

Supplementary material

Table S1 Evaluation of the hematological-biochemical parameters at baseline and after the treatment

| Parameters | Normal range | Baseline | After fortified milk | 95% CI | q Value |
|------------------------------|--------------|----------|----------------------|------------------|---------|
| Total cholesterol (mg/100mL) | 130-200 | 209 ± 36 | 216 ± 43 | 7 (0 - 13) | 0.133 |
| HDL cholesterol (mg/100mL) | ≥ 39 | 55 ± 12 | 55 ± 12 | 0 (-1 - 1) | 0.981 |
| LDL cholesterol (mg/100mL) | ≤ 130 | 127 ± 28 | 132 ± 30 | 5 (-1 - 11) | 0.195 |
| Triglycerides (mg/100mL) | 35-180 | 114 ± 45 | 108 ± 42 | -11 (-23 - 1) | 0.169 |
| Glycaemia (mg/dL) | 67-112 | 97 ± 15 | 102 ± 20 | 3 (-1 - 8) | 0.307 |
| HOMA-IR | 0.22-2.5 | 2 ± 2 | 3 ± 2 | 0.2 (-0.2 - 0.6) | 0.559 |
| Creatinine (mg/dL) | 0.6-1.2 | 1 ± 0.2 | 1 ± 0.2 | 0 (-0.03 - 0.02) | 0.931 |
| Fibrinogen (mg/dL) | 150-400 | 313 ± 48 | 313 ± 47 | -8 (-21 - 4) | 0.356 |
| ALT (U/L) | 8-40 | 18 ± 7 | 20 ± 6 | 3 (1 - 5) | 0.019* |
| ASP (U/L) | 8-40 | 19 ± 5 | 21 ± 5 | 2 (1 - 3) | 0.0006* |

Data are reported as mean ± SD and 95% Confidence Interval (CI). The comparison between the two groups (placebo *versus* fortified milk) was performed by using linear mixed effect model with Benjamini-Hochberg correction, considering $q < 0.05$ (corrected p-value) statistically significant (*). HOMA-IR = homeostasis model assessment of insulin resistance, ALT = alanine aminotransferase, ASP = aspartate aminotransferase.

Table S2 Evaluation of inflammatory parameters at baseline and after the treatment

| Parameters | Normal range | Baseline | After fortified milk | 95% CI | q Value |
|---------------------------|--------------|-----------|----------------------|----------------|---------|
| Interleukin IL-6 (pg/mL) | - | 2 (± 3) | 1 (± 2) | 0 (-0.5 - 0.5) | 0.980 |
| Interleukin IL-10 (pg/mL) | - | 1.4 (± 4) | 1.3 (± 4) | 0 (-0.1 - 0.3) | 0.431 |
| CRP (mg/L) | 0-6 | 3.2 (± 3) | 3.4 (± 3) | 0 (-1 - 0) | 0.508 |

Data are reported as mean ± SD and 95% Confidence Interval (CI). The comparison between the two groups (placebo *versus* fortified milk) was performed by using linear mixed effect model with Benjamini-Hochberg correction, considering $q < 0.05$ (corrected p-value) statistically significant. CRP = C-reactive protein.

