JOURNAL OF
EMERGING INVESTIGATORS

Article

Reducing levels of C-Reactive Protein: An eight-week, open-label clinical trial of three oral supplements

James H. Henter[1], Ioline D. Henter[2]

[1] Monticello High School, Charlottesville, Virginia

[2] National Institute of Mental Health, National Institutes of Health, Bethesda, Maryland

SUMMARY

C-reactive protein (CRP) is a protein in the blood that increases with inflammation, and high CRP levels measured with high-sensitivity CRP (hs-CRP) tests can indicate higher risk of heart attack or stroke. Several over-the-counter oral supplements reduce CRP levels. This eight-week, open-label clinical trial investigated whether Vitamin C, ginger, or curcumin were most effective at reducing hs-CRP levels in healthy individuals with low baseline hs-CRP levels. Thirty healthy male and female participants were enrolled in one of three trial treatment arms: Vitamin C (1000 mg/day), ginger (2000 mg/day), and curcumin (1000 mg/day). hs-CRP levels were collected at baseline and after eight weeks of oral supplements. Paired t-tests were used to analyze data by age, body mass index (BMI), and baseline hs-CRP level. The primary outcome measure was mean difference between time points and 95% confidence intervals. Twenty-six people completed the study. Baseline hs-CRP levels were very low for all three intervention groups. Based on estimated mean difference, all three supplements reduced hs-CRP levels, but change at eight weeks was not statistically significant. Within the groups, ginger most consistently reduced hs-CRP levels even though the ginger group had the lowest mean baseline hs-CRP levels. Curcumin was least likely to reduce hs-CRP levels. Overall, all three interventions reduced hs-CRP levels in this group of healthy participants with low baseline levels, suggesting that these agents, which are available over-the-counter, may provide an alternative for reducing inflammation. Larger clinical trials to assess the utility of these agents are warranted.

INTRODUCTION

C-reactive protein (CRP) is a protein in the blood that increases with inflammation, the body's way of protecting tissues from injury or infection (1). Regular CRP tests are used to detect serious bacterial infections or inflammatory conditions (2). Traditionally, CRP levels lower than 3.0 mg/L are considered normal, levels of 3.0 to 10.0 mg/L represent minor elevations, levels above 10.0 mg/L are considered moderate, and levels of 100 to 500 mg/L are considered elevated (3). Elevated CRP levels can be caused by a wide variety of inflammatory conditions. These include rheumatoid arthritis, chronic lung conditions, cancer, diabetes, hypertension, inflammatory bowel disease and, most commonly, bacterial and viral infections (1; 4; 5). Several other factors are also known to affect CRP levels, including body mass index (BMI), cigarette smoking, phase of menstrual cycle, estrogen replacement therapy, cholesterol levels, and genetic polymorphisms in the *CRP* gene (1). While regular CRP tests are useful for people with serious infections or inflammatory diseases, high-sensitivity CRP (hs-CRP) tests can detect slight elevations in CRP levels that would otherwise go unnoticed but that provide a valuable biomarker for assessing risk of heart disease (6). In particular, high hs-CRP levels can indicate inflammation in the arteries of the heart, meaning that there is a higher risk of heart attack or stroke. In terms of risk for developing heart disease, hs-CRP values of <1.0 mg/L are considered low risk, 1.0 to 2.9 are considered intermediate risk, and >3.0 are considered high risk (7). Several interventions, including a number of over-the-counter oral supplements, have been found to reduce CRP levels, but few studies have compared these supplements head-to-head or studied them in individuals whose baseline CRP levels are low.

Three oral supplements that have previously been shown to reduce CRP levels are Vitamin C, ginger, and curcumin (turmeric). Two recent meta-analyses found that ginger at doses of 1000-3000 mg/day significantly reduced CRP levels in patients with a variety of diagnoses. The first study, a meta-analysis of 16 randomized controlled clinical trials (n = 1010) found that ginger reduced hs-CRP levels by a standardized mean difference of 0.88 points (8). The second meta-analysis of nine studies (n = 449) found that it reduced CRP levels by a weighted mean difference of 0.84 points (9).

