



A Review of Mushroom Safety and Efficacy

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Learning Objectives

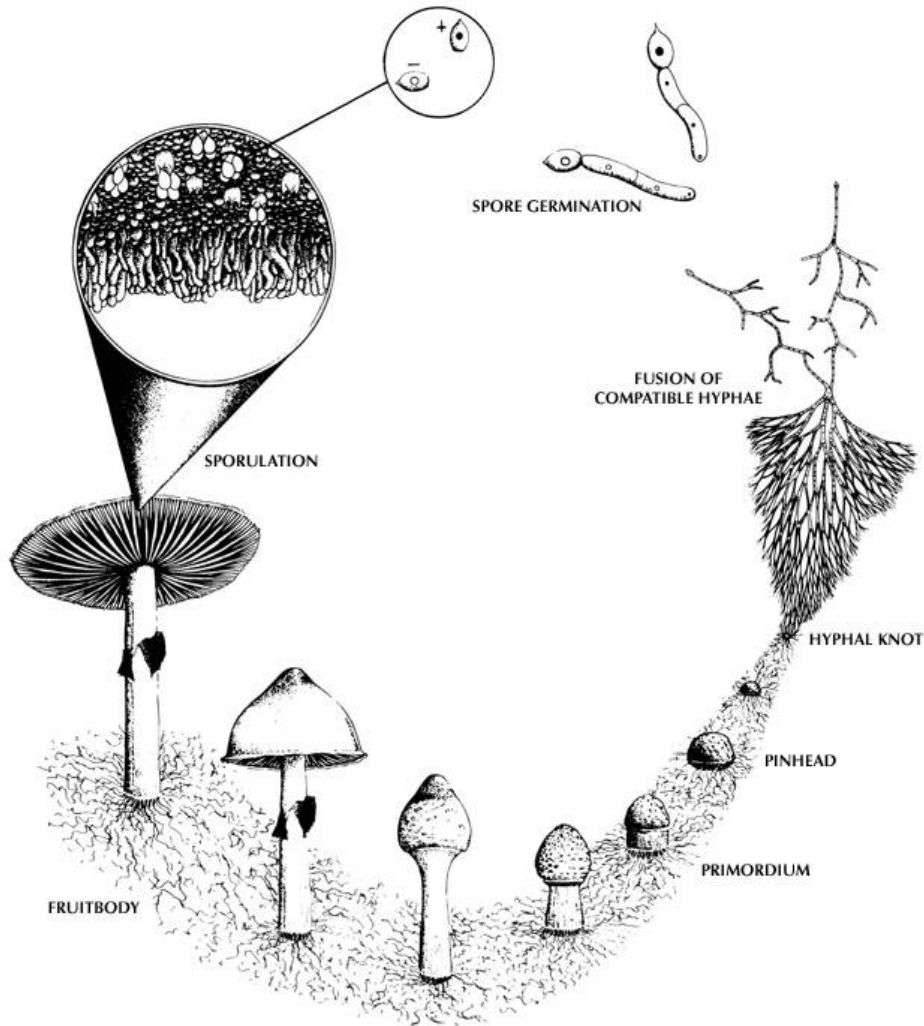
- a. Understanding the similarities and differences between mushroom mycelium and mushroom fruit bodies as well as their potential benefits**
- b. How to gain practitioner/patient confidence with validated testing for product safety, identity, purity, and composition**
- c. Review the research and potential benefits of five mushroom species**

DISCLOSURE



I am an employee of Host Defense Mushrooms as the Practitioner Channel Educator and a member of the National Science Education team.

THE MUSHROOM LIFE CYCLE



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Attributed to Paul Stamets & Jeff Chilton from *The Mushroom Cultivator*

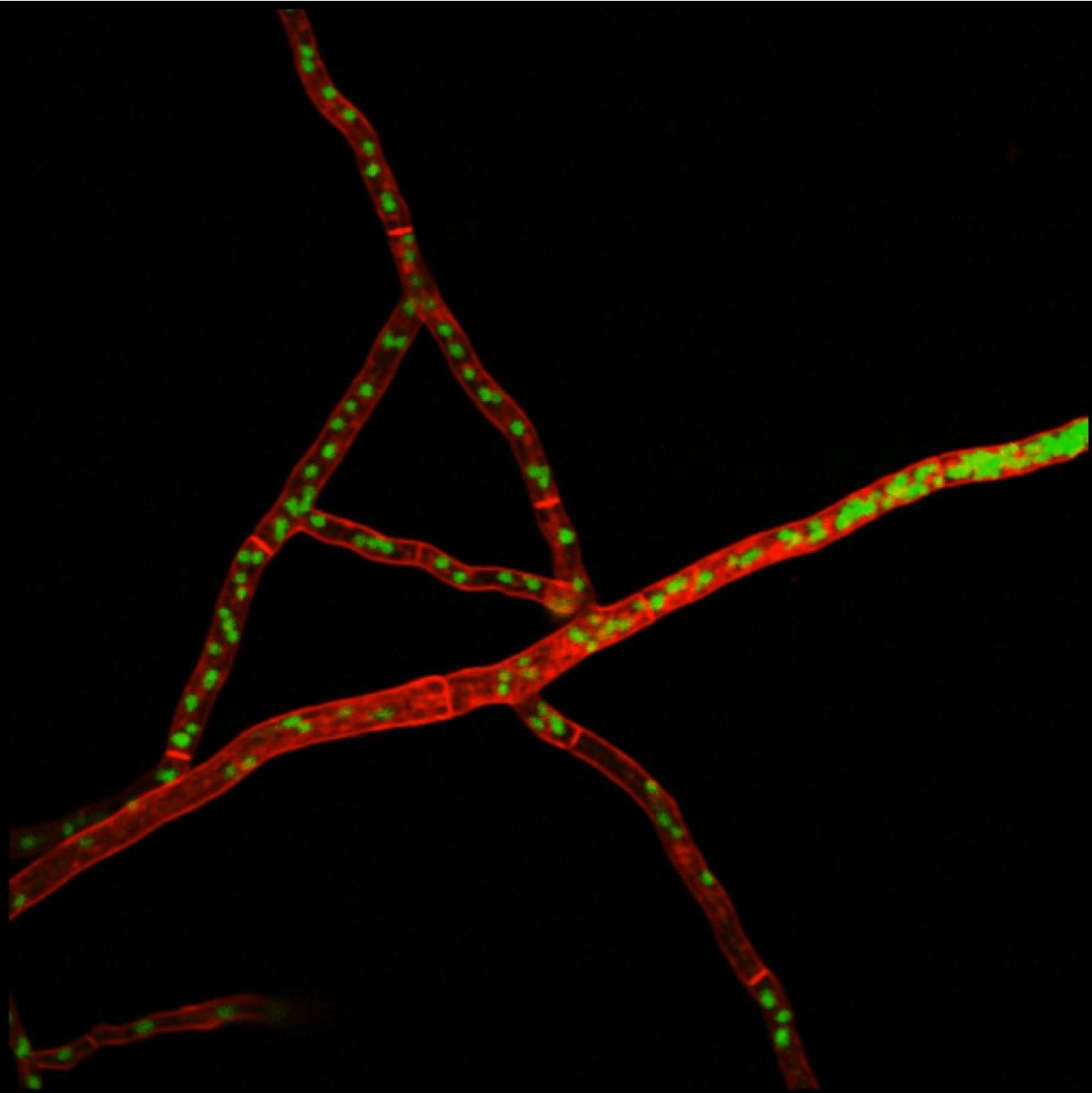
The parts of a mushroom should be scientifically specific:

Mushroom spores
Mushroom mycelium
Mushroom primordia
Mushroom fruit body

Similarly with plants:

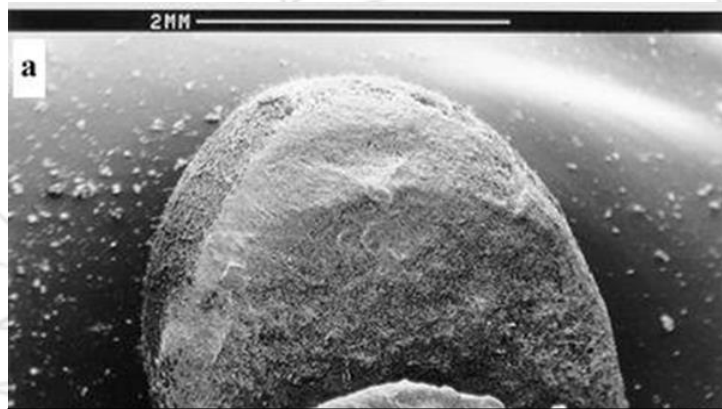
Plant spores/seeds
Plant roots
Plant leaves
Plant stems

DOI: 10.1534/genetics.111.127456

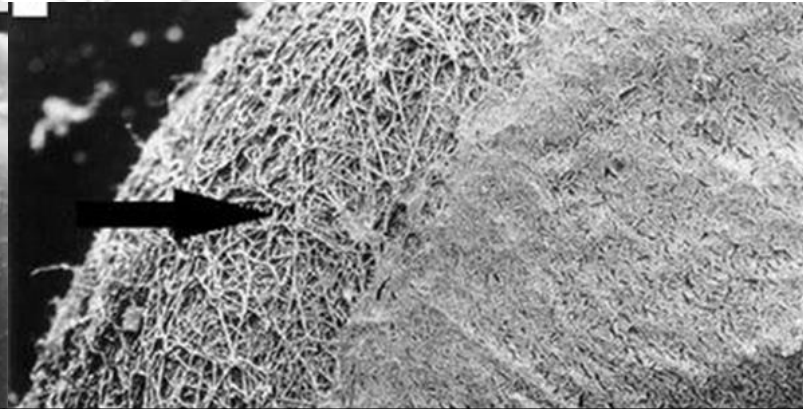


Some people use the term "vegetative" to describe mushroom mycelium. This term does the organism a disservice. It is a term that directly relates to the kingdom plantae which can be confusing. Also, vegetative in medical terminology is descriptive of minimal signs of life, specifically brain functioning. It, in no way, describes this metabolically active stage of the mushroom lifecycle.

