2018

Effects of Ginger Supplementation on Inflammation in Individuals

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EFFECTS OF GINGER SUPPLEMENTATION ON INFLAMMATION IN INDIVIDUALS OF VARYING ACTIVITY LEVELS

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ABSTRACT

Background. Ginger is a widely used ingredient in Southeast Asian countries and has gained increasing popularity in the Western diet due to its purported health benefits. Ginger has high antioxidant power because of its rich phytochemistry profile that contributes to its anti-inflammatory properties. While there have been animal studies, the research of ginger’s effects in humans is limited.

Objective. We sought to understand ginger’s effects on commonly assayed inflammatory biomarkers—C-Reactive Protein (CRP), Interleukin-6 (IL-6), and Tumor Necrosis Factor-Alpha (TNF- α)—in individuals with varying levels of physical activity. We propose that ginger may lower levels of these biomarkers due to its inherent anti-inflammatory characteristics.

Design. We designed an eight-week cohort study. Blood draw measurements were taken at three timepoints: the start of study, at week four, and upon completion of study.

Participants/setting. The study was conducted at Loma Linda University, where we enrolled twelve participants with a mean age of 42.4 ± 11.4 years who exercised at least once/week, did not take any anti-inflammatory medications, and who were free of any chronic inflammatory conditions.

Intervention. Participants were instructed to take three grams of ginger supplement mixed with lemonade powder to improve palatability daily. Participants also completed a pre- and post-intervention Short Form Health questionnaire (SF-36) to evaluate quality of life.

Main outcome measures. Inflammation was measured using three blood biomarkers: CRP, TNF-α, and IL-6. Quality of life was measured using the SF-36 questionnaire.

Statistical analyses performed. The three inflammatory biomarkers were analyzed using the Friedman non-parametric test and the Wilcoxon test where appropriate. The SF-36 questionnaire was analyzed using a paired t-test.

Results. Results of our study indicated a statistically significant reduction in TNF- α (p = .04) and a clinically significant reduction of greater than 15% in IL-6. There was a significant improvement in the domain of emotional well-being on the SF-36 after the ginger supplementation (p = .05).

Conclusions. Ginger may potentially be used as an adjuvant intervention in the prevention and management of chronic inflammatory diseases such as cardiovascular disease, diabetes, and obesity.
INTRODUCTION

Aging is associated with chronic low-grade inflammation, causing an increased risk of numerous diseases, poor physical functioning, and mortality.\textsuperscript{1} When comparing circulating levels of pro-inflammatory cytokines, such as C-reactive protein (CRP), Interleukin-6 (IL-6), and Tumor Necrosis Factor-α (TNF-α) in youth versus the elderly, researchers found a two- to four-fold increase in these markers for the elderly, even if the older individuals did not have any chronic disease present.\textsuperscript{1,2} This may be a result of a significant decline in immune function, antioxidant capacity, increased oxidative stress, and circulating levels of reactive oxygen species (ROS) during the aging process.\textsuperscript{1,2}

Inflammation can be measured using various blood biomarkers, specifically CRP, IL-6, and TNF-α. Environmental factors such as aging, obesity, diet, and smoking result in increased inflammation, and subsequently higher levels of these blood biomarkers.\textsuperscript{3} Sustained elevated levels of these factors can transition to chronic inflammation, leading to more serious medical conditions.

Elevated high sensitivity CRP (hs-CRP) analysis—a test used to detect the lower levels of CRP associated with long-term, low-grade inflammation—supports evidence for induction of prothrombotic pathways and atherosclerosis.\textsuperscript{4} C-reactive protein stimulates the production of monocytes, which then produces tissue factors involved in the coagulation system.\textsuperscript{5} There is also evidence to show that elevated CRP is linked to an increased risk of coronary artery disease, stroke, and myocardial infarction.\textsuperscript{5}

Interleukin-6 is an immune response mediator that plays a role in autoimmune and chronic inflammatory diseases.\textsuperscript{6} When there is a local lesion or stress, IL-6 is produced, followed by
inflammatory proteins including CRP, serum amyloid A (SAA), and others. Prolonged high levels of IL-6 contributes to a progressive degeneration of various organs and organ systems.\textsuperscript{6}

Tumor Necrosis Factor-\(\alpha\), similar to IL-6 in promoting inflammation, also plays a role in immune function. It stimulates macrophages and recruits inflammatory cells to kill various types of infectious bacteria.\textsuperscript{7} This biomarker has additional roles such as anti-viral and anti-tumor properties, to name a few.\textsuperscript{7} Since there is a strong association between high levels of CRP, IL-6 and TNF-\(\alpha\) and chronic inflammation, anti-inflammatory therapy may have the potential to lower these biomarkers and minimize damage caused by chronic inflammatory pathways.\textsuperscript{8}