With regard to Vitamin C, a meta-analysis of 12 studies (n =893) found that Vitamin C in doses ranging from 250-1000 mg/day reduced CRP levels by 0.23 mg/L in patients with a wide variety of diagnoses (10). In addition, a randomized, placebo-controlled, double-blind trial in 151 patients with diabetes and hypertension undergoing hemodialysis found that 250 mg intravenous (IV) three times per week of Vitamin C significantly reduced CRP levels from an average of 16.8 mg/L to 10.7 mg/L (11). Interestingly, an eight-week study found that 1000 mg/day of Vitamin C reduced median CRP levels by 25% in healthy non-smokers with normal CRP levels (12).

In regard to curcumin, an eight-week, randomized, double-blind clinical trial enrolled 70 patients with mild-to-moderate ulcerative colitis and found that 1500 mg/day of curcumin reduced hs-CRP levels by 6.3 points (13). Another study found that four weeks of treatment with 300 mg/day of curcumin significantly reduced CRP levels in patients with Takayasu arteritis compared to placebo (14). In addition, a randomized, double-blind, placebo-controlled, three-armed,

parallel group study of 24 patients with rheumatoid arthritis compared two doses of a curcumin/bioperine complex: 500 mg/day (n = 12) and 1000 mg/day (n = 12) for 90 days. The study found that both doses significantly reduced CRP levels (15).

Most studies that have investigated the effectiveness of over-the-counter oral supplements in reducing CRP or hs-CRP levels have studied individuals whose CRP or hs-CRP levels were already high rather than individuals with hs-CRP levels below 3.0 mg/L. Thus, it remains unknown how these supplements reduce hs-CRP levels in those whose hs-CRP levels fall into the "normal" range of below 3.0 mg/L. One study that looked at CRP levels in healthy individuals found that Vitamin C had no effect in patients with the lowest CRP levels (<0.85 mg/L), but that individuals with the highest CRP levels at baseline had the greatest reductions in their levels after eight weeks (12).

This eight-week, open-label clinical trial investigated whether oral supplements of Vitamin C (1000 mg/day), ginger (2000 mg/day), or curcumin (1000 mg/day) were most effective at reducing hs-CRP levels. Participants were healthy males and females with normal hs-CRP levels at baseline who were not diagnosed with any chronic inflammatory diagnoses. Of the supplements known to reduce CRP, Vitamin C has been studied over many years and has consistently been shown to reduce CRP levels. Thus, the hypothesis was that Vitamin C would lead to the largest reductions in hs-CRP levels. Overall, baseline hs-CRP levels were found to be very low for all three intervention groups, and all three interventions reduced hs-CRP levels in this group of healthy participants, though change at eight weeks was not statistically significant. Within the groups, ginger most consistently reduced hs-CRP levels even though the ginger group had the lowest mean baseline hs-CRP levels. Curcumin was least likely to reduce hs-CRP levels.

RESULTS

Study groups

Thirty people (15M/15F) enrolled in the study, 10 in each study intervention. However, only 26 people completed the study **(Table 1)**. Reasons for not completing the study included having a viral illness that inflated baseline hs-CRP levels (n = 2, one in the Vitamin C group and one in the curcumin group), a second hs-CRP test being lost in the mail and not received by the laboratory (n = 1, in the ginger group), and insufficient blood sample for the lab to process the second hs-CRP test (n = 1, in the Vitamin C group).

Although other studies have found that BMI correlates with CRP or hs-CRP level, the correlation in this sample was only weakly positive (r = 0.21). Similarly, the correlation between age and hs-CRP level was only weakly positive (r = 0.21). Age and BMI showed moderate positive correlation (r = 0.33).

