

ROELMI•HPC
Health & Personal Care



SYNBALANCE®

METSYN

TAKE CARE OF YOU !



ROELMI HPC – Company

ROELMI HPC is now the global expert for actives and functionals in Health & Personal Care.

But its roots date back to 1946 in the Mediterranean area, where the company still finds concepts and innovation-driven technologies, in full respect of nature and people.

Its high quality products are developed thanks to avant-garde research, scientific approach and true passion.



**NO IMPACT
IN PROGRESS®**

*NIP, your P.I.N.
to sustainability*



ROELMI HPC – Commitment

Launched at the beginning of XXI century, NO IMPACT IN PROGRESS® (NIP) is more than a program. It is the key to achieve the sustainability, an ambitious target, an active process as well as an active community.



N = Safe for Nature

We inform customers of the importance to choose, when possible, eco-friendly ingredients that ensure a lower dependence on energy in production with a reduced impact on the environment.



I = Innovation & efficacy

We manufacture high-performance ingredients recognized by their technology and efficiency.



P = Safe for People

The safety of the person is a key component of our philosophy. Our ingredients are subject to stringent controls to ensure consumer's safety.



**NON-EDIBLE
FRACTIONS**



**RENEWABLE
SOURCES**



**SAFETY &
PERFORMANCE**



**ETHICAL SUPPLY
CHAIN**



**CIRCULAR
ECONOMY**



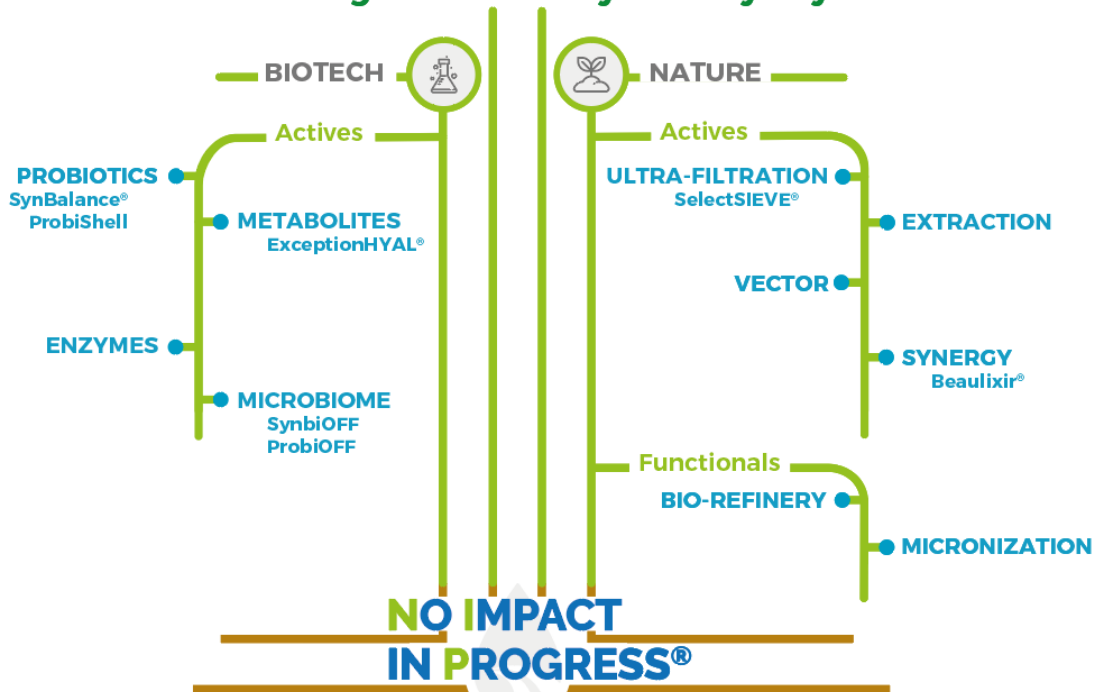
**NO IMPACT IN
PROGRESS**

Our NIP® program applies to all products and technologies.



ROELMI HPC – Active ingredients

Practicing Sustainability in every day life



ROELMI HPC – Focus on Actives

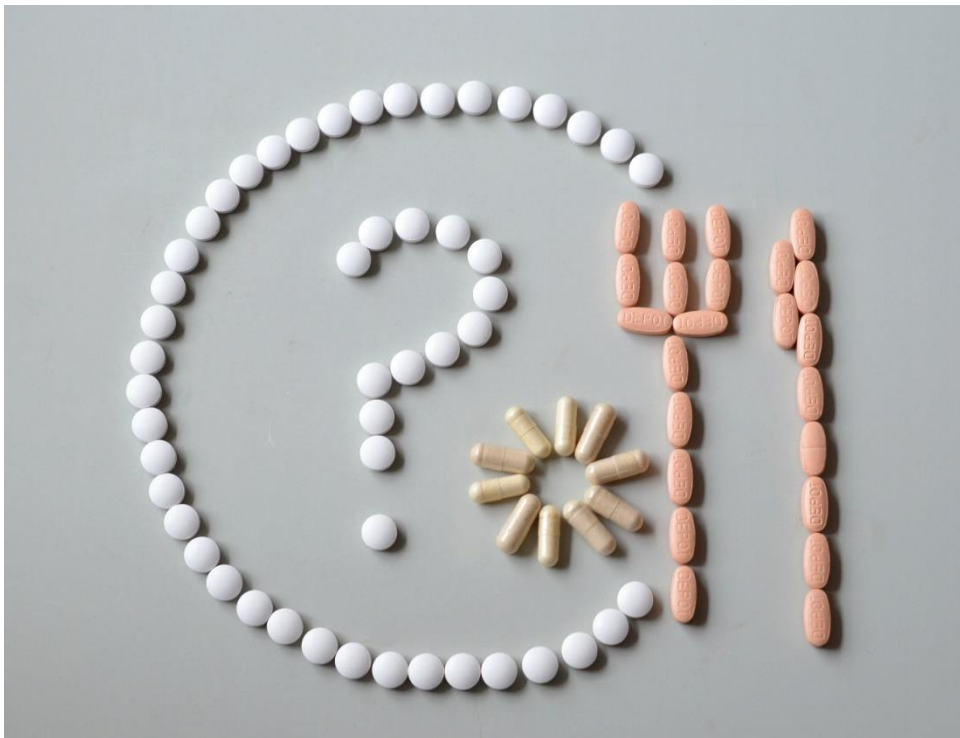
Nutrition

**CLINICALLY
TESTED**



New ingredients in development go through a strict screening of *in-vitro*, *ex-vivo* and *in-vivo* tests not only for the efficacy, but also for safety parameters.

