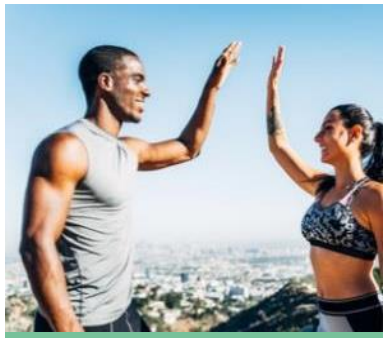
Not All Yeast Beta Glucans Are The Same

A deeper look into Wellmune's unique differentiating molecular structure

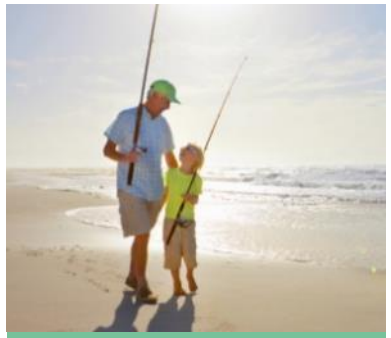
Sonja Nodland, PhD
Principal Scientist, ProActive Health

Consumer Health & Wellness

Consumers are evolving in their behavior by taking a proactive approach to health and wellness.



Vitality



Taking Care

Preventative

Long-term

Proactive

The global health and Wellness market has reached a market evaluation of **1.5 trillion** and growing at a rate of **5-10%** per year.

Consumers continue to prioritize investment in health and wellbeing. **61%** of consumers globally intend to increase their spending on health in the next 12 months.

67% of global consumers agree that "**gut health** is key to achieving holistic wellbeing.

80% of Asan consumers says that due to Covid-19, they have spent time educating themselves on ingredients and procedures that can boost their **immune health**.

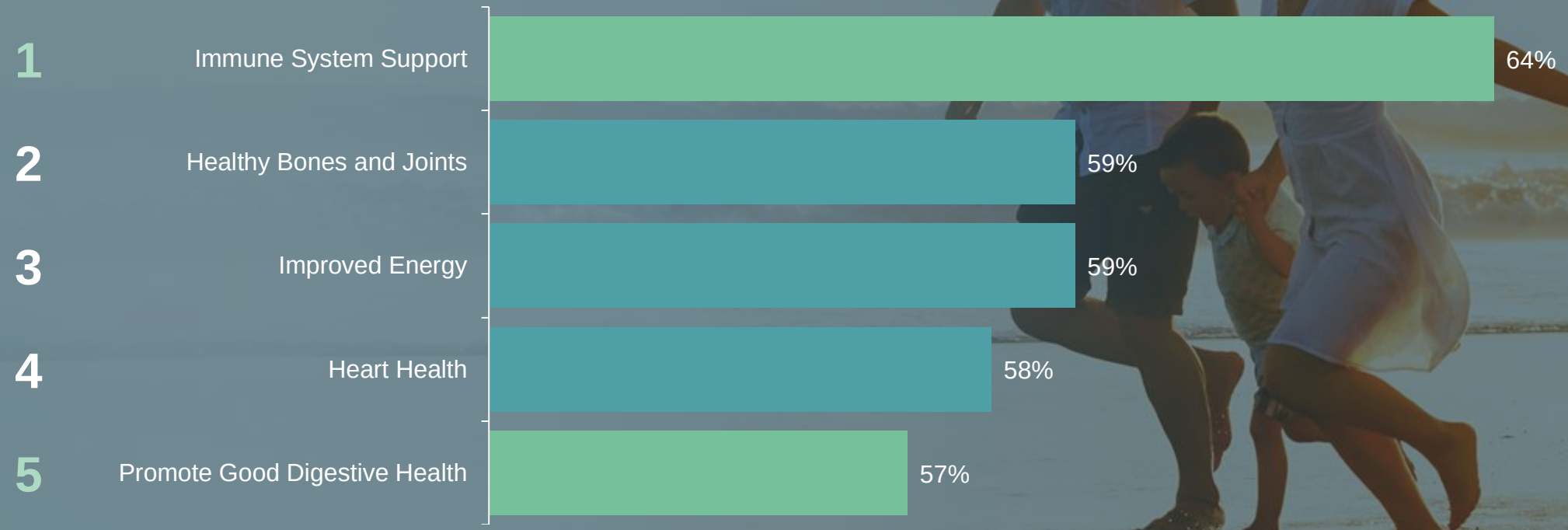
Source: Innova database, McKinsey survey

Reasons for Purchasing Healthy Lifestyle Products in Asia

*Note: Top 5 ranked based on % of sample who selected each reason as a purchase driver. Base: Asia (n=5639)

Source: Kerry Global Consumer Survey - Digestive & Immune Health, 2019-2021

Reasons for Purchasing Healthy Lifestyle Products in Malaysia



*Note: Top 5 ranked based on % of sample who selected each reason was the most important (i.e. ranked first)