	Vitamin C (n = 8; 1M/7F)			Ginger (n = 9; 5M/4F)			Curcumin (n = 9; 6M/3F)		
Age	Mean	SD	Median	Mean	SD	Median	Mean	SD	Median
Baseline	42.1	19.1	49.5	48.2	12.8	50	36.4	17.6	50
At 8 weeks	42.3	18.9	49.5	48.3	12.9	50	36.4	17.6	50
BMI	Mean	SD	Median	Mean	SD	Median	Mean	SD	Median
Baseline	23.7	3.14	24.2	26.2	5.88	25.1	24.7	4.2	23.5
At 8 weeks	23.7	2.96	24.2	26.3	6.28	24.9	24.6	4.3	23.8
hs-CRP Level	Mean	SD	Median	Mean	SD	Median	Mean	SD	Median
Baseline	1.25	1.2	0.8	0.8	1.0	0.3	1.4	2.06	0.4
At 8 weeks	0.74	0.43	0.75	0.49	0.42	0.3	1.2	1.6	0.4

Table 1: Sample characteristics for the three intervention groups. Abbreviations: BMI: body-mass index; hs-CRP: high-sensitivity C-reactive protein; SD: standard deviation.

	Estimated Mean Difference [95% CI] Vitamin C vs Ginger	Estimated Mean Difference [95% CI] Vitamin C vs Curcumin	Estimated Mean Difference [95% CI] Ginger vs Curcumin
Age			
Baseline	6.12 [-10.52, 22.76]	5.66 [-13.31, 24.63]	11.78 [-3.61, 27.17]
At 8 weeks	6.08 [-10.47, 22.63]	5.81 [-13.04, 24.66]	11.89 [-3.54, 27.32]
BMI			
Baseline	2.48 [-2.49, 7.45]	0.92 [-2.96, 4.8]	1.56 [-3.55, 6.67]
At 8 weeks	2.6 [-2.59, 7.79]	0.9 [-2.97, 4.77]	1.7 [-3.68, 7.08]
hs-CRP Level			
Baseline	0.45 [-0.69, 1.59]	0.15 [-1.65, 1.95]	0.6 [-1.0, 2.24]
At 8 weeks	0.25 [-0.19, 0.69]	0.44 [-0.8, 1.69]	0.69 [-0.48, 1.86]

Table 2: Between-group differences at baseline and eight weeks. Abbreviations: BMI: body-mass index; hs-CRP: high-sensitivity C-reactive protein; CI: confidence interval.

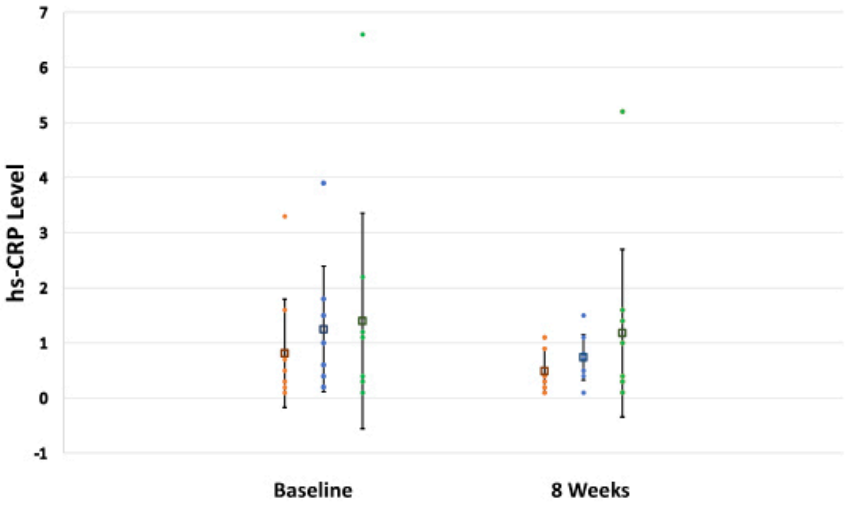

Figure 1: hs-CRP level for all groups at all timepoints. Scatterplot showing the relationship between hs-CRP levels in the ginger (orange), Vitamin C (blue), and curcumin (green) groups at baseline and eight weeks. Black bars represent 95% confidence intervals. Squares mark the mean values.

Reflecting the fact that all participants were healthy volunteers, baseline hs-CRP levels were in the lower end of the normal range for all three intervention groups. Mean hs-CRP levels at baseline were 1.25 mg/L for Vitamin C, 0.8 mg/L for ginger, and 1.4 mg/L for curcumin, and median hs-CRP levels at baseline were 0.8 mg/L for Vitamin C, 0.3 mg/L for ginger, and 0.4 mg/L for curcumin **(Table 1)**.