Besides aging, exercise is also known to impact inflammation levels. When individuals exercise, two types of inflammatory pathways are recruited: acute and chronic inflammation.\textsuperscript{1} An increase in acute inflammation occurs immediately after exercising and can produce short-term discomfort, particularly for those who do not exercise regularly or have just started exercising.\textsuperscript{1,9} Regular moderate exercise can also reduce chronic inflammation, which is among the benefits desired for long-term health.\textsuperscript{1,8,10} For this reason, exercise is an important factor to consider in the multi-faceted approach to the curtailment of inflammation. Exercise alleviates chronic or systemic inflammation in regularly exercising adults over 70, but not to the same degree as in younger individuals.\textsuperscript{8,10} Increased chronic inflammation in individuals over the age of 70 has been hypothesized to be due to general inflammation associated with the aging process.\textsuperscript{1,9} This suggests that individuals over the age of 70 may not be able to alleviate acute inflammation in a normal timeframe as compared to younger individuals.

Foods offer an ideal source of readily-available, relatively inexpensive therapeutic potential for sustained anti-inflammatory actions. Foods with demonstrated anti-inflammatory properties include but are not limited to citrus fruits, strawberries and other berries, and high sources of
omega-3 fatty acids such as spinach, nuts, and fatty fish.\textsuperscript{11,12} Spices, such as ginger and cinnamon, have also been studied for their anti-inflammatory properties.\textsuperscript{13}

Conversely, foods that elevate inflammation levels include refined carbohydrates, added sugar, and certain omega-6 fats.\textsuperscript{14} The effect is initially acute but can transition into chronic inflammation if a diet consisting largely of these foods persists. Therefore, the ideal anti-inflammatory diet would emphasize increased consumption of foods that decrease inflammatory cytokines and decrease foods that are known to trigger inflammation.\textsuperscript{14}

Ginger (\textit{Zingiber officiale}) is commonly used in Southeast Asian foods and as a remedy in alternative medicine because of its rich phytochemical benefits.\textsuperscript{15,16} The non-volatile components of ginger consist of gingerols, shogaols, diarylheptanoids, phenylbutenoids, flavonoids, diterpenoids, sesquiterpenoids, paradols, and zingerone.\textsuperscript{17,18} These bioactive compounds are found in the rhizome of the plant and have been shown to be effective in treating many medical conditions, such as wounds, muscular pains, atherosclerosis, ulcers, and stomach discomfort.\textsuperscript{18} The phenolic compounds in gingerols have been shown to have powerful antioxidant and anti-inflammatory effects through the cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2) enzymatic pathways.\textsuperscript{19} Cyclooxygenase-1 is a pathway involved in maintaining homeostatic function in the body and is always active at a baseline level. The role of the cyclooxygenase-2 system is to halt oxidative stress or injury and is important in regulating inflammation.\textsuperscript{19} If unmanaged and overstimulated, the COX-2 pathway can lead to chronic inflammation over time.\textsuperscript{19}

Because ginger is a rich source of antioxidants, increasing antioxidant levels in the body through the intake of ginger can potentially combat the higher levels of oxidative stress that occur as a result of diet, aging, and environmental stressors.\textsuperscript{16} This can help lower the COX-2
pathway activity. In doing so, ginger may yield great benefits in the management of diseases such as cardiovascular disease, immune system-related illnesses, and cancer.\textsuperscript{16}

There are few studies on ginger’s anti-inflammatory effects post-exercise. The research is rather limited and mainly focus on athletes who engage in high-intensity interval training in a relatively young age group (20s-30s).\textsuperscript{13,20} Historically, IL-6 and hs-CRP were the markers measured in experiments involving ginger supplementation.\textsuperscript{21,22} However, TNF-α has also been found to play an important role in inflammation in the body. Therefore, the purpose of our graduate student research study was to observe the effects of ginger on hs-CRP, IL-6, and TNF-α levels in individuals of varying exercise activity levels.

METHODS AND MATERIALS

All methods and procedures were approved by Loma Linda University’s (LLU) Institutional Review Board prior to the start of the study. We recruited 12 healthy male and female LLU faculty, staff, family members, and friends with a mean age of 42.4 ± 11.4 years who reported varying activity levels. Recruitment was accomplished through email and flyers that were distributed around the LLU campus. Subjects filled out a questionnaire to provide us with demographics.

Inclusion and exclusion criteria were outlined to obtain an unbiased and diverse sample group for this study. The inclusion criteria stipulated that participants must be between the ages of 30-70 years and have participated in various levels of activity outlined by the General Physical Activities Defined by Level of Intensity by the American College of Sports Medicine (ACSM) and the Centers for Disease Control and Prevention (CDC). Individuals were excluded from the study if they were currently taking Aspirin (Acetylsalicylic Acid), Coumadin (Warfarin or Jantoven), supplements containing ginger (Zingiber officinale, ginger root, black ginger,
zingiberis rhizoma) more than one time per week within the last month, or Heparin (Hep-Pak, Heparin Lock Flush, Hep-Pak CVC, Hep-Lock, Heparin Sodium ADD-Vantage). Individuals with chronic inflammatory conditions such as cancer, CVD, diabetes, gastroesophageal reflux disease (GERD), ginger allergies, metabolic syndrome, and/or autoimmune diseases such as rheumatoid arthritis, were also excluded from participating in the study. Individuals with phenylketonuria were also excluded due to the presence of Aspartame in the lemonade flavoring agent.

