

## ***Lactobacillus fermentum* ME-3**

Newly Discovered, Patented, Probiotic  
Proven to Boost Glutathione Levels\*

Unique Multi-Function Probiotic  
With Powerful Antioxidant Activity\*

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## ***Lactobacillus fermentum* ME-3**

Glutathione-Boosting Probiotic\*

Unique Multi-Function Probiotic with Antioxidant Activity\*

### **The Human Microbiome Project (HMP) has accelerated research into probiotics at an exponential rate.<sup>1</sup>**

It is becoming apparent that probiotics provide a wide range of health-promoting benefits that extend well beyond their traditional role in digestive health. Scientists are also learning that probiotics are strain specific, which means an individual probiotic strain can possess properties and produce benefits that are totally unique and specific to that strain, and substantially different from similar strains within the same species.<sup>1</sup>

*Lactobacillus fermentum* ME-3 is a newly identified probiotic strain that was first isolated in 1995 at the University of Tartu in Estonia. Ongoing research indicates that *L. fermentum* ME-3 expresses numerous unique and very exciting health benefits.\* As often transpires with great discoveries, a great deal of serendipity was involved in the discovery of *Lactobacillus fermentum* ME-3.

### **A Brief Background About the Discovery of *Lactobacillus fermentum* ME-3**



In 1994, the University of Tartu hosted a visiting professor from the University of Linköping in Sweden. The professor initiated a joint research project between doctors at the Department of Pediatrics at the University of Linköping and Professor Marika Mikelsaar and the Department of Microbiology at the University of Tartu.<sup>2</sup>

The purpose of the joint research project between the two groups of scientists was to research the relationship between levels of intestinal lactic acid-producing bacteria and the incidence of childhood immune health challenges. This research project was chosen because children in Sweden have a higher incidence of imbalanced immune response while children in Estonia have a very low incidence of imbalanced immune response.

Professor Mikelsaar and her team at the Department of Microbiology at the University of Tartu were well suited for this collaboration because they had been conducting research on *Lactobacillus* bacteria and the ecology of the human gastrointestinal tract for several decades. In fact, for over 20 years, Professor Mikelsaar and her colleagues worked with the Russian Space Program studying the intestinal microflora of Russian astronauts.

While *Lactobacillus fermentum* ME-3 was not the subject of the collaboration between Sweden and Estonia, during the research project, over 200 strains of

*Lactobacillus* bacteria were collected and identified from the intestinal tracts of the study subjects. On March 2, 1995, five separate strains of *Lactobacillus fermentum* were isolated from a healthy Estonian child. Significant differences were found in this child's probiotic fingerprint when compared to the intestinal bacteria of children who demonstrated signs of imbalanced immune response.<sup>3</sup>

### **Serendipity in the Discovery of *Lactobacillus fermentum* ME-3**

In 1996, a Dutch company engaged the University of Tartu to test their collection of *L. acidophilus* strains for possible antioxidant activity. The Dutch company asked the University of Tartu to do this study based on previously published Japanese research, which reported that some *Lactobacillus* species strains expressed antioxidant activity. This research venture turned out to be a disappointment because none of the tested strains of *Lactobacillus acidophilus* exhibited any significant antioxidant properties.<sup>4</sup>

Although the Dutch company's study did not find any strains of *L. acidophilus* with antioxidant activity, scientists at the University of Tartu subsequently decided to test the strains of *Lactobacillus fermentum* that had previously been collected. The Tartu scientists quickly discovered that several strains of *Lactobacillus fermentum* exhibited antioxidant properties. The strain that had been given the designation ME-3 was found to express very strong antioxidant properties.<sup>5</sup> Based on the initial finding that ME-3 produced significant antioxidant activity, follow-up studies were initiated that began to discover a wide range of additional health-promoting properties of *Lactobacillus fermentum* ME-3.\*

But first, a few words about the scientists who discovered *Lactobacillus fermentum* ME-3 and conducted substantial research on this new strain of lactic acid bacteria.



#### **Marika Mikelsaar, M.D., Ph.D.**

Marika Mikelsaar, M.D., Ph.D. is currently professor emeritus and a leading scientist in the department of microbiology at the University of Tartu. She is recognized as a leading expert in the areas of medical microbiology, human microbial ecology and biomedicine.