There were no statistically significant differences in age, BMI, or hs-CRP levels between any of the groups at baseline or at eight weeks **(Table 2; Figure 1)**. All three supplements were well-tolerated; none of the participants in any of the three intervention groups reported any noticeable side effects, either positive or negative.

Within-group differences

All three supplements reduced hs-CRP levels. The estimated mean difference was 0.51 for the Vitamin C group, 0.31 for the ginger group, and 0.22 for the curcumin group. However, there was no statistically significant difference in the overall change at eight weeks because point estimates for change in hs-CRP level were all contained in the other confidence intervals, indicating that the *p*-value for differences between the groups would be >0.05. All 95% confidence intervals also crossed zero **(Table 3)**.

Within the groups, ginger most consistently reduced hs-CRP levels **(Figure 2)**. Specifically, six of the nine participants (67%) in the ginger-treated group demonstrated reduced hs-CRP levels; hs-CRP levels increased in one participant (11%) and stayed the same in two participants (22%). In contrast, in the Vitamin C group, five of the eight participants showed reduced hs-CRP levels (63%), but hs-CRP levels went up in the other three participants (37%). In the curcumin group, only four of the nine participants had reduced hs-CRP levels (44%); hs-CRP levels went up in three participants (33%) and stayed the same in two participants (22%). This suggests that of the three interventions, curcumin was the least likely to reduce hs-CRP levels.

	T Value	*P* Value	Degrees of Freedom	Estimated Mean Difference [95% CI]
Age: Change from Baseline to 8 Weeks				
Vitamin C	-1.0	0.35	7	0.15 [-19.46, 19.76]
Ginger	-1.0	0.35	8	0.10 [-12.73, 12.95]
Curcumin*	n/a	n/a	n/a	n/a
BMI: Change from Baseline to 8 Weeks				
Vitamin C	0.26	0.80	7	0.03 [-3.24, 3.3]
Ginger	-0.36	0.73	8	0.10 [-5.98, 6.18]
Curcumin	0.34	0.74	8	0.06 [-4.19, 4.31]
hs-CRP Level: Change from Baseline to 8 Weeks				
Vitamin C	1.31	0.23	7	0.51 [-0.46, 1.48]
Ginger	1.12	0.29	8	0.31 [-0.46, 1.08]
Curcumin	0.33	0.75	8	0.22 [-1.62, 2.06]

Table 3: Within-group differences from baseline to eight weeks. *Mean age in the curcumin group did not change from baseline to the end of the eight-week study period. Abbreviations: BMI: body-mass index; hs-CRP: high-sensitivity C-reactive protein; CI: confidence interval.

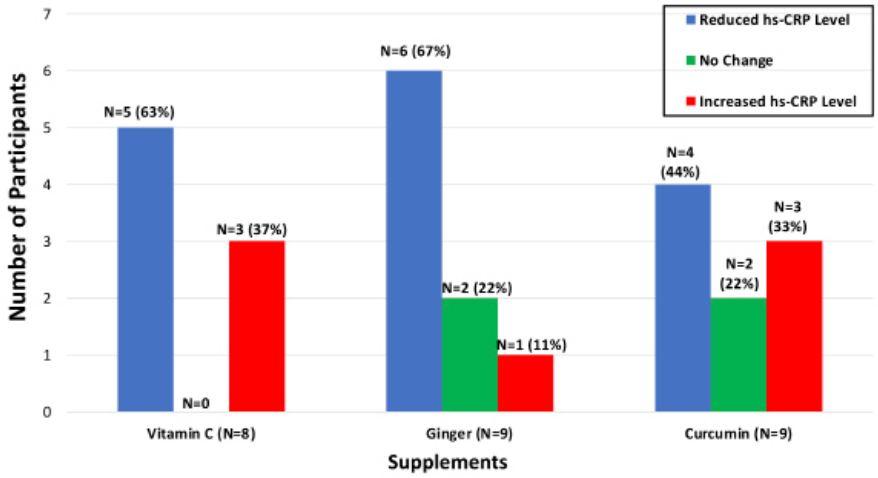

Figure 2: The number of participants whose hs-CRP levels decreased, stayed the same, or increased in the Vitamin C, ginger, and curcumin groups.