The purpose, basic design, and the individual’s role in the study were explained to potential participants. While there were no direct benefits to participants, the results of the study could potentially contribute to researchers’ and clinicians' increased understanding of ginger’s role in inflammation and its possible use as a complementary treatment modality for lowering inflammation. Risks to participants were minimal and involved a potential breach of confidentiality and momentary digestive discomfort. The risks involved in drawing blood included, but were not limited to, momentary discomfort at the site of the blood draw, possible bruising, redness, swelling around the site, bleeding at the site, feeling lightheaded when the blood is drawn, possibly fainting, and rarely, obtaining an infection at the site of the blood draw. If a participant fainted during or after the blood draw, the licensed phlebotomist would safely stop the procedure and place the participant’s head between their knees. A cold compress would then be applied to the back of the neck. Usually, this is a sufficient and effective measure in helping a participant recover from a fainting spell. The phlebotomist would have stayed with the patient for at least 15 minutes to make sure the participant is fully recovered. All recruited participants signed an informed consent form before being admitted into the study.
Once participants signed the informed consent, subjects filled out the following assessment forms:

1) **Demographics Questionnaire** – Developed by the researchers to gather information about the participants. This questionnaire included questions about height, weight, amount of exercise, medications taken, medical conditions, and their use of ginger supplements. The average time for completion of the questionnaire was five minutes.

2) **SF-36** – 36-item Quality of Life Assessment developed by the Research and Development (RAND) Corporation which assesses overall health. It measures eight different dimensions including physical functioning, role limitations due to physical health, role limitations due to emotional problems, energy/fatigue, emotional well-being, social functioning, pain, and general health. The average time for completion of the questionnaire was ten minutes. The participants filled out the survey pre- and post-study.

After participants filled out the consent and surveys, they were scheduled to come in after fasting for 10 hours for their blood draw. A certified phlebotomist proceeded with an 8 mL blood draw (0.5 tablespoons) to establish baseline hs-CRP, IL-6, and TNF-α levels. Test tubes were labeled with the participants’ randomly-assigned numbers, followed by the letter “A” to signify the first sample of the study. Before participants left, they were provided with an eight-week supply of ginger powder (168 g total), pre-portioned Crystal Light® lemonade powder, measuring spoons, and a compliance sheet. Starting on the day of the first blood test, participants took a 3 g powder supplement of ginger mixed with the Crystal Light® lemonade powder and water (as desired) with meals once a day for eight weeks. At the end of week 4 (day 6, 7, or 8), the participants returned to Nichol Hall for another blood test to collect mid-intervention hs-CRP, IL-6, and TNF-α. Test tubes were labeled with the participant’s ID number followed by the letter “B” to
signify the second sample of the study. Participants continued to follow the supplement regimen. At the end of week 8 (day 6, 7, or 8), participants returned to Nichol Hall to fill out the post-intervention SF-36 survey, submit their compliance worksheet, and for their final blood draw. Each subject that completed the 8-week study received a $5 gift card.

**Inflammatory Biomarkers**

**Venipuncture Blood Draw**

Inflammation was assessed using the biomarkers IL-6, hs-CRP, and TNF-α, extracted by a venipuncture blood draw. Blood draws were conducted three separate times on each participant: pre-intervention, mid-intervention, and post-intervention. On the night before each blood test, the participant was able to take regular medications except for over-the-counter non-steroidal anti-inflammatory drugs (NSAIDs) such as Advil, Aleve, Motrin, Excedrin, Midol, Nuprin, etc. The subjects arrived in the morning at the Clinical Molecular Laboratory in Nichol Hall Room A117 after having fasted for 10 hours prior to the blood draw. Blood draws were conducted by certified phlebotomist Kristin Bruhjell. Participants were seated in a comfortable chair and venous blood was drawn from the antecubital vein using a standard venipuncture protocol for a total of 8 mL or 0.5 tablespoons of blood.

**Analysis of hs-CRP**

High sensitive C-reactive protein (hs-CRP) concentrations were measured using a Point of Care Diazyme (POC) SMART 700 | kit, according to the manufacturer's instructions. After calibrating the POC SMART 700 instrument to the specific kit, a 20-μL sample of the whole blood at room temperature was placed into the Diazyme Reagent System cuvette using a pipette. The cuvette was then wiped with a non-abrasive tissue to ensure a clean surface. The sample was
then placed into the instrument to be analyzed. Results were seen in approximately 4 minutes. Samples were run in duplicates to reduce error.