Table S3 Main measured parameters in each time point by treatment

| Parameters | Baseline | After fortified milk | After washout | After placebo |
|-----------------------------------|-----------|----------------------|---------------|---------------|
| Vitamin B9 (ng/mL) | 7 ± 3 | 13 ± 5 | 7 ± 3 | 7 ± 3 |
| Vitamin B6 (µg/L) | 16 ± 18 | 22 ± 10 | 19 ± 18 | 21 ± 20 |
| Vitamin B12 (pg/mL) | 378 ± 158 | 395 ± 153 | 346 ± 133 | 379 ± 177 |
| Vitamin 25(OH)D (ng/mL) | 18 ± 10 | 23 ± 6 | 22 ± 8 | 16 ± 6 |
| Vitamin E (µg/mL) | 12 ± 3 | 13 ± 3 | 13 ± 3 | 12 ± 3 |
| Zinc (µg/L) | 805 ± 89 | 798 ± 102 | 800 ± 93 | 808 ± 81 |
| Selenium (µg/L) | 102 ± 14 | 108 ± 15 | 108 ± 13 | 104 ± 14 |
| Linoleic acid (%) | 11 ± 1 | 11 ± 1 | 11 ± 1 | 11 ± 1 |
| DGLA (%) | 2 ± 0.6 | 2 ± 0.3 | 2 ± 0.4 | 2 ± 0.3 |
| Arachidonic acid (%) | 16.3 ± 1 | 15.9 ± 2 | 16.2 ± 1 | 16.7 ± 1 |
| TFA (%) | 0.2 ± 0.1 | 0.3 ± 0.1 | 0.2 ± 0.1 | 0.2 ± 0.1 |
| SFA (%) | 45 ± 2 | 45 ± 2 | 45 ± 2 | 45 ± 2 |
| MUFA (%) | 19 ± 1 | 19 ± 2 | 20 ± 2 | 19 ± 1 |
| PUFA (%) | 35 ± 2 | 36 ± 2 | 35 ± 2 | 36 ± 2 |
| DHA (% in e. m.) | 5 ± 1 | 6 ± 1 | 4.9 ± 1 | 4.9 ± 1 |
| EPA (% in e. m.) | 0.9 ± 0.4 | 1.1 ± 0.3 | 0.7 ± 0.3 | 0.9 ± 0.3 |
| ω -6/ ω -3 PUFA (%) | 5 ± 1 | 4 ± 1 | 5.7 ± 2 | 5 ± 1.4 |
| ω -3 index (%) | 5.6 ± 1 | 7.3 ± 1 | 5.7 ± 2 | 5.8 ± 1 |
| Homocysteine (µmol/L) | 15.2 ± 6 | 11.6 ± 4 | 14.7 ± 6 | 14.7 ± 6 |
| Total cholesterol (mg/100mL) | 209 ± 36 | 216 ± 43 | 210 ± 31 | 209 ± 36 |
| HDL cholesterol (mg/100mL) | 55 ± 12 | 55 ± 12 | 53 ± 11 | 55 ± 12 |
| LDL cholesterol (mg/100mL) | 127 ± 28 | 132 ± 30 | 129 ± 24 | 127 ± 29 |
| Triglycerides (mg/100mL) | 114 ± 45 | 108 ± 42 | 116 ± 47 | 118 ± 53 |
| Glycaemia (mg/dL) | 97 ± 15 | 102 ± 20 | 95 ± 17 | 98 ± 16 |
| HOMA-IR | 2 ± 2 | 3 ± 2 | 2.6 ± 1 | 2.5 ± 2 |
| Creatinine (mg/dL) | 1 ± 0.2 | 1 ± 0.2 | 1 ± 0.2 | 1 ± 0.2 |
| Fibrinogen (mg/dL) | 313 ± 48 | 313 ± 47 | 330 ± 48 | 323 ± 63 |
| ALT (U/L) | 18 ± 7 | 20 ± 6 | 18 ± 7 | 18 ± 9 |
| ASP (U/L) | 19 ± 5 | 21 ± 5 | 20 ± 5 | 19 ± 4 |

Data are reported as mean ± SD. FP = arm: participants on fortified milk and then placebo, PF = arm: participants on placebo and then fortified milk, DGLA = Dihomo- γ -linolenic acid, TFA = Trans-unsaturated fatty acids, SFA = Saturated Fatty Acids, MUFA = Mono Unsaturated Fatty Acids, PUFA = Poly Unsaturated Fatty Acids, DHA = Docosahexaenoic acid, EPA = Eicosapentaenoic acid, e. m. = erythrocyte membranes, HOMA-IR = homeostasis model assessment of insulin resistance, ALT = alanine aminotransferase, ASP = aspartate aminotransferase.

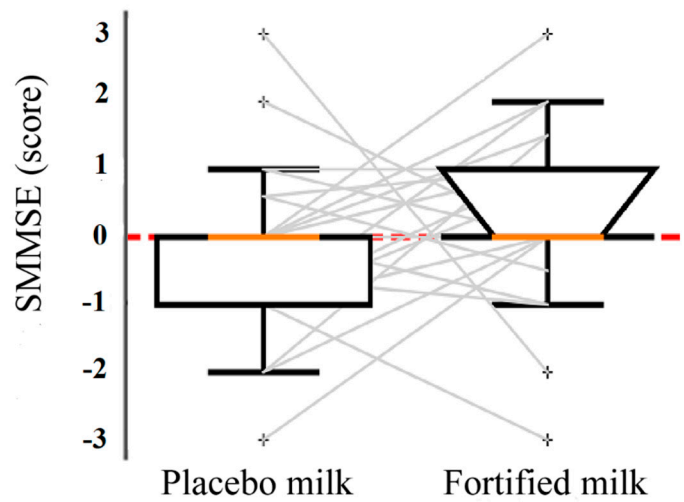


Figure S1. Standardized Mini-Mental State Examination (SMMSE). Boxplot of the variation of SMMSE scores in participants on placebo *versus* those on fortified milk are displayed. A not significant trend of the SMMSE score to increase after fortified milk consumption emerged ($q = 0.749$). Statistical analysis was performed by linear mixed model effect and a q-value (corrected p-value for the Benjamini-Hochberg multiple comparisons) < 0.05 was considered statistically significant.