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Consumption of Dietary Flavonoids and Serum Levels of High-Sensitivity C-Reactive Protein in US Residents: A Cross-sectional Study Based on NHANES 2017-2018

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Abstract. Chronic low-grade inflammation is associated with the occurrence and development of many non-communicable diseases, and serum high-sensitivity C-reactive protein (hs-CRP) is a convenient indicator of systemic inflammation. Flavonoids are natural polyphenols in plants with antioxidant and anti-inflammatory properties, but there is little epidemiological data on various types of flavonoids. Cross-sectional Study of the Correlation between Regular Consumption of Dietary Flavonoids and Serum Levels of High-Sensitivity C-Reactive Protein (hs-CRP) in U.S. Residents Based on NHANES 2017-2018 Data and the USDA Flavonoid Database. A total of 3,426 people were over the age of 20. Weighted regression was used to address the problem of multi-stage sampling and control for confounders related to society and health. The higher the energy-norm total flavonoid intake, the lower the hs-CRP in consecutive quintiles. Subgroup analysis shows that flavan-3-ol and flavonol accounted for most of the decrease, and other groups of flavonoids were not independently related to it. Therefore, causality cannot be deduced from the cross-sectional method. Based on the two studies above, we will find out whether frequent consumption of flavonoids is harmful to or beneficial for prolonged low-grade inflammation in chronic diseases.

Keywords: Dietary flavonoids, Hs-CRP, Chronic low-grade inflammation, NHANES, Plant polyphenols

1. Introduction

Persistent low-grade inflammation is a basic physiological state in many chronic diseases that are not infectious, such as cardiovascular disease, type 2 diabetes and obesity. Serum high-sensitivity C-reactive protein (hs-CRP) is a common indicator of systemic inflammation in public health. Flavonoids are a general category of dietary polyphenols found in fruits and vegetables, tea, legumes, grains, nuts, other plant products, etc. Based on scientific and functional data, flavonoids can reduce oxidative stress and the various inflammatory pathways of nuclear factor kappa B and cytokines [1, 2]. Based on the above biological factors, we believe that frequent consumption of high doses of flavonoids by free-living people may lead to a reduction in systemic inflammation.

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Epidemiological Data Are Dispersed. Based on the analysis of NHANES 1999-2002, after correcting for diet, demographics and behaviour, total flavonoid intake was negatively correlated with serum C-reactive protein (CRP) levels [3]. Later, the NHANES study found that the higher the flavonoid intake, the lower the risk of obesity and elevated CRP levels [4]. Conversely, the Multiethnic Cohort did not find that the different self-reported flavonoid groups were associated with circulating inflammatory markers [5]. Diets that are pro-inflammatory have been associated with high levels of C-reactive protein (CRP) in meta-analyses [6], but recent umbrella reviews have found that the impact of different kinds of flavonoids varies with the time of measurement [7]. Therefore, the research on flavonoids and inflammation should be divided into subcategories and strictly control for energy intake and other confounders.

To correct the problems above, this paper has combined the NHANES 2017-2018 data with the USDA Flavonoid Values for Survey Foods and Beverages 2017-2018 dataset. This paper will present all types of flavonoids consumed by the US population, compare hs-CRP in different groups of flavonoid intakes, determine whether total flavonoids or certain types of flavonoids are associated with hs-CRP, and investigate whether this connection exists after adjusting for demographic information, lifestyle factors and health conditions. Many recent studies have repeatedly found that dietary flavonoids are associated with higher levels of CRP and other unhealthy conditions, according to NHANES data [8], and in 2017-2018, new evaluations were also conducted using the flavonoid database [9].

2. Methodology

2.1. Data source and study population

According to the public data from the NHANES 2017-2018 cycle released by the National Centre for Health Statistics, a cross-sectional observational study was carried out. The multi-stage probability sampling method of NHANES is employed to collect national data on the civilian noninstitutionalised population in the United States. According to the food identification code in the dietary food-level record, the flavonoid content data were obtained from the USDA Flavonoid Values for Survey Foods and Beverages 2017-2018 database [9].

The subjects were all over the age of 20. The reasons for exclusion were: pregnancy, lack of serum hs-CRP data, insufficient 24-hour dietary recall information, and excessively high self-reported caloric intake. Based on the above criteria, 3,426 subjects were finally selected for the observation group.

2.2. Dietary flavonoid intake assessment

The subject reported their food intake in the last 24 hours. All the listed items have been cross-referenced with the relevant data in the USDA flavonoid database, and 29 new flavonoids have been obtained from the six main categories [9]. Daily total flavonoid intake is the sum of the number of flavonoids in all food and drink. The six divisions were evaluated individually: anthocyanidin, flavan-3-ol, flavanone, flavone, flavonol and isoflavone.