**Analysis of IL-6 and TNF-α**

Whole blood serum samples were frozen until all the participants completed the study. When all samples were collected, the samples were packaged and shipped to the Cytokine Reference Laboratory (CRL) at the University of Minnesota. Samples were analyzed by Mr. Michael Ehrhardt, BSc. Samples were analyzed for IL-6 & TNF-α simultaneously using the Luminex platform and conducted as a high-sensitivity multi-plex analysis according to the manufacturer’s instructions. In brief, fluorescent color-coded beads, pre-coated with anti-human (IL-6, TNF-α) capture antibodies, were added. After incubation and washing, biotinylated anti-human detection antibodies were added, followed by phycoerythrin-conjugated streptavidin. The beads were read on a Luminex instrument (Bioplex 200) which is a dual-laser, fluidics-based instrument. One laser determines the analyte being detected via the color coding of the beads; the other measures the magnitude of the red phycoerythrin signal from the detection antibody, which is proportional to the amount of analyte bound to the bead. Samples were run in duplicate and values were interpolated from 5-parameter fitted standard curves generated on each 96-well plate.

Changes in inflammatory levels were analyzed by comparison of the mean blood marker levels of individuals at three different time points. Significance was set at $p \leq 0.05$. The three inflammatory biomarkers were analyzed using the Friedman non-parametric test. The eight different categories of the SF-36 questionnaire were analyzed using a paired t-test.

**RESULTS**
The demographic data of all 12 participants are displayed in Table 1. Our population consisted of an equal distribution of men and women, six per group, with ages ranging from 30 to 59 and a mean age of 42.4 ± 11.4 years. For the analysis of data, one large group was used instead of the two proposed groups of exercisers vs. non-exercisers, due to an imbalance with respect to both age and gender.

Nonparametric measures were used for statistical analysis of the three blood inflammatory biomarkers: hs-CRP, IL-6, and TNF-α. The statistical tests used were the Friedman test of differences among repeated measures and the one-way ANOVA. Each participant’s initial inflammatory biomarker measurement served as the control.

Based on our results, hs-CRP levels did not differ over the three-time points, \( \chi^2 (2, n=12) = 1.03, p = .60 \) (Table 2). Interleukin-6 was not significantly different over the three-time points, \( \chi^2 (2, N=12) = 3.30, p = .19 \) (Table 2). Tumor Necrosis Factor-α levels over the three-time points were significantly different, \( \chi^2 (2, n=12) = 6.50, p = .04 \) (Table 2).

Post hoc analysis with Wilcoxon signed-rank tests was conducted for TNF-α. There were no significant differences between the middle vs. end time points (Z = -0.275, p = .78). However, there was a statistically significant reduction in TNF-α levels between the beginning vs. middle time points (Z = -2.353, p = .02), and between beginning vs. end time points (Z = -1.963, p = .05). The results of the statistical analysis are shown in Table 2.

There was no observable statistically significant trend with hs-CRP or IL-6. There was a noted downward trend for IL-6, although not significant. Aside from statistical significance, it is important to note that the reduction in values was clinically significant. Percent change was calculated for both hs-CRP and IL-6 to determine if clinical significance was present. There was
an average increase of 76\% for hs-CRP and reduction of 16.3\% for IL-6 when comparing the beginning to the end levels.

A paired-samples t-test was conducted to compare the responses of the SF-36 questionnaire’s eight-areas of quality of life before and after the ginger intervention. The eight areas tested on the survey included physical functioning, role limitations due to physical health, role limitations due to emotional problems, energy/fatigue, emotional well-being, social functioning, pain, and general health. There were no significant differences in the SF-36 questionnaire responses before and after the study with the exception of emotional well-being. There was a significant increase in the score for emotional well-being post ginger supplementation (87.3 ± 4.5), compared to pre-ginger supplementation (84.0 ± 6.2), (p = .05). Results are seen in Table 3.

### TABLE 1. MEAN (SD) OF DEMOGRAPHIC CHARACTERISTICS OF STUDY PARTICIPANTS (n = 12)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>6</td>
</tr>
<tr>
<td>Male</td>
<td>6</td>
</tr>
<tr>
<td>Age (years)</td>
<td>42.4 (11.4)</td>
</tr>
<tr>
<td>BMI (Kg/m$^2$)</td>
<td>26.4 (4.9)</td>
</tr>
<tr>
<td>Exercise (days/week)</td>
<td>3.7 (1.7)</td>
</tr>
</tbody>
</table>