Professor Mikelsaar has published over 100 papers in international scientific journals. Her current research focuses on the impact of microbiota and *Lactobacillus sp.* on

host metabolic functions in health and disease. Professor Mikelsaar is past president of the International Society for Microbial Ecology (SOMED) and is a member of the editorial board of several microbiological journals.<sup>6</sup>

In 2007, Professor Marika Mikelsaar received the European Union (EU) award “European Union Woman Inventor and Innovator” for the discovery of *L. fermentum* ME-3.<sup>7</sup>



**Mihkel Zilmer, M.D., Ph.D.**

Professor Mihkel Zilmer is the head of Department of Biochemistry at the University of Tartu. He has had over 140 papers published in scientific journals, has ten scientific patents, and has contributed to over 20 medical textbooks. Professor Zilmer has conducted extensive research on ME-3 determining that it exhibits surprising antioxidant properties—through producing glutathione.\*

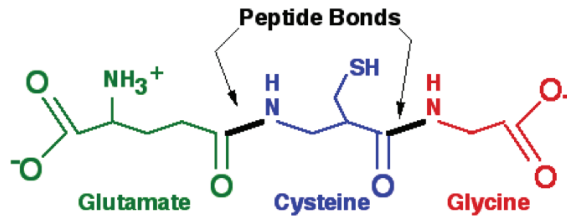
Professor Zilmer’s studies have looked at how ME-3’s glutathione-production lends support not only to the immune system, but also to the cardiovascular system, the liver, and other core body systems.\* Research on this unique *Lactobacillus* strain continues today.

**The Benefits of *Lactobacillus fermentum* ME-3**

After initially discovering that *Lactobacillus fermentum* ME-3 exhibits antioxidant activity, Professor Mikelsaar and her team of scientists at the University of Tartu initiated studies that began to reveal that ME-3 produces a wide range of additional health benefits.\* ME-3’s multiple benefits fall within three broad categories, which are: helps with normal inflammatory response, antioxidant support, and detoxification.\* ME-3 has now been studied for nearly 20 years, and its unique health-promoting benefits are summarized below.\*

**1. The Glutathione “Story”:** *Lactobacillus fermentum* ME-3 **increases glutathione levels!**\* This is a remarkable story because glutathione is recognized as one of the most important antioxidants in the body. ME-3 is often referred to as a “**complete glutathione system**” because it increases glutathione levels by three different mechanisms.\* ME-3 synthesizes glutathione itself; it accumulates glutathione from the environment; and it recycles or regenerates oxidized or “used up” glutathione back to its reduced or “active” state.\* ME-3 is the only organism

or substance we know of at this time that is able to increase glutathione levels by three different mechanisms, simultaneously.\*<sup>8</sup>

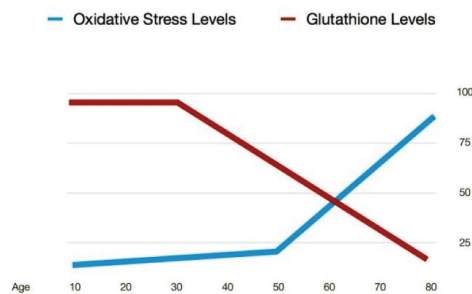


Glutathione is made in every cell throughout the body. It neutralizes a wide range of free radicals and adequate levels of glutathione are critical for good health.\* However, many things people are exposed to deplete glutathione levels such as: alcohol, artificial sweeteners, tobacco smoke, acetaminophen/Tylenol, toxic metals like mercury, artificial food dyes, and many common household chemicals. Also, the diet of many Americans is nutritionally deficient, which contributes to low glutathione levels.

