# Lactobacillus fermentum ME-3

#### HUMAN ORIGIN

Isolated from the intestinal tract of a healthy 1-year old child in 1995 by scientists at the University of Tartu, Estonia

#### PATENTED STRAIN

Patented in Russia, Europe and USA

### **SURVIVAL CHARACTERISTICS**

ME-3 has strong resistance to stomach acid, digestive enzymes and bile acids. Its cell surface lectin profile enables it to adhere to the gut epithelium. It is also temperature tolerant. Hence, it does not need to be refrigerated and can be taken with or without food.

#### SAFETY

ME-3 has been tested in animals and it has been used in human clinical trials over a period of twenty years without side effects. Hence, *Lactobacillus fermentum* ME-3 is very safe for human consumption

# Human Clinical Trials

#### STUDY 1

Probiotic reduces postprandial lipemia and oxidative stress Healthy subjects aged 40-65 years

2 weeks, ME-3 kefir (min. 8,5 log cfu/day) or placebo (kefir without M									
	ME-3 kefir (n=	ME-3 kefir (n=12)		(n=25)					
	T=0	2 weeks	T=0	2 weeks					
LDL	$3,9\pm0,8$	3,7±0,8	$3,9\pm0,7$	4,1±0,6					
HDL	1,5±0,3	1,6±0,3	1,5±0,3	1,5±0,3					
	EQ 1 10	67 1 15	E2 + 1E	64 17					

Kullisaar et al. 2008 Proceedings, 4th Central European Congress on Food

#### STUDY 2

#### Atopic dermatitis

Subjects ages 20 - 42 years old 3 months, goat milk with ME-3 (min 3x 10 log cfu per day) or placebo

	ME-3 (n=5)		Placebo (n=6)	
	T=0	3 months	T=0	3 months
DC (skin)	299±85	205±72	289±71	319±98
GSSG/GSH (skin)	0,19±0,04	0,11±0,04	0,16±0,03	0,16±0,03
oxLDL in blood	87±14	61±15	103±28	109±19
TAC in blood	34±1	46±3	37±1	35±4

Kullisaar et al. 2008 Proceedings, 4th Central European Congress on Food

#### STUDY 3

#### Post-stroke patients

Subjects aged 71-89 who had experienced a stroke between 8 - 22 days earlier 3 weeks, 6 capsules per day at 9 log cfu/capsule or placebo

	ME-3 (n=10)		Placebo (n=11)	
	T=0	3 weeks	T=0	3 weeks
LDL	3,9±2,2	3,8±1,9	3,2±0,8	3,2±1,1
oxLDL	121±35	109±35	130±23	128±22
DC	50±9	45±8	45±16	45±14
GSSG	64±16	52±18	73±28	71±18
GSSG/GSH	0,07±0,01	0,05±0,01	0,07±0,02	0,06±0,01
TAA	34±1	46±3	37±1	35±4

DC : diene conjugates, a marker of LDL oxidation - GSSG : oxidized glutathione - GSSG/GSH : ratio oxidized/reduced glutathione

TAA : total antioxidant capacity in serum

Kullisaar et al. 2008 Proceedings, 4th Central European Congress on Food

#### RESULTS

Volunteers ingesting kefir containing ME-3 exhibited the following:

- -16% in oxidized LDL-cholesterol
- -20% in 8-isoprostanes
- 10% increase in HDL-cholesterol
- 18% increase in paraoxonase enzyme activity (PON1)
- 10% decline in triglycerides

#### RESULTS

Individuals receiving *Lactobacillus fermentum* ME-3 experienced significant improvements in skin condition, blood markers and in self-assessment rating.

#### RESULTS

Subjects consuming ME-3 exhibited significant improvements in both the Scandinavian Stroke Scale and the Functional Independece Measure inventory. Stroke patients also experienced impressive improvements in the following blood markers: oxidized LDL-cholesterol, glutathione levels and ratio of reduced to oxidized glutathione, total antioxidant capacity, paraoxonase enzyme activity, as well as reductions in markers of inflammation and free radical damage.

# Lactobacillus fermentum ME-3 A Glutathione Producing Strain of Probiotic Bacteria





# **Strain Properties**

## Glutathione production and regeneration

Antioxidant Activity: Glutathione (GSH) is called the Master Antioxidant. Glutathione contains a thiol group (also called a sulfhydryl group) which is a sulfur atom bonded to a hydrogen atom (SH). Reduced glutathione can "donate" the hydrogen atom from its sulfhydryl group to neutralize free radicals, which is what makes it a powerful antioxidant.

GSH directly scavenges free radicals such as reactive oxygen species (ROS) and reactive nitrogen species (RNS). It is also a required cofactor for important antioxidant enzymes such as glutathione peroxidase which inactivates dangerous lipid peroxides. GSH also recycles and regenerates other antioxidants like vitamin C, vitamin E, coenzyme Q10 and lipoic acid back to their active form.