SD: Standard Deviation

### TABLE 2. MEAN RANKS OF BLOOD BIOMARKERS (CRP, IL-6, TNF-α) OVER TIME (n = 12)

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Mean Ranks Beginning</th>
<th>Mean Ranks Middle</th>
<th>Mean Ranks End</th>
<th>$\chi^2$</th>
<th>df</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRP</td>
<td>1.88</td>
<td>2.21</td>
<td>1.92</td>
<td>1.03</td>
<td>2</td>
<td>.60</td>
</tr>
<tr>
<td>IL-6</td>
<td>2.25</td>
<td>2.17</td>
<td>1.58</td>
<td>3.30</td>
<td>2</td>
<td>.19</td>
</tr>
<tr>
<td>TNF-α</td>
<td>2.58</td>
<td>1.58</td>
<td>1.83</td>
<td>6.50</td>
<td>2</td>
<td>.04</td>
</tr>
</tbody>
</table>
Figure 1. Median and Range of TNF-α Concentrations Over Time (n = 12)

Figure 2. Median and Range of IL-6 Concentrations Over Time (n = 12)

Figure 3. Median and Range of hs-CRP Concentrations Over Time (n = 12)
TABLE 3. PRE AND POST SF-36 MEAN (SD) SCORES BY DOMAIN (n = 12)

<table>
<thead>
<tr>
<th>Domain</th>
<th>Pre</th>
<th>Post</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical Functioning</td>
<td>98.8</td>
<td>97.5</td>
<td>.28</td>
</tr>
<tr>
<td>Role limitations d/t physical health</td>
<td>97.9</td>
<td>97.9</td>
<td>1.00</td>
</tr>
<tr>
<td>Role limitations d/t emotional prob.</td>
<td>91.7</td>
<td>94.4</td>
<td>.34</td>
</tr>
<tr>
<td>Energy/fatigue</td>
<td>68.3</td>
<td>76.0</td>
<td>.12</td>
</tr>
<tr>
<td>Emotional well-being</td>
<td>84.0</td>
<td>87.3</td>
<td>.05</td>
</tr>
<tr>
<td>Social Functioning</td>
<td>97.9</td>
<td>95.8</td>
<td>.17</td>
</tr>
<tr>
<td>Pain</td>
<td>82.9</td>
<td>85.6</td>
<td>.47</td>
</tr>
<tr>
<td>General health</td>
<td>81.9</td>
<td>85.8</td>
<td>.12</td>
</tr>
</tbody>
</table>

SD: Standard Deviation

DISCUSSION

The present study was designed to determine if ginger supplementation (3 g/day) has an effect on lowering inflammation in individuals of varying activity levels. Three blood biomarkers—TNF-α, IL-6, and CRP—were chosen as indicators of inflammatory status. These three inflammatory biomarkers have been previously used to assess inflammation levels related to ginger, exercise, and in chronic diseases such as diabetes and cancer.\(^{24-26}\) Due to ginger’s known anti-inflammatory phytochemical compounds—gingerols, shogaols, diarylheptanoids, phenylbutenoids, flavanoids, diterpenoids, sesquiterpenoids, paradols, and zingerone—it was hypothesized that ginger can potentially be effective at systemic reduction of inflammation in individuals of varying activity levels.

The results of the eight-week study provided promising results. Tumor Necrosis Factor-α levels from the start to the end of the study showed statistically significant differences; the
greatest difference was seen from the beginning and middle time points. Tumor Necrosis Factor-α has a variety of roles in the body, and the most notable function for our study is its ability to recruit inflammatory cells. Greater reduction in TNF-α was observed between the beginning and middle timepoints vs. the middle and end timepoints. This could be due to higher compliance in daily ginger regimen at the beginning of the study. Although the total compliance for the entire duration of the study was high (96.2%), there was a 1% reduction in compliance when comparing the first 4 weeks (96.8%) with the last 4 weeks (95.8%). Another possible reason we suggest could have been the reduction of TNF-α due to ginger supplementation stabilized after four weeks. The significant reduction in TNF-α levels in the middle and end timepoints compared to the beginning timepoint, strengthens the evidence discussed by Mashhadi et al. and Ricciotti et al. in their respective studies, which suggest that ginger supplementation can inhibit the inflammatory COX-2 pathway that causes an increase in undesirable cytokine inflammation and oxidative stress. Toda et. al. (2016) evaluated TNF-α in the soleus muscle of physically active mice who consumed black ginger extract for 4 weeks and found that the mRNA expression levels were lower in the ginger group than in the control group. This suggests that the anti-inflammatory effects of ginger could benefit one’s health in a short period of time.

Interleukin-6 and hs-CRP did not yield statistically significant results. The results of IL-6 levels in our study were consistent with the findings by Mashhadi et al. (2013), which showed there was an overall reduction in IL-6 levels after ginger consumption, although not statistically significant. A possible explanation could be that the ginger dose and/or duration of supplementation was insufficient to yield a significant reduction in inflammatory cytokines. Based on a study by Yimin and Kohanawa (2006), there is a potential negative feedback
relationship that exists between TNF-α and IL-6. Experiments on mice revealed that these biomarkers have a direct relationship, where the rise in one led to a suppression in the other and vice versa. The exact nature of this relationship and differences in the roles of TNF-α and IL-6 remains to be discovered.