Results are confirmed by clinical trials performed in Universities, CRO or in collaboration with specialists.



SynBalance® MetSyn

- High potency probiotics selection (LP, LA and LR)
- Biofermentation origin for nutraceutical applications
- Designed for metabolic modulation
- Gut health symptoms improvement
- Effective on obesity markers
- Reduction of systemic inflammation and oxidative stress



Mechanism of action

HEALTHY GUT MICROBIOTA

SynBalance® MetSyn supports metabolic health by:

1. Enhancing lipids metabolism & by reducing glucidic metabolism and absorption
2. Producing useful metabolites as short chain fatty acids
3. Turning the typical unbalanced microbiota of overweight people into healthier one
4. Slowing down systemic intestinal inflammatory processes and oxidative stress
5. Ameliorating the symptoms of GI alterations and promoting gut wellbeing



SynBalance[®] MetSyn – Biological target

How to recognize if you suffer from Metabolic Syndrome?

At least, 3 of the following:

**Overweight
/ obesity**

**High
triglycerides**

**Low HDL/
High LDL**

**High fasting
blood
glucose**

**High blood
pressure**

Metabolic Syndrome is a set of conditions that can increase the risk of having:

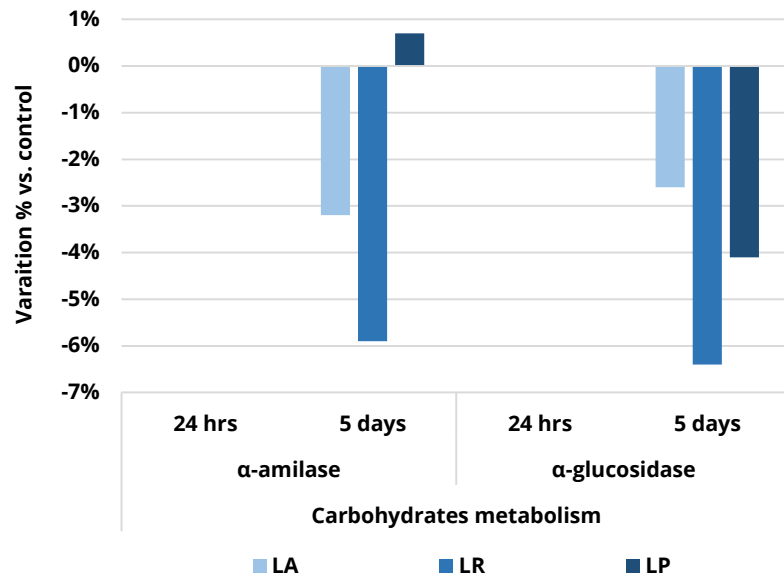
- Type 2 diabetes
- CV disease
- Nonalcoholic fatty liver disease
- Osteoarthritis
- Some types of cancer: breast, colon, endometrial and kidney
- Stroke
- Musculoskeletal disorders



SynBalance® MetSyn – Efficacy dossier

CARBOHYDRATES METABOLISM

- **α -amylase**, **α -glucosidase** are the enzymes involved in the digestion-absorption of carbohydrates and hydrolyzation of oligosaccharides to release glucose.
- SynBalance® MetSyn is effective in inhibiting the enzymatic activity and the corresponding starch digestion, modulating the carbohydrate digestion and reducing the absorption of sugars.



Protocol: enzymatic activity of α -amylase was evaluated by Lugol reactive assay and α -glucosidase was evaluated by Fehling assay .

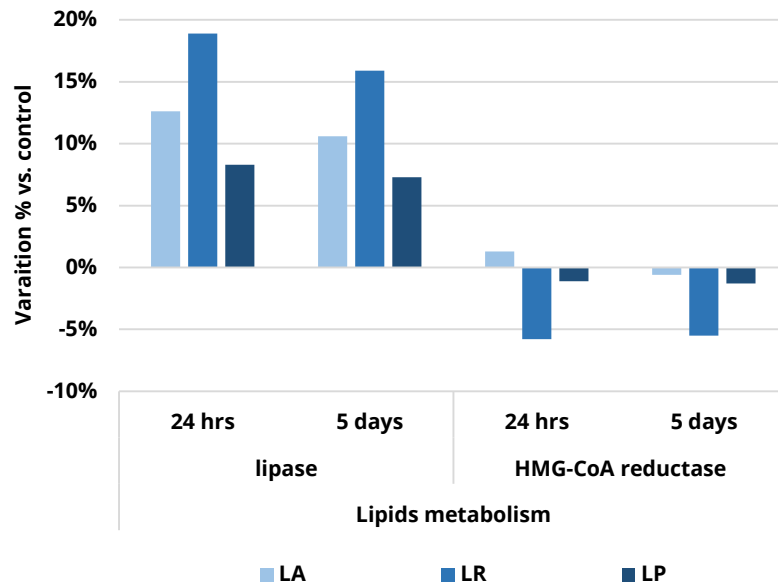
In-vitro efficacy dossier



SynBalance[®] MetSyn – Efficacy dossier

LIPIDS METABOLISM

- Modulation of lipolysis and cholesterol biosynthesis as biological markers of hyperlipidemia and hypercholesterolemia.
- SynBalance[®] MetSyn improves the exploitation of lipid mass and keep under control the cholesterol blood level.

