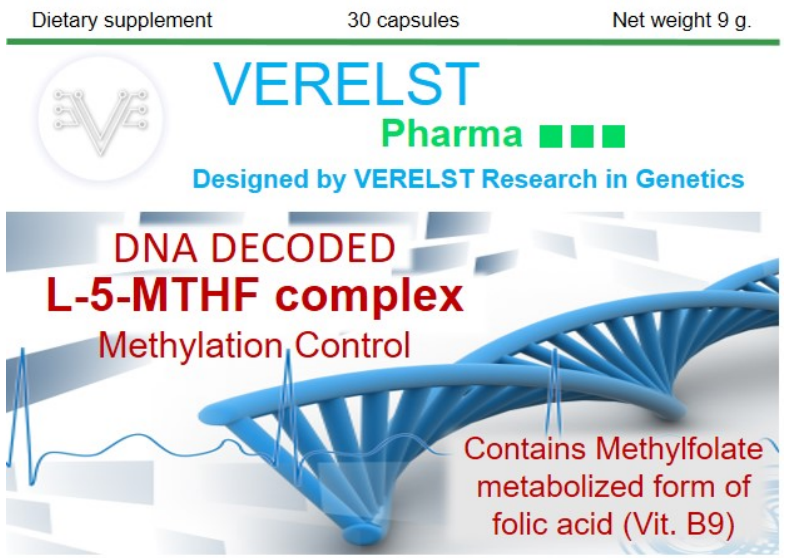
DNA DECODED
L-5-MTHF COMPLEX



CLINICAL EVIDENCE THAT SUPPORT THE EFFECTIVENESS OF THE MAIN INGREDIENTS:

L-5-MTHF, Methylcobalamin and Pyridoxal-5-Phosphate

L-5-MTHF lowers homocysteine levels in plasma by 14,6 % and is more effective than folic acid

Plasma total homocysteine (tHcy), plasma folate, and red blood cell folate (RCF) concentrations in the intervention groups at each time point[1]

Treatment	Baseline[2]	Week 8	Week 16	Week 24	Percentage difference from baseline at week 24[3]
Plasma tHcy (μmol/L)	Homocysteine levels drop continuously when taking L-5-MTHF. This is protective against cardiovascular disease.				
Placebo (n = 50)	8.5 (8.0, 9.1)	8.8 (8.2, 9.4)	8.8 (8.2, 9.4)	8.5 (7.9, 9.1)	
L-MTHF (n = 53)	8.8 (8.0, 9.6)	8.3 (7.7, 9.1)	8.1 (7.4, 8.8)	7.4 (6.9, 8.0)	−14.6 (−9.3, −19.5)[4]
Folic acid (n = 52)	8.4 (7.7, 9.1)	8.1 (7.5, 8.7)	7.8 (7.2, 8.4)	7.6 (7.1, 8.2)	−9.3 (−3.7, −14.6)[4,5]
Plasma folate (nmol/L)					
Placebo (n = 50)	19.7 (17.4, 22.3)	19.0 (16.4, 22.0)	18.5 (15.9, 21.5)	20.5 (17.6, 24.0)	
L-MTHF (n = 53)	17.5 (15.4, 20.0)	22.3 (19.7, 25.2)	23.0 (19.8, 26.7)	25.6 (22.6, 28.9)	34 (14, 56)[4]
Folic acid (n = 52)	23.3 (20.5, 26.5)	28.9 (25.8, 32.4)	28.5 (24.6, 33.1)	34.5 (30.5, 39.0)	52 (30, 78)[4]
RCF (nmol/L)					
Placebo (n = 50)	884 (804, 972)	866 (781, 959)	884 (789, 991)	848 (752, 956)	
L-MTHF (n = 53)	814 (739, 897)	899 (822, 983)	1003 (926, 1087)	984 (910, 1064)	23 (12, 35)[4]
Folic acid (n = 52)	915 (838, 999)	999 (924, 1079)	1057 (959, 1164)	1137 (1053, 1227)	31 (19, 44)[4]

[1] Geometric $\bar{x}$; 95% CIs in parentheses. L-MTHF, L-5-methyltetrahydrofolate.
[2] There were no significant differences among the 3 groups at baseline.
[3] Relative to the placebo group.
[4] Significantly different from placebo group after adjustment for baseline, $P < 0.01$ (Bonferroni adjusted for multiple comparisons).
[5] Significantly different from the L-MTHF group after adjustment for baseline, $P < 0.05$ (Bonferroni adjusted for multiple comparisons).

Reference:

Bernard J. Venn, Rudolf Moser, Jim I Mann TJG. Comparison of the effect of low-dose supplementation with L-5-methyltetrahydrofolate or folic acid on plasma homocysteine: a randomized placebo-controlled study. Am Soc Clin Nutr. 2003;77(April):658-662.