Nutrient density is employed to reduce the confounding effect of total food and calorie intake. Energy-adjusted flavonoid consumption is the number of flavonoids per 1,000 kcal of total daily energy expenditure. Both the total daily intake in mg per day and the energy-adjusted intake in mg per 1,000 kcal were kept for quantitative analysis.

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2.3. Variables and confounders

Serum hs-CRP was the main end point. In the NHANES 2017-2018 period, the dual-reagent immunoturbidimetric laboratory method was employed to measure hs-CRP [10]. Given that the distribution of the raw HS-CRP data is highly right-skewed, we have taken the logarithm of it to obtain a continuous dependent variable for the survey-weighted linear regression model. According to the weights in the survey, logistic regression was applied to the group of people with hs-CRP ≥ 3.0 mg/L.

The first causes of bias were derived from epidemiology. Demographic factors are age, sex, race/ethnicity, income and poverty. Lifestyle factors are smoking, drinking alcohol, exercising regularly and total daily calories. Health Factors: Body Mass Index (BMI) and self-reported history of chronic diseases. All these were added to the regression.

2.4. Statistical analysis

All the investigations have taken into account the particular population factors, sampling groups and central sampling units of NHANES in their work on probability sampling. Continuous and nominal attributes are presented as survey-estimated descriptive statistics.

Multiple linear regression is used to determine how the total intake and some kinds of flavonoids affect log-transformed hs-CRP. Gradually add the factors of sociodemographics, behaviour and health to the model as independent variables. Then, the energy-adjusted total flavonoid intake was divided into five groups to see if it was higher among high consumers.

Multivariate logistic regression with survey weights was used to examine the association between flavonoid intake and high hs-CRP. The same step-by-step addition of covariates was carried out for the linear models. Based on a two-tailed test, it was decided that the significance level was $P < 0.05$.

3. Results

According to the above inclusion and exclusion criteria, finally, 3,426 eligible US residents were included in the analysis. Demographic and Clinical information are shown in Table 1. The weighted mean age was 47.2 years, and females accounted for 51.2 per cent of the whole. The mean BMI of the subjects was 29.4 kg/m², and 42.7 per cent of them were obese (BMI ≥ 30 kg/m²); among these, 26.8 per cent had hs-CRP levels exceeding 3.0 mg/L (Table 1).

Table 1. Weighted baseline characteristics of study participants

Variable	Weighted mean ± SE / Weighted %
Age, years	47.2 ± 0.7
Female, %	51.2
BMI, kg/m²	29.4 ± 0.3
Current smoker, %	31.4
Obesity (BMI ≥ 30), %	42.7
hs-CRP > 3.0 mg/L, %	26.8

The median daily consumption of the six flavonoid groups is shown in Table 2. Flavan-3-ols had the highest median daily consumption at 186.5 mg/day; flavanones were 87.1 mg/day and

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anthocyanidins were 62.3 mg/day. Isoflavones had the lowest median intake at 2.8 mg/day, and the total exposure of all these flavonoid groups was relatively small (Table 2).

Table 2. Median daily intake of flavonoid subclasses

Flavonoid subclass	Median intake (mg/day)
Anthocyanidins	62.3
Flavan-3-ols	186.5
Flavanones	87.1
Flavones	13.8
Flavonols	37.4
Isoflavones	2.8

Figure 1 shows the geometric mean of hs-CRP in quintiles of energy-modified total flavonoid consumption. The geometric mean of hs-CRP was lower in the higher quintiles than in the lower quintiles. The concentration of inflammatory markers in Q1 was the highest, and it was lowest in Q5. Therefore, it is proposed that increased consumption of total flavonoids may reduce inflammation in the body.

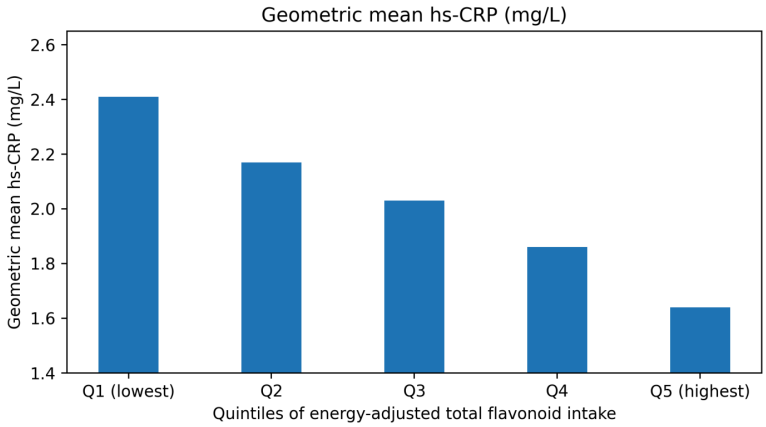


Figure 1. Mean hs-CRP in the quintiles of total flavonoid intake (energy-adjusted) (original image source)

Geometric mean concentrations of hs-CRP are in Table 3. Adjusting for covariates, the geometric mean hs-CRP in Q1 was 2.41 mg/L, and it had dropped to 1.64 mg/L by Q5. The Q5 was about 32% lower than the Q1, and the drop in each subsequent category of intake also showed the same inverse relationship with exposure (Table 3).