Every system in the body is influenced by glutathione levels, especially the immune system, the nervous system, the gastrointestinal system, and the lungs and liver.\* Hence, ME-3's ability to increase glutathione levels is a benefit that can help promote and maintain the health of virtually everyone.\*

**2. Powerful antioxidant:** Antioxidants neutralize damaging free radicals, which promotes health.\* Free radicals are one contributor to the aging process.\* In addition to producing the antioxidant glutathione, ME-3 also produces antioxidant enzymes (glutathione peroxidase and glutathione reductase), which contribute to glutathione function and regeneration\*.<sup>9</sup> As mentioned above, ME-3 is the only substance we currently know of that functions as a “complete glutathione system” to synthesize, increase cellular uptake and recycle/regenerate glutathione.\*

## DECREASED GLUTATHIONE LEVELS AS YOU AGE



*Lactobacillus fermentum* ME-3 also produces a powerful antioxidant enzyme called manganese superoxide dismutase (MnSOD)\*.<sup>10</sup> MnSOD is the primary antioxidant enzyme in mitochondria, which are the energy-producing sites in cells. Mitochondria consume over 90 percent of the oxygen used by cells, which makes them especially vulnerable to oxidative free radical damage.<sup>11</sup> Healthy levels of MnSOD are associated with overall health.

*Lactobacillus fermentum* ME-3 provides additional antioxidant power because it helps regenerate or return the antioxidants vitamin C and vitamin E to their active forms.\*

*Lactobacillus fermentum* ME-3 has been shown to have the highest Total Antioxidant Activity (TAA) and the highest Total Antioxidant Status (TAS) of any probiotic tested to date.<sup>12</sup>

**3. Supports cardiovascular health\*:** *Lactobacillus fermentum* ME-3 has been shown to help maintain triglyceride levels already in the normal range and increase levels of the “good” HDL-cholesterol<sup>13</sup>.\* More importantly, ME-3 has been shown to help maintain healthy levels of oxidized LDL-cholesterol that are already within the normal range.\*<sup>14,15</sup>

**4. Promotes detoxification\*:** Since ME-3 substantially increases glutathione levels, scientists deduce it will increase glutathione’s detoxification capabilities.\* Glutathione helps promote the body’s normal detoxification processes, particularly with regard to heavy metals such as mercury, lead and arsenic.\* It is also involved in neutralizing and eliminating toxic air pollutants and many agricultural pesticides.\*<sup>16</sup>

**5. Promotes liver health\*:** The liver is the primary site for detoxification. The glutathione pathway is one of the mechanisms for neutralizing and removing a wide range of toxins from the body.\* Excess free radicals are generated during detoxification and *Lactobacillus fermentum* ME-3’s ability to increase total antioxidant activity (TAA) may help support a healthy liver.\*<sup>17</sup>

**6. Promotes Healthy Bacterial Balance\*:** ME-3 has the ability to produce significant levels of short-chain fatty acids (SCFAs), hydrogen peroxide, and nitric oxide.\*<sup>18</sup> This ability helps promote healthy bacterial balance.\*

**7. Reduces Activity-related Inflammation\*:** *Lactobacillus fermentum* ME-3 has been shown to help maintain healthy levels of several key markers such as high sensitivity C-reactive protein (hs-CRP) and interleukin 6 (IL-6) that are already within the normal range, and it is also capable of stimulating production of the peptide adiponectin and of reducing levels of glycated hemoglobin.<sup>19</sup> This is important for supporting a normal inflammatory response.\*

**8. Detoxifies Organophosphate Pesticides\*:** Organophosphates are one of the most widely used pesticides worldwide. They are commonly sprayed on commercial food crops and occur in many pesticide and insecticide products used in homes and gardens. They are also used in plasticizers, as antifoaming agents in lubricants and hydraulic fluids and flame retardants.

*Lactobacillus fermentum* ME-3 increases the production of an enzyme called PON1, which helps detoxify organophosphates.\*<sup>20</sup> A 2004 report stated the following, “Almost every person is, or has been, exposed to organophosphate insecticides in their home, work or environment.”<sup>21</sup> It is very exciting to have a probiotic that helps the body respond to typical exposure to organophosphates.\*

**9. Survivability:** In order to be effective, a probiotic must be able to withstand and survive exposure to the highly acidic conditions in the stomach and exposure to the digestive bile acids present in the small intestine.

In *in vitro* studies, *L. fermentum* ME-3 was found to survive at pH values ranging from 4.0 to 2.5 (which is highly acidic) without a loss in viable cell count. Even at pH 2.0, the ME-3 strain survived for up to 6 hours. When exposed to bile acids, ME-3 survived for 24 hours without significant loss of live bacteria.<sup>22</sup> Thus, while testing in the human body has not been conducted, *in vitro* testing suggests that *Lactobacillus fermentum* ME-3 can likely tolerate exposure to harsh acidity in the stomach as well as exposure to bile acids in the small intestine. *Lactobacillus fermentum* ME-3 is a survivor!