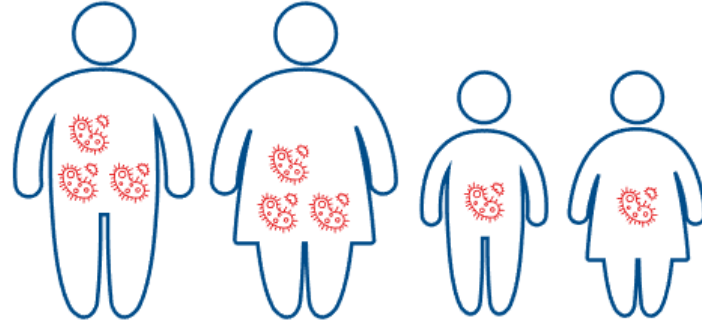
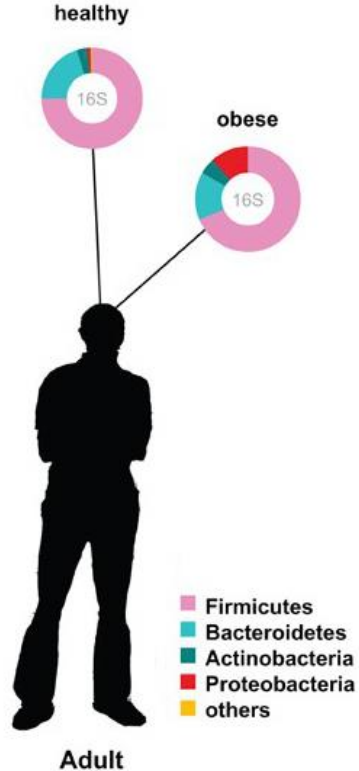


Protocol: enzymatic activity was assayed by colorimetric method evaluating the synthesis of fatty acids (lipase) and Mevalonic acid (HMG-CoA reductase)

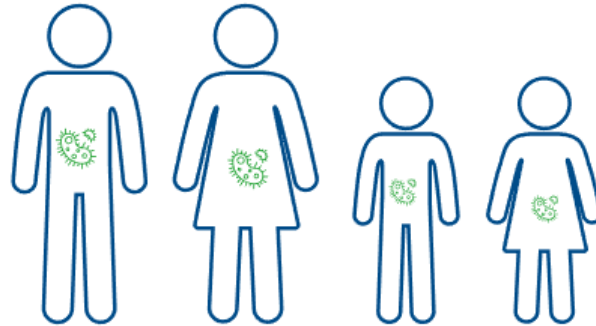
In-vitro efficacy dossier



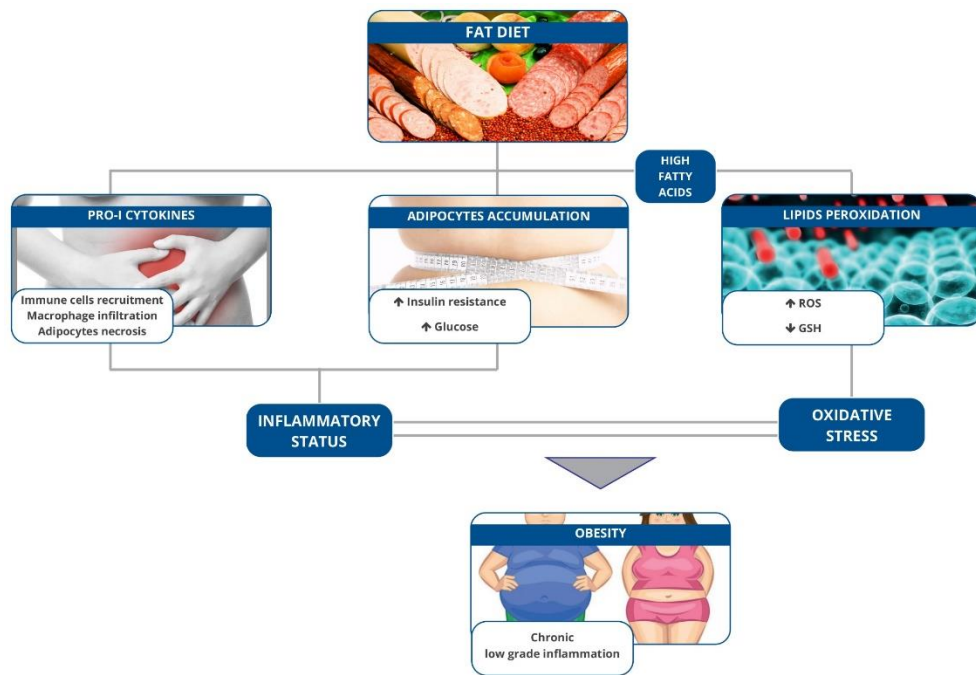
Promotion of healthy microbiota



SynBalance® MetSyn probiotic strains help to rebalance intestinal microbiota



Inflammatory status linked to obesity



Adipose tissue expresses cytokines which inhibit insulin signalling pathways. Obesity also results in impairment of endothelium-dependent vasodilatation to insulin.

Local deposits of fat around blood vessels have a vasoregulatory role, which may contribute both to insulin action and to vascular endothelial dysfunction.

In normal conditions, insulin activates both endothelin-1- mediated vasoconstriction and nitric oxide-mediated vasodilatation.