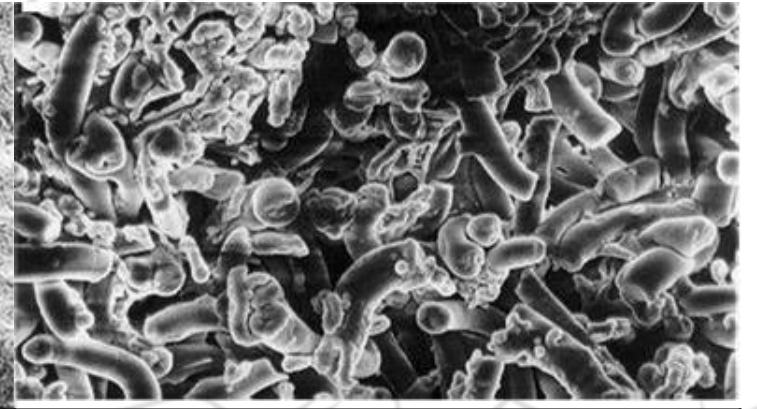
The Mushroom Life Cycle: Fruit bodies are made of densely-packed hyphae



A. Bisporus Pinhead or Primorida



B. Magnification of the Pinhead or Primordia



C. Hyphae Forming Mycelia



Lion's Mane at 5 weeks incubation

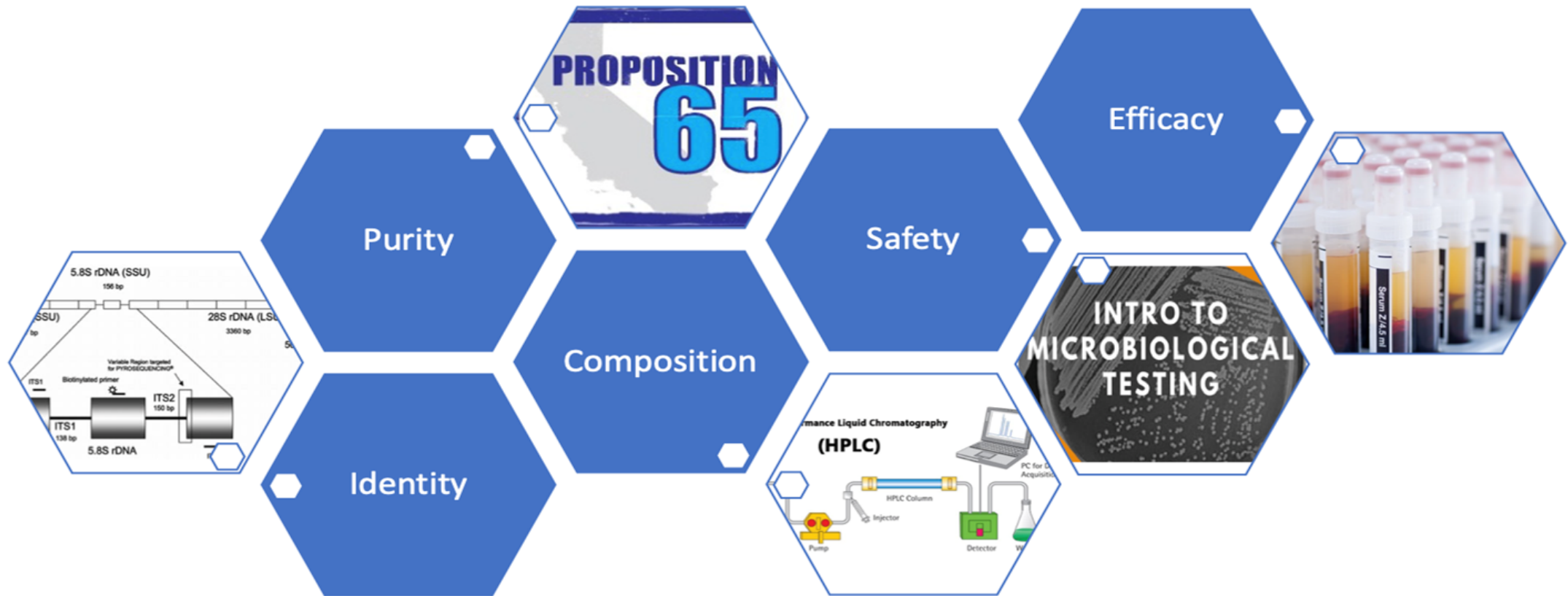


Lion's Mane fruit body magnification



Lion's Mane at 6 weeks incubation

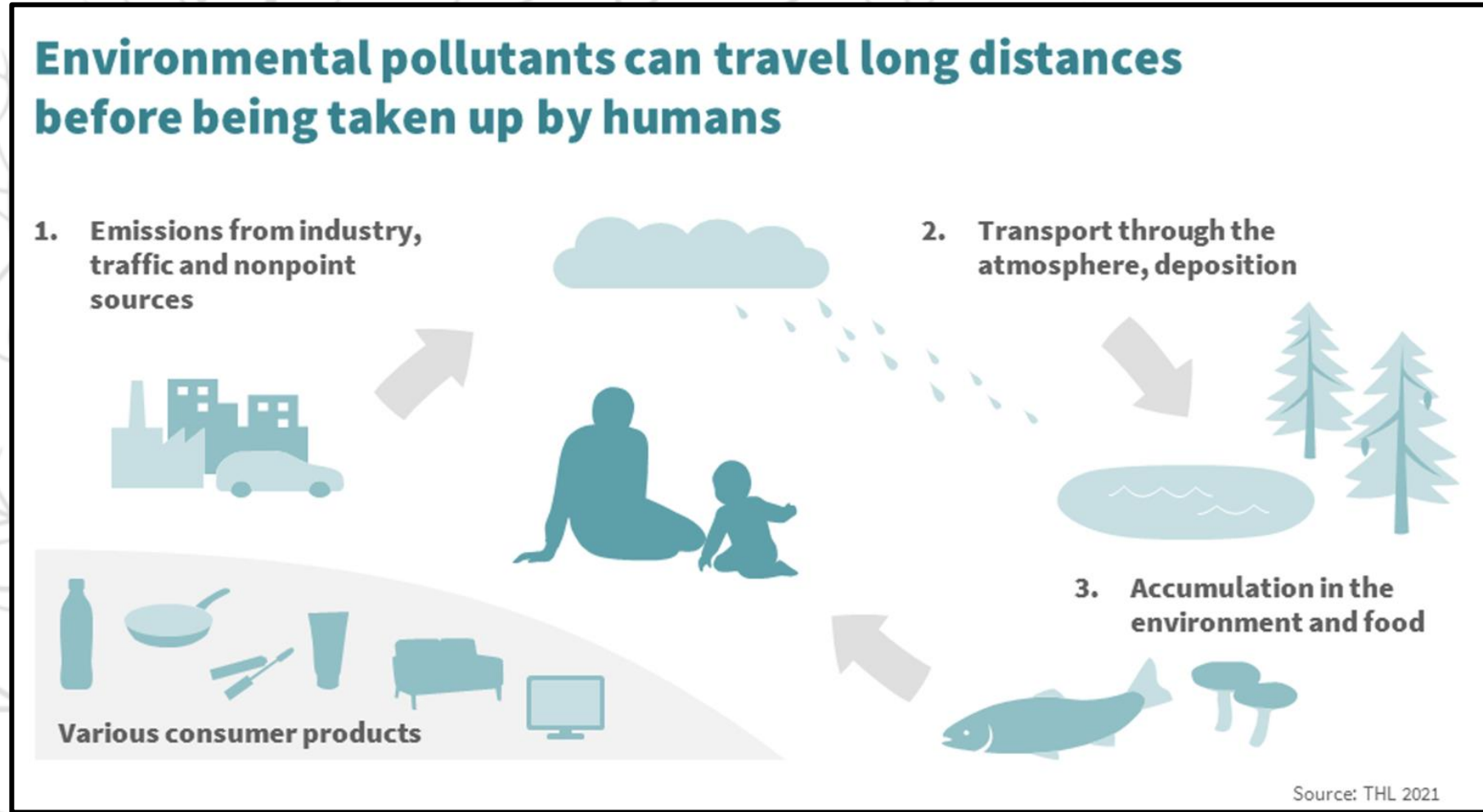
Testing Methods & Metrics



Testing Methods & Metrics: Environmental Pollutants

Know the Source

Certified organic substrate & filtered water may reduce exposures to environmental pollutants present in unsuspected ecosystems.



Testing Methods & Metrics

Endotoxin contamination

Endotoxin contamination, naturally present in forest ecosystems, can unknowingly find their way into a product intended to support health and wellness. Sustainable cultivation can significantly increase the safety of products.