### **Concluding Remarks**

*Lactobacillus fermentum* ME-3 substantially increases glutathione levels, which is an amazing new health “story.”\* Further, as reported above, ME-3 is a “multi-tasking” probiotic that provides a wide range of additional health-promoting benefits including antioxidant activity; helping to maintain healthy cholesterol markers that are already within the normal range; and supporting the body’s natural detoxification processes.\*

*Lactobacillus fermentum* ME-3 is truly a breakthrough new probiotic that provides a wide range of benefits that promote good health.\*

**With its wide range of documented benefits, *Lactobacillus fermentum* ME-3 may qualify as one of the strongest multi-function probiotics ever discovered.\***

## References

1. Konstantinidis KT, Tiedje JM, Towards a Genome-Based Taxonomy for Prokaryotes. J Bacteriol. Sep 2005; 187(18):6258-6264.
2. Mikelsaar M, Zilmer M., *Lactobacillus fermentum* ME-3...Microb Ecol Health Dis. Apr 2009;21(1):1-27.
3. Sepp E., et al., Intestinal microflora of Estonian and Swedish infants. Acta Paediatr. 1997 Sept;86(9):956-61.
4. Mikelsaar M, Zilmer M., *Lactobacillus fermentum* ME-3...Microb Ecol Health Dis. Apr 2009;21(1):1-27.
5. Mikelsaar M, Zilmer M., *Lactobacillus fermentum* ME-3...Microb Ecol Health Dis. Apr 2009;21(1):1-27.
6. Mikelsaar M., Probiotic lactobacilli in antioxidative defence. [http://omicsonline.org/speaker/Marika\\_Mikelsaar\\_University\\_Of\\_Tartu\\_Estonia\\_Probiotics2013](http://omicsonline.org/speaker/Marika_Mikelsaar_University_Of_Tartu_Estonia_Probiotics2013).
7. UT Professor Marika Mikelsaar Receives Prestigious EU Award: <http://www.ut.ee/en/ut-professor-marika-mikelsaar-receives-prestigious-eu-award>.
8. Kullisaar T., et al., Complete glutathione system in probiotic *Lactobacillus fermentum* ME-3. Applied Biochemistry & Microbiology; Sep 2010, 46(5):481.
9. Ibid., p. 481.
10. US Patent, 20040151708 A1.: <http://www.google.com/patents/US20040151708>.
11. Fariss MW, et al., Role of Mitochondria in Toxic Oxidative Stress. Molecular Interventions. April 2005; 5(2):94-111.
12. Hutt P, et al.,. Journal of Applied Microbiology. 2006; Vol. 100:1324-1332.
13. Central European Journal of Biology 2011, vol. 6(1).
14. Mikelsaar M, Zilmer M., *Lactobacillus fermentum* ME-3...Microb Ecol Health Dis. Apr 2009;21(1):1-27.
15. Holvoet P.. Acta Cardiol. 2004 Oct;59(5):479-84.
16. Pastore A., et al., Analysis of glutathione: implication in redox and detoxification. Clin Chim Acta. 2003 Jul 1:333(1):19-39.
17. Wu G., et al., Glutathione metabolism and its implications for health. J Nutr. 2004 Mar;134(3):489-92.
18. Mikelsaar M, Zilmer M., *Lactobacillus fermentum* ME-3...Microb Ecol Health Dis. Apr 2009;21(1):1-27.
19. US Patent WO 2014102692 A1: Method of treatment using *Lactobacillus fermentum* me-3. <http://www.google.com/patents/WO2014102692A1?cl=en>
20. Mikelsaar M, Zilmer M., *Lactobacillus fermentum* ME-3...Microb Ecol Health Dis. Apr 2009;21(1):1-27.
21. Casida J, Quistad G., (2004). Organophosphate Toxicology: Safety Aspects of Nonacetylcholinesterase Secondary Targets. Chemical Research in Toxicology, Vol.17, No.8, pp. 983-992,
22. Songisepp E. Evaluation of technological and functional properties of the new probiotic *Lactobacillus fermentum* ME-3. Diss Med Univ Tartuensis; 2005.

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