



MUSHROOM BIOSCIENCE

Bringing evidence to the clinic: medicinal mushrooms for mental health

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Agenda

- 1. Medicinal Mushrooms (MM): prebiotics for the gut-brain axis**
- 2. Clinical cases and Hifas da Terra studies**
- 3. Products and recommendations**
- 4. Why Hifas da Terra? Quality, Safety and Efficacy**



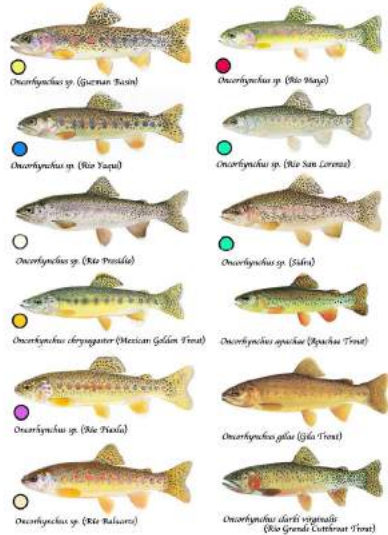
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Part 1

**Medicinal Mushrooms (MMs):
prebiotics for the gut-brain axis**

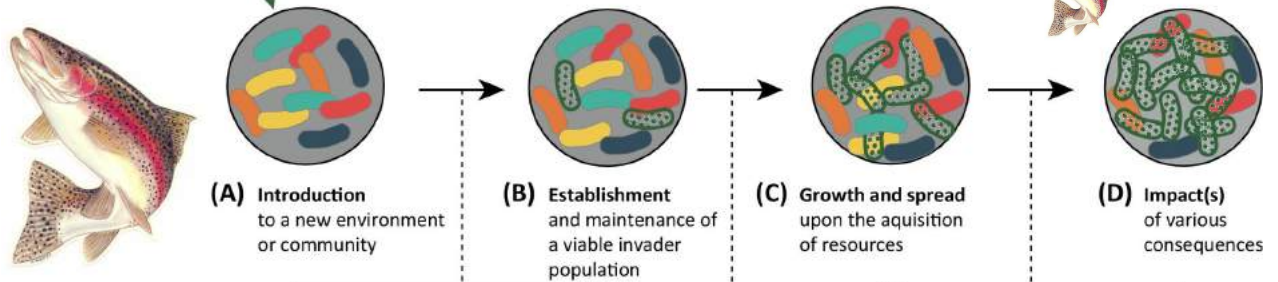
Medicinal mushrooms as prebiotics

Prebiotic effect: the similarity with the diverse gene pool of river trouts



Traits that increase an invader's chance of success:

- High growth rates
- Dispersal capability
- Phenotypic plasticity
- Genetic diversity



Abiotic resistance as a barrier to invasion:

- pH
- Temperature
- Salinity

Biotic resistance as a barrier to invasion:

- Competition
- Antagonism
- Predation

A successful invasion may:

- Displace or shift resident taxa
- Alter community functioning

How can mushrooms support gut health?

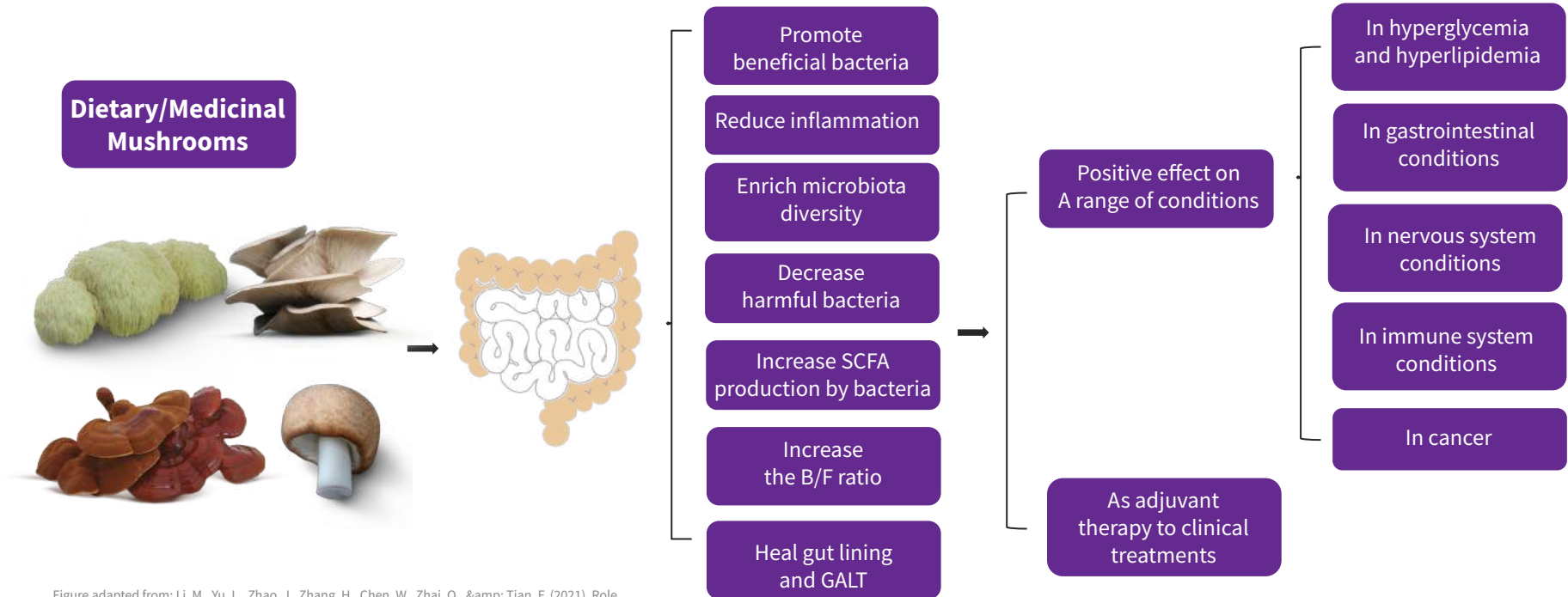
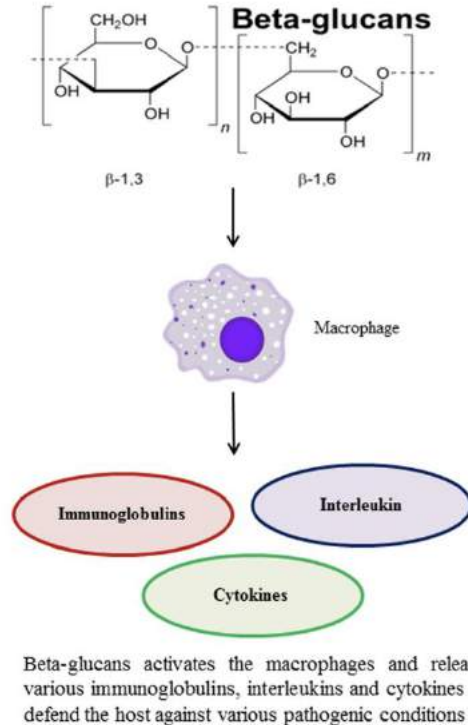