Source: Kerry Global Consumer Survey - Digestive & Immune Health, 2019-2021

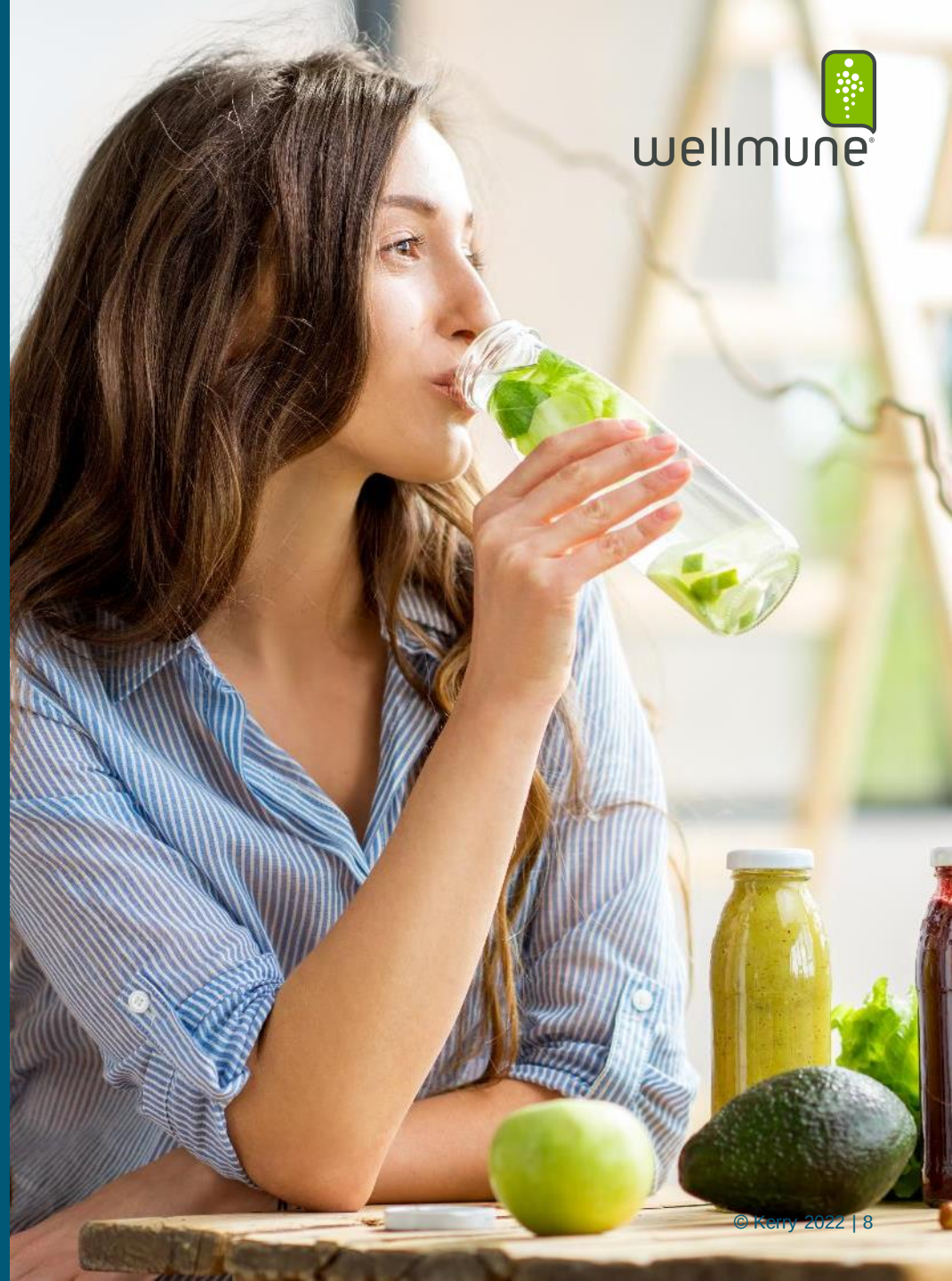
What is Wellmune® and How Does it Work?

Introducing Wellmune®

- Wellmune® is a natural food, beverage and supplement ingredient clinically proven to help strengthen the immune system.
- A proprietary baker’s yeast beta 1,3/1,6 glucan, Wellmune makes it easier for people of all ages to be well and stay well.

Wellmune’s Mechanism of Action

Beta Glucans 101



Beta Glucan Sources

Beta glucans are fibers naturally found in foods such as mushrooms, cereal grains (like oats) and yeast. They are growing in awareness for their benefits.

Oats

Notable for promoting heart health and helping manage LDL (bad) cholesterol.

Mushrooms

Have been shown to have immune health benefits but their potency is lower and research on benefits is mixed.

Yeasts

- Yeast-derived beta glucans usually originate in either baker's yeast or brewer's yeast.
- The source matters and not all strains are the same.
- The manufacturing or processing methods used to extract them can impact their and structure affects function.

Differences in β-glucan Molecular Structures

Each beta glucan source has a different structure (molecular backbone and level of branching), which affects its biological activity.

	Bacterial	linear β-1,3-glucan (Curdlan)
	Fungal	short β-1,6 branched β-1,3-glucan (*i.e.* schizophyllan) & β-1,4 main chains with β-1,3/1,6 branching (*i.e.* Krestin)
	**Yeast**	**long β-1,6 branched β-1,3-glucan**
	Cereal	linear β-1,3/ β-1, 4-glucan (*i.e.* oats, barley, rye)

 linear β-1,3-glucan

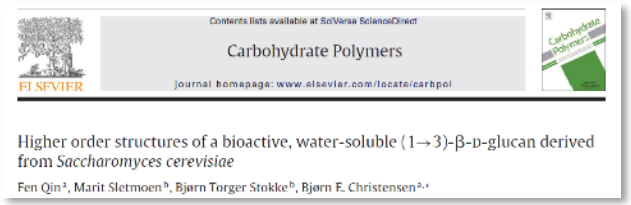
 β-1,6 branched b1,3-glucan branch

β-1,6 branch

 β-1, 4-glucan

Just like when you refer to a maple tree (like yeast beta glucans), there are variations in those maple trees that make them different - branch numbers, placements and lengths.

Structure - Bioactivity Relationship for Beta Glucans is Well Known



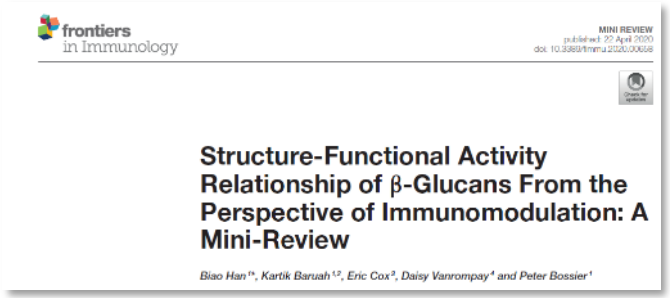
Contents lists available at SciVerse ScienceDirect

Carbohydrate Polymers

journal homepage: www.elsevier.com/locate/carbpol

Higher order structures of a bioactive, water-soluble (1→3)-β-D-glucan derived from *Saccharomyces cerevisiae*

Fen Qin[a], Marit Sletmoen[b], Bjørn Torger Stokke[b], Bjørn E. Christensen[a,*]



frontiers in Immunology

MINI REVIEW

Structure-Functional Activity Relationship of β-Glucans From the Perspective of Immunomodulation: A Mini-Review