doi: 10.1186/1476-9255-8-4

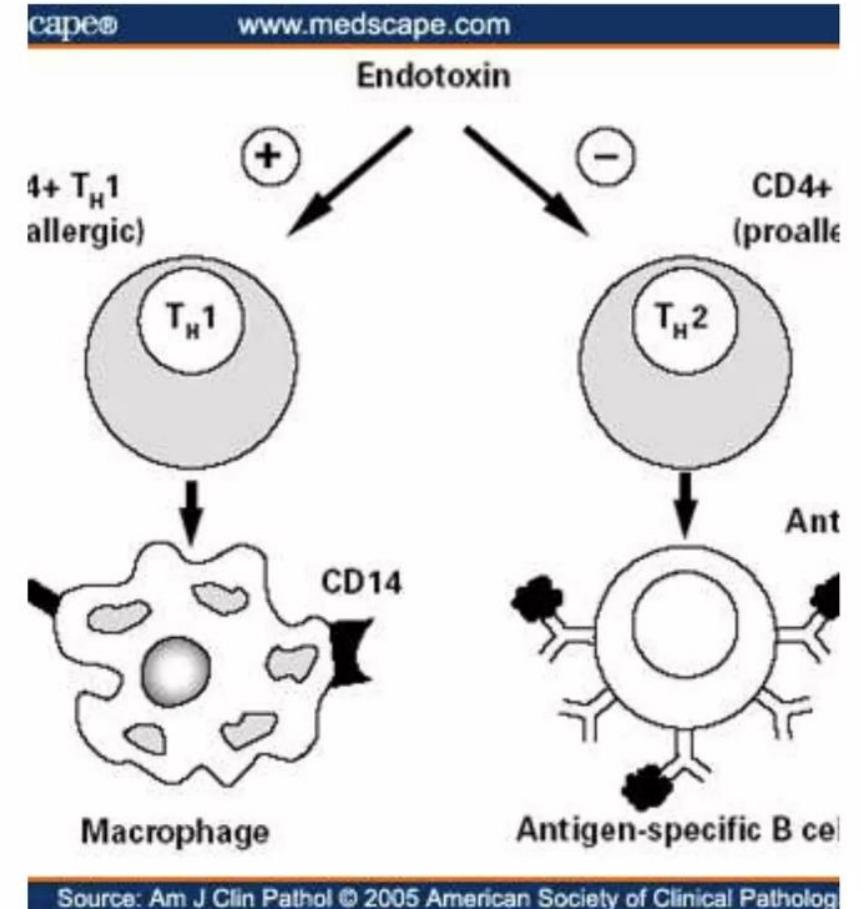
doi: 10.1055/s-0032-1328023

doi: 10.1039/c9fo01707k

doi: 10.1016/j.intimp.2008.03.007

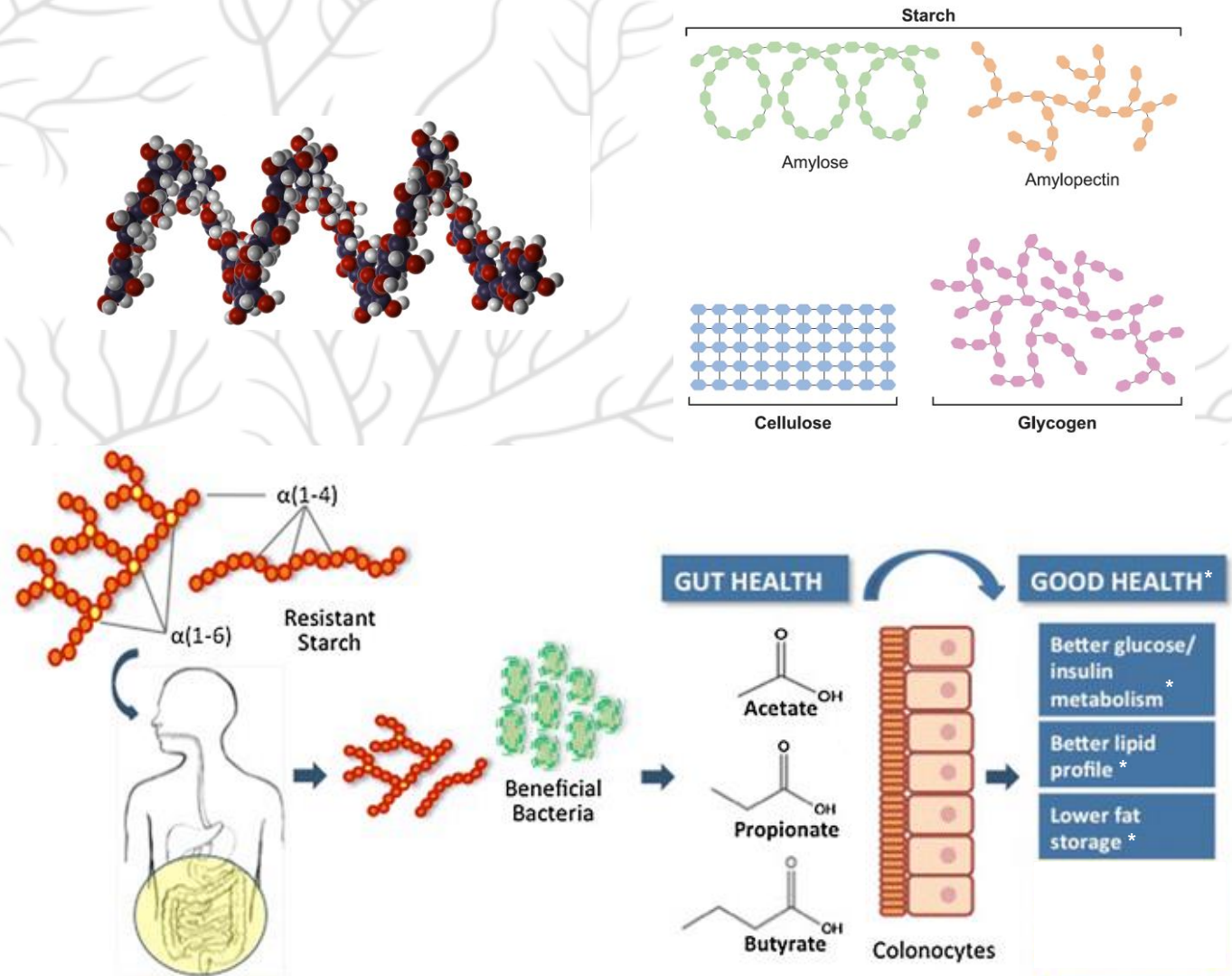
Endotoxins

The lipopolysaccharide endotoxins on Gram-negative bacteria cause fever, changes in blood pressure, inflammation, lethal shock, and many other toxic events.



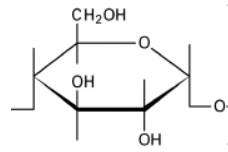
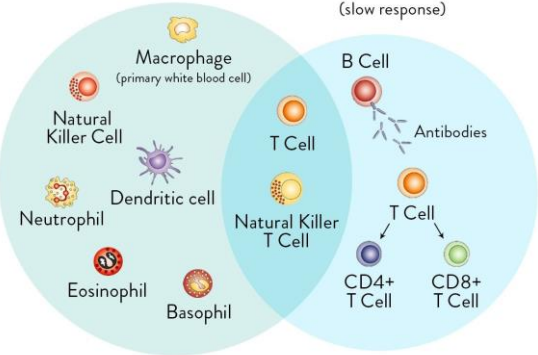
Testing Methods & Metrics: Iodine Testing

- Iodine Testing was first noted in 1814 – colorimetric response.
- Iodine will turn blue/black in the presence of amylose and purple in the presence of amylopectin. Iodine determines presence or absence not relative amounts.
- This color change is due to Iodine atoms dispersing and binding to the branching molecular structure of amylose. It's very pretty.
- **What is amylose?** Amylose is a **digestion resistant, prebiotic starch** (doi: 10.3945/an.114.007419)



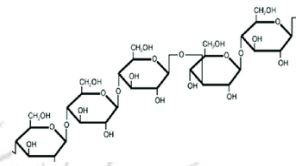
INNATE IMMUNITY
(rapid response)

ADAPTIVE IMMUNITY
(slow response)



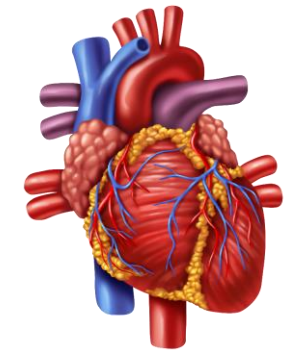
Algal Molecule

Cereal
Linear: 1,3;1,4
Branched:
1,3 1,4
i.e. Oat, Barley,
Rye

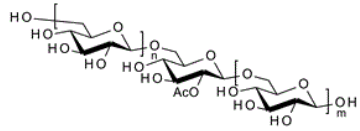


Cereal Molecule

Yeast
Linear: 1,3
Branched:
1,3;1,6
i.e. Zymosan,
Cerevan



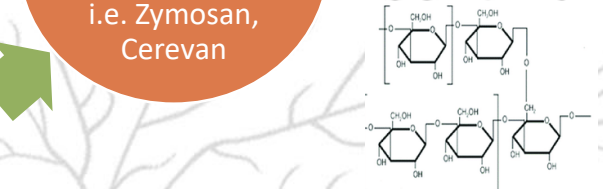
Lichen Molecule



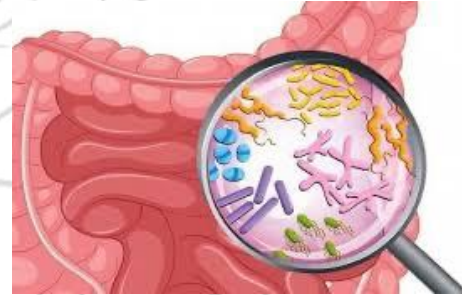
Seaweed/Algal
Linear: 1,3 i.e.
Laminaran,
Leucosin

**BETA
GLUCAN
SOURCES**

Lichen
Linear: 1,3
Branched:
1,3; 1,6 & 1,4; 1,6
i.e. Pustulan,
Lichenan

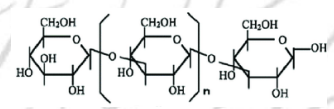


Yeast Molecule

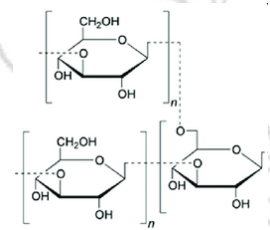
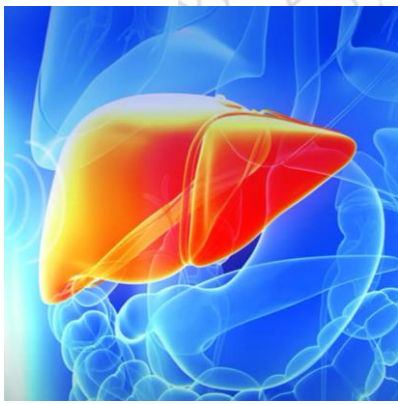
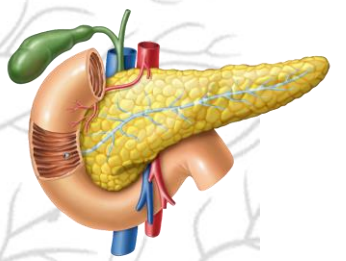


Bacterial
Linear: 1,3
Cyclic:
1,2;1,3 & 1,2;1,6
i.e. Curdlan

Fungal
Linear
Branched: 1,3;1,6
& 1,4;1,6, &
1,3;1,4;1,6 i.e.
Lentianan, Grifolan,
PSK