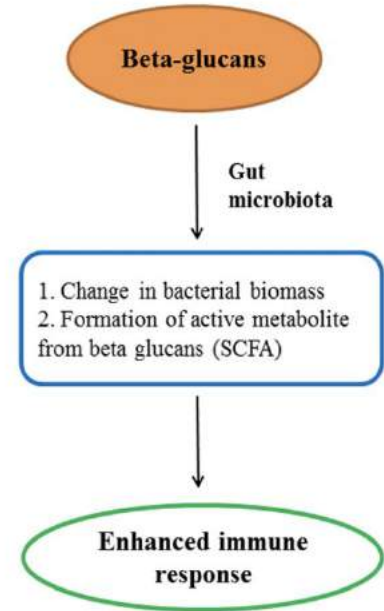
Figure adapted from: Li, M., Yu, L., Zhao, J., Zhang, H., Chen, W., Zhai, Q., & Tian, F. (2021). Role of dietary edible mushrooms in the modulation of gut microbiota. *Journal of Functional Foods*, 83.

Medicinal mushrooms as prebiotics

- β -(1 \rightarrow 3, 1 \rightarrow 6)-D-glucans contribute to production of SCFAs
- Activate & sustain microbiota
- Regulate dysbiosis
- Immunomodulation

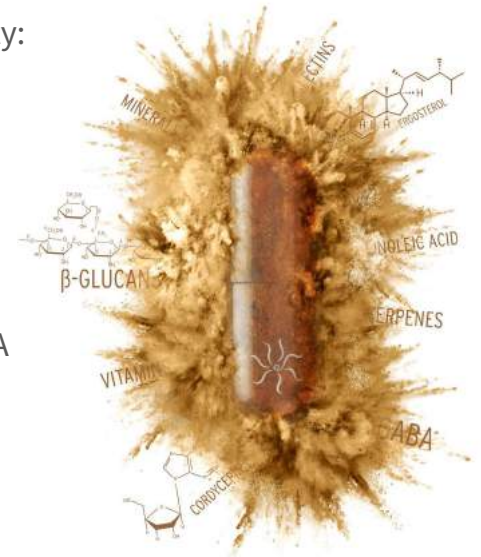


Possible involvement of gut microbiota in beta-glucans immunomodulatory action



Main bioactive molecules in medicinal mushrooms

- **Polysaccharides** (particularly **β -D-glucans**): main prebiotic and immunomodulatory activity
- **Terpenes**: myelin regeneration, NGF synthesis, antioxidant and antiinflammatory activity:
e.g. *G. lucidum* **ganoderic acids** and **erinacines & hericenones** (*H. erinaceus*).
- Complete essential amino acid profile and non essential aminoacids
- Vitamins and minerals
- Sterols: main one is **Ergosterol** – precursor of Vitamin D2
- **GABA**: natural neurotransmitter: Reduced levels contribute to stress and insomnia. GABA supplementation improves cognitive functions such as temporary visual attention.
- **Ergothioneine** levels decrease from the age of 60 onwards: Subjects with mild cognitive impairment have significantly lower levels.
- Others: statins: e.g. natural Lovastatin, polyphenols (rich source of antioxidants)..