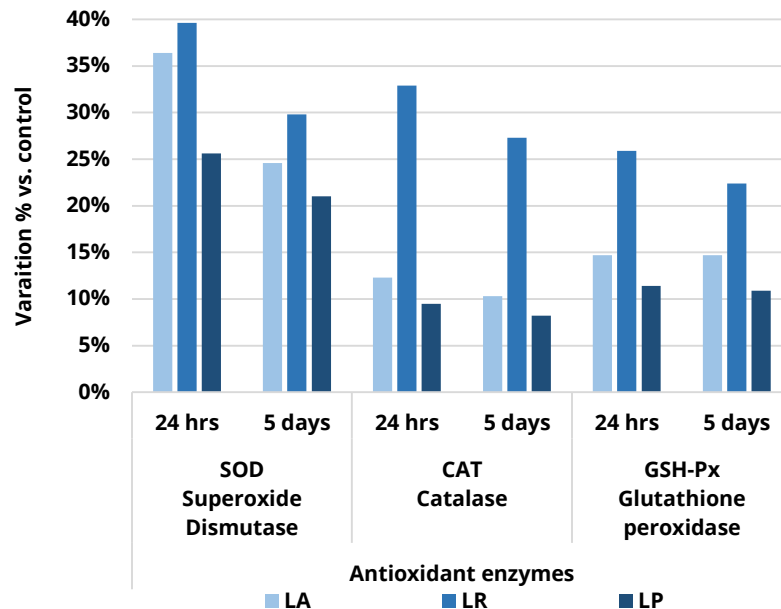
In obese people, insulin-stimulated nitric oxide synthesis is impaired due to TNF-alpha production, resulting in unopposed vasoconstriction.



SynBalance® MetSyn – Efficacy dossier

PROTECTION FROM OXIDATIVE STRESS ENZYMATIC MODEL

- The antioxidant power of SynBalance® MetSyn was proven through positive modulation of antioxidant enzymes.
- The activity of the enzymes is strongly improved helping the reduction of the oxidative stress.



Protocol: Spectrofluorometric assay for the evaluation of the enzymatic activity of SOD as described by Flohè and Otting (1984), of CAT as described by Aebi (1984) and of GPx as described by Flohè and Gunzler (1984).

In-vitro efficacy dossier

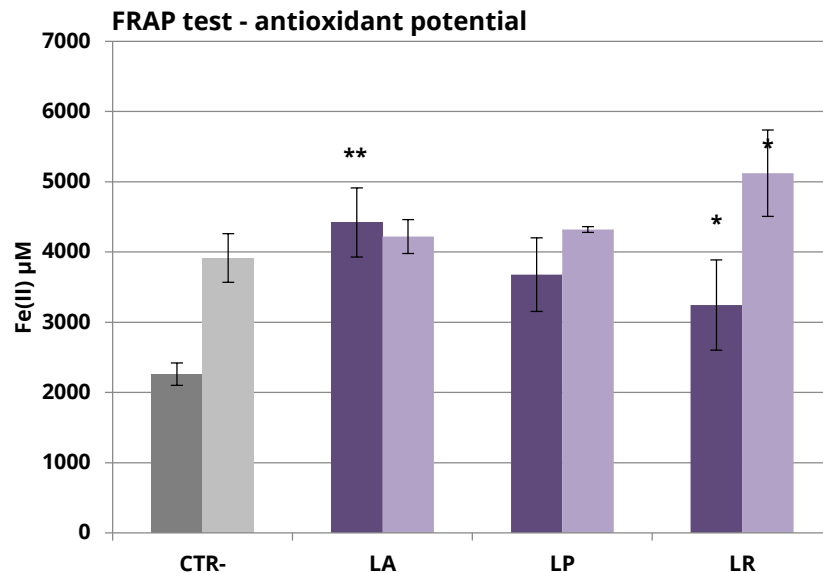


SynBalance[®] MetSyn – Efficacy dossier

PROTECTION FROM OXIDATIVE STRESS⁽¹⁾ FRAP MODEL

- The antioxidant power was confirmed through the protection of cell culture from the oxidative stress.
- SynBalance[®] MetSyn demonstrates a strong synergic antioxidant potential.

(1) I. Presti, G. D'Orazio, M. Labra, et al., "Evaluation of the probiotic properties of new Lactobacillus and Bifidobacterium strains and their in vitro effect". *Applied Microbiology and Biotechnology*, 2015, 99:13, 5613.



Protocol: Protection from inflammatory stress induced by sodium dodecyl sulphate, antioxidant power (AOP) & reducing properties. Murine model: Fibroblasts line (BALB/c3T3, clone A31). Outcomes at 24h (acute, darker) and 5dd (chronic, lighter). CTR+: SDS/ CTR-: no treatment

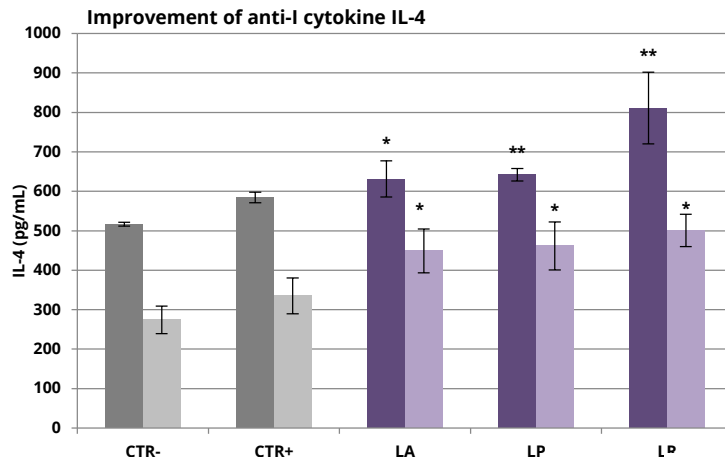
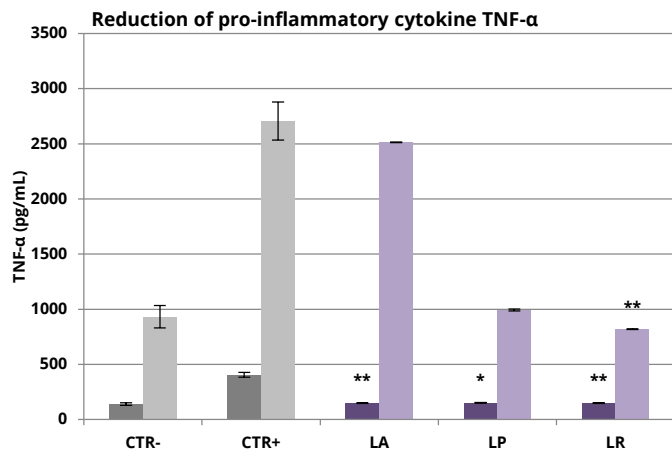
In-vitro efficacy dossier



