eon Longevity +Plus Clinically Reduces Systemic Inflammation and Symptoms of Prediabetes and Metabolic Syndrome

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1. Background

Fine Hygienic Holding is a company devoted to improving people's health and lives, providing reliable and high-quality baby and adult care products since 1958. In 2018 the company decided to diversify its product range by adopting health foods and drinks as well as food supplements. Its first flagship product is eon Longevity +Plus.

eon Longevity +Plus is a herbal drink infused with water-soluble curcumin. Curcumin, the most widely researched phytochemical in the drink, is a phytochemical derived from the roots of the *Curcuma longa* plant. The dried and ground roots are commonly known as turmeric, of which 2-3% comprises the bioactive compound curcumin. Curcumin has widespread use as a food supplement with clinically proven health benefits [1]. Studies have demonstrated that the compound is effective in reducing inflammation in patients with osteoarthritis [2] and rheumatoid arthritis [3] (joints), ulcerative colitis (intestines) [4], and psoriasis (skin) [5]. Curcumin acts as an anti-oxidant [6] that neutralizes free radicals in the body that form during mild and chronic inflammation [7,8]. Curcumin also has a beneficial effect in subjects with features of metabolic syndrome [9], promoting a reduction in blood cholesterol, low-density lipoprotein (LDL) [10], serum triglycerides [8] as well as liver fat [11]. Through its lowering action on free fatty acids in the blood, the compound has been shown to exert a glucose-lowering effect in diabetics [12] and prevented prediabetics from developing type 2 diabetes [13]. Athletes experience better recovery when using curcumin after strenuous exercise [7,14]. The compound is effective against certain forms of pain [15-17] and ameliorates anxiety and feelings of depression [18,19]. Owing to its effects on blood coagulation and fibrinolysis [20,21], curcumin is a blood thinner (just like aspirin), which can be advantageous to patients who suffer from certain cardiovascular diseases. These medicinal effects are likely enhanced by bioactive, health-promoting substances in the other herbs in eon Longevity +Plus [22-25]. For example, thyme extract contains compounds with antioxidant [26], anti-inflammatory [26-28], antimicrobial [29], and antitussive [30] properties. Similarly, eucalyptus has been reported to possess antioxidant [23,31], anti-inflammatory [31,32], antimicrobial [33,34], and potentially antidiabetic properties [32,35,36]. The carob is an interesting additive in that it increases satiety and serves as a low-glycemic index ingredient [37], thereby controlling the glycemic response after intake [38] while conferring sweetness to the herbal drink. Moreover, long-term consumption of carob improves lipid oxidation [39] and postprandial insulin sensitivity in healthy individuals [38], and lowers total cholesterol and low-density lipoprotein (LDL) in hypercholesterolemic subjects [40]. The manuka honey has antimicrobial efficacy and may be beneficial for oral health [41]. Altogether, the medicinal properties of the ingredients are expected to favorably modulate physiological and biochemical processes in the body that will lead to improved longevity, vitality, and psychological well-being.

To build a scientific foundation for these hypotheses, a pilot experiment was initially conducted where the eon Longevity +Plus was provided to 29 volunteers to gauge their experience with the product. After twice daily use for 8 weeks, the participants reported the following effects: felt happier (N = 5), felt more relaxed / better mood (N = 12), constipation relief (N = 6 volunteers), greater vitality and health (N = 24), more energy (N = 5), pain relief throughout body (N = 4), headache relief (N = 2), improved breathing (N = 3), more regular bowel movement (N = 6), body feels cleaner (N = 20), better sports performance (N = 6), and improved sleep (N = 5). Based on these positive reports, a more systematic trial was conducted in a larger cohort of overweight participants to assess the therapeutic efficacy and safety of eon Longevity +Plus. The most significant findings of the trial were that (1) daily consumption of eon Longevity +Plus reduced a number of symptoms associated with prediabetes and metabolic syndrome, particularly markers of chronic inflammation, (2) decreased cortisol, a stress hormone, and that (3) the product was safe. It is a putative contention that chronic inflammation, which is a significant feature of diabetes and metabolic syndrome, and stress lead to various diseases that reduce lifespan. On the basis of the outcomes, the study essentially justified the herbal drink's name: eon Longevity +Plus.

2. Methods

To keep this white paper accessible and readable, only the most important parts of the study are described in the main text. A supplemental document featuring all data and more detailed explanations (e.g., statistical analysis methods) is available online for a more in-depth account. R. It is further important to underscore that outcomes that appear different numerically and graphically but lack statistical significance (i.e., a *P*-value of > 0.05) are considered not to be different, in line with general statistics practices.

The study was conducted in compliance with national laws of Jordan and volunteers provided informed written consent before inclusion in the study. Volunteers received financial compensation for their participation (650 Jordanian Dollars). The cohort comprised 29 volunteers from the Amman, Jordan area; 15 men and 14 women, with a mean ± standard deviation (SD) age of 34 ± 6 and 36 ± 9 years ($P = 0.4866$). The demographics of the participants are detailed in Table 1. No gender-specific differences were found for any of the demographic parameters ($P \geq 0.1343$). Consequently, the data from the male and female cohorts were analyzed collectively as well as separately. Only statistically significant findings are reported in the main text.

Study participants were examined at the Amman branch office of Fine Hygienic Holdings using a dedicated investigation room that contained the necessary equipment. On day 0, a total of 52 baseline parameters were sampled after an overnight fast, which were stratified into the following categories: anthropomorphic, cardiovascular, hematological, metabolic and endocrinological (substratified into general, carbohydrates, lipids, and vitamins), urine markers, organ function and tissue damage markers, and inflammation markers. All procedures were conducted by board-certified physicians and registered nurses. Next, the participants were instructed to come to the FHH office in Amman and take 1 serving in the morning and 1 serving in the evening every day for 8 weeks but not to change their lifestyle. This ensured exact dosing. The visits were logged for compliance purposes. At 4 weeks and at 8 weeks the participants returned to the clinic to undergo follow-up measurements and sampling after an overnight fast.

The anthropomorphic parameters were measured on-site on an InBody 230 machine (InBody, Seoul, Republic of Korea). Urine was collected into a sterile collection cup (Vacutainer, BD Biosciences, Franklin Lakes, NJ, USA). Venous blood was drawn into EDTA-containing vacuum tubes (Vacutainer, BD Biosciences) and kept at room temperature. Serum samples were obtained by collecting blood into empty Vacutainer tubes (BD Biosciences) according to GLP procedures (10 min clotting and centrifugation). Serum was transferred to sterile 1.5-mL Eppendorf tubes. Part of the tubes was stored on ice for same-day analysis, whereas the remaining tubes were snap-frozen in liquid nitrogen. Whole blood, urine and serum samples were taken to an independent laboratory (MedLabs Consultancy Group, Amman, Jordan) under the required storage conditions. Whole blood was analyzed for complete blood count on a hematology analyzer (Pentra DX Nexus SPS Evolution, Horiba, Kyoto, Japan) within 1 h after collection. Urine and serum samples were analyzed on a modular analyzer (Cobas 8000, Roche Diagnostics, Basel, Switzerland). Snap-frozen serum samples were stored at -20 °C until shipment on dry ice to a third-party laboratory. The analysis of IL-1β, TNF-α, and 8-hydroxy-2'-deoxyguanosine in serum samples was performed by a specialized independent lab (Bioscientia International, Ingelheim, Germany).