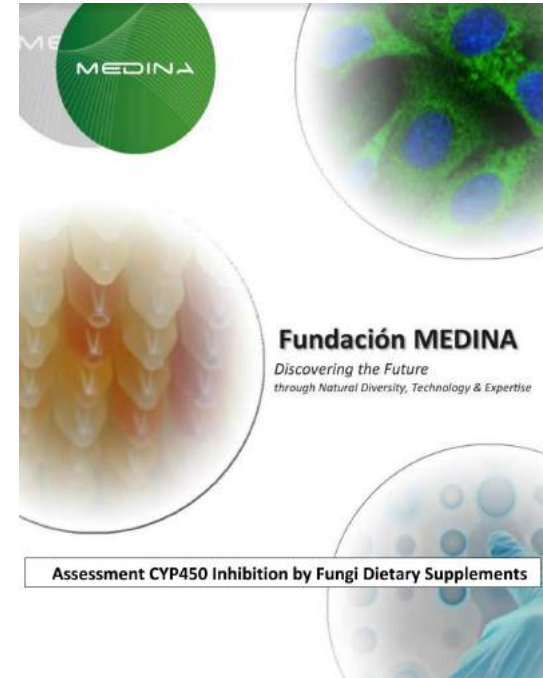


Medicinal mushrooms are natural immunomodulators

Why recommend MM?

- **Natural** products with potential pharmacological and beneficial effects
- **Safe & well-tolerated:** no toxicity (*Zhao et al., 2020*)
- **Perceived as safer vs. synthetic or semi-synthetic** compounds
- **Demonstrated prebiotic effect:** support healthy microbiota status
- **Immune balance:** promote dynamic balance between Th1/Th2 response
- **Wellbeing** & regulation of a healthy emotional-stress-mood-energy status

Hifas da Terra demonstrates the non-significant interaction of our fungal extracts with CYP450 enzymes, cytochromes involved in the metabolism of chemotherapy agents and other drugs





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Part 2

Clinical cases and Hifas Da Terra studies

Case study: Depression and dysbiosis



NUTRACEUTICAL PROTOCOL HDT

DEPRESSION			
Protocol	Morning	Afternoon	Night
Mico-Rei	1	0	0
Mico-Leo	1	0	0



BACKGROUND

40-year-old woman with 20 years of depression who, despite previous psychiatric and nutritional interventions, continued to suffer from depression.

Decreased total colonisation of microorganisms, especially protective microbiota (greatly reduced Bifidobacteria) and muconutritive microbiota (very low Akkermansia).

Proteolytic microbiota and yeast overgrowth.

pH 6.5, the upper limit of normal.

In this patient, due to the evaluation of her history of marked intestinal dysbiosis, it was decided to add Bio-Intestin to the protocol. **The protocol used was as above plus 3 capsules of Bio-Intestin in the morning.**

Case study: Depression and dysbiosis

June 2019

Microbiota Aerobia	Unidad	Resultado	Evaluación	Valores normales	Legenda
E <i>Escherichia coli</i>	CFU/g	8 x10 ⁶	✓	>=1 x10 ⁶	CUL
P <i>E. coli</i> <i>Biovare</i>	CFU/g	9 x10 ⁵	↑↑	<1 x10 ⁴	CUL
P <i>Proteus spp.</i>	CFU/g	<1 x10 ⁴	✓	<1 x10 ⁴	CUL
P <i>Pseudomonas spp.</i>	CFU/g	<1 x10 ⁴	✓	<1 x10 ⁴	CUL
P Otros microorganismos proteolíticos	CFU/g	<1 x10 ⁴	✓	<1 x10 ⁴	CUL
I <i>Enterococcus spp.</i>	CFU/g	4 x10 ⁶	✓	>=1 x10 ⁶	CUL

Microbiota Anaerobia	Unidad	Resultado	Evaluación	Valores normales	Legenda
S <i>Bifidobacterium spp.</i>	copias/g	<4 x10 ⁷	↓↓↓	>=1 x10 ⁸	PCR
S <i>Bacteroides spp.</i>	copias/g	3 x10 ⁸	↓	>=1 x10 ⁹	PCR
S <i>Lactobacillus spp.</i>	CFU/g	4 x10 ⁶	✓	>=1 x10 ⁵	CUL
S <i>H₂O₂-Lactobacillus</i>	CFU/g	1 x10 ⁶	✓	>=1 x10 ⁶	CUL
P <i>Clostridium spp.</i>	CFU/g	<2 x10 ⁴	✓	<1 x10 ⁵	CUL
M <i>Faecalibacterium prausnitzii</i>	copias/g	7 x10 ⁷	↓↓	>=1 x10 ⁹	PCR
M <i>Akkermansia muciniphila</i>	copias/g	4 x10 ⁴	↓↓↓	>=1 x10 ⁸	PCR

Análisis cuantitativo de Levaduras					
Levaduras	CFU/g	<1 x10 ³	✓	<1 x10 ³	CUL
Análisis Cuantitativo de Hongos					
Hongos		Sin crecimiento		Sin crecimiento	CUL
Número total de Microorganismos					
	copias/g	4 x10 ¹⁰	↓	>=1 x10 ¹¹	PCR

Características de las Heces					
pH de las Heces		6,5	✓	5,8 - 6,5	PH
Consistencia de las heces		Pastosa			