SynBalance® MetSyn – Efficacy dossier

MODULATION OF SYSTEMIC INFLAMMATION⁽¹⁾

- SynBalance® MetSyn is effective in slowing down the inflammatory status activated by TNF- α both in early and late responses
- SynBalance® MetSyn helps to activate the immunity response by improving IL-4 cytokine release



Protocol: Inhibition of pro-inflammatory TNF-alpha. Improvement of anti-inflammatory IL-4. Murine model: Fibroblasts line (BALB/c3T3, clone A31). Outcomes at 24h (acute, darker) and 5dd (chronic, lighter). CTR+: SDS/ CTR-: no treatment

(1) I. Presti, G. D’Orazio, M. Labra, et al., “Evaluation of the probiotic properties of new Lactobacillus and Bifidobacterium strains and their in vitro effect”. *Applied Microbiology and Biotechnology*, 2015, 99:13, 5613.

In-vitro efficacy dossier



Clinical study

AIM OF THE STUDY: RDBPC clinical trial to evaluate the efficacy of a probiotic (SynBalance® MetSyn) in improving metabolic syndrome-associated conditions.

SUBJECTS: 60 males and females (randomized as 30 active/ 30 placebo), 65-80 years old, with metabolic syndrome diagnosis.

STUDY PROTOCOL: initial screening and observation 2 weeks before treatment then followed by 2 months of administration. Checks are scheduled at T0, T30 and T60. QoL questionnaires collected after wash-out (one month of follow-up)

MEASURED PARAMETERS

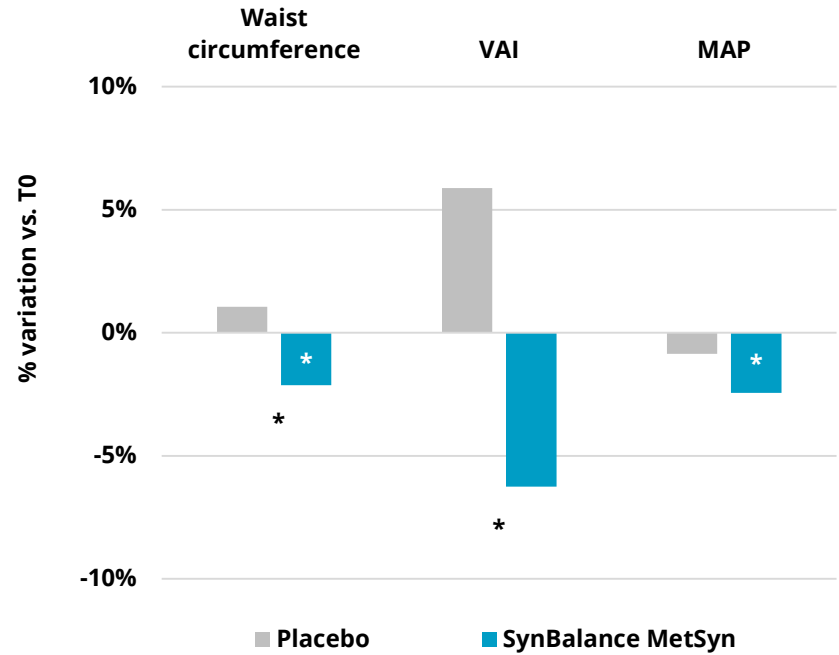
- **Anthropometric evaluation:** body mass index, waist circumference, central obesity index, visceral adiposity index, blood arterial pressure (systolic, diastolic, average, pulse), heart rate, endothelial function (Endocheck)
- **Hematochemical analysis:** Metabolic markers: Glycaemia, Basal insulin, HOMA-IR, Complete lipid profile {Total Cholesterol, LDL, HDL, triglycerides}, GOT, GPT, gamma-GT, NAFLD indexes (LSI, HSI, FLI), Uric acid, Creatinine, Estimated glomerular filtration rate (eGFR). Immune markers: hsPCR, TNF-alpha, Hemocromo e Lymphocytes typization + 2 Adipocytokines (Leptin, Adiponectin)
- **Self-assessment:** Quality of Life questionnaire or MNA (mini-nutritional assessment)



Anthropometric evaluation

IMPROVEMENT OF OBESITY MARKERS

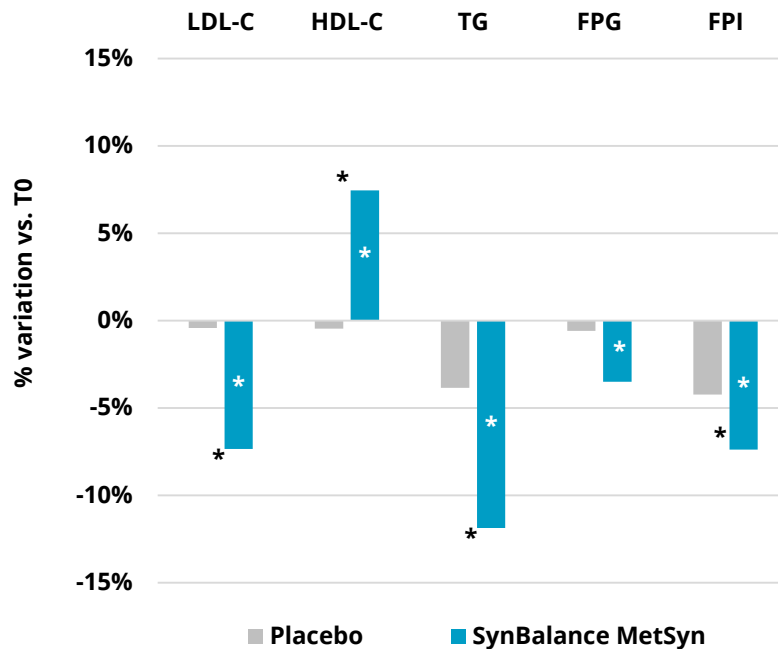
- Waist circumference in overweight people was reduced by 4 cm in the active group together with visceral adipose index (-10%).
- In another study, typical symptoms correlated to GI dysfunction in overweight and obese people such as constipation and bloating, were also improved by the same probiotics.
- Slight decrease of MAP (mean arterial pressure) has been reported.