Biao Han[†], Kartik Baruah[†,2], Eric Cox[2], Daisy Vanrompay[4] and Peter Bossier[1]

ELSEVIER

Carbohydrate Polymers **28** (1995) 3–14

0144-8617(95)00076-3

(1→3)-β-D-Glucans as biological response modifiers: a review of structure–functional activity relationships

John A. Bohn & James N. BeMiller*

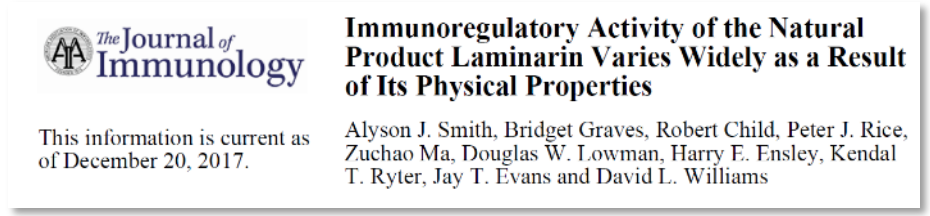
Contents lists available at ScienceDirect

Carbohydrate Polymers

journal homepage: www.elsevier.com/locate/carbpol

The linear structure of β-glucan from baker's yeast and its activation of macrophage-like RAW264.7 cells

Xing Zheng[a], Siwei Zou[a], Hui Xu[a], Qingye Liu[a], Jianhui Song[b], Min Xu[b], Xiaojuan Xu[a,*], Lina Zhang[a]

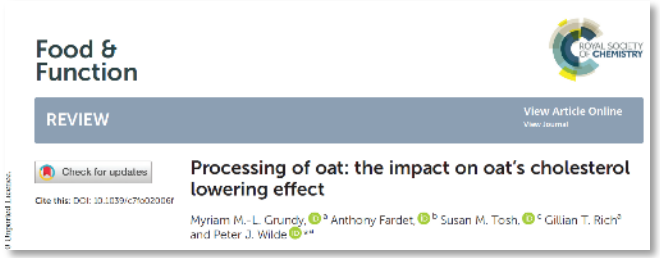


The Journal of Immunology

This information is current as of December 20, 2017.

Immunoregulatory Activity of the Natural Product Laminarin Varies Widely as a Result of Its Physical Properties

Alyson J. Smith, Bridget Graves, Robert Child, Peter J. Rice, Zuchao Ma, Douglas W. Lowman, Harry F. Ensley, Kendal T. Ryter, Jay T. Evans and David L. Williams



Food & Function

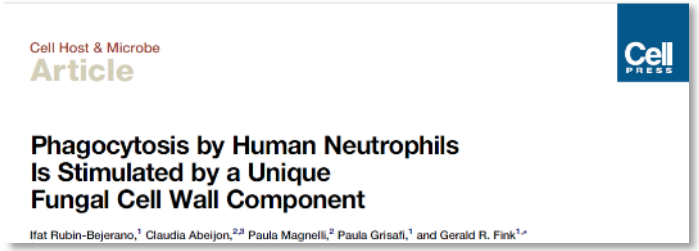
REVIEW

View Article Online

Check for updates

Processing of oat: the impact on oat's cholesterol lowering effect

Myriam M.-L. Grundy, Anthony Fardet, Susan M. Tosh, Gillian T. Rich and Peter J. Wilde

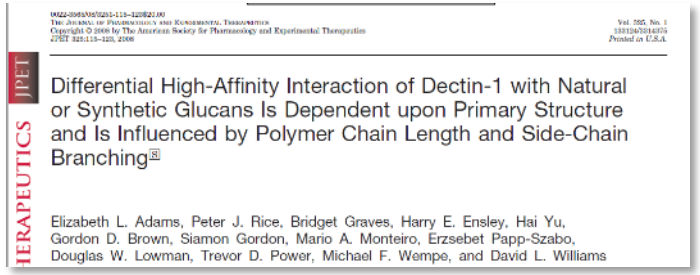


Cell Host & Microbe

Article

Phagocytosis by Human Neutrophils Is Stimulated by a Unique Fungal Cell Wall Component

Ifat Rubin-Bejerano,[1] Claudia Abeijon,[2,3] Paula Magnelli,[2] Paula Grisafi,[1] and Gerald R. Fink[1,*]



JPET

Differential High-Affinity Interaction of Dectin-1 with Natural or Synthetic Glucans Is Dependent upon Primary Structure and Is Influenced by Polymer Chain Length and Side-Chain Branching

Elizabeth L. Adams, Peter J. Rice, Bridget Graves, Harry E. Ensley, Hai Yu, Gordon D. Brown, Siamon Gordon, Mario A. Monteiro, Erzsebet Papp-Szabo, Douglas W. Lowman, Trevor D. Power, Michael F. Wempe, and David L. Williams

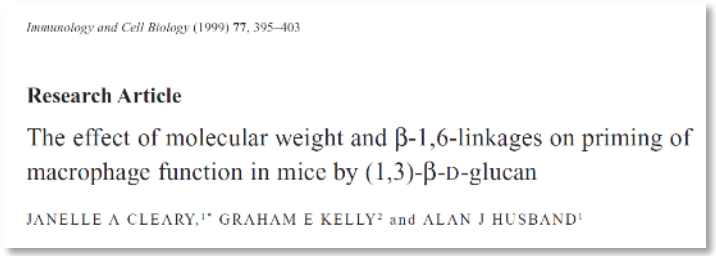
BIOMOLECULES & THERAPEUTICS

Invited Review

Biomol Ther 20(5), 433-445 (2012)