September 2019

Microbiota Aerobia	Unidad	Resultado	Evaluación	Valores normales	Legenda
I <i>Escherichia coli</i>	CFU/g	5 x10 ⁶	✓	>=1 x10 ⁶	CUL
P <i>E. coli</i> <i>Biovare</i>	CFU/g	<1 x10 ⁴	✓	<1 x10 ⁴	CUL
P <i>Proteus spp.</i>	CFU/g	<1 x10 ⁴	✓	<1 x10 ⁴	CUL
P <i>Pseudomonas spp.</i>	CFU/g	<1 x10 ⁴	✓	<1 x10 ⁴	CUL
P Otros microorganismos proteolíticos	CFU/g	<1 x10 ⁴	✓	<1 x10 ⁴	CUL
I <i>Enterococcus spp.</i>	CFU/g	3 x10 ⁶	✓	>=1 x10 ⁶	CUL

Microbiota Anaerobia	Unidad	Resultado	Evaluación	Valores normales	Legenda
S <i>Bifidobacterium spp.</i>	copias/g	2 x10 ⁸	✓	>=1 x10 ⁸	PCR
S <i>Bacteroides spp.</i>	copias/g	8 x10 ⁸	↓	>=1 x10 ⁹	PCR
S <i>Lactobacillus spp.</i>	CFU/g	3 x10 ⁶	✓	>=1 x10 ⁵	CUL
S <i>H₂O₂-Lactobacillus</i>	CFU/g	2 x10 ⁶	✓	>=1 x10 ⁵	CUL
P <i>Clostridium spp.</i>	CFU/g	<2 x10 ⁴	✓	<1 x10 ⁵	CUL
M <i>Faecalibacterium prausnitzii</i>	copias/g	2 x10 ⁹	✓	>=1 x10 ⁹	PCR
M <i>Akkermansia muciniphila</i>	copias/g	1 x10 ⁶	↓↓	>=1 x10 ⁸	PCR

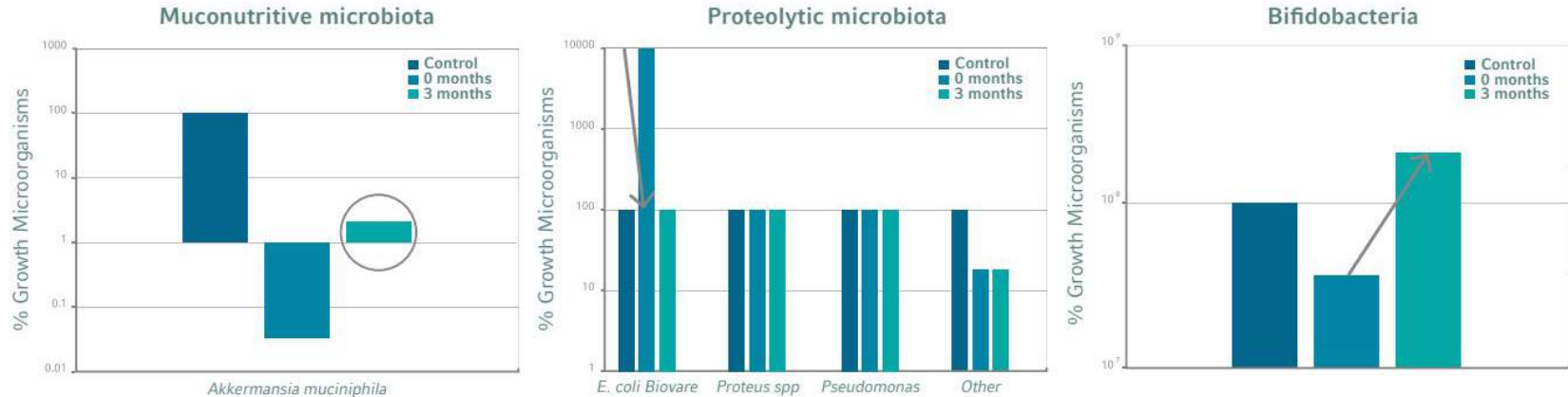
Análisis cuantitativo de Levaduras					
Levaduras	CFU/g	<1 x10 ³	✓	<1 x10 ³	CUL
Análisis Cuantitativo de Hongos					
Hongos		Sin crecimiento		Sin crecimiento	CUL
Número total de Microorganismos					
	copias/g	3 x10 ¹¹	✓	>=1 x10 ¹¹	PCR

Características de las Heces					
pH de las Heces		6,0	✓	5,8 - 6,5	PH
Consistencia de las heces		Viscosa			

Case study: Depression and dysbiosis

RESULTS

Favourable progression of both the intestinal dysbiosis and the patient's condition.