Hematochemical parameters

MODULATION OF METABOLIC PROFILE

- All dyslipidemic markers were improved in MetSyn group during the treatment: especially TG and LDL-C were statistically reduced and HDL-C increased with respect to placebo.
- Also fasting plasma insulin (FPI) and fasting plasma glycaemia (FPG) diminished thanks to a more efficient use of endogenous insulin and an enhanced carbohydrates metabolism.



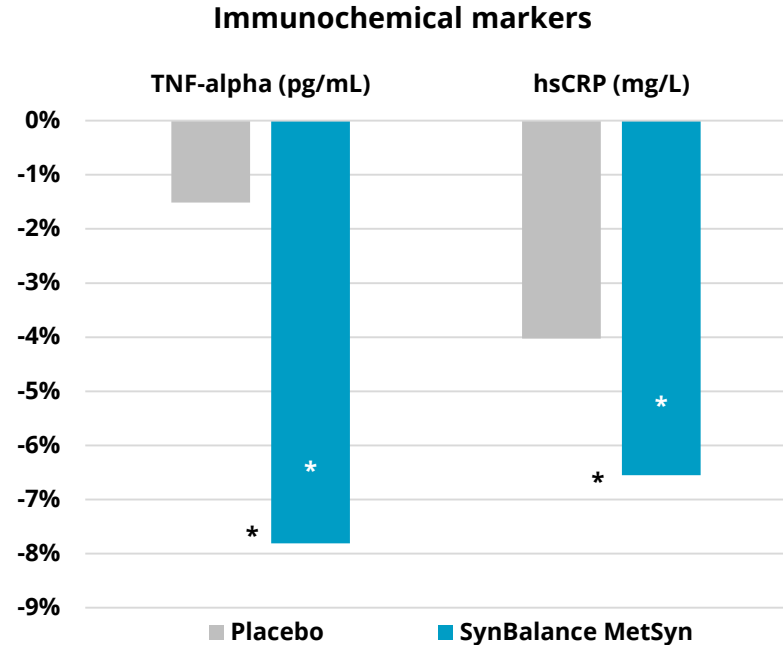
Chronic inflammation

REDUCTION OF SYSTEMIC INFLAMMATION

Low-grade systemic inflammation is a key player in the onset of metabolic syndrome. The pro-I state associates with both insulin resistance and endothelial dysfunction, providing a connection between inflammation and metabolic processes which is highly deleterious for vascular functions.

C-reactive protein is elevated in patients with CVD. TNF-a is enhanced by the resistance to the anti-inflammatory actions of insulin and is overproduced by adipose tissue.

- Both pro-I cytokine and C- reactive protein were reduced by the implementation of a healthier life style, but SynBalance® MetSyn consistently improved these immunochemical markers, showing its positive influence on chronic (low grade) inflammation.



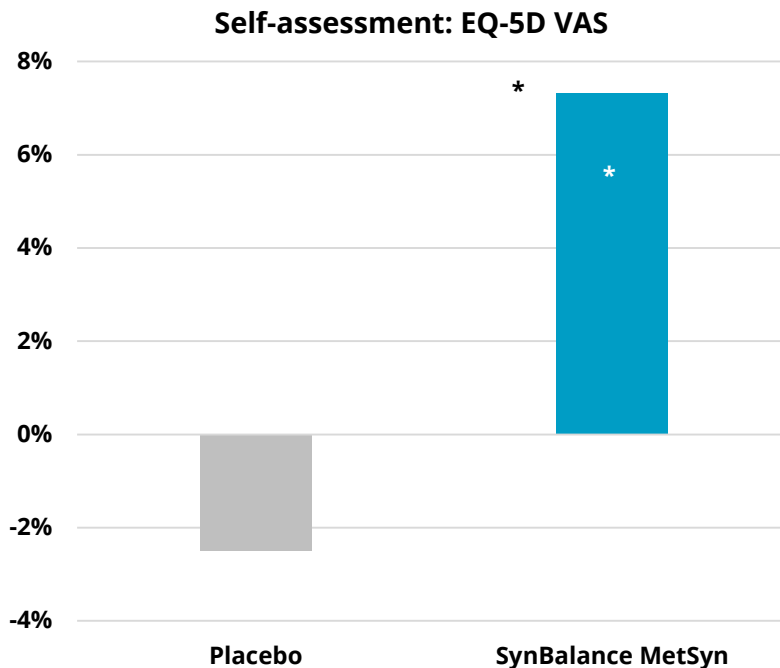
Self-assessment

IMPROVEMENT OF QUALITY OF LIFE

The EQ-5D-5L consists of:

- a descriptive system comprising 5 dimensions: mobility, self care, usual activities, pain/discomfort, anxiety/depression, rated by 5 levels (no problems, slight problems, moderate problems, severe problems, and extreme problems);
- EQ VAS recording the respondent's self-rated health on 0-100 vertical, visual analogue scale.

SynBalance® MetSyn significantly improved the self-perceived healthy status of patients with respect to placebo group showing a stronger effect of the probiotic treatment on quality of life against the sole life-style changes.