Data were processed, analyzed, and plotted in GraphPad Prism software (GraphPad Software, San Diego, CA, USA) and presented as mean ± SD. The statistical methods are detailed in section S2. A *P*-value of ≤ 0.05 was considered statistically significant.

3. Results and Discussion

The percentual changes in every parameter are presented for the overall study population per clinical outcome category in Forest plots at the bottom of the main text: anthropomorphic parameters, Figure 1; cardiovascular parameters, Figure 2; hematological parameters, Figure 3; metabolic and endocrinological (general, carbohydrates, and vitamins) parameters, Figure 4; metabolic and endocrinological (lipids) parameters, Figure 5; urine markers, Figure 6; organ function and tissue damage markers, Figure 7; and inflammation markers, Figure 8.

3.1. Volunteers were overweight and presented with prediabetes and metabolic syndrome-related symptoms before the start of the study

The cohort consisted of demographically equivalent male and female volunteers who were overweight and who presented with prediabetes and symptoms related to metabolic syndrome. Metabolic syndrome harnesses at least three of the five following medical conditions simultaneously: abdominal obesity, high blood sugar, high serum triglycerides, low serum high-density lipoprotein (HDL), and high blood pressure. The rationale behind including overweight individuals in the study was twofold: (1) the manifestation of disease symptoms are revealed by anthropomorphic measurements and clinical chemistry, and allow for normalization by the intervention (eon Longevity +Plus intake) as an objective measure of efficacy, and (2) the phytochemical properties of eon Longevity +Plus are well-attuned to combatting the symptoms of prediabetes and metabolic disease as explained in the Background section.

The baseline body mass index (BMI) of male participants was 26.1 ± 3.5. The overweight BMI in men concurred with an above-normal body fat percentage (22.6 ± 6.9%), a waist:hip ratio of 0.90 ± 0.06 (signifying overweight), and a waist:height ratio of 0.53 ± 0.06 (signals an increased medical risk). Male participants had elevated levels of creatine phosphokinase (CPK; 116 ± 46 U/L), which is a biomarker for obesity [42]. Moreover, men had borderline high triglyceride levels (119 ± 52 mg/dL) and low yet still acceptable HDL levels (42.4 ± 7.5 mg/dL) that put them at an increased risk for cardiovascular disease. The male participants also presented with above-normal fasting insulin (10.9 ± 10.8 µIU/mL) and insulin resistance score (2.2 ± 2.2). These metabolic manifestations are inherent to the relationship between fat build-up and disrupted sugar metabolism [43]. In response to enduring overnutrition and fat accumulation, the liver and other organs become less responsive to insulin and the body gradually develops insulin resistance. The pancreas, which produces insulin, attempts to counter the developing resistance by secreting more insulin into the blood. When increased blood insulin levels can no longer compensate for the impaired insulin response of all metabolic organs, including fat tissue, liver, muscle, pancreas, and even the central nervous system [44], type 2 diabetes develops [45]. With increasing BMI, the HDL, serum triglycerides, and visceral fat would ultimately become abnormal [46,47] and exacerbate the prediabetes and metabolic syndrome. It is therefore imperative that no further deterioration of health occurs, e.g., through lifestyle changes and/or nutritional support. Hyperhomocysteinemia (17.7 ± 4.2) was found in men and indicates deficiency in vitamin B12, vitamin B6, and/or folic acid (vitamin B_9) [48]. Elevated levels of homocysteine are most likely caused by improper diet and are also linked to heart- [49] and cerebrovascular disease [50]. Furthermore, a state of low-grade inflammation was measured in overweight men. Tumor necrosis factor-α (TNF-α) was elevated (8.5 ± 2.0 pg/mL) but interleukin 1β (IL-1β) and C-reactive protein (CRP) were in-range, making the inflammation low-grade [51]. TNF-α is a pro-inflammatory cytokine that mediates systemic inflammation [52]. This acute-phase protein is released by mainly innate immune cells called macrophages. In this particular cohort of participants, elevated TNF-α levels can be explained by two mechanisms. First, persistent hyperglycemia due to insulin resistance can lead to shedding of the endothelial glycocalyx [53], a protective layer covering the inner surface of almost all blood vessels. The shed glycocalyx constituents activate macrophages, which in turn release of TNF-α into the blood [54]. Second and more important, the participants carried excessive body fat that is composed of several different cell types, including fat cells and macrophages that produce pro-inflammatory cytokines including TNF-α [55] and interleukin 6 (IL-6, not measured in this study). The released TNF-α subsequently causes and exacerbates inflammation and insulin resistance [56]. Finally, male participants exhibited below-normal serum creatinine levels (0.73 ± 0.12 mg/dL), indicating good renal function despite the potentially deleterious effects of obesity on the kidneys [57].

The baseline BMI of the female participants was 26.9 ± 3.9 . Overweight women presented with above-normal body fat percentage (39.2 ± 6.4%) and visceral fat (135 ± 39 cm^2), a waist:hip ratio of 0.81 ± 0.05, a waist:height ratio of 0.54 ± 0.06, aberrant CPK levels (75 ± 23 U/L), and near-borderline high triglyceride levels (112 ± 51 mg/dL). Visceral fat is body fat that is stored within the abdominal cavity around internal organs such as the liver, pancreas, and intestines, affecting their function. Visceral fat in itself augments insulin resistance [58]. Correspondingly, overweight female participants exhibited problematic sugar metabolism, as evidenced by elevated fasting insulin levels (9.9 ± 6.3 µIU/mL) and insulin resistance scores (2.0 ± 1.4). In addition to having elevated levels of TNF-α (9.5 ± 2.7 pg/mL) in the blood, the included women also expressed abnormally high levels of CRP (4.1 ± 3.5 mg/L), underpinning their low-grade inflammatory state. As TNF-α, CRP is an acute phase protein whose blood concentration rises in response to inflammatory signaling mediated by macrophage- and fat cell-derived IL-6. CRP is synthesized in the liver [59] and its production is stimulated by biochemical factors (adipokines) released from macrophages and fat cells [60]. People who are overweight and obese possess so-called overweight/obese white adipose tissue. The expansion of white adipose tissue in overweight and obese individuals leads to mechanical and cellular stress in fat cells, resulting in the release of free fatty acids such as triglycerides and inflammatory cytokines [61,62]. Various types of immune cells are subsequently recruited to the overweight/obese white adipose tissue, driving local and systemic inflammation [63]. The general rule is that the more visceral fat (i.e., the higher the BMI), the greater the inflammatory response. Not only do the infiltrated macrophages locally produce TNF-α and IL-6 to propel an inflammatory state [62], but the IL-6 triggers the synthesis and release of CRP by the liver, further compounding the local and systemic inflammation and insulin resistance [64]. Moreover, CRP is a strong independent predictor of incident diabetes [65,66] and incident cardiovascular disease [67-69] and is correlated with other elements of metabolic syndrome such as fasting insulin and microalbuminuria [70]. Again, it is imperative to curtail further development of prediabetes and symptoms of metabolic syndrome through diet, exercise, and effective dietary supplementation. In contrast to men, the female participants had in-range homocysteine levels and, in similarity to men, renal function was not perturbed (below-normal serum creatinine of 0.47 ± 0.09 mg/dL).