C-reactive protein levels had the greatest variability throughout the three timepoints. Multiple factors such as obesity, diet, exercise, smoking, and exposure to environmental toxins play a role in hs-CRP levels, and could have been possible confounders causing levels to vary throughout the eight weeks. Based on findings from Carpenter et. al, high plasma C-reactive protein concentrations were significantly correlated with body mass index, lower quality physical health, fatigue and pain. Although 33% of our subjects in our sample met the basal metabolic index criteria for obesity, most participants were generally healthy adults without major medical disorders. Furthermore, all participants were recruited from the Loma Linda area, which is America’s Blue Zone region. Most of the population in this area live longer than other Americans due to vegetarianism, regular exercise, and omitting smoking and alcohol.

Although not statistically significant, it is of benefit to note the clinical importance of lowered IL-6 levels throughout the study. With the clinically significant reduction of IL-6, we suggest ginger can potentially be used as a complementary dietary intervention in managing inflammatory issues as opposed to the use of medications that often yield more serious side effects. Interleukin-6 plays an important role to the transition between acute and chronic inflammation. Within a short period of time, this biomarker is able to destroy the injurious agent in a localized area while promoting an immune response through local leukocyte recruitment, death and migration. Interleukin-6 is also able to develop specific cellular and humoral immune
responses, such as end-stage B cell differentiation, immunoglobulin secretion, and T cell activation.³

Ginger was also shown to increase the levels of self-reported emotional well-being in individuals. This is important considering that health encompasses not only physical, but also psychological and emotional well-being.³¹ Research has established a link between depression and premature mortality, coronary heart disease, diabetes, and other chronic disorders.³²-³⁴ Positive subjective well-being has been associated as a protective factor for health.³⁵ Increased emotional well-being is associated with regular physical activity, increased cardiovascular health, maintenance of muscle, increased immune regulation, and reduced inflammatory responses.³⁵-³⁷ High inflammation levels have been associated with a lower quality of life.³⁸ The findings of this study suggest that ginger can reduce inflammation levels and increase emotional health; therefore, ginger can potentially increase quality of life.

There were limitations to our study. Both sample size and short duration of study do not allow for generalizability to the public and does not speak to long-term effects. Eight weeks may not be sufficient to observe ginger’s overall effects. Additionally, a larger sample may yield greater variability in data among individuals of different socioeconomic status and ethnic background, among others. Secondly, the fact that some of the participants were enrolled during the holidays is important to take into consideration. The stress of the holidays could have negatively influenced their inflammatory biomarkers to a greater degree, potentially overshadowing ginger’s effects. Some of the stressors include lack of sleep, increase in consumption of refined and high-sugar foods, flu season, decreased activity and exercise, and greater financial demands.³⁹-⁴¹
Further research is warranted with a larger sample size and longer duration (possibly six months to a year) to uncover any significant reductions in IL-6 levels, and to establish appropriate amounts and duration for therapeutic effect. Due to the small sample size, participants were not evenly distributed among exercise categories. Including individuals with a wider age and gender range of varying activity levels could increase the generalizability of the results.

CONCLUSION

The outcome of our study indicates that ginger may be an effective adjuvant treatment intervention in the management of chronic inflammatory diseases that have become so widespread in our society. Perhaps the use of ginger as a complement to other medical treatment modalities can minimize patients’ reliance on medications and lessen the negative side effects experienced. In addition, ginger may have auxiliary benefits that go beyond improvement in clinical biomarkers but incorporate other aspects of health that ultimately contribute to whole person care. Since chronic inflammation has an additive effect over time, older individuals are more prone to suffering from the drawbacks of living with such conditions, leading to an increased reliance on medications and decreased physical activity, both of which may be detrimental to their emotional state. Lowering inflammation can therefore improve quality of life. Furthermore, the information provided by our research can help educate other healthcare professionals on the value of nutrition and how specific foods can address certain conditions. Food can be used as a first step in a treatment plan, rather than an afterthought.
THE EFFECTS OF GINGER SUPPLEMENTATION ON INFLAMMATION IN EXERCISING INDIVIDUALS

Each participant will fill out a questionnaire prior to the start of the study. The questionnaire will include questions about the participant’s demographics and lifestyle. Average completion time is 10 minutes or less.

by Sara Kashlan, Brenda Rodriguez, Monique Vuong

1 GROUP 1 - 2 PAPERWORK
Once recruited, participants will go to Clinical Molecular Psychoneuroimmunology Lab Nichol Hall Allied Health Provision to fill out an informed consent as well as a demographic/lifestyle survey. We will also explain the nature of the study in more detail.