Final consideration

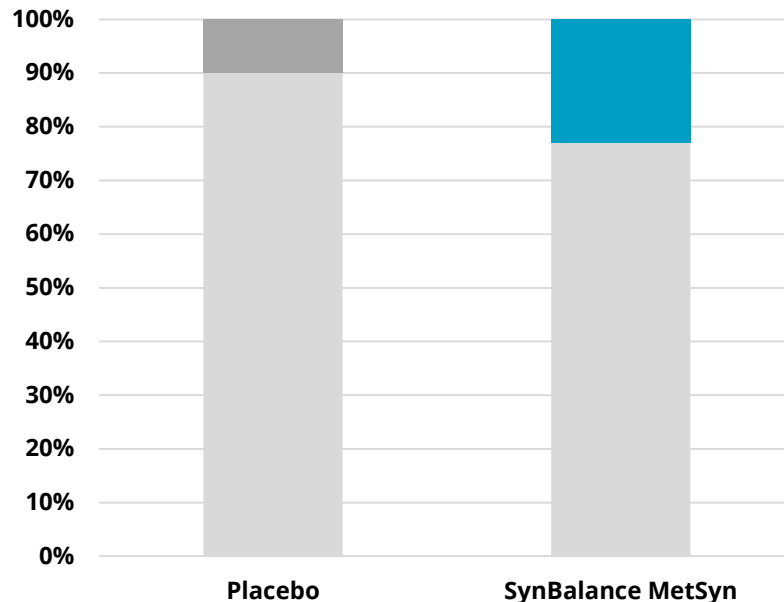
DIAGNOSIS OF METABOLIC SYNDROME

To be recruited, each patient needs to fulfil the International Diabetes Federation criteria (at least 3 among 5):

- 1) waist circumference ≥ 94 cm in men and ≥ 80 cm in women (not BMI)
- 2) systolic AP ≥ 130 and/or diastolic AP ≥ 85 ,
- 3) Basal glycaemia >100 mg/dL,
- 4) TG >150 mg/dL,
- 5) HDL-C ≤ 40 in men and ≤ 50 in women

At the end of the study, the number of patients not complying with the MetS diagnosis anymore, significantly increased in SynBalance® MetSyn group (23%), compared with the placebo (10%).

Reduction in MetS-diagnosis

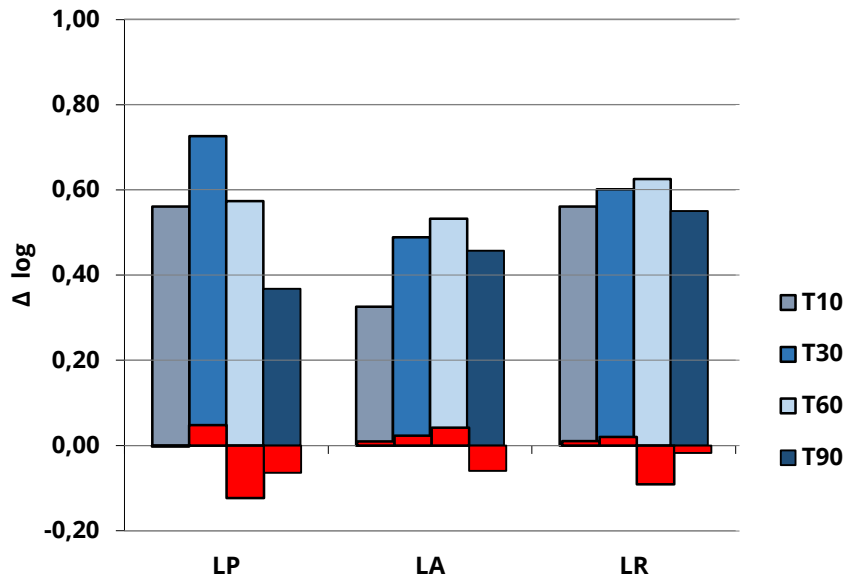


SynBalance[®] MetSyn – Efficacy dossier

CLINICAL EVIDENCE OF GI COLONIZATION⁽²⁾

Quantification of strains with respect to T0 (confirmed by qPCR tests on blinded samples) during the treatment (60 days) and follow-up (additional 30 days):

- No significant increase in the placebo group (red color) for any specie
- Selective, consistent and significant improvement of administered strains (blue colors) in the study group



Protocol: Oral intake: 1B CFU/day/strain for 60 days. Subjects: 50/group. Inclusion criteria: patients with a condition similar to irritable bowel syndrome IBS. *Randomized, double blind, placebo controlled.* Method: collection of stools & HR-QOL questionnaire. Outcome: GI-tract colonization, clinical evaluation of symptoms. Analytical technique: Real time – qPCR. Analysis performed at T0, T10, T30, T60, T90 (30dd wash out).

(2) V. Mezzasalma et al., "A Randomized, Double-Blind, Placebo-Controlled Trial: The Efficacy of Multispecies Probiotic Supplementation in Alleviating Symptoms of Irritable Bowel Syndrome Associated with Constipation" *BioMed Research International*, 2016.