3.2. An 8-week regimen of daily eon Longevity +Plus intake restores parameters related to prediabetes and metabolic syndrome to normal levels

Given the plethora of physiology- and biochemistry-modulating properties of curcumin and other ingredients in eon Longevity +Plus (Background section), we hypothesized that daily intake of the drink over the course of 8 weeks would lead to an improvement in parameters tied to mainly prediabetes and metabolic syndrome. It was expected that such improvements would be characterized by restoration of some of the parameters to normal levels. The baseline measurements confirmed that several of the measured parameters were out-of-range, as discussed in the previous section. The majority of the aberrant parameters were connected to prediabetes and metabolic syndrome.

As was projected, daily consumption of eon Longevity +Plus resulted in the normalization of multiple outcome measures. When the entire study cohort is considered as a whole, a decrease in insulin resistance score, triglyceride levels, and homocysteine fell back to normal range after 8 weeks, while TNF-α declined to healthy levels after 4 weeks of intake. In the male cohort, the results were echoed with the exception of homocysteine, which remained high throughout the trial period. In the female cohort, fasting insulin and insulin resistance score normalized after 8 weeks, which was preceded by normalization of TNF-α levels at the 4-weeks follow-up. Also, cortisol levels in women decreased to below the bottom reference limit. Since the participants were explicitly instructed not to change their lifestyle and daily routine, there is a high probability that the normalization of several key parameters is ascribable to eon Longevity +Plus. With the herbal drink comprising multiple active principals with proven health benefits, it is impossible to accurately pinpoint the contribution of each ingredient. It is also possible that the ingredients collectively impart a non-linear effect (i.e., '1 + 1 = 3').

The most important result was the normalization of inflammatory markers (TNF-α in men and women and CRP in women) (Figure 8). The reduction in TNF-α was statistically significant in the overall cohort ($P < 0.001$) and in the female participants ($P = 0.01$). Chronic inflammation is a state that

encompasses the non-stop activation of cells of the innate immune system (e.g., macrophages) and the corollary production and release of pro-inflammatory cytokines into inflamed tissue and the bloodstream. Chronic inflammation is deleterious to health [71] in that it potentiates the development of cancer [72], cardiovascular disease [73], ageing [73], rheumatoid arthritis [74], type 2 diabetes [75], non-alcoholic fatty liver disease [76], asthma [77], and neurodegenerative diseases such as Alzheimer's [78]. Controlling chronic inflammation is therefore key to a healthy life.

Furthermore, 4-week and 8-week consumption of eon Longevity +Plus reduced circulating levels of cortisol ($P < 0.045$) (Figure 5). Cortisol is a steroid hormone that is produced mainly by the kidneys' adrenal gland and released in response to stress and low blood glucose concentrations. Chronic exposure to elevated levels of the hormone promotes insulin resistance [79]. Cortisol also modulates the immune system by preventing the release of substances that cause inflammation, including TNF-α [80], while at the same time making certain adaptive immune cells less amenable to pro-inflammatory ques [81] and suppressing the activity and cytotoxic potential of natural killer cells [82]. So, on the one hand cortisol works as an anti-inflammatory but on the other hand the hormone impairs our ability to fend off infections. Its control is therefore important in maintaining immune function and ameliorating the symptoms of prediabetes and metabolic syndrome. What is particularly striking is that the reduction in TNF-α (Figure 8) occurred concomitantly with lowered cortisol levels, which normally exist in an inverse relationship. These findings suggest that metabolic factors other than cortisol, probably primed by constituents of the herbal drink, were responsible for the anti-inflammatory effects.

Readers should note that this study was not designed to provide mechanistic insight into the pharmacology of eon Longevity +Plus. This study was conducted to establish whether any physiological modulation could be achieved with eon Longevity +Plus in the sense that it promoted people's health. It is clear that eon Longevity +Plus can reduce symptoms of prediabetes and metabolic syndrome. Accordingly, it can be concluded that the consumption of eon Longevity +Plus is restorative as well as beneficial in preventing the further escalation of already out-of-balance medical conditions that could culminate in more profound insulin resistance, diabetes, and cardiovascular problems. It is expected that the daily intake of eon Longevity +Plus with a good diet and exercise will expedite the restoration of an overweight body to metabolic normalcy [83].

3.3. eon Longevity +Plus may reduce stress

As indicated in the previous section, cortisol is a stress hormone. Maladaptive cognitive responses to stress, such as magnification, rumination, and helplessness, may intensify cortisol release and with it forge a physiological stress response to psychological stress. Such a response is referred to as a psychosomatic reaction. The psychological stress is a relative concept that is subject to a person's perception of potential stressors, and can therefore manifest even at basically inconsequential external stimuli such as an unpleasant co-worker's body odor, chaotic morning traffic, or adversity to certain sounds (misophonia). Failure to cope properly with stressors may lead to prolonged or exaggerated stress and exacerbation of the physiological response, namely sustained hypercortisolemia, which is detrimental to health [84]. The fact that eon Longevity +Plus was able to significantly reduce cortisol levels suggests the anxiolytic potency of the product and validates the testimonials of users in the pilot study who reported feeling more elated and destressed.