DISCUSSION

This eight-week, open-label study investigated whether oral supplements of Vitamin C (1000 mg/day), ginger (2000 mg/day), or curcumin (1000 mg/day) were most effective at reducing hs-CRP levels. Twenty-six healthy male and female participants with normal hs-CRP levels who were not diagnosed with any chronic inflammatory diagnoses took part in this study. The key finding was that all three interventions reduced hs-CRP levels, even though baseline hs-CRP levels were very low across all three groups. Despite not being statistically significant, these results may still be clinically meaningful.

Few studies have investigated whether oral supplements can reduce CRP or hs-CRP levels in individuals whose levels are low to begin with (<3.0 mg/L). For instance, one study that looked at CRP levels in healthy individuals found that Vitamin C had no effect in participants with the lowest CRP levels (<0.85 mg/L), but that individuals with the highest CRP levels at baseline had the greatest reductions after eight weeks of Vitamin C (12).

In the present study, all three interventions reduced hs-CRP levels in this group of healthy participants; the initial study hypothesis that Vitamin C would most successfully reduce hs-CRP levels was not supported. These results are especially impressive when one considers that the baseline hs-CRP levels were very low for these three groups. All three oral supplements in this study were well-tolerated, and participants reported no side effects. Surprisingly, even though the ginger group had the lowest mean baseline hs-CRP level, it most consistently reduced hs-CRP levels—67% of participants in the ginger group had lower hs-CRP levels after the eight-week period versus 63% for the Vitamin C group and 44% for the curcumin group **(Figure 2)**. These findings corroborate two large recent meta-analyses that found that ginger at doses ranging from 1000-3000 mg/day significantly reduced CRP or hs-CRP levels (8; 9). It also suggests that ginger may be useful for reducing inflammation even in those whose CRP or hs-CRP levels are already considered low, a finding that has potential public health implications.

Interestingly, although all three supplements reduced mean hs-CRP levels across the eight weeks of the study, there was still significant variability in hs-CRP levels. For instance, across all three interventions, 15 of the 26 participants had hs-CRP levels that went down (58%), but seven of the 26 participants (27%) had hs-CRP levels that went up. Studies have found large intra-individual variations in circulating CRP levels that can be due to a variety of factors, including phase of menstrual cycle, BMI, cholesterol levels, and genetic polymorphisms (1). In addition, hs-CRP tests, like the type used in this study, are more sensitive than standard CRP tests to even small changes in CRP levels; such minor elevations in hs-CRP levels do not have to be clinically meaningful and may explain the variability observed in this study (16).

This study had several limitations. First, the sample size was small. It is possible that given the trends observed here, statistically significant results might have been identified with larger sample sizes. In addition, the fact that each intervention contained so few people made it impossible to compare hs-CRP levels by sex. Second, all participants were white, which suggests that the findings cannot be generalized to other racial groups. Third, there was no control group; because environmental factors like stress, diet, exercise, and seasonal variations in temperature might affect hs-CRP levels over an eight-week period, it would have been helpful to compare these results to a control group that received no supplements. Finally, the study was open-label and not randomized. All participants chose the intervention they were most interested in joining. To truly measure the effectiveness of these supplements, a randomized, double-blind, placebo-controlled study would be necessary. Because several other factors also affect CRP levels—for instance, higher BMI and cigarette smoking—it would also be interesting to repeat this experiment in non-healthy individuals who might be expected to have higher baseline CRP levels but no formal diagnosis.

Despite these limitations, this eight-week, open-label study in 26 healthy male and female participants found that over-the-counter oral supplements could effectively reduce hs-CRP levels in those with normal CRP levels at baseline. In particular, ginger reduced or did not alter hs-CRP levels in 89% of the participants in that study group, even though

baseline hs-CRP levels of ginger were only 0.8 mg/L. Though not statistically significant, this finding suggests that ginger may lower CRP or hs-CRP levels in a clinically meaningful way. Because lower CRP levels indicate lower levels of inflammation in the body, these findings could be important for public health reasons. Given the promising nature of this preliminary finding, future studies with larger sample sizes could help clarify the full extent of ginger's anti-inflammatory properties in individuals with low CRP or hs-CRP levels.