L-5-MTHF improves pregnancy outcome for MTHFR mutation carriers

Reference of the couple | Gene MTHFR status: Mutation or not (WT) | Nr. of pregnancy failures before treatment | Treatment | Outcome after the L-5-MTHF treatment

Case (women age)	Genetic background		Infertility/failures	TT duration (months)	Result (of treatment with L-5-MTHF) SPr = Spontaneous Pregnancy
	Women	Man			
AS/EJS (31)	HMZ 1298CC	WT	4 misc	4	SPr: normal delivery (male)
BE/EJS (29)	HMZ 677TT	HMZ 1298CC	Unexplained	4	SPr: pregnant 28 weeks
RK/EJS (31)	HMZ 677TT	WT	4 years, 4 failed IUI	4	SPr: pregnant 21 weeks
BL/EJS (34)*	HMZ 677TT	WT	2 misc./POF	4	SPr: pregnant 18 weeks
KD/EJS (28)	HMZ 1298CC	WT	Failed ovarian Stim	4	Ovarian stimulation: Pregnant 30 weeks
JP/LF (38)	HTZ677CT	HTZ677CT	8 misc. (4IUI), 1 IVF	4	SPr: delivery (female)
ND/LF (37)	HTZ677CT	HTZ677CT	6 misc	4	Pr post ovarian stimulation: delivery (female)
Ma/ LF (32)	HTZ677CT	HTZ677CT	3 misc	4	SPr: delivery (female)
Va/LF* (37)	HTZ677CT	HTZ677CT	2 misc., 1 ectopic	4	SPr: 30 weeks
HS/EJS (26)	HTZ677CT	HTZ677CT	3 misc	3	SPr: 32 weeks
Ca/LF (40)	HMZ677TT	HTZ677CT	6 misc	4	Twin Pregnancy post ovarian Stimulation: 20 week
Bou/LF (33)	HTZ677CT	HMZ677TT	3 misc	6	One failed ovarian stimulation, then SPr: 14 weeks
BBM/DC (36)	HMZ677TT	HTZ677CT	4 misc	4	Two failed IUI
DC/DC (38)	HMZ677TT	HTZ677CT	2 failed IVF	7	Pregnant post IVF, 6 mths
Ib/MC (38)	HTZ677CT	HTZ677CT	2 failed IVFs	4	Failed 3rd IVF
La/MC (33)	HTZ677CT	HTZ677CT	2 failed IVFs	4	Failed 3rd IVF
Du/MC (42)	HMZ677TT	HTZ677CT	2 failed IVFs	4	IUI: Twin pregnancy 6 months
Go/MC (28)	HTZ677CT	HTZ677CT	5 failed IUI	4	Pr post IVF, 6.5 months
Ha/MC (38)	HTZ677CT	HTZ677CT	2 misc	4	SPr: miscarriage
Be/MC (39)	HMZ677TT	HTZ677CT	Unexplained Primary	4	Spr: delivery (male)
Be/MC (39)	HMZ677TT	HMZ677TT	Unexplained	4	Pr post IVF: delivery female baby
Ba/MC (31)	HMZ677TT	HTZ677CT	PCOS, high Hcy	5	Pregnancy post IVF: delivery (female)
Bi/MC (26)	HMZ677TT	HMZ677TT	PCOS, endometriosis	6	Pr post IVF: delivery female baby
Sa/MC (37)	HMZ677TT	HTZ677CT	Unexplained primary	4	Pr post IVF: delivery female baby
Vi/MC (34)	HMZ677TT	HMZ677TT	Unexplained primary	4	Pr post IVF: delivery female baby
Yi/MC (26)	HMZ677TT	HTZ677CT	Unexplained primary	6	3 failed IUI, Pr post IVF, delivery female baby
GSt/MC (35)	HMZ677TT	HMZ677TT	8 misc	4	Spr 6.5 months
VM/EJS (35)	677CT/1298AC	HTZ1298AC	Biochemical Pr	4	Spr: 10 weeks
AyM/MC (23)	HTZ677CT	HTZ677CT	3 misc	4	Pr 6 months post IVF
MS/MC (32)	HMZ677TT	HTZ677CT	7 misc	5	SPr 10 weeks

HMZ homozygote, *HTZ* heterozygote, *WT* wild type (no mutation), *POF* premature ovarian failure

*Patients counseled for oocyte donation before entering the program

30 couples with recurrent pregnancy failure were treated with L-5-MTHF. After treatment all couples except 3 were able to successfully achieve pregnancy, mostly spontaneous.

Conclusions of the clinical trial:

The conventional use of large doses of folic acid (5 mg/day) has become obsolete. Regular doses of folic acid (100–200 µg) can be tolerated in the general population but should be abandoned in the presence of MTHFR mutations, as the biochemical/genetic background of the patient precludes a correct supply of 5-MTHF, the active compound. A physiological dose of 5-MTHF (800 µg) bypasses the MTHFR block and is suggested to be an effective treatment for these couples. **Moreover, it avoids potential adverse effects of the UMFA (Unmetabolized Folic Acid) syndrome, which is suspected of causing immune dysfunction and other adverse pathological effects such as cancer (especially colorectal and prostate)**

Reference:

Servy EJ, Jacquesson-fournols L, Cohen M, Menezo YJR, Natecia C, Clement L. MTHFR isoform carriers. 5-MTHF (5- methyl tetrahydrofolate) vs folic acid : a key to pregnancy outcome : a case series. 2018:1-10.