3.4. The daily consumption of eon Longevity +Plus is safe

Toxicological assessment was performed in the entire cohort using two distinct approaches. First, the urine markers and the organ function and tissue damage markers were evaluated because these are the most sensitive barometer for xenobiotic toxicity. Any changes compared to baseline measurements could signal an adverse reaction or impaired organ function in response to daily consumption. As reported in Figures 6 and 7, the only marker that increased was the 8-hydroxy-2'-deoxyguanosine:creatinine ratio in spot urine, while the only marker that decreased was total protein content in serum. 8-Hydroxy-2'-deoxyguanosine is a marker of oxidative stress in cell nuclei and constitutes a DNA breakdown product [85]. This DNA oxidation metabolite is in fact part of normal cell metabolism, as its formation occurs at an

average frequency of 2400 per cell [86]. Once formed, the DNA damage is repaired and the 8-hydroxy-2'-deoxyguanosine is removed quickly via the renal system (elimination half-life is 11 min) and it ends up in urine [87]. The presence of 8-hydroxy-2'-deoxyguanosine in urine signifies that radicals formed in our body have damaged nuclei, but in the wake of no apparent damage in organs/tissues (liver, biliary system, heart, kidneys, brain, muscle, blood cells), perturbed function (kidneys), and decreased inflammation (Figure 8) there is no reason to assume eon Longevity +Plus -induced toxicity. Moreover, compared to baseline, the creatinine levels in urine had decreased at the 4-week and 8-week follow-up, albeit not significantly. Nevertheless, the lowered creatinine levels could have skewed the 8-hydroxy-2'-deoxyguanosine:creatinine ratio in urine in favor of the former, which is standardly corrected for total creatinine. With respect to the hypoproteinemia, although protein levels dropped significantly at 8 weeks, these were still within normal range. This phenomenon, also in the context of the abovementioned reasons, therefore cannot be considered to reflect toxicity.

The second approach was to look at parameters that were in normal range at the baseline measurement but became out of range at the follow-ups. This was only noted for CRP (4.7 ± 6.6 mg/L at 8 weeks versus 3.2 ± 2.9 mg/L at baseline). The mean CRP level was elevated because of 3 outliers (Figure 8), which is also reflected by the very high standard deviation. In this instance the elevated CRP can be dismissed as a general indicator of toxicity. The increase is not statistically significant and, when these outliers are omitted, the CRP becomes in-range.

In summary, there were no objective signs that the eon Longevity +Plus was harmful. These findings confirm the subjective reports from the volunteers in the pilot study.

4. Conclusions

A clinical study was conducted in prediabetics and overweight individuals with symptoms of metabolic syndrome, who consumed twice daily eon Longevity +Plus and who were followed up at 4 weeks and at 8 weeks after the start of eon Longevity +Plus consumption to determine the effects on health. Analysis of 52 clinical parameters demonstrated that the eon Longevity +Plus reduced and/or normalized key metabolic parameters and markers of inflammation. Subset analysis of certain outcome measures, although not addressed per se or presented in this white paper, further revealed that some participants exhibited rather drastic reductions in several parameters such as diastolic blood pressure, cholesterol:HDL ratio, LDL, CPK, and others. Further studies are therefore planned to provide greater insights into the physiological modulation by eon Longevity +Plus and its effect on stress levels, and to devise means (e.g., eon Longevity +Plus in combination with diet and exercise) to maximize a person's health through this product. With the current results it can be concluded that eon Longevity +Plus deters the progression of clinical conditions that would de facto reduce a person's longevity. It can therefore be posited that the product has earned its name.

Table 1. Demographics of the study cohort.

	Age	Employment	Education*	Smoker#	Physical activity	Per day (hours)	Frequency (per week)	Meals (per day)	Meals skipped	Snacks (per day)	Outside meals, fast food	Water intake (cups‡/day)
MEN												
1	40	telecom engineer	3	Y - 2	walking, swimming	1-2	1-2	2	breakfast	1	1-3/mo	>5
2	27	civil engineer	4	N - 0	weightlifting, jogging	1-2	4	>3	none	2	never	>5
3	27	industrial technician	1	Y - 1	horse riding	2-3	1-2	3	none	1	<1/mo	>5
4	30	driver	4	N - 0	none	0	0	1	breakfast, dinner	2	<1/mo	3-5
5	29	unemployed	3	Y - 1	swimming	1-2	2	2	dinner	1	1-3/mo	>5
6	33	driver	3	Y - 1	fitness exercises	1-2	1-2	2	lunch	1	1-3/wk	>5
7	27	engineer	3	N - 0	weightlifting	1-2	4	>3	none	2	1-3/wk	>5
8	37	did not disclose	0	N - 0	none	0	0	3	none	3	4-6/wk	>5
9	37	administrative	3	Y - 3	weightlifting	1-2	3-4	2	dinner	2	1-3/mo	3-5
10	41	teacher	3	Y - 2	none	0	0	3	none	2	1-3/mo	>5
11	24	unemployed	3	N - 0	jogging	1-2	1-2	2	dinner	2	1-3/wk	3-5
12	43	driver	1	Y - 1	football	1-2	1-2	3	none	2	daily	3-5
13	31	unemployed	2	N - 0	fitness exercises	<1	1-2	2	breakfast, dinner	2	1-3/wk	3-5
14	41	guard/ handyman	1	N - 0	Swedish exercises	<1	3-4	2	lunch	3	<1/mo	>5
15	39	administrative	1	N - 0	none	0	0	2	dinner	1	never	1-3
WOMEN												
1	42	local NGO	3	N - 0	none	0	0	2	dinner	1	1-3/wk	>5
2	27	dentist assistant	3	N - 0	walking	<1	1-2/wk	3	none	2	<1/mo	3-5
3	42	unemployed	2	Y - 2	aerobics/ machines	1-2	3-4/wk	2	breakfast	2	<1/mo	>5
4	30	logistics/ clearance	3	Y - 3	none	0	0	2	breakfast	2	1-3/wk	3-5
5	33	unemployed	3	N - 0	none	0	0	3	none	3	1-3/mo	3-5
6	44	secretary	1	N - 0	walking	1-2	3-4/wk	3	none	1	1-3/mo	>5
7	30	lab technician	3	N - 0	none	0	0	2	dinner	2	1-3/mo	3-5
8	29	unemployed	4	N - 0	aerobics	1-2	4/wk	3	none	2	1-3/mo	1-3
9	33	mechanical technician	3	N - 0	none	0	0	2	dinner	1	1-3/mo	3-5
10	39	unemployed	3	N - 0	cardio/machines	<1	3-4/wk	3	none	2	<1/mo	>5
11	57	unemployed	4	Y - 1	machines	1-2	3-4/wk	>3	none	3	1-3/mo	>5
12	33	engineer	4	N - 0	different sports	<1	1-2/wk	3	none	1	1-3/wk	3-5
13	23	industrial engineer	3	N - 0	none	0	0	2	dinner	>3	1-3/mo	>5
14	38	administrative	3	Y - 2	aerobics	<1	1	2	dinner	2	<1/mo	>5

* Education: 0, primary education; 1, higher education; 2, diploma; 3, bachelor's degree; 4, master's degree; 5, post-graduate level

Smoker: Y, yes; N, no; 0, no smoker; 1, cigarettes; 2, sisha/hooka; 3, cigarettes and hooka