Case study: Delayed cognitive development in a 3 year old boy

BACKGROUND

The patient has poor cognitive development for his age in terms of language and communication skills, as well as a dysbiosis characterised by:

<p>Decrease of <i>Akkermansia muciniphila</i>, a muconutritive bacterium.</p>	<p>Decreased <i>Lactobacillus H₂O₂</i>. These hydrogen peroxide-producing <i>Lactobacillus</i> may prevent colonisation or invasion of opportunistic pathogens.</p>	<p>Concomitant overgrowth of proteolytic microorganisms and yeasts leading to their conversion to pathogens. Thus it was important to regulate their levels.</p>
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HDT NUTRACEUTICAL PROTOCOL

DELAYED DEVELOPMENT - 3 YEAR OLD

Protocol

Dr. GB

0.5 ml/kg



Case study: Delayed cognitive development (August 2019)

Microbiota Aerobia		Unidad	Resultado	Evaluación	Valores normales	Legenda
E	<i>Escherichia coli</i>	CFU/g	2×10^7	✓	$\geq 1 \times 10^8$	CUL
P	<i>E. coli</i> Biovar	CFU/g	$< 1 \times 10^4$	✓	$< 1 \times 10^4$	CUL
P	<i>Proteus</i> spp.	CFU/g	$< 1 \times 10^4$	✓	$< 1 \times 10^4$	CUL
P	<i>Pseudomonas</i> spp.	CFU/g	$< 1 \times 10^4$	✓	$< 1 \times 10^4$	CUL
P	Otros microorganismos proteolíticos	CFU/g	1×10^5	↑↑	$< 1 \times 10^4$	CUL
E	<i>Enterococcus</i> spp.	CFU/g	6×10^5	↓	$\geq 1 \times 10^8$	CUL
Microbiota Anaerobia						
S	<i>Bifidobacterium</i> spp.	copies/g	$< 4 \times 10^7$	↓↓↓	$\geq 1 \times 10^8$	PCR
S	<i>Bacteroides</i> spp.	copies/g	6×10^5	↓	$\geq 1 \times 10^9$	PCR
S	<i>Lactobacillus</i> spp.	CFU/g	7×10^5	✓	$\geq 1 \times 10^5$	CUL
S	<i>H₂O₂-Lactobacillus</i>	CFU/g	7×10^5	✓	$\geq 1 \times 10^5$	CUL
P	<i>Clostridium</i> spp.	CFU/g	$< 2 \times 10^4$	✓	$< 1 \times 10^5$	CUL
M	<i>Faecalibacterium prausnitzii</i>	copies/g	1×10^5	↓	$\geq 1 \times 10^9$	PCR
M	<i>Akkermansia muciniphila</i>	copies/g	7×10^5	↓↓	$\geq 1 \times 10^8$	PCR
Análisis cuantitativo de Levaduras						
C	<i>Candida albicans</i>	CFU/g	2×10^3	↑	$< 1 \times 10^3$	CUL
Análisis Cuantitativo de Hongos						
H	Hongos		Sin crecimiento		Sin crecimiento	CUL
	Número total de Microorganismos	copies/g	4×10^{10}	↓	$\geq 1 \times 10^{11}$	PCR
Características de las Heces						
	pH de las Heces		8,0	↑↑↑	5,8 - 6,5	pH
	Consistencia de las heces		Pastosa			

CUL (cultivo)

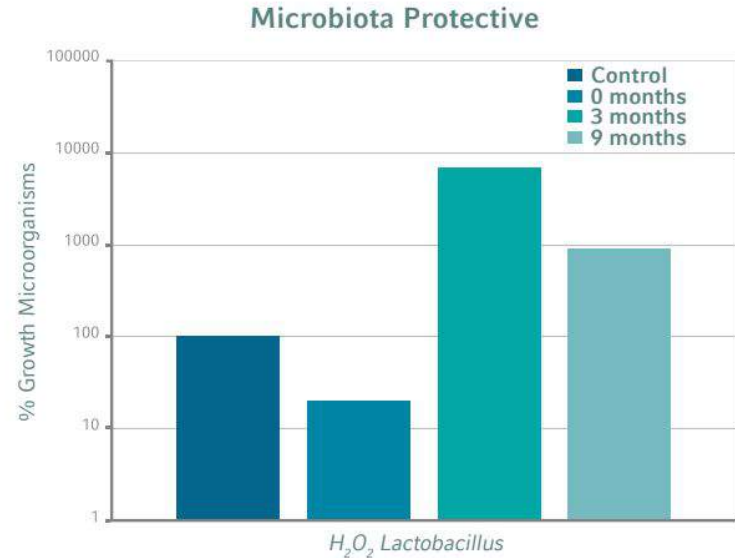
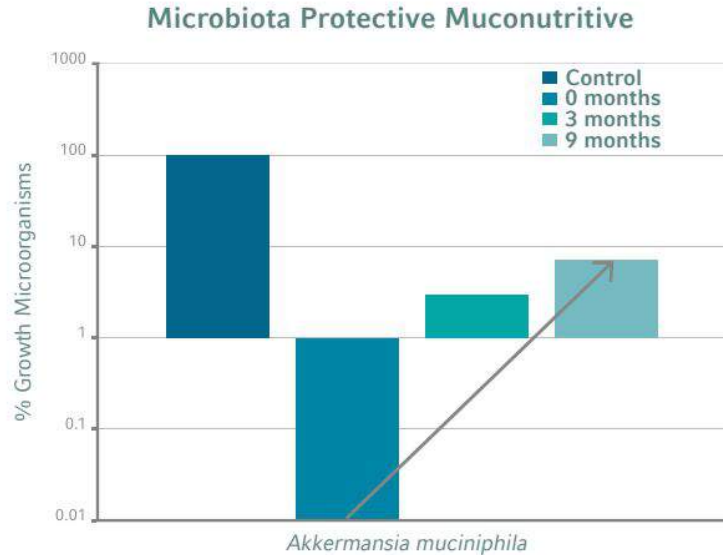
PCR (reacción en cadena de la polimerasa)

pH (colorimétrico con tres reactivos)