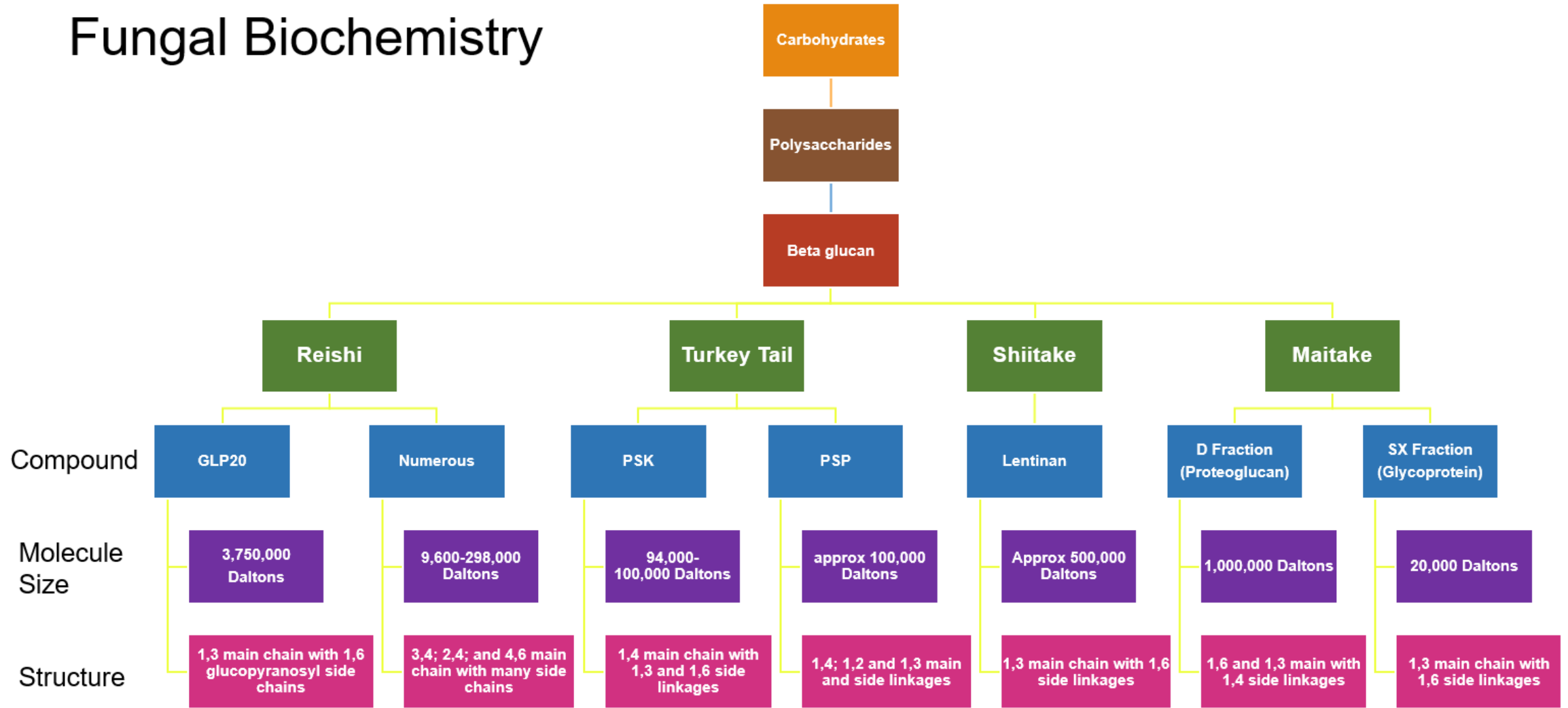


Bacterial Molecule



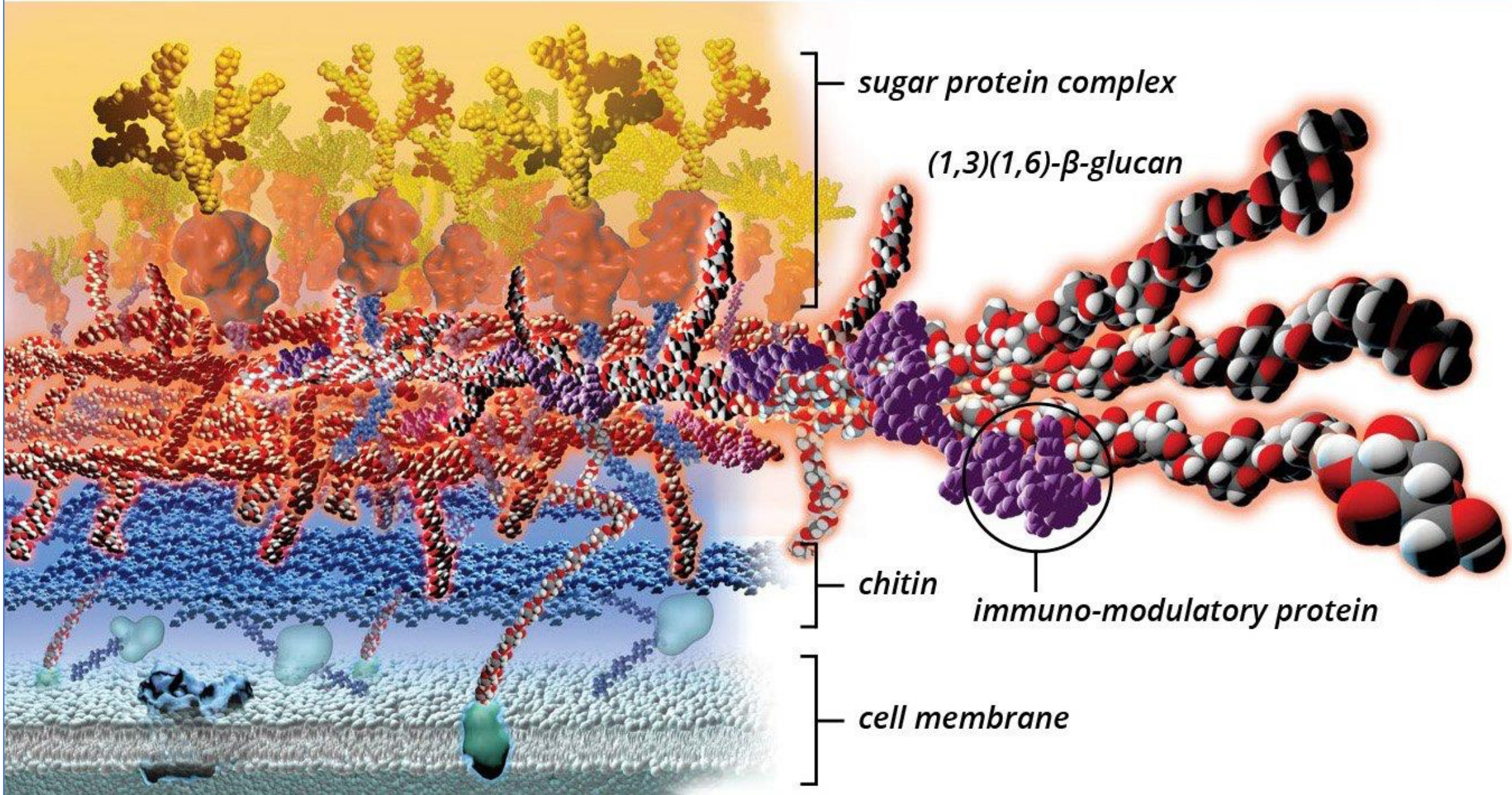
Fungal Molecule

Fungal Biochemistry



Fungal Cell Wall

Extracted Triple Helix Structure



sugar protein complex

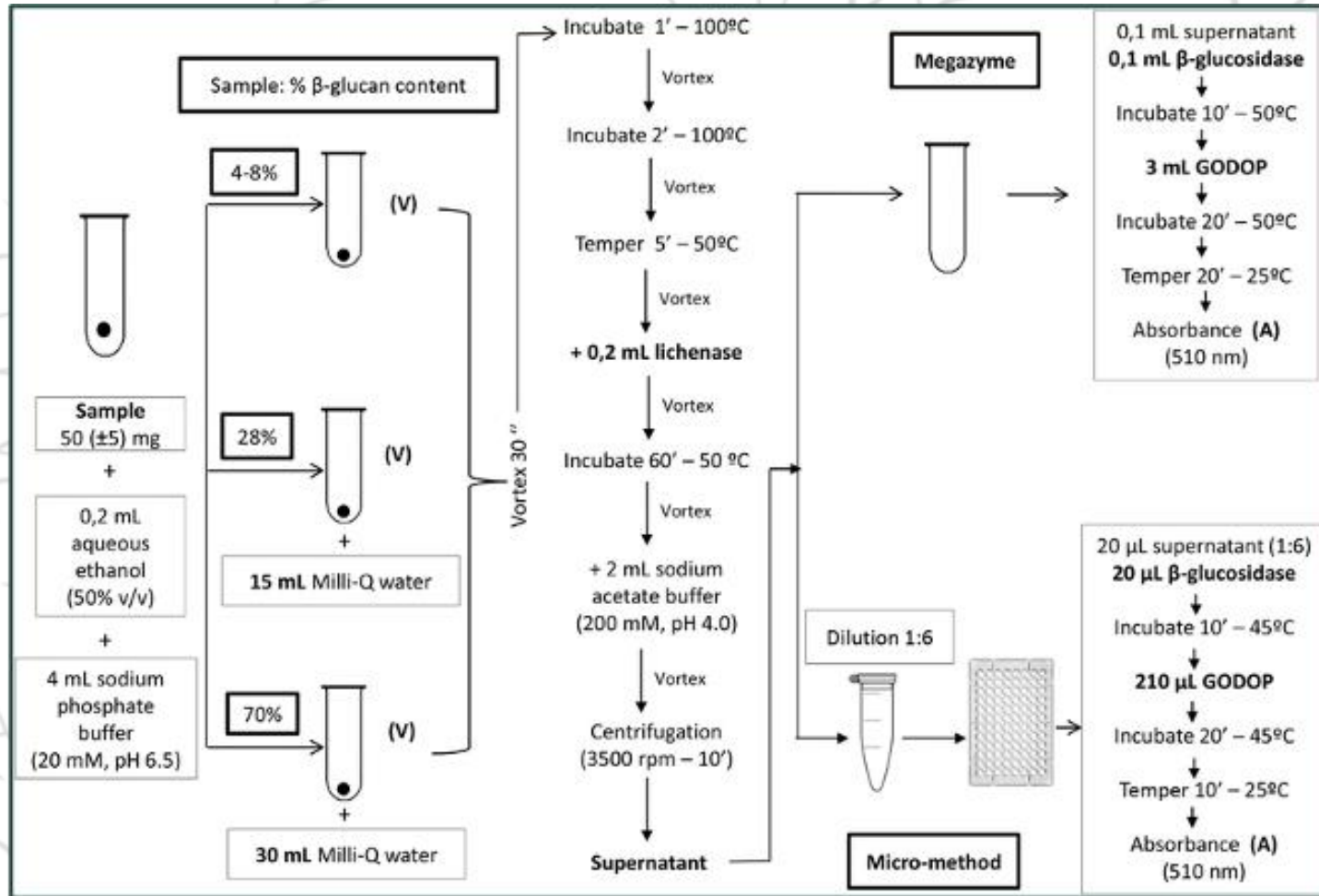
(1,3)(1,6)-β-glucan

chitin

immuno-modulatory protein

cell membrane

Testing Methods & Metrics



The megazyme test is a reductive test that uses enzymes to digest compounds that are not beta glucans. It is not a direct test of what is present.

It is AOAC validated testing for beta glucans in:

-Cereal grains

The megazyme assay is not a validated AOAC method for testing beta glucans in:

-Mushroom fruit bodies

-Mushroom mycelium

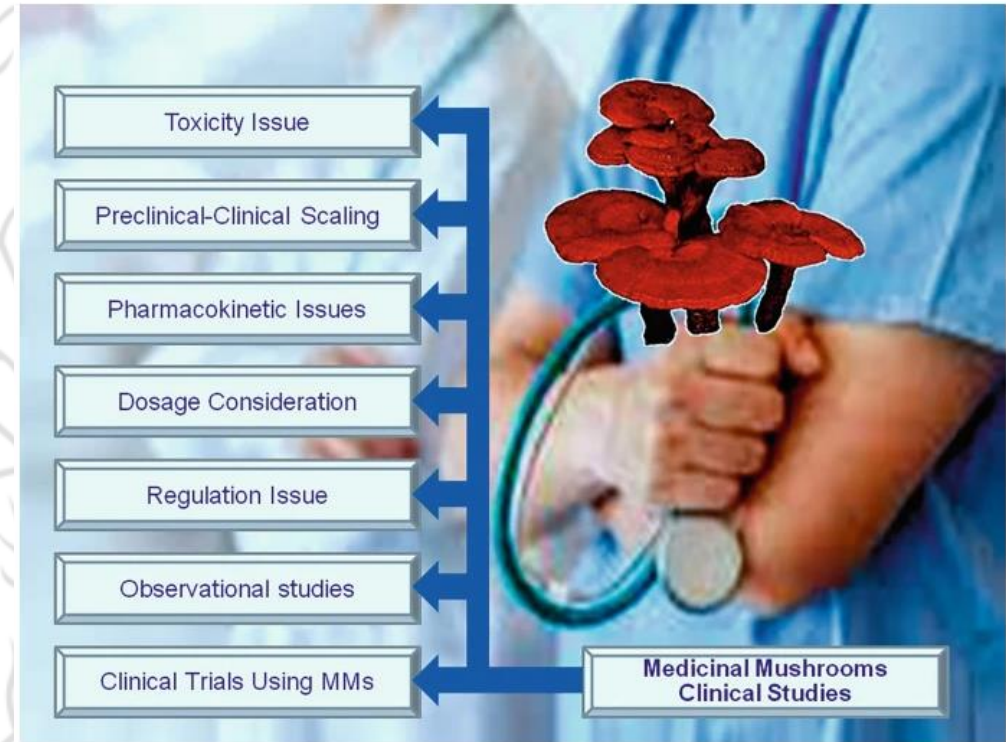
Testing Methods & Metrics

DSHEA parameters reinforce the importance of testing for:

- Identity – is it the substance that is on the label
- Purity – are there any contaminants/adulterants
- Composition – can we discern if there are any compounds of interest present
- Safety – first do no harm.

Critical to use RECOGNIZED and VALID testing methods that are repeatable with high confidence intervals, not theatrical or antiquated methods such as:

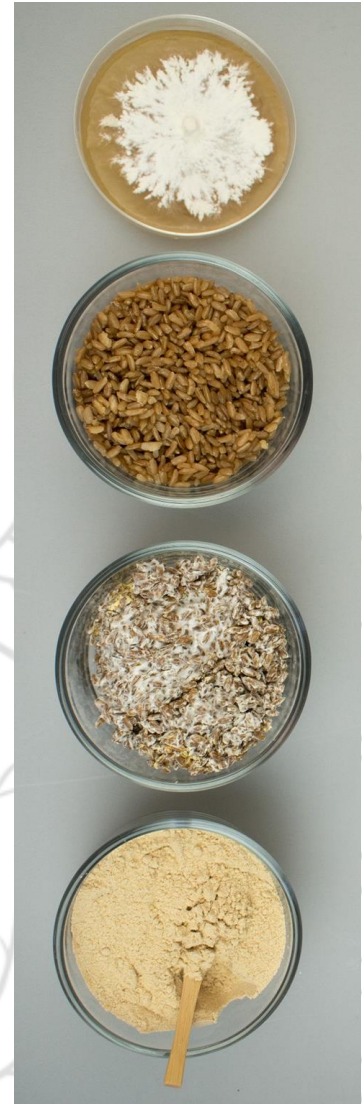
- Iodine testing
- Beta glucan testing



Testing Methods & Metrics

Results that Have Been Tested In Vitro Cell Model and in Human Clinical Trials with Independent Labs

- 3RD party research confirms mycelium-based products show significant beneficial impact on immune functioning. (doi: 10.2147/JIR.S229446)
- Research confirms that mycelium, fermented rice, and fruit bodies of mushrooms are ALL excellent allies for our health and wellness.
- Fermented rice is different than unfermented rice. (doi: 10.1186/s12906-019-2681-7.)
- Liquid vs solid state fermentation impact quality testing standards.
- There is an increased number of beneficial fermentation metabolites associated with solid state fermentation. (doi: 10.1016/j.procbio.2011.11.016)
- Human blood cell model and human clinical trials provide safety data along with outcome measures.



Solid state fermentation creates a biologically active, easily absorbable, food-based product.

Process Biochemistry 47 (2012) 175–185

Solid-state fermentation: Physiology of solid medium, its molecular basis and applications

Javier Barrios-González

Abstract

Solid-state fermentation is an alternative culture method that has gained researchers attention over the past 20 years. There are several advantages in employing many SSF processes over the conventional submerged fermentation (SmF) ones, like higher yields of secondary metabolites or enzymes. Moreover, certain enzymes and secondary metabolites can only be produced in SSF. Many of these advantages are related to the special physiology shown by fungi in SSF. This