‡ One cup equates to approximately 175 mL

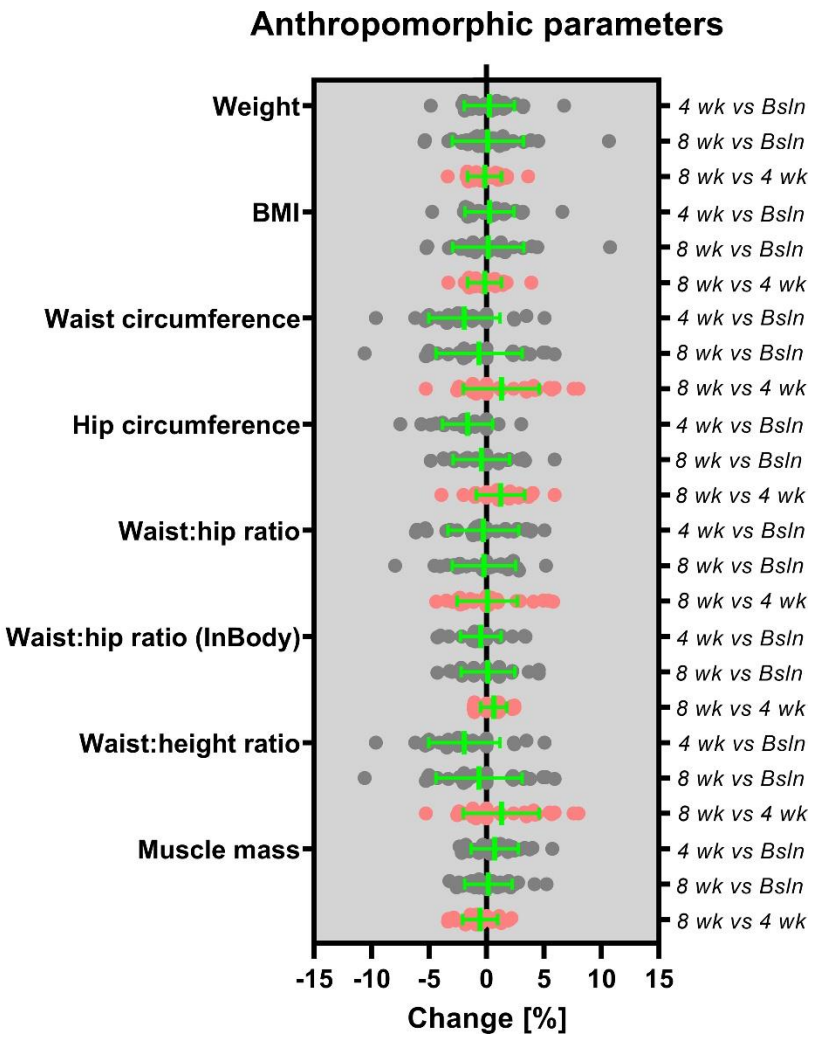

Figure 1. Forest plot of the percentage change (*x*-axis) in anthropomorphic parameters (left *y*-axis) over time following twice daily intake of eon Longevity +Plus. The periods compared are provided on the right *y*-axis. Plotted data feature individual data points (dark gray, light red), the mean percentage change (central vertical green line), and the ± standard deviation (lateral green vertical lines). Statistically significant changes are indicated by a green (increase) or red (decrease) highlight of the periods compared on the right *y*-axis. The absence of such highlights means that there were no statistically significant differences between the 2 periods compared, and that therefore the values did not change over the respective time frame. Abbreviations: BMI, body mass index; wk, weeks; Bsln, baseline (day 0 measurement).

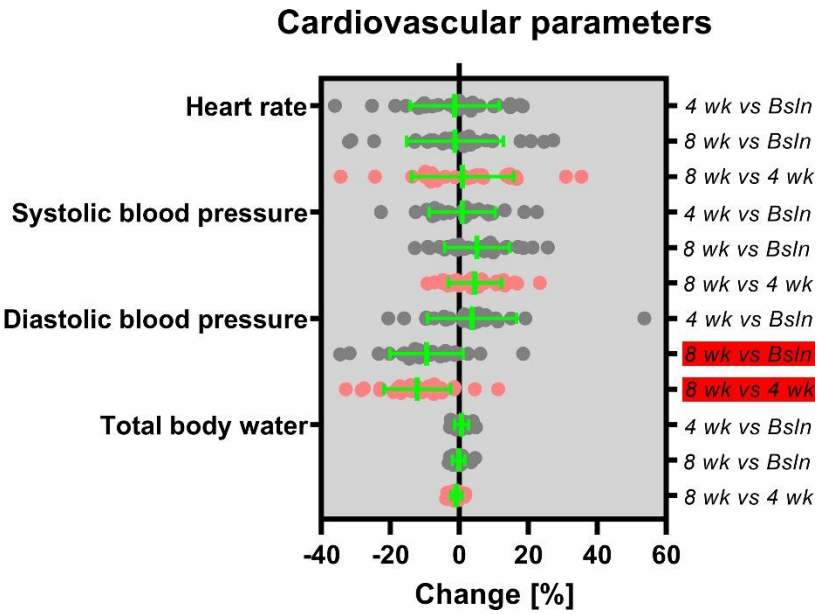

Figure 2. Forest plot of the percentage change (*x*-axis) in cardiovascular parameters (left *y*-axis) over time following twice daily intake of eon Longevity +Plus. The periods compared are provided on the right *y*-axis. Plotted data feature individual data points (dark gray, light red), the mean percentage change (central vertical green line), and the ± standard deviation (lateral green vertical lines). Statistically significant changes are indicated by a green (increase) or red (decrease) highlight of the periods compared on the right *y*-axis. The absence of such highlights means that there were no statistically significant differences between the 2 periods compared, and that therefore the values did not change over the respective time frame. Abbreviations: wk, weeks; Bsln, baseline (day 0 measurement).