Immunomodulation of Fungal β-Glucan in Host Defense Signaling by Dectin-1

Sainkhuu Batbayar, Dong Hee Lee* and Ha Won Kim*



Immunology and Cell Biology (1999) **77**, 395–403

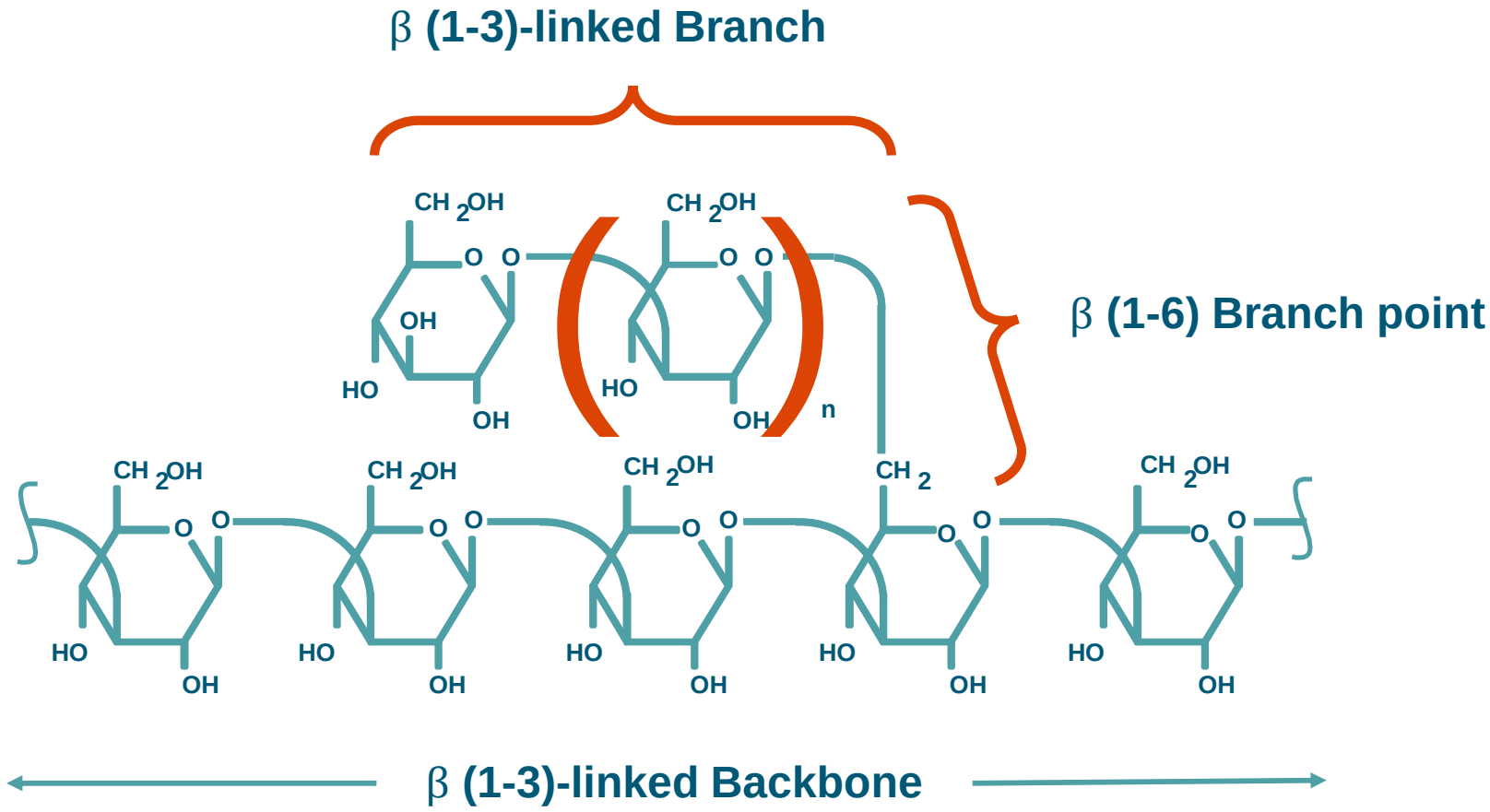
Research Article

The effect of molecular weight and β-1,6-linkages on priming of macrophage function in mice by (1,3)-β-D-glucan

JANELLE A CLEARY,[1*] GRAHAM E KELLY[2] and ALAN J HUSBAND[1]

The Wellmune® Difference

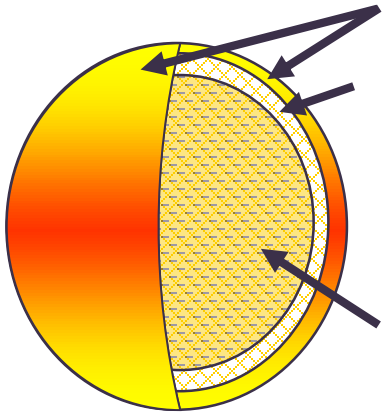
Health Benefits Begin with Structure



Wellmune Uses Proprietary Strains and Methods

Wellmune uses a proprietary strain of baker's yeast (Saccharomyces cerevisiae) and a proprietary method of obtaining the beta glucan from the baker's yeast.

Yeast Cell



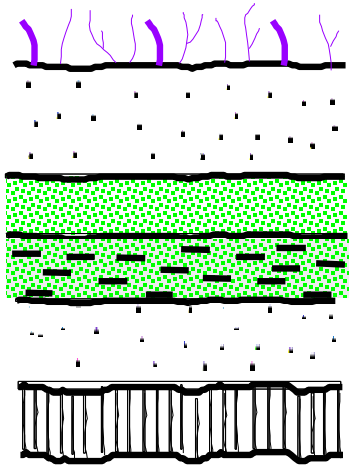
Mannoprotein

Beta 1,3/1,6 Glucan

Beta 1,3/1,6 Glucan

Lipids, Proteins, Nucleic Acids and cellular contents

Yeast Cell Cross Section



Fibrillar Layer

Mannoprotein

Beta 1,3/1,6 Glucan

Mannoprotein
Plasma Membrane
Cytoplasm. Lipids

Yeast Beta Glucan Uniqueness

Not all yeast beta glucans are the same

Structural differences between Wellmune® baker's yeast beta glucan and competitor yeast beta glucans:

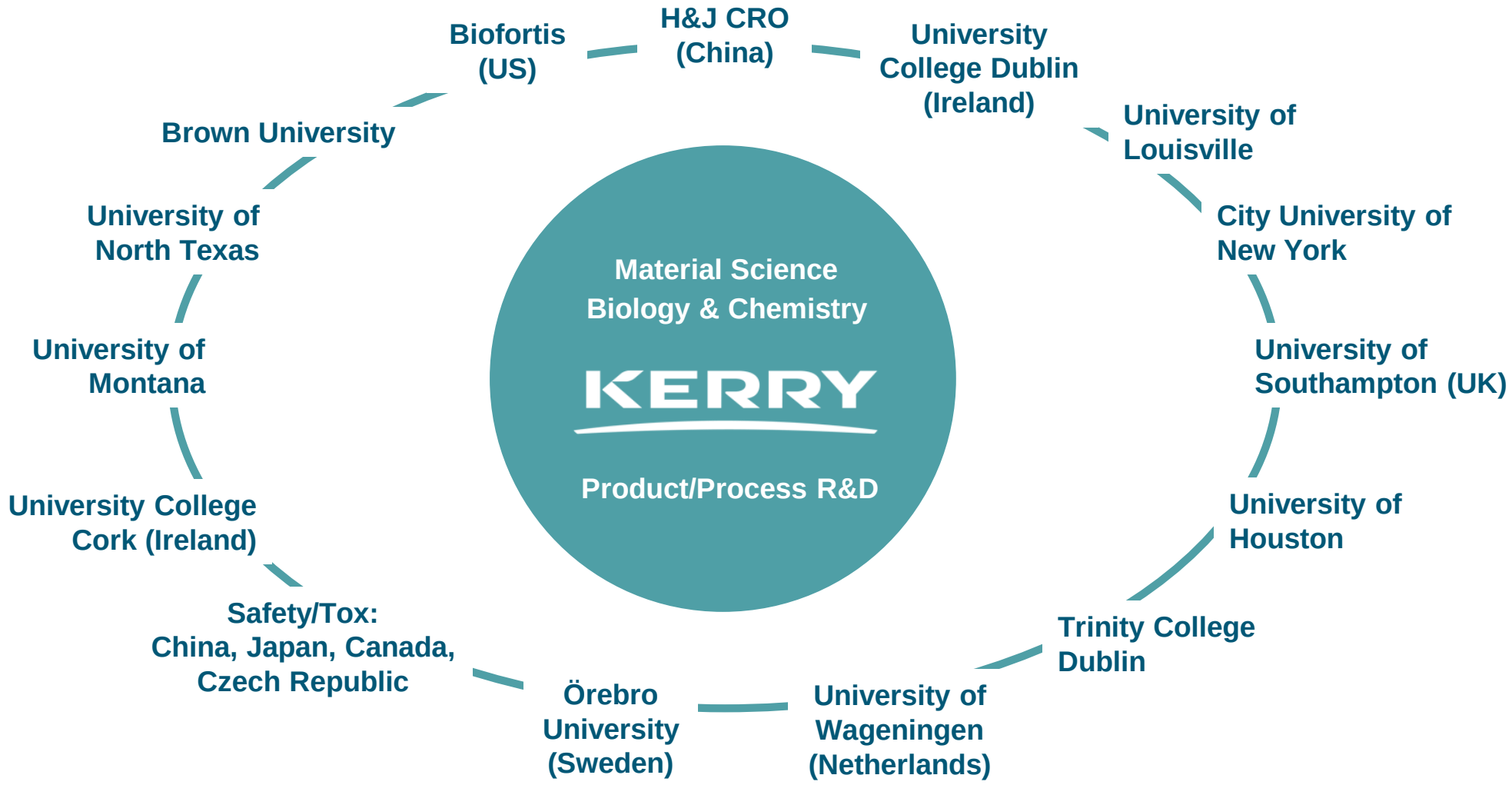
- We know from previous research[1] that some beta glucans affect immune activity, but the benefits depend on their chemical structure.
- New research[2] clearly demonstrates that yeast beta glucans also have complex structures, and they differ based on sources and processing methods.
- Wellmune and competitor yeast beta glucans are all yeast beta glucans but are very different in structure.
- Wellmune has over a dozen studies on its unique strain to show that its structure has functional benefits. Wellmune's well-researched benefits cannot be applied to another strain with a different structure.
- Further research is being done to look at how yeast beta glucan structure differences affect immune activity.