review refers to this physiology (i.e. a behavior that deviates from the one displayed by the fungus in liquid medium), sometimes referred to as “physiology of solid medium”, and its molecular basis. The reason for this different physiology in SSF is not fully understood, but recent advances are beginning to draw an interesting and wide panorama. Higher secondary metabolites production has been related to higher transcription of the biosynthetic genes; while studies on enzymes production in SSF have identified SSF-specific genes and provided deeper insight into their genetic expression and regulation. Moreover, some solid culture environmental stimuli (signals) have been identified. Many of these basic findings are also starting to be applied to new genetic improvement methods, novel culture systems, and other technological advances.

What's In a Product: Proper Labeling

Regulations at a Glance

FDA-regulated products	Pre-market approval (FDA)	Pre-market notification (FDA)	Labeling (FDA)	Mandatory adverse event reporting (FDA)	GMPs (FDA)	Facility registration (FDA)	Advertising (FTC or FDA)
Foods		✓	✓		✓	✓	✓ FTC
Dietary supplements		✓	✓	✓	✓	✓	✓ FTC
Drugs	✓		✓	✓	✓	✓	✓ FDA
Biologics	✓		✓	✓	✓	✓	✓ FDA
Medical devices	✓		✓	✓	✓	✓	✓ FDA

Supplement Facts

The Federal Trade Commission (FTC) enforces the federal laws requiring that dietary supplement claims in advertising are truthful and not misleading, and substantiated with scientific evidence.

Council for Responsible Nutrition

www.crnusa.org

What's In a Product: Labeling Concerns

Supplement Facts	
Serving Size: 2 capsules Servings Per Container: 30	
Amount Per Serving	% Daily Value
Calories	5
Total Carbohydrate	<1g <1% [◇]
Turkey Tails (<i>Trametes versicolor</i>) mycelium [‡] /fermented brown rice biomass [‡]	1g †
◇ Percent Daily Values are based on a 2,000 calorie diet † Daily Value not established	
Other Ingredients: Pullulan (capsule). ‡ Certified Organic	

Supplement Facts		
Serving Size 2 capsules		
Amount per serving		%DV
Organic Turkey Tail Mushroom Extract	1000 mg	*
<i>Trametes versicolor</i>		
Beta-(1,3)(1,6)-glucans	300 mg	
* Daily Value (DV) not established.		

Other ingredients: Hypromellose (vegetable capsule), silicon dioxide, microcrystalline cellulose, may contain stearic acid.

MICROCRYSTALLINE CELLULOSE & SILICON DIOXIDE ARE IN FACT FILLERS / EXCIPIENTS

Research Data Categorization

Level A:

Human clinical trials
Double blind, randomized
Meta-analysis

Level B:

Blinded, non-randomized
Clinical cohort & case reports
Epidemiological studies

Level C:

Expert opinion & consensus

Level D:

Animal trials
Mechanism of action research
Theoretical Pharmacology



Resources:

Natural Medicines Database TRC
Scholar.google.com
Pubmed.gov
Mushroomreferences.com
Drugs.com

Reishi

Ganoderma lucidum s.l.