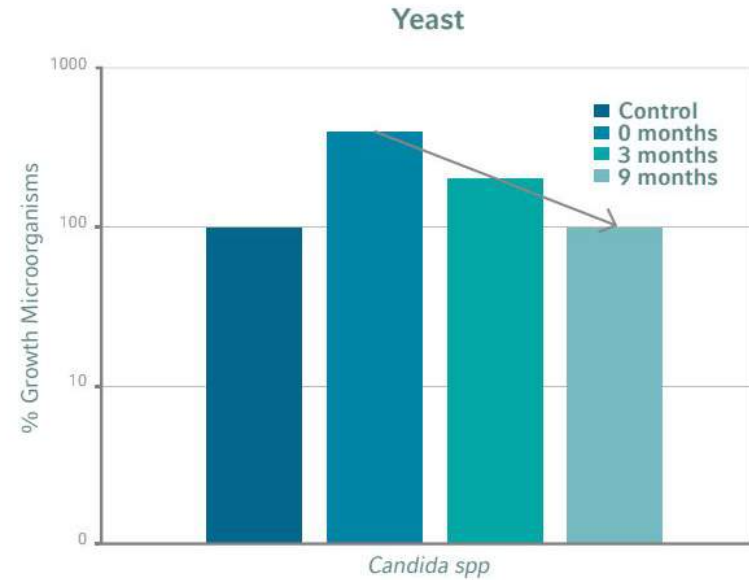
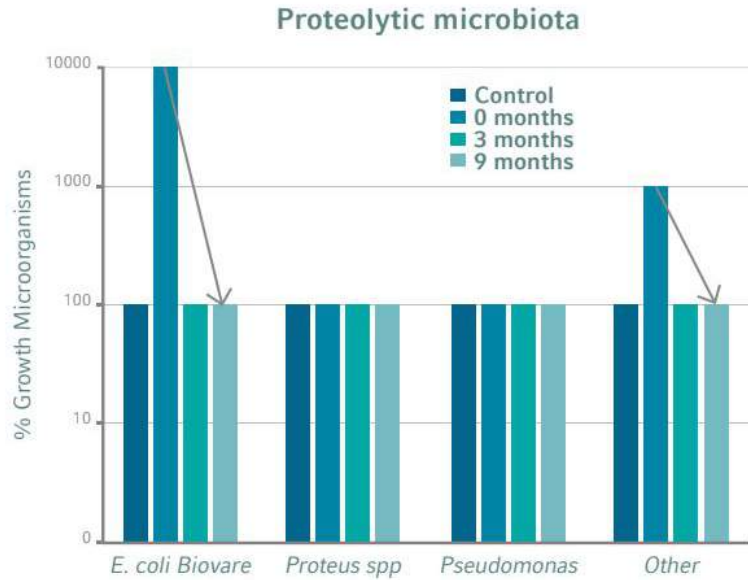
Case study: Delayed cognitive development (August 2019)

RESULTS

Favourable evolution of the intestinal dysbiosis and the patient's condition.



Case study: Delayed cognitive development



Case study: Dysbiosis and constipation in 10 year old boy

Case background: Young Male, Aged 10, symptoms - chronic constipation since 3yrs. of age. Evacuates every 3-5 days. Stools offensive. Type 2 on British Stool Chart. Early antibiotic use, first 3 days of life and at 1 ½ yrs, due to chest infection. Food intolerance, wheat and yeast identified. Intestinal permeability and dysbiosis, stomach distention and cramping after certain foods. Mood disorder - Outbursts of anger / anxiety predominantly with delayed emptying of bowels. Focus and concentration weak, family history of IBD & Celiac.

HdT products used:

- Dr. Leo now replaced with Dr. GB, taken for 3 months, continued taking post recovery as health plan support
- Dosage - was 0.5ml x body weight of 32 kg = 16ml of HdT mushroom syrup daily

Results: Improved

- Great benefits; evacuating stool with ease more regularly every 1-2 days, non-offensive smell
- Stool formed on the British Stool Chart Type 3-4 = normal formation
- Stomach distention reduced dramatically, no cramping
- Food intolerances reduced, reduced daily mood swings and anxiety, overall improvement in wellbeing, more focus at school

Additional therapeutic intervention:

- 5R protocol, nervous system support, immune support, lifestyle support - breathing and relaxation
- Exercise, movement, bedtime routine, Epsom salt baths

HdT 2019 study: Mico-Rei for stress, anxiety, and sleep

Aim: demonstrate potential therapeutic benefits of *Ganoderma lucidum* (Mico-Rei[®]) for the improvement of anxiety, and the ability to fall asleep and sleep quality.