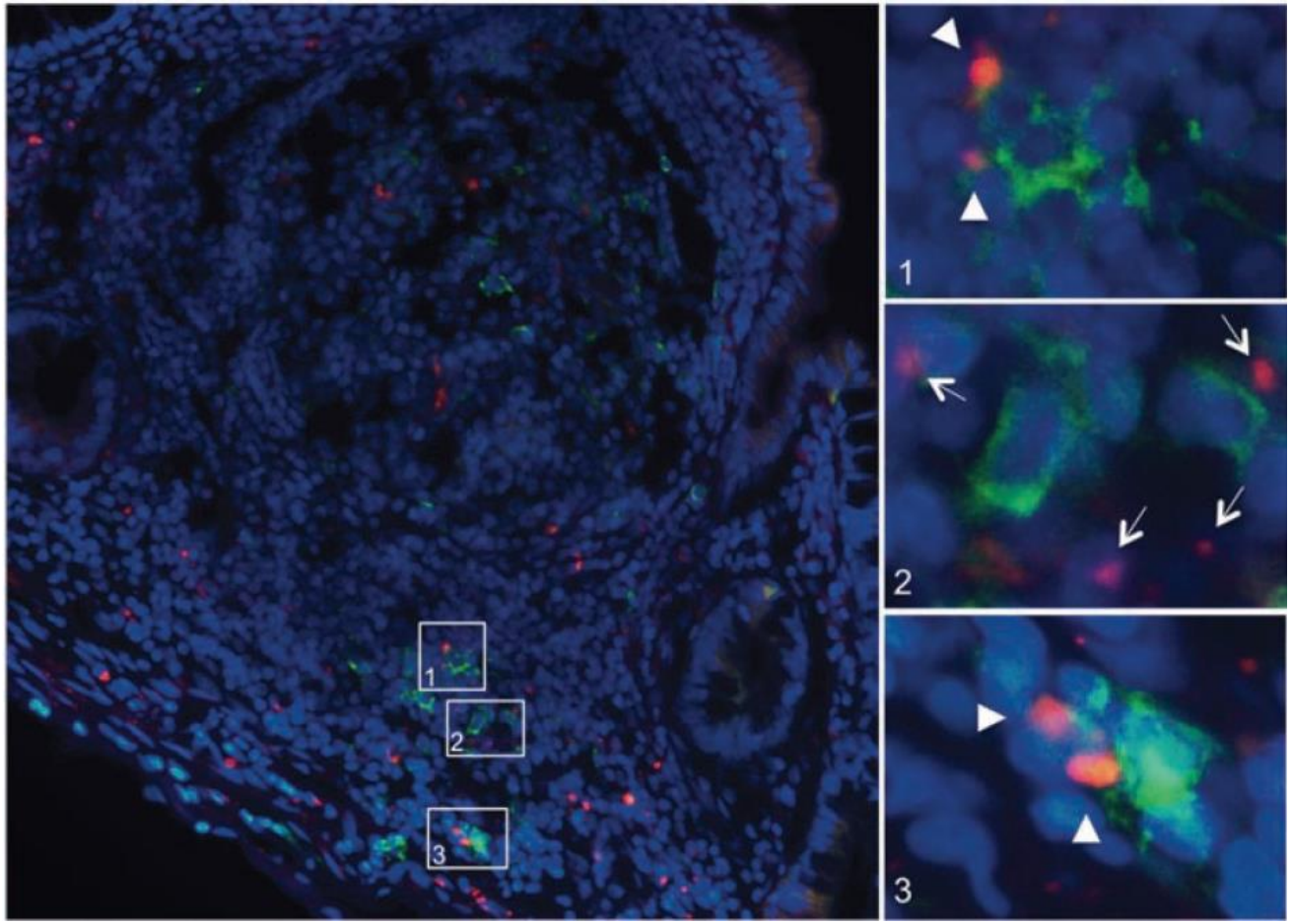
	Wellmune® baker's yeast beta glucan (W1)	Competitor #1 (G1)	Competitor #2 (B1)	Competitor #3 (L1)
% 1,3 linkage	>80%	<78%	<50%	>80%
% 1,6 linkage	>4%	<4%	>4%	<4%
% 1,4 linkage (glycogen)	<1%	>20%	>2%	<1%
Other linkages	<3%	>4%	>15%	>4%
% of total branches	>3	<2	>9	>3
% of short branches	<78	>80	>80	>80
% of long branches	>20	<20	<15	<15

1 Han, B., et al. (2020). "Structure-Functional Activity Relationship of Beta-Glucans From the Perspective of Immunomodulation: A Mini-Review." Front Immunol 11: 658.

2 Boutros JA, Magee AS, Cox D. 'Comparison of structural differences between yeast β-glucan sourced from different strains of saccharomyces cerevisiae and processed using proprietary manufacturing processes' Food Chem. 2021 Jul 28;367:130708

Wellmune® Research Collaboration Model





Percent of Immune Cells in Proximity to Wellmune		
Cell Type	Intestinal Villus	Intestinal FAE (near Peyer's Patch)
Macrophages	10%	23%
Dendritic Cells	30%	33%

Adapted from Ganda-Mall et al 2018. Inflamm Bowel Dis 24(1):166-178

Study: Exercise Stress

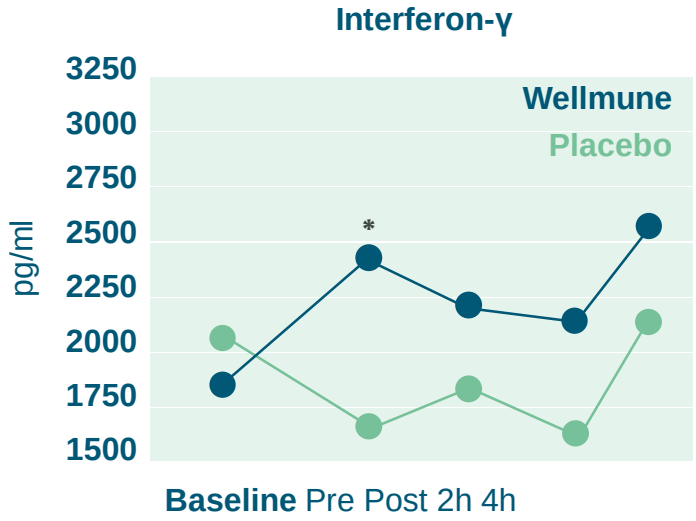
Study Protocol

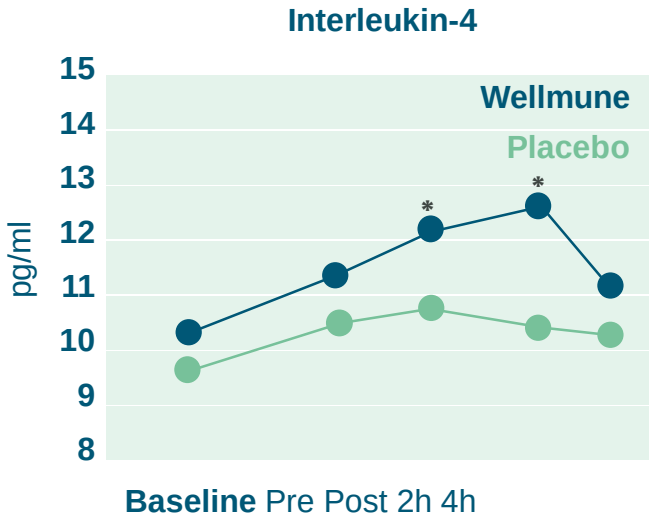
Study Site	Applied Physiology Laboratory, University of North Texas, USA
Population	109 healthy adults (50 men, 59 women)
Age	18-40 (average 21 years)
Design	Randomized, double-blinded, placebo-controlled, crossover study
Duration	10 days supplementation with Wellmune or placebo; seven-day wash out period; 10 days supplementation with Wellmune or placebo.
Serving	Participants were split into two groups, and consumed the following once daily for 10 days, in two separate instances: • 250mg Wellmune • Placebo

Additional Study Details:
After the 10 day supplementation period, participants jogged on a treadmill for 90 minutes in a hot, humid environment.