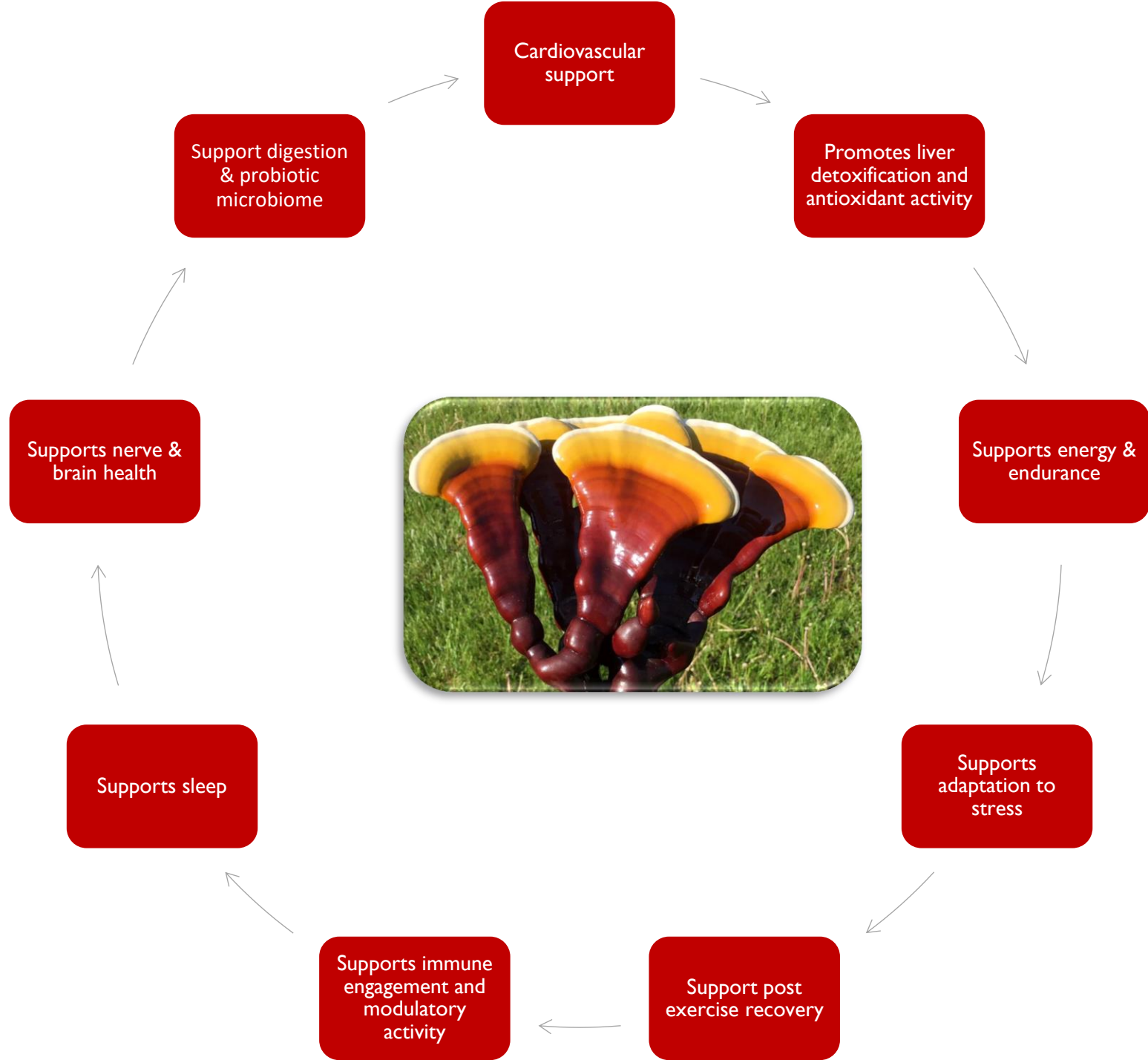
KEY

Potential Adverse Events:

- Estrogen receptor agonist and non-hemostatic

Potential Drug Interactions:

- NO **Level A** nor **Level B** interactions
- Blood thinners or blood pressure medication
- Blood glucose regulatory medication
- Immunosuppressive medication



REISHI

1 gram – daily immune modulatory activity, glycemic balance, metabolic detoxification, cardiovascular support, and prebiotic activity for intestinal cell integrity and immune support, support of daily stressors, mood, sleep architecture, and antioxidant activity

2-3 grams – moderate support of antioxidant activity, modulation of the flight or fight response, day long energy, post-exercise recovery, immune modulation, glycemic balance, and metabolic detoxification, mood, sleep architecture, and cardiovascular support

3-4.5 grams - for significant immune modulatory support and prebiotic activity, metabolic detoxification, antioxidant activity, cognitive functions, neurotransmitters functioning, and mood, adaptation to stressors, post-exercise recovery, cardiovascular support, sleep architecture, mood, and immune support

Reishi - *Ganoderma lucidum* Research

Mushroom	Research Model	Supports	DOI
Reishi	Human clinical trial	Supports adaptation to low oxygen environments, supports post exercise recovery	10.1136/bjism.2007.038620
Reishi	Review of literature	Supports immune engagement and modulatory activity	10.2174/1872213x08666140619110657
Purified FB polysaccharide	Human clinical double blinded 5.4 grams/day 8 weeks 132 patients 50 male, 62 female 43 +/- 7 years	Mild adverse events 5: 2 nausea, 2 dry mouth, 1 vomiting, otherwise well tolerated. Reported and observed clinical global improvement of well being and fatigue.	10.1089/jmf.2005.8.53
Fruit body preparation	Human clinical double blinded 6 grams/day 6 weeks 48 women 53 +/- 11 years	Mild adverse events of nausea, diarrhea, discomfort and nervousness Fibromyalgia patients reported and observed significant increases in endurance, walking velocity and lower limb flexibility	10.3305/nh.2015.32.5.9601
Purified FB polysaccharide	Human clinical double blinded 5.6 grams/day 12 weeks 71 patients	Fasting plasma glucose and HbA1c improved significantly compared to placebo group.	10.1615/IntJMedMushr.v6.i1.30
FB extract	Human clinical soluble blinded 1.4 grams/day 12 weeks 23 patients	Well tolerated, and no adverse events reported or observed	10.1017/S0007114511003795

Concerns: Out of 19 Reishi products in the US supplement market, only 5 tested with the accordance with their labels. 3 different extracts of *G. lucidum* fruit bodies in both adults' and children's peripheral blood mononuclear cells suggest that extracts of *G. lucidum* should be used with caution as there appears to be potential for toxicity. Reishi has conflicting evidence associated with estrogen receptor activation and potential immune support for hormonally responsive tumors, therefore proceed with caution or consider non-hormonally responsive mushrooms for immune support (*Trametes versicolor*).

Lion's Mane

Hericium erinaceus

KEY

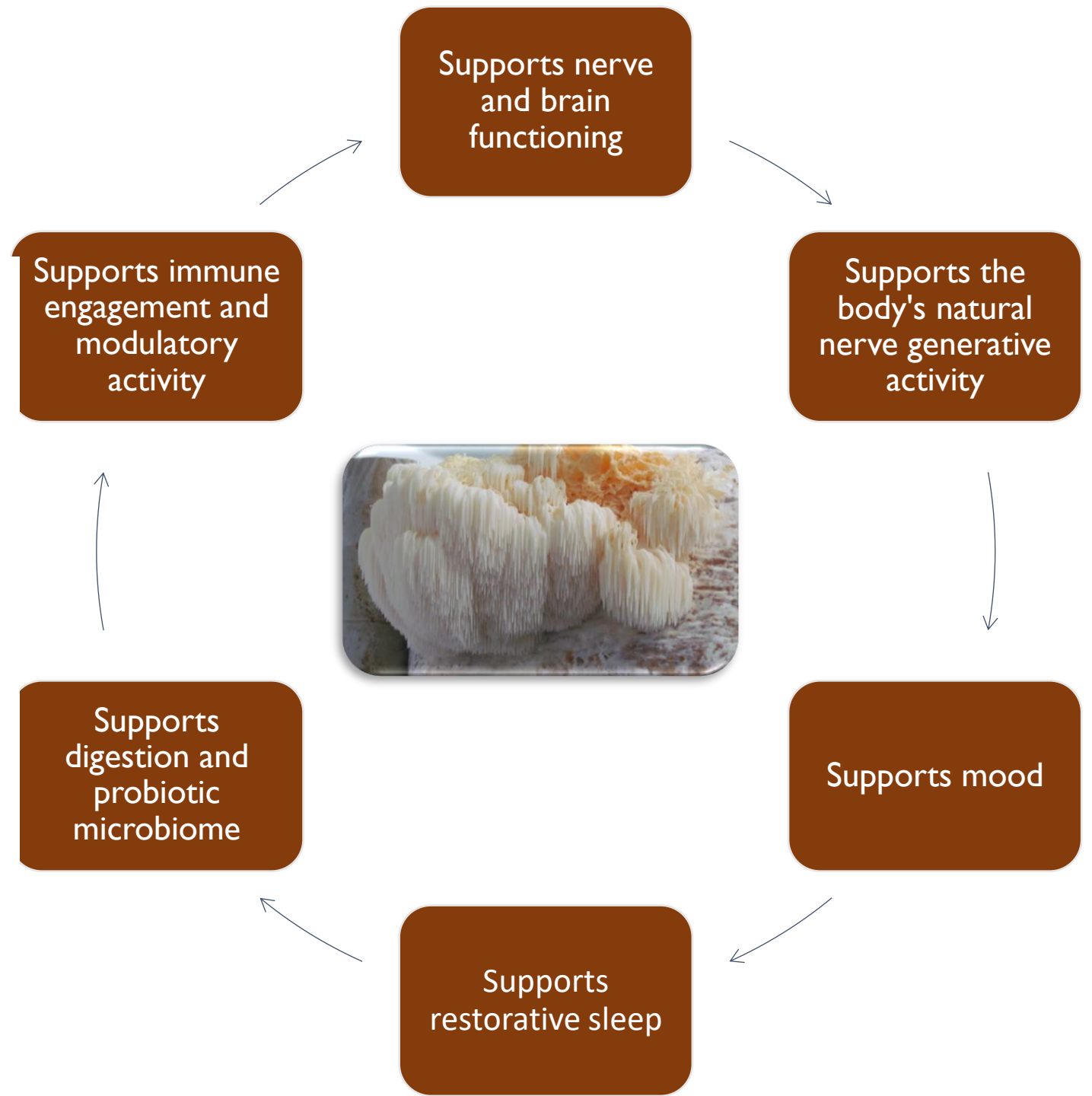
Potential Adverse Events:

- Low potential for GI discomfort

Potential Drug

Interactions:

- NO **Level A** nor **Level B** interactions



LION'S MANE

1 gram – for daily support of targeting nerve functioning for mood, cognition, memory, sleep architecture, prebiotic activity, intestinal cell integrity, immune modulatory activity, glycemic balance, sleep architecture and liver functioning

2-3 grams – to support advanced antioxidant activity, targeting nerve functioning for mood, cognition, memory, sleep architecture, prebiotic activity, intestinal cell integrity, immune modulatory activity, glycemic balance, and liver functioning

3-4.5 grams – significant support mood, cognition, daily nerve generative activity, and memory, as well as a prebiotic support, robust antioxidant activity, more advanced support for glycemic balance, advanced increased intestinal cell integrity and immune modulatory activity

Lion's Mane – *Hericium erinaceus* Research

Lions Mane Mushroom	Study Design	Structure & Function	Publication Information
Fruit body extract	Human clinical trial	Supports cognitive function*	10.1002/ptr.2634.
Mycelium enriched with Erinacine A	Human clinical trial	Supports cognitive functioning, mental status and activities of daily living*	10.3389/fnagi.2020.00155
Fruit body extract	Human clinical trial	Supports mood*	10.1155/2019/7861297
80% Mycelium and 20% Fruit body extract preparation	Human clinical trial	Supports mood & sleep & pro-BDNF increase*	10.1155/2019/7861297
Mycelium	In vivo animal study	Supports recognition memory and central nervous system generative activity*	10.3390/nu11040715
Fruit body extract	In vivo animal study	Supports nerve generative activity in healthy animals*	10.1615/IntJMedMushr.v14.i5.10
Solid-fermented mycelia in rice	Human clinical trial	Dietary and lifestyle changes along with Lion's Mane supplementation supports cognitive function, daily activities and overall health and wellness.*	10.1186/s13195-024-01482-z
Mycelium	In vivo animal study	Supports probiotic microflora, immune cell engagement and immune modulatory activity*	10.1016/j.intimp.2019.02.038
Mycelium	Human clinical trial	Supports probiotic microflora proliferation, short chain fatty acid production, liver function and cholesterol metabolism already within the normal range.*	10.3390/nu13031008

Concerns: In a group of middle-aged women Lion's Mane was able to help balance moods in mild and moderate mood disturbances for the duration of use. Benefits were seen to revert after about a month when discontinued.

Cordyceps

Cordyceps militaris

KEY

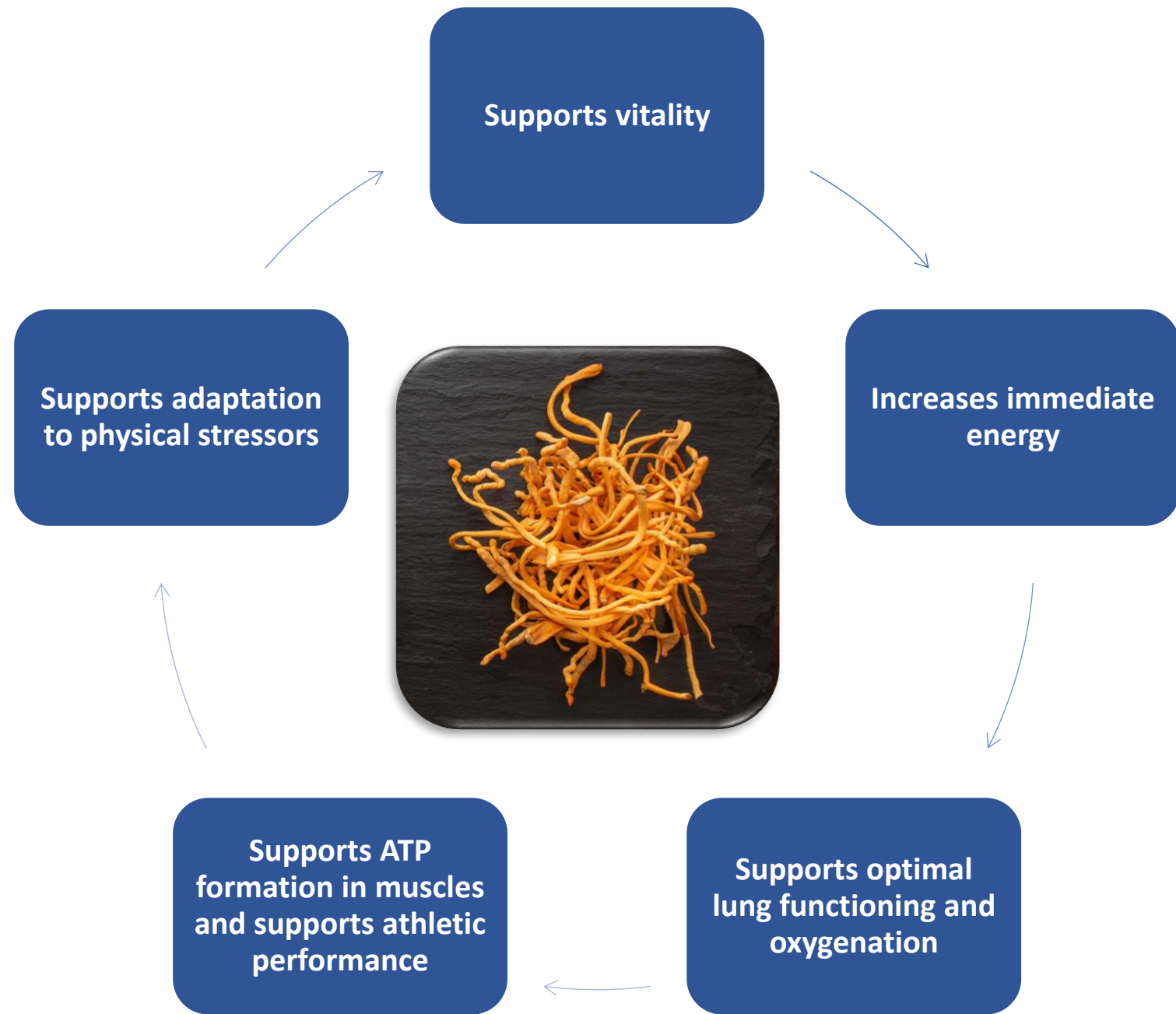
Potential Adverse Events:

- Low probability of mild diarrhea, constipation and abdominal discomfort

Potential Drug Interactions:

NO **Level A** nor **Level B** interactions

- Blood glucose regulatory medication
- Blood pressure medications
- Immunosuppressive medication



CORDYCEPS

1 gram – for daily support targeting lung and kidney functioning, antioxidant activity, cardiovascular support, increase V_{O_2} , supports oxygenation and lung functioning, increases volume of we can take into our lungs, immediate energy support, blood pressure, glycemic balance, cognition, mood, and cholesterol metabolism

2-3 grams – advance support advanced antioxidant activity, targeting lung and kidney functioning, cardiovascular support, increase V_{O_2} , supports oxygenation and lung functioning, increases volume of we can take into our lungs, immediate energy support, glycemic balance, blood pressure, cognition and mood, and cholesterol metabolism

3-4.5 grams – significant support for oxygenation & graceful breathing, targeting lung and kidney functioning, antioxidant activity, cardiovascular support, increase V_{O_2} , supports oxygenation and lung functioning, increases volume of we can take into our lungs, immediate energy support, blood pressure, glycemic balance, cognition, and mood, and cholesterol metabolism

Cordyceps – *Cordyceps militaris* Research

Mushroom	Research Model	Supports	DOI
Cordyceps	Animal cell model	Supports balanced immune response, supports granulocyte/mast cell pacification activity*	10.1016/j.jep.2011.03.030
Cordyceps	Animal in vivo model	Supports balanced bronchial immune response, supports function of bronchial alveolar lavage fluids*	10.1016/j.resp.2020.103412
Blend of multispecies mushroom mycelium biomass with grain substrate	Human clinical trial 4 grams/day 1 week & 3 weeks 30 patients, 16 female, 12 male 22.7 +/- 4.1 years old	Phase I & II, double blinded, Significant increase in VO2 max, ventilatory threshold and time to exhaustion 3-week trial observed greater results than 1 week trial	10.1080/19390211.2016.1203386
Fruit body extract	Human clinical 1.5 grams/day 4 weeks 39 male patients (19-64)	Well tolerated, no adverse events reported Increased INF gamma, IL-2 and lymphocyte cell proliferation observed	10.1089/jmf.2014.3350
Fruit Body extract	Human Clinical 1 gram/day 90 days 64 male patients (45-86 years)	Given concurrent with any preexisting medication treatments for diabetes, hypertension, dementia. Increased urinary flow, decreased prostate volume, increased sexual function and satisfaction	10.1016/j.prmcm.2022.100143

Concerns: *Cordyceps militaris* is a very energizing, so avoid taking past 2 PM. Cordyceps has conflicting data associated with hormonally responsive tumors. Since it may increase testosterone levels, use with caution or consider a non-hormonally responsive mushrooms for supporting immunity where hormonally responsive tumors are present (*Trametes versicolor*).