Duration: 16 weeks of supplementation of 2 capsules/day of Mico-Rei[®]

Results - All patients experienced improvement in anxiety and stress levels

- 50% reported absence of anxiety
- 38% presented with mild anxiety (a reduction in pre-study levels)
- Only 12% continued with severe anxiety

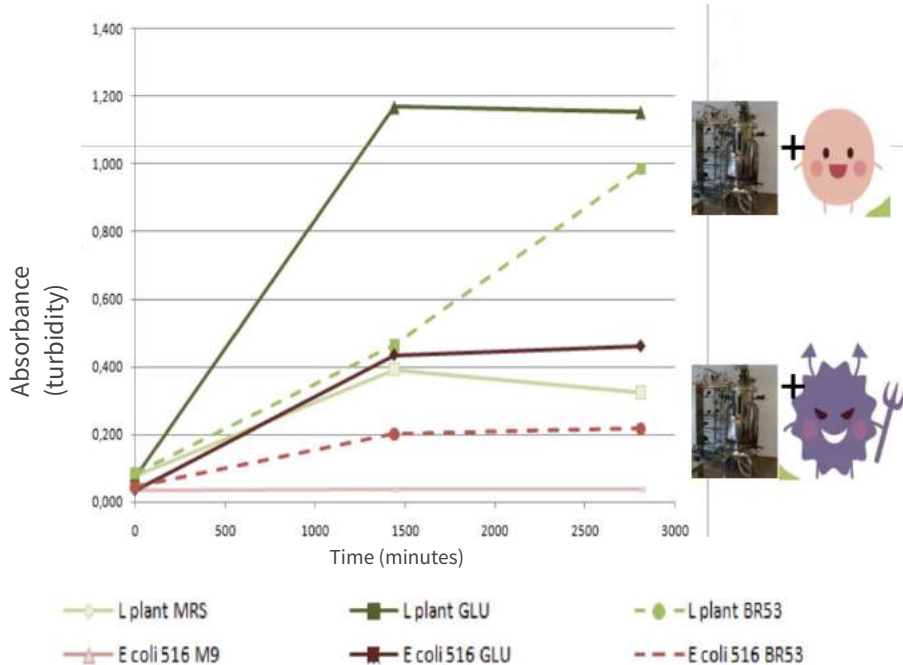
Sleep:

- Sleep onset time decreased by 41.25% in 100% of cases. Sleep onset and sleep duration improved in all participants
- Average hours of sleep increased by more than 2 hours
- All patients had reduced severity of insomnia after use of Mico-Rei[®]
- Insomnia was completely resolved in half of the patients

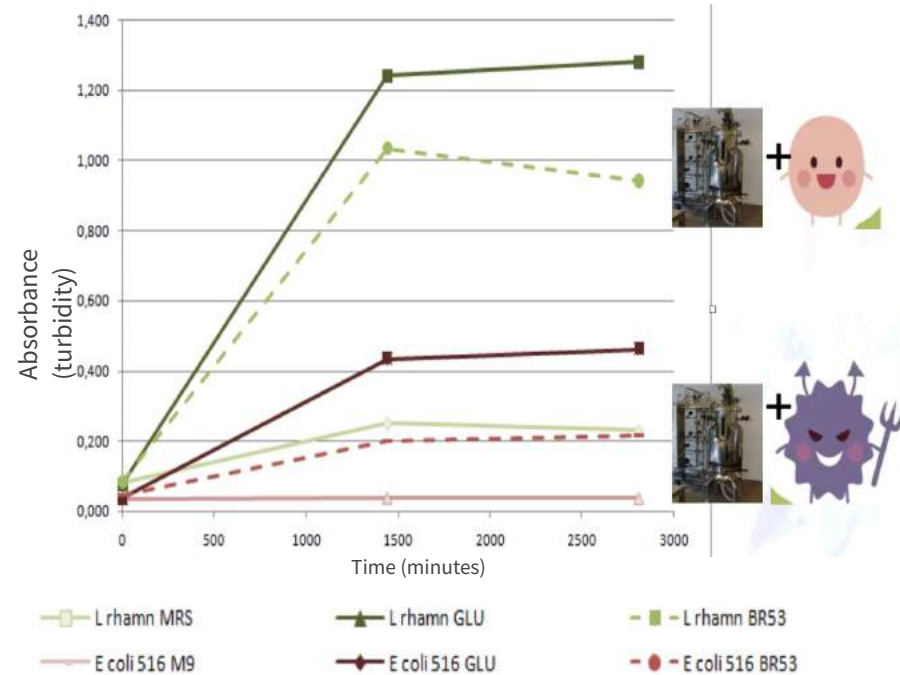


3 months results of prebiotic activity from HDT Lion's Mane strain cultured in Bioreactor

Lactobacillus plantarum



Lactobacillus rhamnosus





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Part 3

Products & Recommendations

Mico-Leo (Lion's Mane - *Hericium erinaceus* 12:1 extract)

100% organic, pure and standardised **extract of Lion's Mane** (*Hericium erinaceus*) with a high concentration of Beta-glucans, Hericenones, Erinacines, Ergothioneine, GABA, B-vitamins, ergosterol (pro-vitamin D2) and naturally occurring minerals.