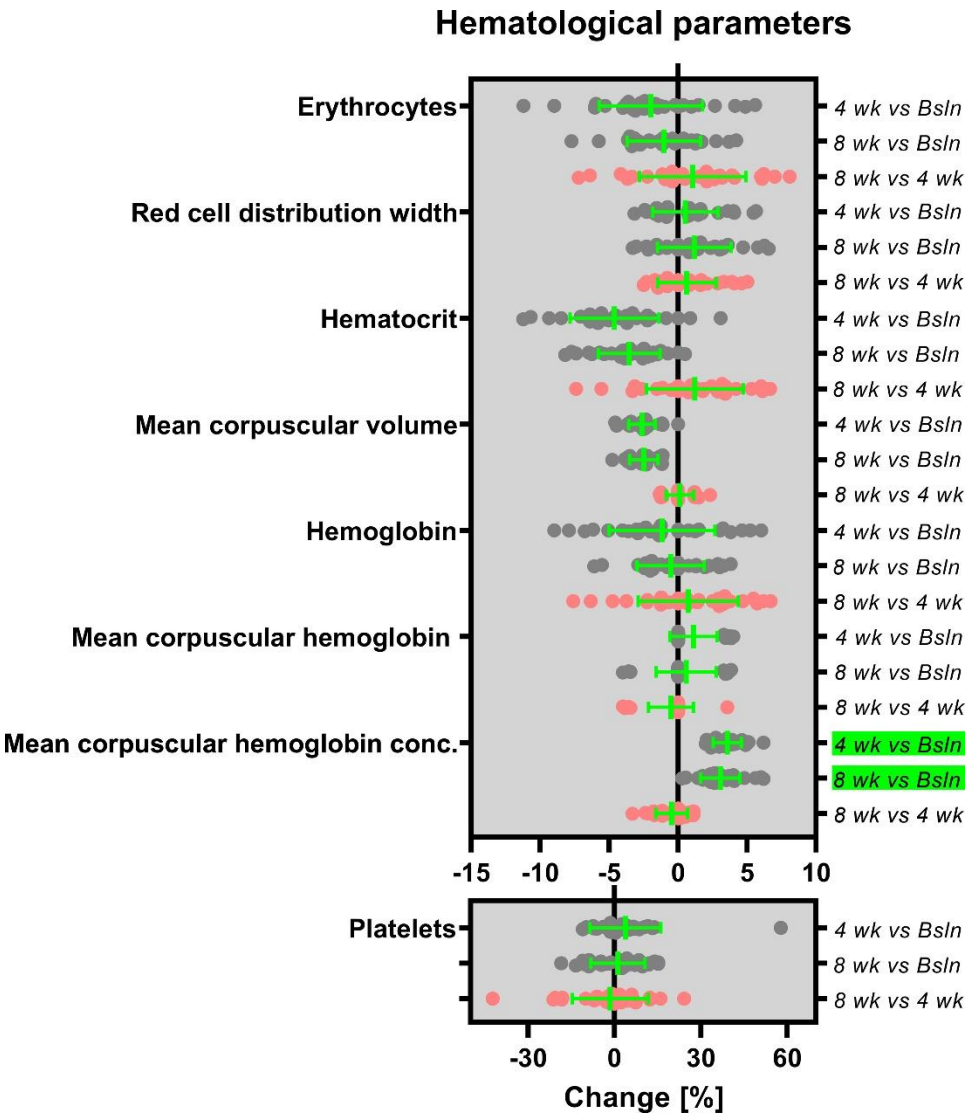

Figure 3. Forest plot of the percentage change (*x*-axis) in hematological parameters (left *y*-axis) over time following twice daily intake of eon Longevity +Plus. The periods compared are provided on the right *y*-axis. Plotted data feature individual data points (dark gray, light red), the mean percentage change (central vertical green line), and the ± standard deviation (lateral green vertical lines). Statistically significant changes are indicated by a green (increase) or red (decrease) highlight of the periods compared on the right *y*-axis. The absence of such highlights means that there were no statistically significant differences between the 2 periods compared, and that therefore the values did not change over the respective time frame. Abbreviations: conc., concentration; wk, weeks; Bsln, baseline (day 0 measurement).

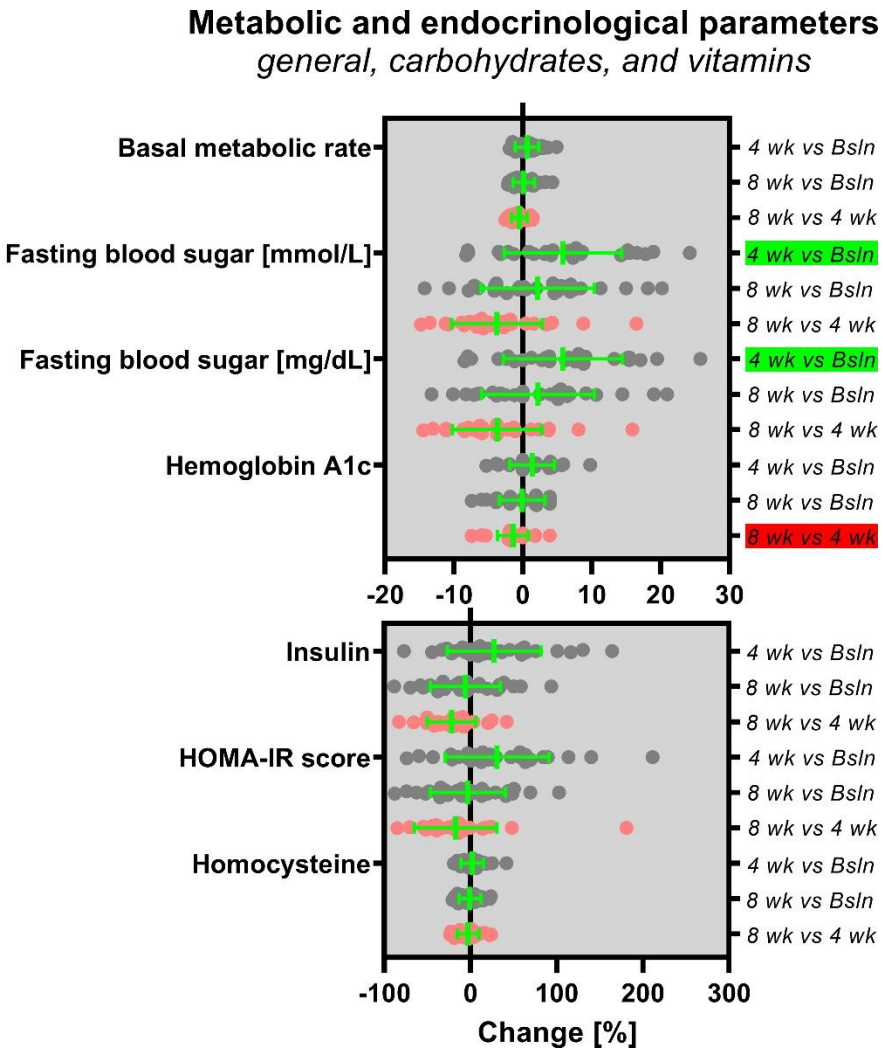

Figure 4. Forest plot of the percentage change (*x*-axis) in metabolic and endocrinological (general, carbohydrates, and vitamins) parameters (left *y*-axis) over time following twice daily intake of eon Longevity +Plus. The periods compared are provided on the right *y*-axis. Plotted data feature individual data points (dark gray, light red), the mean percentage change (central vertical green line), and the ± standard deviation (lateral green vertical lines). Statistically significant changes are indicated by a green (increase) or red (decrease) highlight of the periods compared on the right *y*-axis. The absence of such highlights means that there were no statistically significant differences between the 2 periods compared, and that therefore the values did not change over the respective time frame. Abbreviations: HOMA-IR, homeostatic model assessment of insulin resistance; wk, weeks; Bsln, baseline (day 0 measurement).