2 WEEK 1 - BLOOD TEST #1
Subjects will then proceed to their first blood test to establish baseline CRP, IL-6, and TNF-α levels.

3 3G SUPPLEMENT GINGER
Participants will take a 3g supplement of ginger in powder form with meals once/day for 8 weeks (preferably in the morning)

4 WEEK 4 - BLOOD TEST #2
At the end of Week 4, participants will return to Nichol Hall to do another blood test for mid-intervention CRP, IL-6, and TNF-α levels.

5 3G SUPPLEMENT GINGER
Participants will continue to take a 3g supplement of ginger in powder form with meals once/day (preferably in the morning).

6 WEEK 8 - BLOOD TEST #3
At the end of Week 8, participants will return to Nichol Hall for a final blood test for post-intervention CRP, IL-6, and TNF-α levels.

Research on this study is done with the help of Dr. Bains and Loma Linda University.
REFERENCES


37. Steptoe A, O'Donnell K, Badrick E, Kumari M, Marmot M. Neuroendocrine and


Appendix A

LOMA LINDA UNIVERSITY
School of Allied Health Professions
INFORMED CONSENT

THE EFFECTS OF GINGER SUPPLEMENTATION ON INFLAMMATION IN EXERCISING INDIVIDUALS

PRINCIPAL INVESTIGATOR: JeJe Noval, PhD, RDN - Assistant Professor, Department of Nutrition and Dietetics, School of Allied Health Professionals

WHY IS THIS STUDY BEING DONE?

The purpose of this graduate student research is to study the effect of ginger supplementation on inflammation levels in individuals of varying activity levels.

You are invited to be in this study because you are a healthy individual between the ages of 30-70 years and exercise at least once per week for 30 minutes.

You are excluded from the study if you are currently taking steroids, aspirin, Tylenol, Advil, Alleve, Motrin, Excedrin, Midol, Nuprin, etc., Coumadin, Ginger supplements, pain meds, and heparin more than 1x/week within the last month.

You will also be excluded if you have any chronic inflammatory conditions such as Cancer, CVD, Diabetes, Gastroesophageal reflux disease (GERD), Ginger allergies, Metabolic Syndrome, autoimmune diseases such as Rheumatoid Arthritis, and/or Phenylketonuria (PKU).

If you are currently taking Vitamin D, you must continue with your supplement regimen throughout the duration of the 8-week study.

You will be divided into one of two groups based on your level of exercise: regular exercisers (3-7 times per week) and non-regular exercisers (1-2 timer per week).

Approximately 30 subjects will participate at Clinical Molecular Psychoneuroimmunology Lab located in Nichol Hall Allied Health Provision at Loma Linda University.

Your participation in this study will last 8 weeks. Upon completing the 8-week study, you will receive a $5 gift card.
HOW WILL I BE INVOLVED?

Participation in this study involves the following:

Visit 1
- You will go to Clinical Molecular Lab Nichol Hall Room A117 to fill out a demographics survey and a quality of life survey (SF-36). After you fill out the consent and survey, a certified phlebotomist will immediately proceed with a blood draw to establish baseline CRP, IL-6, and TNF-α levels. Before you leave, we will provide you with an 8-week supply of ginger powder (168g total), teaspoon set, lemonade powder, and a compliance sheet.
- You will begin taking a 3g (1.5 teaspoons) supplement of ginger in powder form daily with meals. The ginger powder must be mixed with lemonade powder that we have provided.

Visit 2
- At the end of Week 4, you will return to Nichol Hall to do another blood test to determine your CRP, IL-6, and TNF-α levels.
- You will continue taking the ginger supplement twice/day with food.

Visit 3
- At the end of Week 8, you will return to Nichol Hall to fill out the SF-36 survey and for a final blood test to determine your final CRP, IL-6, and TNF-α levels.

*A total of 8 mL or 0.5 tablespoons of blood will be drawn at each visit.

*ON THE NIGHT BEFORE EACH VISIT, participant may take regular medications except for over-the-counter non-steroidal anti-inflammatory drugs (NSAIDs) such as Advil, Aleve, Motrin, Excedrin, Midol, Nuprin etc. Participant may only consume water 10 hours prior to blood draw visit.

WHAT ARE THE REASONABLY FORESEEABLE RISKS OR DISCOMFORTS I MIGHT HAVE?

Participating in this study will involve the following risks: possible breach of confidentiality. In addition, the risks involved in drawing blood may include, but are not limited to, momentary discomfort at the site of the blood draw, possible bruising, redness, swelling around the site, bleeding at the site, feeling of lightheadedness when the blood is drawn, the possibility of fainting, and rarely, an infection at the site of the blood draw.