Neurocognitive and intestinal regenerator: NGF synthesis, myelin and neurotransmitter enhancement

Prebiotic: gut-brain axis connection



Mico-Rei (Reishi - *Ganoderma lucidum* 15:1 extract)

Highly concentrated **100% organic**, pure and standardised **extract of Reishi (*Ganoderma lucidum*)** with guaranteed levels of Beta-D-glucans and triterpenoid compounds (ergosterol, ganoderic acids).

Mood balancing, anxiety-stress relief, depression and insomnia:
antidepressant and anxiolytic due to its 5-HT_{2A} receptor antagonist activity, sedative-hypnotic compounds and hormone balancing.



HdT recommendations



Depression

Product	AM	MID	PM
Mico- Rei	1	0	0
Mico-Leo	1	0	0

Anxiety and stress

Product	AM	MID	PM
Mico- Rei	1	1	0

Insomnia

Product	AM	MID	PM
Mico- Rei	1	0	1

Dysbiosis

Product	AM	MID	PM
Bio-Intestin	1	1	1

Leaky Gut

Product	AM	MID	PM
Mico- Leo	1	1	0
Mico- Rei	1	1	0



*As per Reishi study, 16 weeks treatment is recommended

Dysbiosis in behavioural disorders in children

Bioactive molecules in **Reishi and Lion's mane** such as erinacines, hericenones, ganoderic acids and terpenes contribute to the proper functioning of the central nervous system and microbiota balance.

Dr. GB Gut & Brain is a natural syrup (250 ml) containing organic Reishi (*Ganoderma lucidum*) and Lion's Mane (*Hericium erinaceus*), with vitamins A and C, specifically formulated for children to support their digestive, nervous and immune systems.



Pediatric Dysbiosis

Product

Dr. GB (Gut & Brain)

Microbiota balancing effect
Epithelial regeneration

0.5 ml/kg of
child's weight





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Part 4

Why Hifas da Terra?
Quality, Safety & Efficacy

WHY HIFAS?

Improving health worldwide

NATURE MADE SCIENCE

- NUTRACEUTICALS FROM ORGANIC CERTIFIED MEDICINAL MUSHROOMS
- ENVIRONMENTAL PHILOSOPHY
- ORGANIC PRODUCTION

EUROPE'S
LARGEST
MEDICINAL
MUSHROOM
BIOTECH COMPANY



THE VANGUARD OF BIOTECH INNOVATION IN MEDICINAL MUSHROOMS

- THE ONLY EUROPEAN MCO THERAPY COMPANY WITH CLINICAL TRIALS OF OUR PRODUCTS

QUALITY, EFFICACY & SAFETY

MicoQuality

- 100% PURE
- HIGHLY CONCENTRATED EXTRACTS
- NO DRUG INTERACTION
- SELECTION OF SPECIFIC STRAINS



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*Join our
professional area*



Secado en condiciones naturales



Ensayos clínicos



Certificado GMP buenas prácticas de producción



Apto para veganos y vegetarianos



Aptos para intolerantes a la lactosa



Aptos para celíacos



Cápsulas 100% vegetales



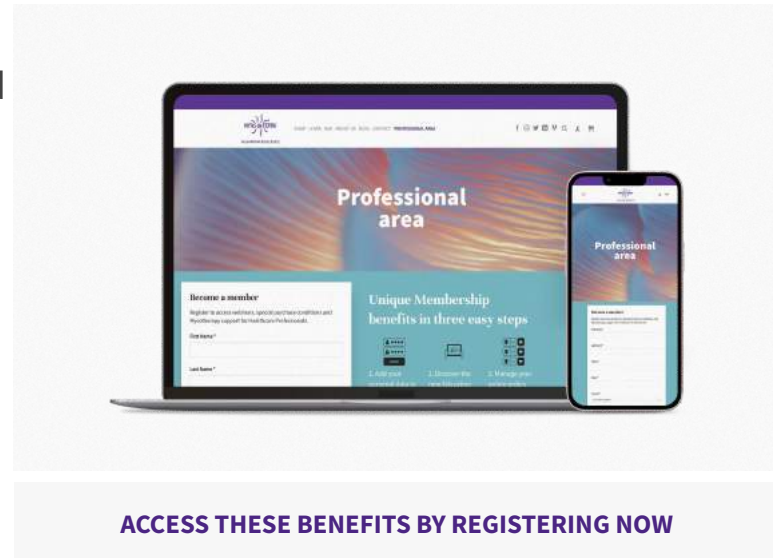
Producción ecológica certificada

Professional Area

Exclusive benefits for health professionals

Visit www.hifasdaterra.co.uk/professionals for:

- **Access to resources:** vademecum, webinars, papers and publications by Hifas da Terra I+D
- Continue your **training on HdT's e-learning platform** with scientifically validated content - *coming soon*
- Get free **professional advice on mycotherapy** from our biomedical department
- Receive HdT's free **newsletter** for professionals





HIFAS da TERRA®

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Thank you!

The gut, the second brain

Key actions of Lion's mane:



EPITHELIUM REGENERATOR

Regenerates epithelium of gastrointestinal mucous membranes



HEALS/PROTECTS GASTRIC MUCOSA

Regenerates damaged gut mucosa



Consider supplementation with *H. erinaceus* in:

- Dysbiosis
- *Helicobacter pylori*
- IBD: Crohn's and ulcerative colitis
- Leaky gut
- IBS