Agarikon

Fomitopsis officinalis

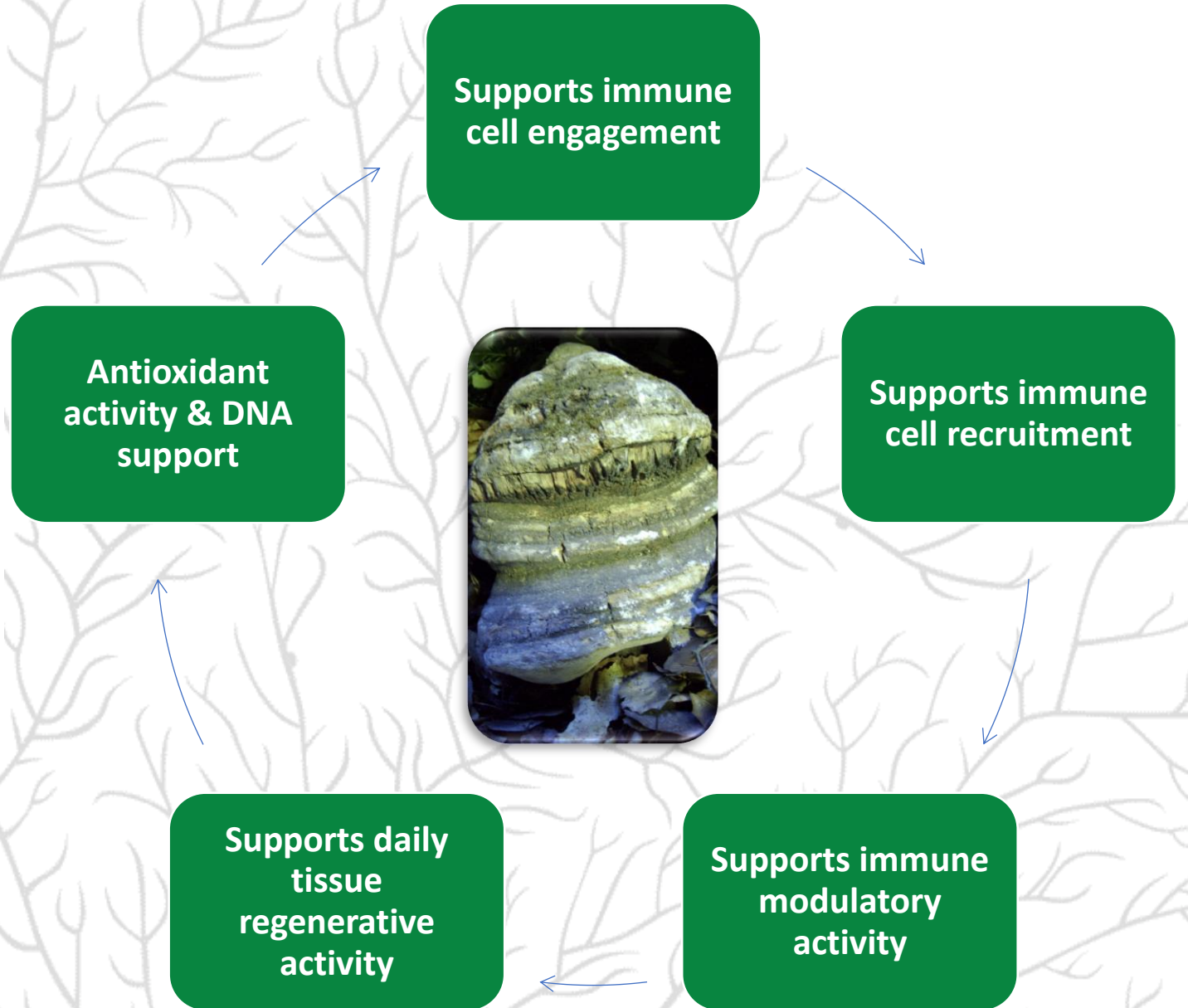
KEY

Potential Adverse Events:

- None found

Potential Drug Interactions:

- NO **Level A** nor **Level B** interactions



AGARIKON

0.5-1 grams –daily immune engagement, daily generative tissue, antioxidant activity, and modulatory support

2-3 grams – significant immune engagement and modulatory support

Agarikon – *Fomitopsis officinalis* Research

Mushroom	Research Model	Supports	DOI
Agarikon	Review of cells studies and ethnomycological practices	Supports immune competence, immune modulatory activity and intracellular immunity	10.1002/cbdv.202000213
Agarikon	Review of cell studies and Ethnomycological practices	Supports immune competence, immune modulatory activity and intracellular immunity	https://doi.org/10.1080/21501203.2018.1536680

Concerns: Agarikon is a rare, slow growing mushroom, predominantly found in the old growth forests in the PNW. It is so rare that Agarikon has been placed on the endangered fungal species list since 2019, including being on the Red List of Threatened Species by the International Union for Conservation of Nature.

Turkey tail

Trametes versicolor

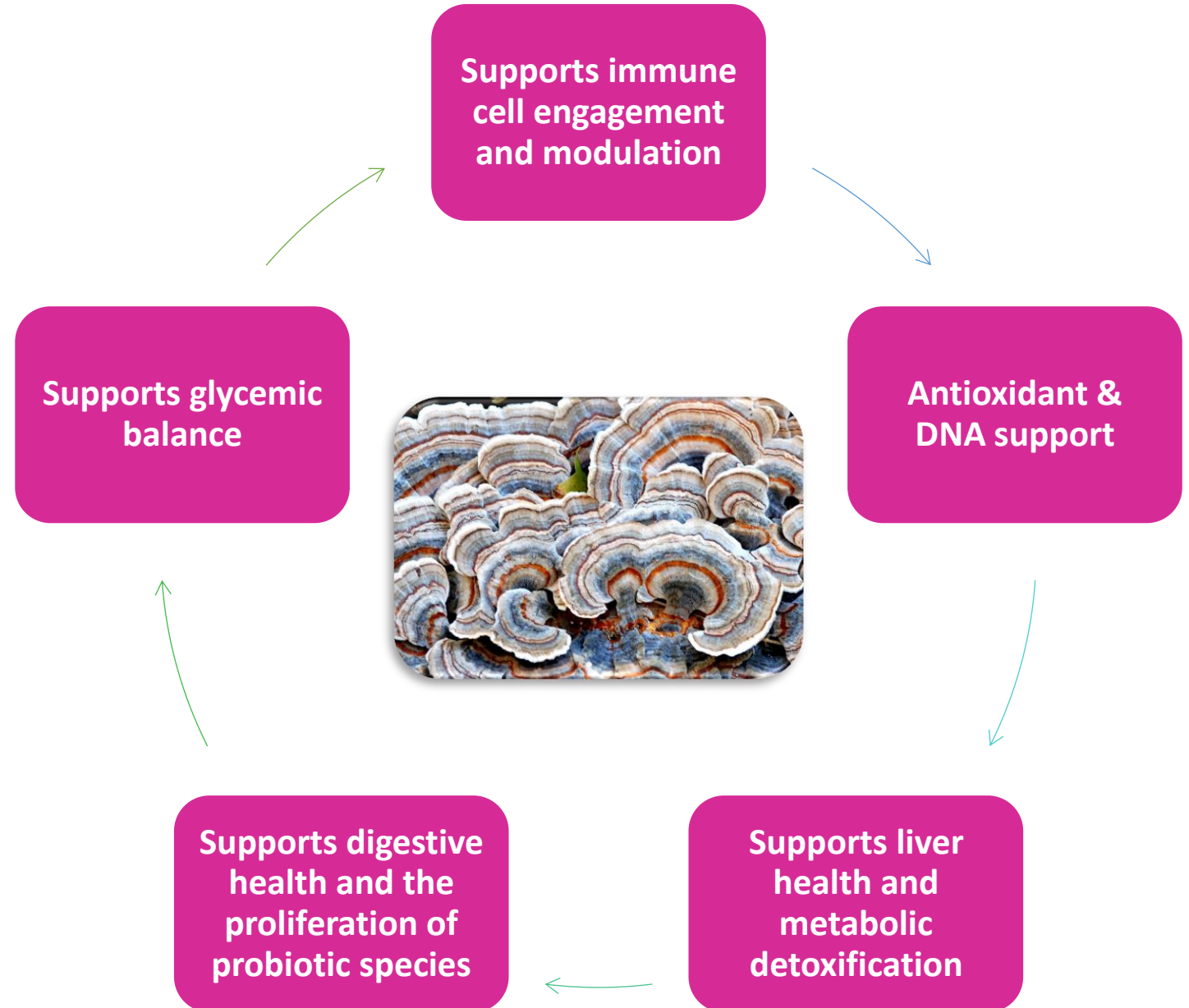
KEY

Potential Adverse Events:

- None reported

Potential Drug Interactions:

- NO **Level A** nor **Level B** interactions
- **Immunosuppressive medication**



TURKEY TAIL

1 gram – daily immune support and PRE-biotic support for microbiome, intestinal cell integrity, glycemic balance, liver, and immune modulatory activity.

2-3 grams – significant immune support and PRE-biotic activity for microbiome, intestinal cell integrity, glycemic balance, liver, and immune modulatory activity.

3-4.5 grams – advanced immune and PRE-biotic support for microbiome, intestinal cell integrity, glycemic balance, liver, and immune modulatory activity.

Turkey Tail – *Trametes versicolor* Research

Mushroom(s)	Research Model	Supports	DOI
TurkeyTail mycelia fermented in rice	Human clinical trial, Phase 1 over six weeks	Turkey Tail modulated immune cell populations and activity in the context of 23 women with breast cancer. Safety dose of 9 grams a day.	10.5402/2012/251632
Turkey Tail mycelial extract of polysaccharopeptide	Human randomized clinical trial of 22 participants over 8 weeks	Polysaccharopeptide (PSP) from <i>T. versicolor</i> acts as a prebiotic to modulate human intestinal microbiome composition.	10.4161/gmic.29558
Turkey Tail and Reishi	Human clinical trial 61 patients 2 months	Supported an oral probiotic microbiome and supported mucosal associated lymphoid tissue.	10.1615/IntJMedMushrooms.v16.i5.80

Concerns: Be sure all mushroom fruit body and mycelium are well heat treated to breakdown the chitin and beta-glucan molecules to gain access to beneficial biological compounds

Thank You!!



Xochitl Palomino, ND
xochitl.p@fungi.com