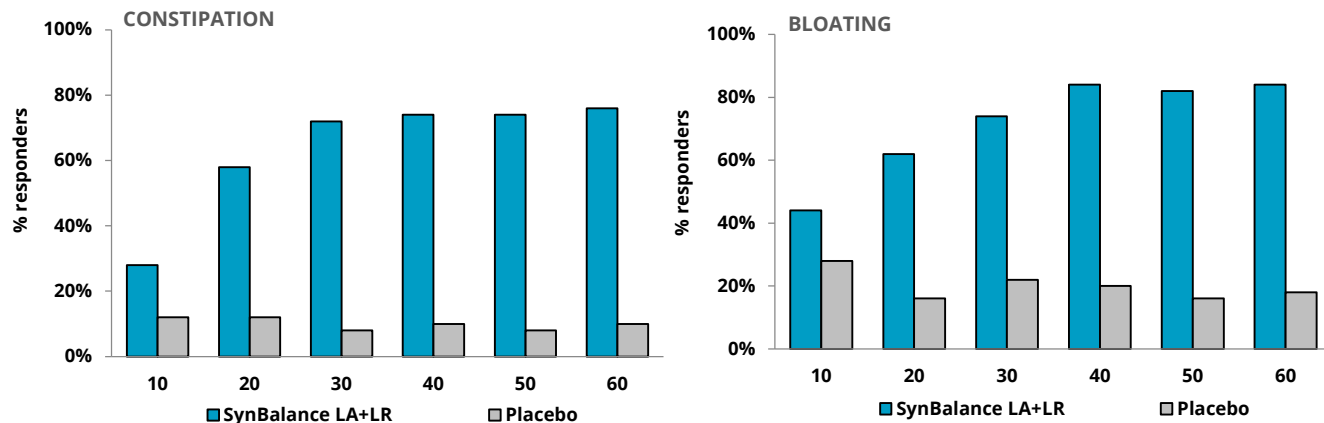
SynBalance® MetSyn – Efficacy dossier

CLINICAL IMPROVEMENT: RESPONDERS %

GI diseases are commonly found in overweight and obese people.

Variation of symptoms during the active treatment (60 days) compared to placebo expressed as % of responders

RESPONDER: subject reporting a decrease of symptoms of at least 30% compared to the basal condition.



Protocol: Oral intake: 1B CFU/day/strain for 60 days. Subjects: 50/group. Inclusion criteria: patients with a condition similar to irritable bowel syndrome IBS. *Randomized, double blind, placebo controlled.* Method: collection of stools & HR-QOL questionnaire. Outcome: GI-tract colonization, clinical evaluation of symptoms. Analytical technique: Real time – qPCR. Analysis performed at T0, T10, T30, T60, T90 (30dd wash out). VAS score based on symptoms scale: Bloating, Abdominal pain, Constipation, Abdominal cramps, Flatulence, Data recorded for study group in active phase and follow-up period compared to placebo.

(2) V. Mezzasalma et al., "A Randomized, Double-Blind, Placebo-Controlled Trial: The Efficacy of Multispecies Probiotic Supplementation in Alleviating Symptoms of Irritable Bowel Syndrome Associated with Constipation" *BioMed Research International*, 2016.

Human Model

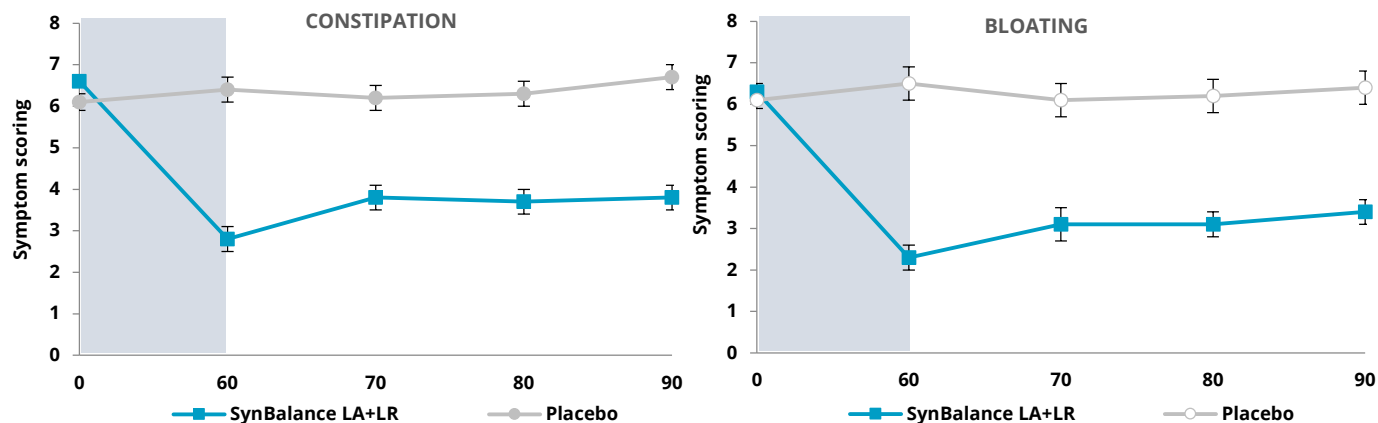


SynBalance[®] MetSyn – Efficacy dossier

FOLLOW-UP IMPROVEMENT

Variation of symptoms during the follow-up period (from day 60 to day 90) compared to placebo and with respect to treatment period.

The positive effect is kept along the wash-out period and even if a slight worsening of the symptom is perceived, it does not reach the basal value and it significantly differs from placebo



(2) V. Mezzasalma et al., "A Randomized, Double-Blind, Placebo-Controlled Trial: The Efficacy of Multispecies Probiotic Supplementation in Alleviating Symptoms of Irritable Bowel Syndrome Associated with Constipation" BioMed Research International, 2016.

Human Model



SynBalance[®] MetSyn – Summary

Description: Probiotic complex (*L. plantarum* LP - PBS067, *L. acidophilus* LA – LA001, *L. reuteri* LR – PBS072)

Typical dosage: 6B CFU/day (2B CFU/strain) – minimum 60 days treatment

RESULTS:

- ✓ Control of carbohydrates digestion
- ✓ Modulation of lipid metabolism
- ✓ Protection from oxidative stress
- ✓ Inhibition of inflammatory stress
- ✓ Improvement of GI symptoms

TYPICAL APPLICATIONS:

- ✓ Improvement of metabolic functions
- ✓ Decreased hyperglycemia
- ✓ Lower calories intake
- ✓ Control of cholesterol synthesis
- ✓ Modulation of chronic inflammation
- ✓ Weight management



Sachets / Sticks



Vials



Capsules



Bulk / Full service



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