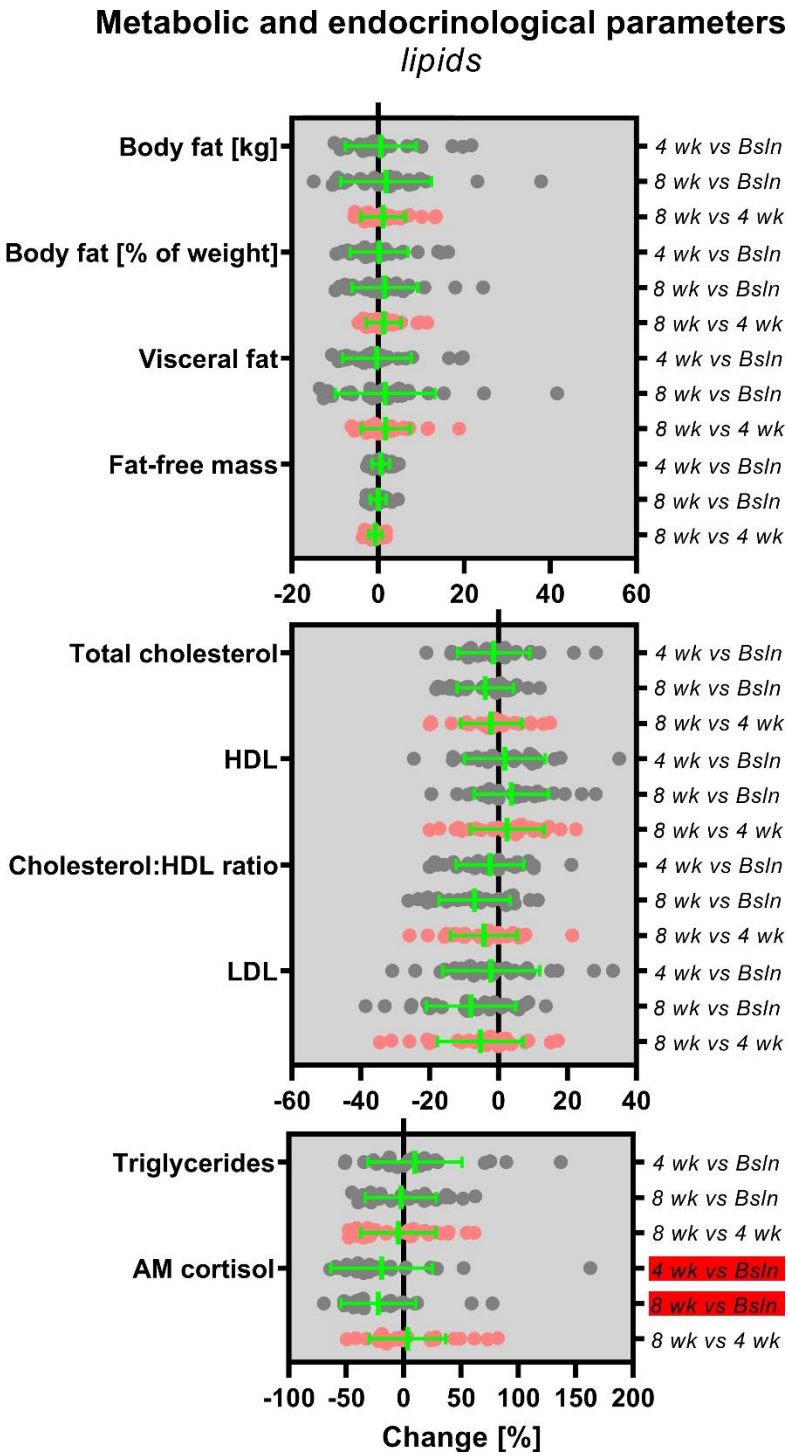

Figure 5. Forest plot of the percentage change (*x*-axis) in metabolic and endocrinological (lipids) parameters (left *y*-axis) over time following twice daily intake of eon Longevity +Plus. The periods compared are provided on the right *y*-axis. Plotted data feature individual data points (dark gray, light red), the mean percentage change (central vertical green line), and the ± standard deviation (lateral green vertical lines). Statistically significant changes are indicated by a green (increase) or red (decrease) highlight of the periods compared on the right *y*-axis. The absence of such highlights means that there were no statistically significant differences between the 2 periods compared, and that therefore the values did not change over the respective time frame. Abbreviations: HDL, high-density lipoprotein (good cholesterol); LDL, low-density cholesterol (bad cholesterol); wk, weeks; Bsln, baseline (day 0 measurement).