Combination of L-5-MTHF, Methylcobalamin and Pyridoxal-phosphate improves cutaneous sensitivity in diabetics.

Diabetic peripheral neuropathy is a condition of nerve damage that is caused by long-term high blood sugar levels, and precedes foot ulcerations and amputations in patients with Diabetes Mellitus. An oral intake of L-5-MTHF (LMF), Methylcobalamin (MC) and Pyridoxal-5-Phosphate (PP) restores the loss of sensation in toes and heels and reverses the symptoms of diabetes.

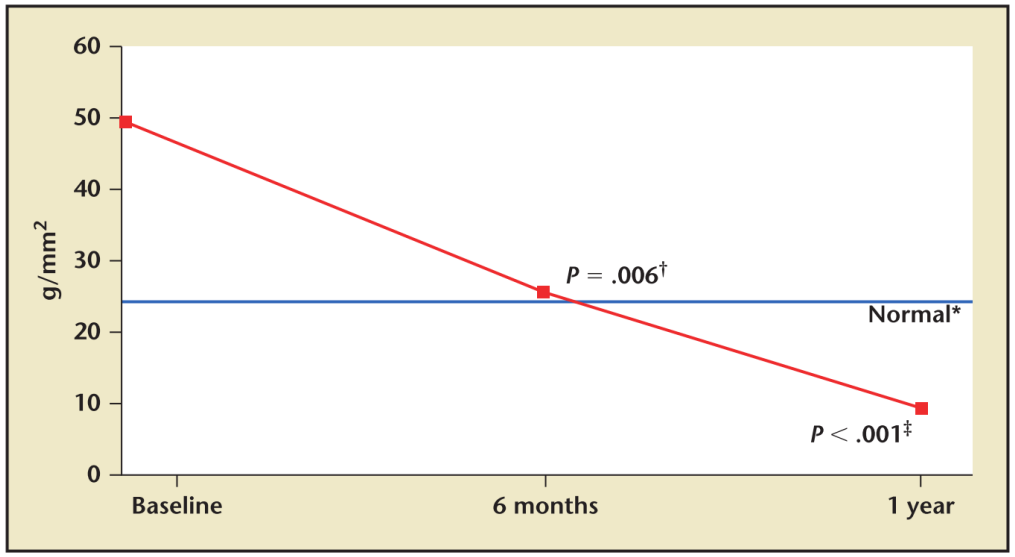


Figure 1. Effect of oral LMF-PP-MC treatment on great toes (left/right combined) of patients with DPN (Diabetic Peripheral Neuropathy). Results from testing the great toes with PSSD (Pressure Specific Sensory Device) show improvement in 2-point sensory discrimination.

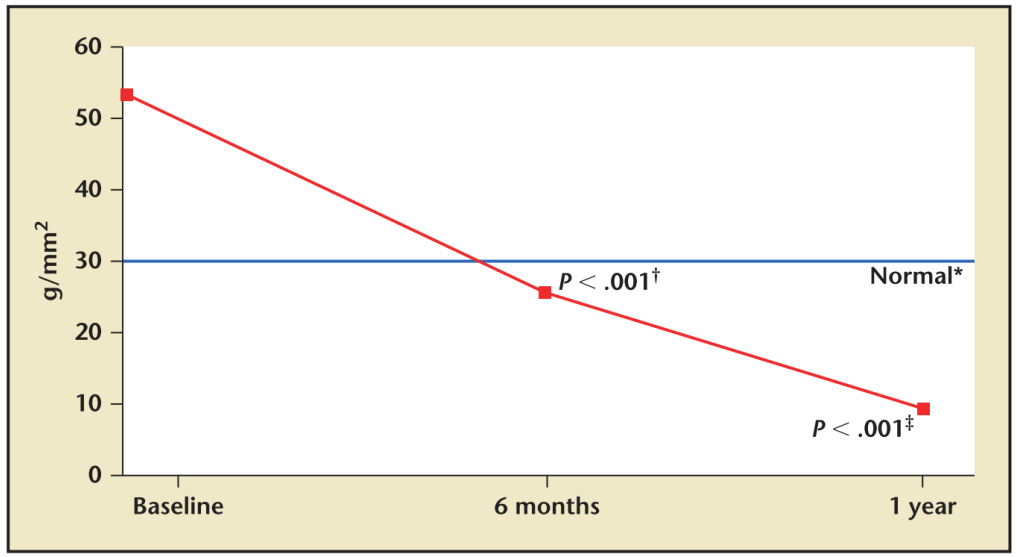


Figure 2. Effect on medial heels (left/right combined) of patients with DPN. Results reveal decline in absolute PSSD 2-point static test values (showing improvement in 2-point sensory discrimination).

Reference:

M. J. Walker, L. M. Morris, and D. Cheng, “Improvement of cutaneous sensitivity in diabetic peripheral neuropathy with combination L-methylfolate, methylcobalamin, and pyridoxal 5’-phosphate.,” Rev. Neurol. Dis., vol. 7, no. 4, pp. 132–9, 2010.