To minimize the risk of breach of confidentiality, we will store all subject data in a locked cabinet in a locked office. An ice pack will be used for swelling, bruising, and redness at the blood draw site. If you faint during or after the blood draw, the licensed phlebotomist will safely...
discontinue the procedure and place your head between your knees. A cold compress will then be applied to the back of the neck. Usually, this is a sufficient and effective measure in helping a participant recover from a fainting spell. The phlebotomist will stay with you for at least 15 minutes to make sure you are fully recovered.

All records and research materials that identify you will be held confidential. Any published document resulting from this study will not disclose your identity without your permission. Information identifying you will only be available to the study personnel.

WILL THERE BE ANY BENEFIT TO ME OR OTHERS?

Although you may not personally benefit from this study, your participation may help practitioners better identify/provide insights into utilizing ginger supplements in order to decrease inflammation.

WHAT ARE MY RIGHTS AS A SUBJECT?

Your participation in this study is entirely voluntary. You may refuse to participate or withdraw once the study has started. You do not give up any legal rights by participating in this study.

WHAT COSTS ARE INVOLVED?

There is no cost to you for participating in this study.

WILL I BE PAID TO PARTICIPATE IN THIS STUDY?

You will receive a $5 gift card upon completion of the 8-week study.

WHO DO I CALL IF I AM INJURED AS A RESULT OF BEING IN THIS STUDY?

If you feel you have been injured by taking part in this study, consult with a physician or call 911 if the situation is a medical emergency. No funds have been set aside nor any plans made to compensate you for time lost for work, disability, pain or other discomforts resulting from your participation in this research.

WHO DO I CALL IF I HAVE QUESTIONS?

Call 909-558-4647 or e-mail patientrelations@llu.edu for information and assistance with complaints or concerns about your rights in this study.
SUBJECT'S STATEMENT OF CONSENT

- I have read the contents of the consent form and have listened to the verbal explanation given by the investigator.
- My questions concerning this study have been answered to my satisfaction.
- Signing this consent document does not waive my rights nor does it release the investigators, institution or sponsors from their responsibilities.
- I may call JeJe Noval during routine office hours at (909) 558-1000 ext:87462 if I have additional questions or concerns.
- I hereby give voluntary consent to participate in this study.

I understand I will be given a copy of this consent form after signing it.

Signature of Subject ___________________________ Printed Name of Subject ___________________________

Date ___________________________

INVESTIGATOR'S STATEMENT

I have reviewed the contents of this consent form with the person signing above. I have explained potential risks and benefits of the study.

Signature of Investigator ___________________________ Printed Name of Investigator ___________________________

Date ___________________________
Appendix B

Demographics Questionnaire

Subject #

Please answer all of the following questions. If the question is not applicable please write N/A.

1. How old are you? ______ years

2. What is your height? ______ ft. ______ in

3. What is your weight? ______ lbs.

4. Please circle: Male Female

5. How many days per week do you exercise for at least 30 minutes? ________

6. What type of exercise do you do? If multiple types of exercise, please list below (ex: weightlifting and cardio)

7. Do you have the following? If so, check the appropriate condition.
   _____ Cardiovascular Diseases _____ Gastroesophageal Reflux Disease
   _____ Diabetes _____ Rheumatoid arthritis
   _____ Cancer _____ Other autoimmune disease: ________
   _____ Metabolic Syndrome

8. Are you taking any of the following medications? If so, check the appropriate medication and how often.
   _____ Aspirin _____ Counadin
   _____ Pain medication _____ Heparin
   _____ NSAIDs (Advil, Aleve, Motrin, Excedrin, Midol, Nuprin)
   How often? ____________________________

9. Are you currently taking ginger supplements more than once per week?

10. Are you taking any other supplements? If so, what are they & how long have you been taking them?

11. Would you like to be contacted for compliance?
    _____ Email - weekly  _____ Text message - weekly
Volunteers Needed for Inflammation Study!

We are looking volunteers for a graduate research study titled, "The Effects of Ginger Supplementation on Inflammation in Exercising Individuals"

WHO: Healthy LLU faculty & staff, family, or friends between 30 and 70 years of age, who exercise at least once per week for 30 minutes.

You are excluded from the study if you are currently taking steroids, aspirin, NSAIDS, Coumadin, Ginger supplements, pain meds, and heparin more than 1x/week within the last month.

You will also be excluded if you have any chronic inflammatory conditions such as Cancer, CVD, Diabetes, GERD, Ginger allergies, Metabolic Syndrome, autoimmune diseases such as Rheumatoid Arthritis, and/or Phenylketonuria (PKU).

WHAT: 3 g ginger supplement daily for 8 weeks, demographic questionnaire & Quality of Life Survey (SF-36)

WHERE:
Clinical Molecular Lab Nichol Hall A117

3 sessions only – approximately 30-45 minutes per session

PRINCIPAL INVESTIGATOR: JeJe Noval, PhD, RDN

* A $5 gift card will be provided at the end of the study.*

For further information

CONTACT: Graduate Student Investigator: Sara Kashlan – skashlan@llu.edu