A Complete Glutathione System: Lactobacillus fermentum ME-3 is capable of boosting glutathione levels by three different mechanisms. The bacteria synthesize glutathione, they can extract it from the surrounding environment and they can also recycle oxidized glutathione back to its active or "reduced" form. Consequently, scientists are calling ME-3 a "Complete Glutathione System" and emphasize that this is the first time anything has been discovered with the capability of boosting glutathione levels via three independent mechanisms

**Detoxification:** Glutathione is also the **Master Detox Agent** because it plays a central role in virtually all detoxification reactions. It helps neutralize and eliminate chemical preservatives, agricultural pesticides, heavy metal toxins like mercury, lead, cadmium and arsenic, alcohol, and both OTC and prescription drugs. In addition to regulating detoxification in the trillions of cells throughout the body, glutathione is vitally important to liver function since the liver is our primary organ of detoxification.

## Stimulation of paraoxonase 1 (PON1) enzyme activity

*Lactobacillus fermentum* ME-3 up regulates PON1, which is an antioxidant enzyme produced in the liver. PON1 helps prevent oxidation of both HDL and LDL cholesterol particles which reduces plaque deposits and cardiovascular disease risks. PON1 also inactivates some toxic derivatives of homocysteine, which is a molecule associated with inflammation and cardiovascular disease. Consumption of ME-3 has been found to increase levels of PON1 in HDL-cholesterol particles.



# **Strain Properties Continued**

# Additional Anti-inflammatory & Antioxidant Effects

In human trials, consumption of *Lactobacillus fermentum* ME-3 decreased key markers of inflammation such as hs-CRP and interleukin-6 (IL-6). Experiments in mice have shown a significant reduction of inflammation due to a decrease in the pro-inflammatory cytokine TNF-alpha, an increase in levels of the anti-inflammatory cytokine IL-10, and a reduction of intestinal permeability using the Citrobacter rodentium mouse model.

In mice infected with salmonella (*S. Typhimurium*), ME-3 treated mice exhibited reduced lipid peroxidation, improved ratio of reduced to oxidized glutathione and improved gut mucosal antioxidant status.

In human clinical trials, treatment with ME-3 resulted in significant improvement in the ratio of reduced to oxidized glutathione in individuals infected with *Heliobacter pylori* and in patients with atopic dermatitis.

*Lactobacillus fermentum* ME-3 has also been shown to produce manganese superoxide dismutase or Mn-SOD, an important intracellular antioxidant enzyme that specifically helps protect mitochondria from free radical damage. Mn-SOD is also a key anti-inflammatory agent due to its ability to scavenge highly pro-inflammatory superoxide anions. Furthermore, increasing Mn-SOD may reduce risks to other illnesses since levels of Mn-SOD are known to be reduced in cancers, neurodegenerative diseases and psoriasis.

## **Anti-bacterial effect**

Lactobacillus fermentum ME-3 has shown potent anti-bacterial activitiy against several common gastrointestinal pathogens such as *E. coli, Salmonella enterica, Shigella sonnei* (in vitro studies); *Salmonella typhimurium* (mouse model for enteric fever), *Citrobacter rodentium* (mouse model for *E. coli* infections). These anti-microbial properties correlate with the production of lactic acid, acetic acid and succinic acid.

## Improvement of lipid profiles

In human clinical trials, consumption of *Lactobacillus fermentum* ME-3 resulted in the following improvements: reductions in elevated LDL Cholesterol, elevated triglycerides, oxidized LDL-cholesterol, oxidation of HDL-cholesterol and reduction in prostprandial lipemia.



# L. fermentum ME-3 In Summary A Multi-function Glutathione-Producing Biological Probiotic

- Isolated in 1995 from the GI tract of a healthy 1-year old child during a broad search for probiotics with strong antioxidant properties.
- Boosts glutathione via 3 mechanisms: increases production, uptake & recycling of glutathione. Scientists are calling ME-3 a "Complete Glutathione System"
- Produces manganese superoxide dismutase (Mn-SOD)
- Regenerates other antioxidants like vitamin C, vitamin E & coenzyme Q10
- Lowers LDL-cholesterol & decreases oxidative damage of LDL-cholesterol
- Promotes liver and cellular detoxification; promotes liver health
- Potent anti-bacterial activity against various strains of harmful bacteria
- Protects and improves gut barrier function
- Reduces local and systemic levels of inflammation; lowers CRP, IL-6
- Increases activity of PON1 enzymes which detoxify organophosphates (OPs). OPs are widely used agricultural pesticides that are linked to lower IQ, and diseases such as autism and ADHD.