Louisville, Department of Pathology, 511 S. Floyd, Louisville, KY 40202, USA, E-mail: vaclav.vetvicka@louisville.edu

Citation: Richter Josef, Král Vlastimil, Svozil Vladimír, Rajnohova Dobiasova Lucie, Pohorska Jitka, et al. (2014) Effects of Transfer Point Glucan #300 Supplementation on Children exposed to Passive Smoking - Placebo-driven Double-blind Clinical Trials. *J Nutr Health* 1: 105

Received Date: April 1, 2014 Accepted Date: May 16, 2014 Published Date: May 20, 2014

Regulation of Hematopoiesis in Cancer Patients: Placebo-Driven, Double-Blind Clinical Trials of β -Glucan

Vaclav Vetvicka, Josef Richter, Vlastimil Král, Lucie Rajnohová Dobiášová, Ivana Stiborova, Jitka Pohorska

findings in glucan-supplemented cancer patients treated three to five months after finishing cancer treatment.

MATERIALS AND METHODS

Protocol

▲ randomized, double-blind, placebo-controlled trial compared β -glucan #300 and a placebo in cancer patients after surgery and chemotherapeutic and radiotherapeutic treatment. We evaluated

RESULTS

Table 1 summarizes the levels of tested parameters in both groups of patients. In both groups, levels found at the beginning and the end of the study are given. Levels of CRP were not statistically significant in any group, similar to the levels of transferrin, ferritin and soluble transferrin receptor. Index of sTfR/log ferritin shows insignificant differences in the placebo group, with highly significant differences



Anti-Inflammatory Effects of β -Glucan in Cancer Related Fatigue

Richter J¹, Kral V¹, Stiborova I¹, Rajnohova D¹ and Vetvicka V^{*2}

¹Zdravotní ústav se sídlem v Ústí nad Labem, Czech Republic

²Department of Pathology, University of Louisville, Louisville, KY, USA

*Corresponding author: Vetvicka V, Department of Pathology, University of Louisville, 511 S. Floyd, Louisville, KY 40292, USA, E-mail: vaclav.vetvicka@louisville.edu

Citation: Richter J, Kral V, Stiborova I, Rajnohova D, Vetvicka V (2015) Anti-Inflammatory Effects of β -Glucan in Cancer Related Fatigue. J Nutr Health Sci 2(3): 304

Glucan

Yeast-derived insoluble **glucan #300** was purchased from Transfer Point (Columbia, SC, USA). This glucan is over 85% pure. A single daily dose of 200 mg was used for 60 days.

Glucan Supplementation Has Strong Anti-melanoma Effects: Role of NK Cells

VACLAV VETVICKA and JANA VETVICKOVA

University of Louisville, Department of Pathology, Louisville, KY, U.S.A.

Correspondence to: Vaclav Vetvicka, University of Louisville, Department of Pathology 511 S. Floyd, Louisville, KY 40404, U.S.A. Tel: +1 5028521612, Fax: +1 5028521177, e-mail: Vaclav.vetvicka@louisville.edu

Key Words: Glucan, melanoma, NK cells, immunity, antibodies, cancer.

lymphocytes (16), or through inhibition of tumor-induced angiogenesis (17).

In the current study, we decided to evaluate the potential anti-melanoma effects of yeast-derived Glucan #300, which was consistently shown to be the most active glucan (18). This glucan had strong anti-tumor potential in a mouse

0250-7005/2015 \$2.00+.40

5287

Materials. Yeast-derived insoluble Glucan #300 was purchased from Transfer Point (Columbia, SC, USA); its purity was over 85%.

Assay from Promega (Promega, Madison, WI, USA) according to the manufacturer's instructions. Briefly, 10 µl of lysis solution was added into appropriate control wells 45 min before the end of incubation.