Study: Exercise Stress

Confirming previous biomarker research with athletes, Wellmune was found to support immune health during and after strenuous exercise in people of average fitness levels by maintaining higher levels of LPS-stimulated cytokines.





No effect on IL-10, MCP-3, MIP-1β, or TNF-α.

*p≤0.05, **p≤0.01, ***p≤0.001

"Oral Supplementation with Baker's Yeast Beta Glucan is Associated with Altered Monocytes, T Cells and Cytokines Following a Bout of Strenuous Exercise." (2017) Frontiers in Physiology 8:786.

Wellmune® Clinical Studies

Dozens of peer-reviewed published studies on Wellmune. Health benefit studies include over 2,300 adults and children.

- **1,713 healthy normal adults**
  - Physical stress studies (944)
  - Psychological stress studies (372)
  - Aging population (100)
  - Other studies (297)
- **669 healthy children, ages 1-4**
  - Wellmune children's study (156)
  - Sponsored children's studies (513)

A recent research review published in 2020 on the role of beta glucans in immune health provides a comprehensive overview of yeast beta glucan clinical studies and highlights the depth of evidence that demonstrates Wellmune's ability to help support the immune system.

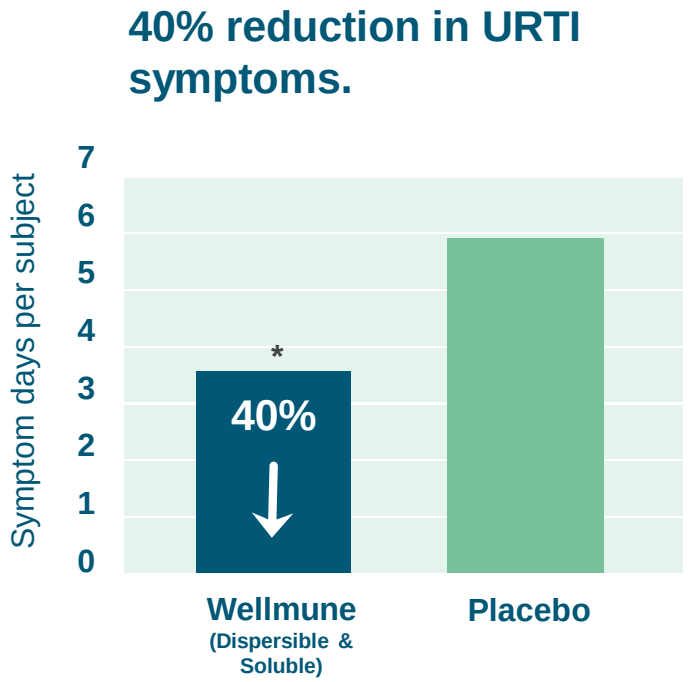
Study: Texas Marathon

Study Protocol

Study Site	Department of Health and Human Performance, University of Houston, USA
Population	182 runners (96 men, 86 women) who completed the 2011 LiveStrong Marathon in Austin, Texas with an average finish time of 4 hours
Age	29-46 (average 34 years)
Design	Randomized, double blinded, placebo controlled, parallel arm study
Duration	4 weeks
Serving	Participants were split into three groups, and consumed one of the following once daily: • 250mg Wellmune soluble • 250mg Wellmune dispersible • Placebo

Study: Texas Marathon

Wellmune supplementation significantly reduced the number of days that subjects reported both general health problems as well as cold/flu symptoms. Participants taking Wellmune had:



*p≤0.05, **p≤0.01, ***p≤0.001

"Baker's Yeast Beta Glucan Supplementation Increases Salivary IgA and Decreases Cold/Flu Symptomatic Days After Intense Exercise." (2013) Journal of Dietary Supplements 10:171-183.

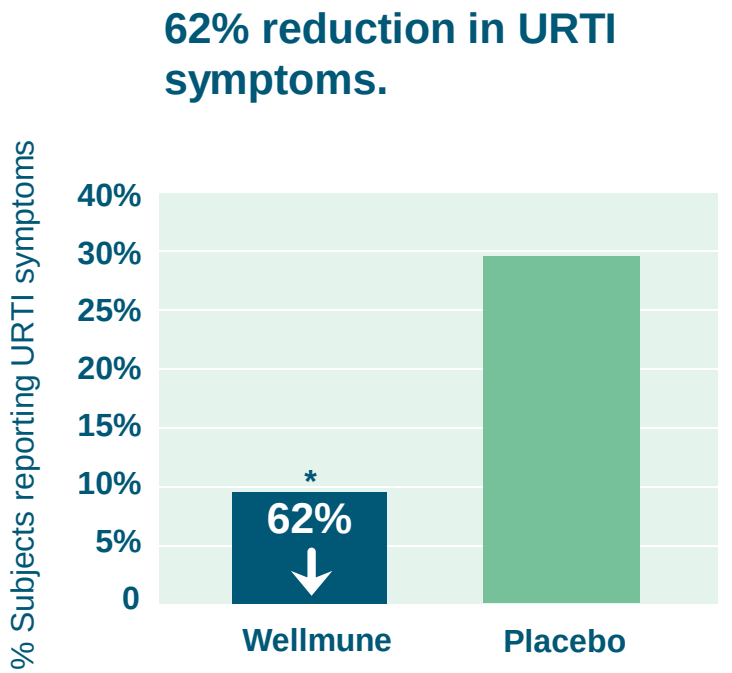
Study: Lifestyle Stress, 12 Weeks

Study Protocol

Study Site	SupplementWatch, Draper, UT USA
Population	77 healthy female volunteers
Age	18-65 (average 41 years)
Design	Randomized, double-blinded, placebo-controlled, parallel arm study
Duration	12 weeks
Serving	Participants were split into two groups, and consumed one of the following once daily: • 250mg Wellmune • Placebo

Study: Lifestyle Stress, 12 Weeks

Wellmune reduced upper respiratory tract infection (URTI) symptoms and improved mood state for moderately stressed women. Participants taking Wellmune had a:



*p≤0.05, **p≤0.01, ***p≤0.001

"Baker's Yeast Beta-Glucan Supplement Reduces Upper Respiratory Symptoms and Improves Mood State in Stressed Women." (2012) Journal of the American College of Nutrition 31:295-300.