MATERIALS AND METHODS

Participants

Healthy male and female participants were enrolled in one of three trial treatment arms (n = 10 each): Vitamin C supplements (1000 mg/day), ginger supplements (2000 mg/day), and curcumin supplements (1000 mg/day). The group assignment was not random and was based on the interest of the participants in joining a particular treatment group. There were no age restrictions in the study. All participants were white, and none were cigarette smokers. Participants were recruited through the researchers' social network, and all gave written, informed consent to participate in the study. hs-CRP levels as well as age and BMI were collected twice: at baseline, before beginning the study intervention, and after eight weeks of oral supplements.

Exclusion criteria for all three groups included being diagnosed with an inflammatory condition (e.g., rheumatoid arthritis, ulcerative colitis, diabetes, etc.), regularly taking any anti-inflammatory medication (e.g., NSAIDs, aspirin, steroids, statins, blood pressure medications, diabetes medications, etc.), and not altering one's diet or exercise habits. In addition, individuals in the ginger group could not have a history of bleeding disorders, and those in the curcumin group could not have a history of gallstones or kidney stones or have an iron deficiency.

Supplements and CRP Testing

To collect hs-CRP levels, each participant was mailed two hs-CRP kits from an independent online laboratory (ZRT Labs, Beaverton, Oregon). The standard CRP test measures high levels of the CRP protein to find different diseases that cause inflammation. The hs-CRP test can measure CRP levels even when they are low and is typically used to focus on the risk of heart disease and stroke. Participants performed a finger stick test in their own homes and returned the test kit to the laboratory by mail, who informed them of the results. hs-CRP levels were measured twice—at baseline and after eight weeks.

All participants were also mailed an eight-week supply of oral supplements. For Vitamin C, this was either a 1000 mg/day capsule (Nature's Bounty; Ronkonkoma, NY), taken once per day, or a 500 mg chewable gummy, taken twice per day (KOS; Goleta, CA), depending on whether the participant requested a swallowable or chewable Vitamin C tablet. For ginger, capsules were 1000 mg each, taken twice per day (Pure Mountain Botanicals; Cheyenne, WY). For curcumin, capsules were 500 mg each, taken twice per day (Doctor's Best DRB-00107 high absorption curcumin with C3 Complex and BioPerine; Tustin, CA).

Costs for both the hs-CRP tests and the eight-week supply of supplements were borne by the researchers; there was no cost to any of the participants.

Data Analysis

The study sought to enroll 10 participants per treatment arm because this number was thought to be sufficient to observe an effect from the interventions; previous studies have suggested that all three interventions consistently reduce CRP or hs-CRP levels across different age groups (8-11; 13-15).

Correlations between hs-CRP levels, age, and BMI were run for the whole group. Within groups, data were analyzed by age, BMI, and baseline hs-CRP level to measure the impact of each of these variables. Because this was a within-subjects analysis, paired *t*-tests were used. T-values, *p*-values, and degrees of freedom were calculated. This study attempted to see whether there was an interaction between time point and intervention, so the primary outcome measure was mean difference between time points with 95% confidence intervals.

For all three groups (Vitamin C, ginger, and curcumin), mean and median values were calculated for age, BMI, and hs-CRP levels both at baseline and after eight weeks; change between treatment groups was also compared after eight weeks using estimated mean difference between time points and 95% confidence intervals.

All statistics were run in Microsoft Excel (version 16.46) except for confidence intervals, which were run using an online statistical calculator (17). The alpha value was 0.05, therefore a *p*-value <0.05 was considered statistically significant.

CLARIFICATION

Ms. Henter is a full-time employee of the National Institute of Mental Health. This work was conducted in her private capacity and the views expressed do not necessarily reflect the views of the NIH, the Department of Health and Human Services, or the United States Government.