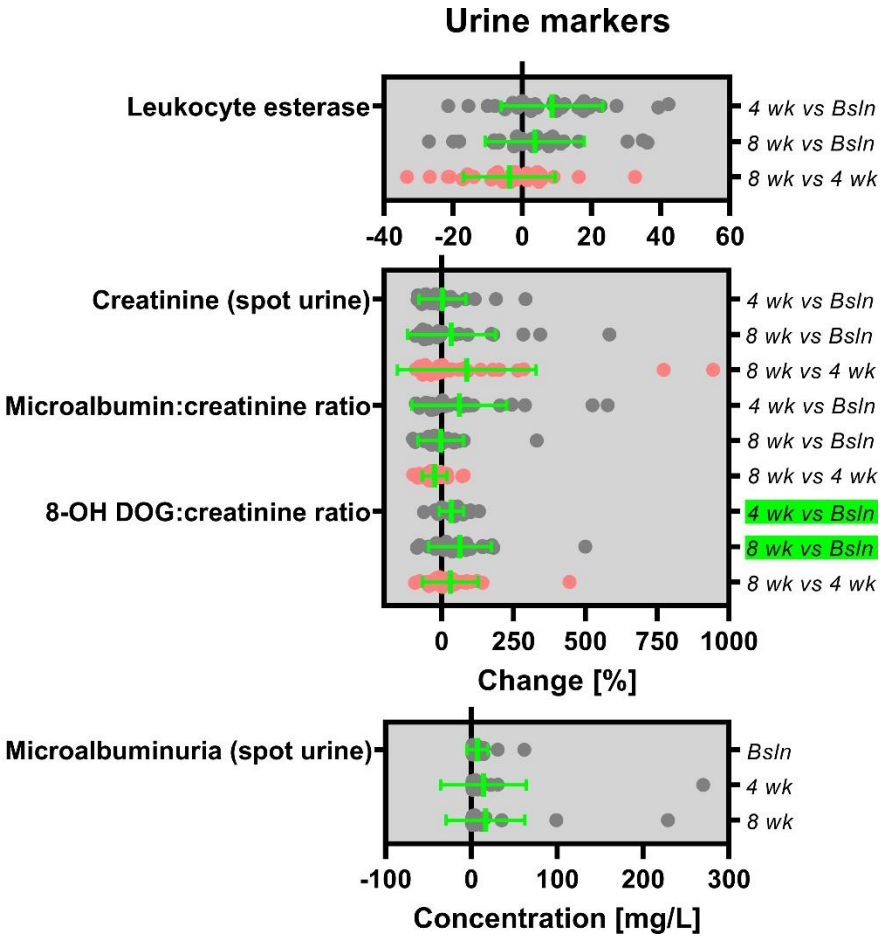

Figure 6. Forest plot of the percentage change (*x*-axis) in urine markers (left *y*-axis) over time following twice daily intake of eon Longevity +Plus. The periods compared are provided on the right *y*-axis. Plotted data feature individual data points (dark gray, light red), the mean percentage change (central vertical green line), and the ± standard deviation (lateral green vertical lines). Statistically significant changes are indicated by a green (increase) or red (decrease) highlight of the periods compared on the right *y*-axis. The absence of such highlights means that there were no statistically significant differences between the 2 periods compared, and that therefore the values did not change over the respective time frame. Abbreviations: 8-OH DOG, 8-hydroxy-2'-deoxyguanosine; wk, weeks; Bsln, baseline (day 0 measurement).

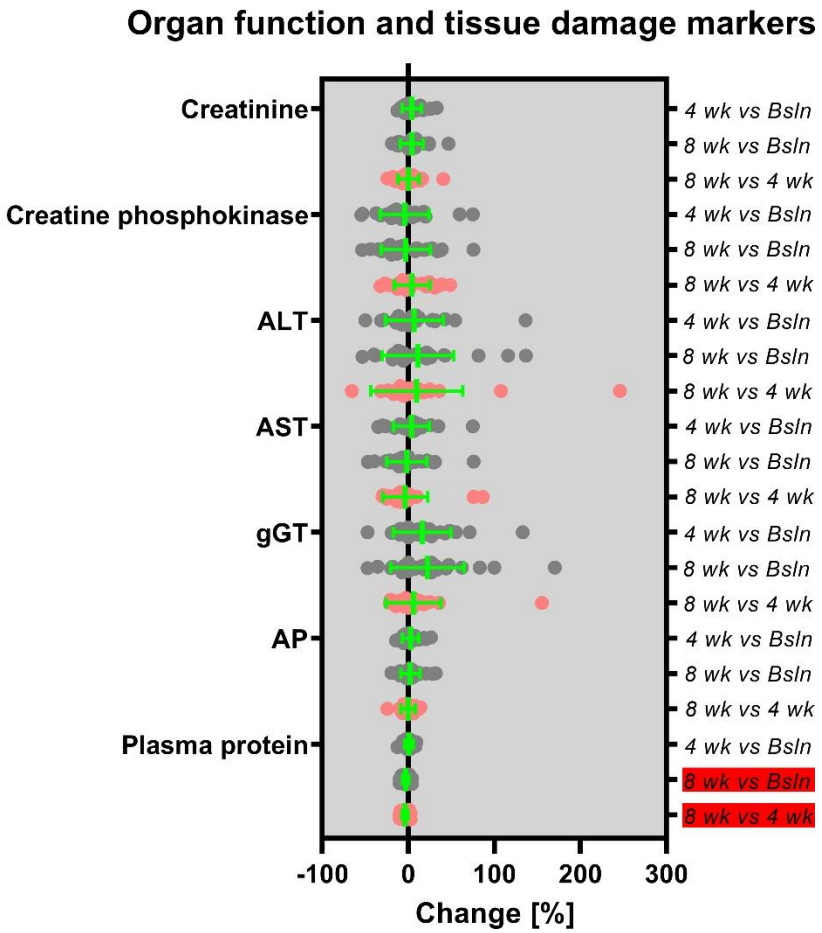

Figure 7. Forest plot of the percentage change (*x*-axis) in organ function and tissue damage markers (left *y*-axis) over time following twice daily intake of eon Longevity +Plus. The periods compared are provided on the right *y*-axis. Plotted data feature individual data points (dark gray, light red), the mean percentage change (central vertical green line), and the ± standard deviation (lateral green vertical lines). Statistically significant changes are indicated by a green (increase) or red (decrease) highlight of the periods compared on the right *y*-axis. The absence of such highlights means that there were no statistically significant differences between the 2 periods compared, and that therefore the values did not change over the respective time frame. Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; gGT, gamma glutamyl transpeptidase; AP, alkaline phosphatase; wk, weeks; Bsln, baseline (day 0 measurement).

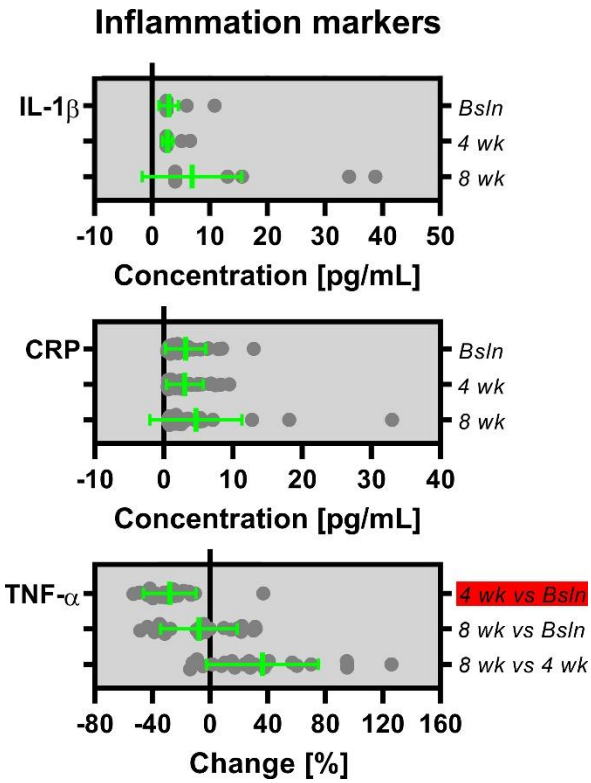

Figure 8. Forest plot of the percentage change (*x*-axis) in inflammation markers (left *y*-axis) over time following twice daily intake of eon Longevity +Plus. The periods compared are provided on the right *y*-axis. Plotted data feature individual data points (dark gray, light red), the mean percentage change (central vertical green line), and the ± standard deviation (lateral green vertical lines). Statistically significant changes are indicated by a green (increase) or red (decrease) highlight of the periods compared on the right *y*-axis. The absence of such highlights means that there were no statistically significant differences between the 2 periods compared, and that therefore the values did not change over the respective time frame. Abbreviations: IL-1β, interleukin 1 beta; CRP, C-reactive protein; TNF-α, tumor necrosis factor-alpha; wk, weeks; Bsln, baseline (day 0 measurement).

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