Study: Children

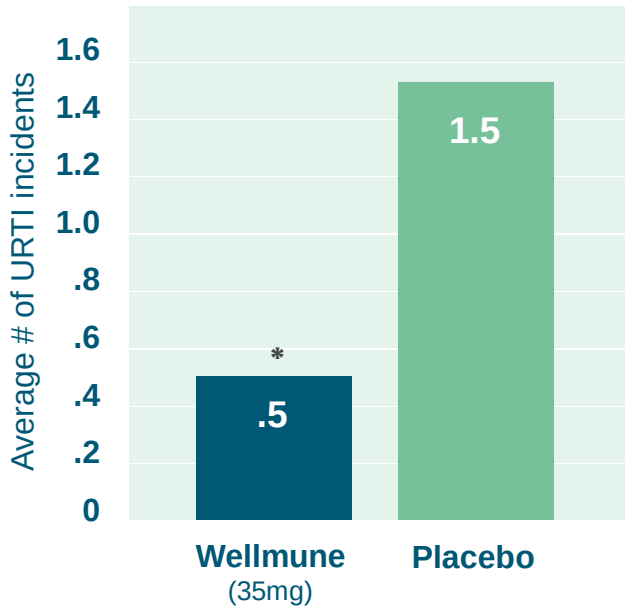
Study Protocol

Study Site	Department of Pediatrics, Chang Ping Women and Children Health Care Hospital, PR China
Population	156 healthy children (73 boys, 83 girls)
Age	12-48 months (average 36 months)
Design	Randomized, double blinded, placebo controlled, parallel arm study
Duration	12 weeks
Serving	Participants were split into three groups and consumed one of the following once daily (beverage based): • 75mg Wellmune • 35mg Wellmune • Placebo

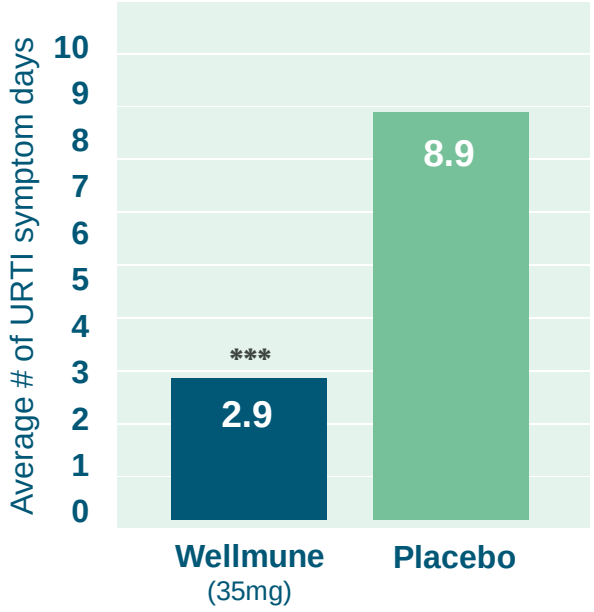
Study: Children

Wellmune helped keep children significantly healthier by decreasing episodes of common childhood illnesses and symptoms of illness, such as upper respiratory tract infections (URTIs).
Children taking Wellmune:

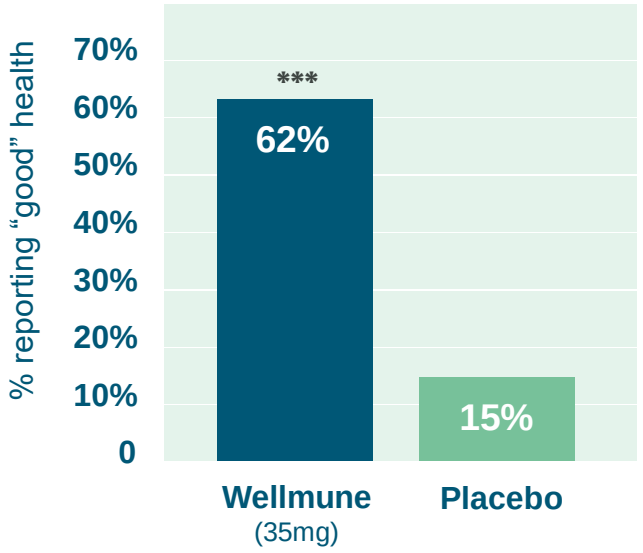
Had 2/3 fewer URTIs.



Had 6 fewer sick days in 12 weeks.



Were significantly healthier, with 62% reporting "good" health status.



*p≤0.05, **p≤0.01, ***p≤0.001

"Baker's Yeast Beta-Glucan Decreases Episodes of Common Childhood Illness in 1 to 4 Year Old Children during Cold Season in China." (2016) Journal of Nutrition & Food Sciences 6:518.

Safety & Regulatory

Safety & Toxicology Studies

- Published safety and toxicology data.
  - Food & Chem. Tox., 45:1719-1730 2007
- Two 90-day subchronic rat toxicology studies.
  - 1,000 times standard dose
- Acute toxicity study.
  - 1,000 times standard dose
- Demonstrated safety throughout multiple human clinical studies.

Setting Industry Standards

Collaboration w/ U.S. Pharmacopeia to develop monographs for beta glucan from baker's yeast.

- Published in the USP Food Chemical Codex and the USP Dietary Supplements Compendium.
- Identification method (NMR) and GEM® assay used in the monograph were developed by Wellmune team.
- Methods were validated in USP labs.
- They represent the only internationally recognized standards for bakers yeast beta glucan used in foods or supplements.

Wellmune® Global Regulatory Approvals

- U.S. FDA GRAS status with FDA letter.
- Novel Foods approval in China and Europe.
- Wide approvals for use in food, beverage and supplements in:
  - North America
  - Latin America
  - Asia & Australia
  - Middle East & Africa
  - Europe
- **Approved nutrient with permitted health claim under Malaysia Food Regulations 1985.**