Received: September 6, 2021
Accepted: November 12, 2021
Published: January 20, 2022

REFERENCES

1. Dhingra, Ravi *et al*. "C-Reactive Protein, Inflammatory Conditions and Cardiovascular Disease Risk." Am J Med, vol. 120, 2007, pp. 1054-1062, doi:10.1016/j.amjmed.2007.08.037.
2. Verbakel, J.Y. *et al*. "Should All Acutely Ill Children in Primary Care Be Tested with Point-of-Care CRP: A Cluster Randomised Trial." BMC Med, vol. 14, 2016, p. 131.
3. Nehring, S.M. *et al*. "C Reactive Protein [Updated 2021 May 10]. Available Online at Https://Www.Ncbi.Nlm.Nih.Gov/Books/Nbk441843." Statpearls [Internet], StatPearls Publishing, 2021.
4. Landry, Alexander *et al*. "Causes and Outcomes of Markedly Elevated C-Reactive Protein Levels." Can Fam Physician, vol. 63, 2017, pp. e316-e323.
5. Ridker, Paul M. "C-Reactive Protein, Inflammation, and Cardiovascular Disease: Clinical Update." Tex Heart Inst J, vol. 32, 2005, pp. 384-386.
6. Kamath, D.Y. *et al*. "High Sensitivity C-Reactive Protein (hsSCRP) & Cardiovascular Disease: An Indian Perspective." Indian J Med Res, vol. 142, 2015, pp. 261-268.
7. Musunuru, Kiran *et al*. "The Use of High Sensitivity

Assays for C-Reactive Protein in Clinical Practice." Nat Clin Pract Cardiovasc Med, vol. 5, 2008, pp. 621-635, doi:10.1038/ncpcardio1322.
8. Morvaridzadeh, Mojgan *et al*. "Effect of Ginger (Zingiber Officinale) on Inflammatory Markers: A Systematic Review and Meta-Analysis of Randomized Controlled Trials." Cytokine, vol. 60, 2020, p. 155224, doi:10.1016/j.cyto.2020.155224.
9. Mazidi, Mohsen *et al*. "The Effect of Ginger Supplementation on Serum C-Reactive Protein, Lipid Profile and Glycaemia: A Systematic Review and Meta-Analysis." Food Nutr Res, vol. 60, 2016, p. 32613, doi:10.3402/fnr.v60.32613.
10. Jafarnejad, Sadegh *et al*. "A Meta-Analysis of Randomized Control Trials: The Impact of Vitamin C Supplementation on Serum CRP and Serum hs-CRP Concentrations." Curr Pharm Des, vol. 24, 2018, pp. 3520-3528, doi:10.2174/1381612824666181017101810.
11. Binaiz, Vajihe *et al*. "Effect of Vitamin C Supplementation on C-Reactive Protein Levels in Patients Undergoing Hemodialysis: A Randomized, Double Blind, Placebo-Controlled Study." Nephrourol Mon, vol. 6, 2013, p. e13351, doi:10.5812/numonthly.13351.
12. Block, Gladys *et al*. "Vitamin C Treatment Reduces Elevated C-Reactive Protein." Free Radic Biol Med, vol. 46, 2009 pp. 70-77, doi:10.1016/j.freeradbiomed.2008.09.030.
13. Sadeghi, Narges *et al*. "The Effect of Curcumin Supplementation on Clinical Outcomes and Inflammatory Markers in Patients with Ulcerative Colitis." Phytother Res, vol. 34, 2020, pp. 1123-1133, doi:10.1002/ptr.6581.
14. Shao, Nan *et al*. "Curcumin Improves Treatment Outcome of Takayasu Arteritis Patients by Reducing TNF-A: A Randomized Placebo-Controlled Double-Blind Clinical Trial." Immunol Res, vol. 65, 2017, pp. 969-974, doi:10.1007/s12026-017-8917-z.
15. Amalraj, Augustine *et al*. "A Novel Highly Bioavailable Curcumin Formulation Improves Symptoms and Diagnostic Indicators in Rheumatoid Arthritis Patients: A Randomized, Double-Blind, Placebo-Controlled, Two-Dose, Three-Arm, and Parallel-Group Study." J Med Food, vol. 10, 2017, pp. 1022-1030, doi:10.1089/jmf.2017.3930.
16. Kushner, Irving *et al*. "What Does Minor Elevation of C-Reactive Protein Signify?." Am J Med, vol. 119, 2006, pp. 166e117-166e128, doi:10.1016/j.amjmed.2005.06.057.
17. Social Science Statistics. "Available At: Www.Socscistatistics.Com."