Table 3. Adjusted geometric mean hs-CRP by quintile of total flavonoid intake

Quintile of total flavonoid intake	Geometric mean hs-CRP (mg/L)	95% CI
Q1 (lowest)	2.41	2.27-2.56
Q2	2.17	2.04-2.31

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Table 3. (continued)

Q3	2.03	1.91-2.16
Q4	1.86	1.74-1.99
Q5 (highest)	1.64	1.53-1.76

All the multivariate models show that a high energy-adjusted consumption of comprehensive flavonoids is related to lower levels of serum hs-CRP and an increased risk of overt inflammation. The above results indicate that the protective correlation is mainly among flavan-3-ols and flavonols. Anthocyanins, flavanones, flavones and isoflavones did not show a significant individual association after all multivariate corrections.

4. Discussion

4.1. Main findings

A nationwide survey of U.S. citizens found that people have different amounts of dietary flavonoids, and the more flavonoids in their diet, the lower their plasma hs-CRP levels are. Add the demographic, behaviour and wellness confounding variables, and then check again. Subgroup analysis shows that flavan-3-ols and flavonols are associated with a higher level of hs-CRP, and the other subgroups do not have an independent effect. According to the previous NHANES studies [3, 4], flavonoid consumption is also associated with lower levels of hs-CRP. Based on the above, it is known that several flavonoids can reduce oxidative stress and inflammation, and also regulate the immune system [1, 2].

The individual differences in the amounts of flavonoids and their functions are relatively small. Previous cohort studies have not uniformly linked all categories of flavonoids to changes in inflammatory markers in the blood [5], and, on the other hand, various groups of flavonoids have shown different effects on health [7]. Therefore, this paper proposes that the subclasses should be studied individually rather than as a whole. Recent studies on NHANES have also found that CRP may be involved in the relationship between flavonoid consumption and the duration of illness [8], and widespread inflammation is now regarded as one of the reasons.

4.2. Limitations and future perspectives

Many constraints must be addressed. First of all, a cross-sectional design cannot show changes over time, so it is not causal. Second, the amount of dietary flavonoids was obtained from 24-hour recall records and may not reflect long-term regular intake; it is also subject to memory errors and daily fluctuations in diet. Thirdly, there is still residual confounding after several regressions. Fourthly, the observed correlations may be due to the overall diet of people who eat flavonoid-rich food, rather than a direct effect of flavonoid molecules. Finally, the results at the subclass level may have lower precision because the intake distributions and main food sources of different subgroups are quite different.

A prospective cohort study will be carried out to collect long-term data on diet and changes in inflammatory markers to determine if diet causes inflammation. Regularly adjust the diet to see if adding more foods rich in flavonoids can reduce levels of hs-CRP and other inflammation markers. Further research should differentiate among the main sources of diet, such as tea, fruits, vegetables

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and legumes; explore possible nonlinear exposure-response relationships; determine how these effects are modified by age, obesity, cardiometabolic conditions, smoking and other factors, etc. The above studies will help us know if the inverse associations in cross-sectional population data are also clinically significant anti-inflammatory effects.

5. Conclusion

Based on the cross-sectional study of nationally representative U.S. citizens, as energy-adjusted total dietary flavonoid intake increased on average, so too did the levels of circulating hs-CRP, a marker of systemic inflammation. The higher the quintile of flavonoid consumption, the lower the adjusted geometric mean hs-CRP; that is to say, the highest quintile had approximately 32% lower levels than the lowest quintile. Based on subgroup analysis, the main reason was flavan-3-ol and flavonol content; anthocyanidin, flavanon, flavone and isoflavone did not show an independent association after multiple adjustments for other variables. Therefore, the total flavonoid content may not adequately represent the differences among various groups of flavonoids, and separate assessments of these subclasses can provide additional information on the association between plant-based food components and inflammation.

The results are only observational correlations and do not prove that they are caused by anti-inflammation. The cross-sectional NHANES framework cannot determine whether the increase in flavonoid intake occurred before the decrease in hs-CRP levels, and a single day's dietary recall may not be representative of regular food intake. Unmeasured residual confounding may be due to general diet and lifestyle, other unobserved clinical factors, etc. However, there is also a general decrease in hs-CRP as the lower quintiles of intake increase; this will be investigated further. Regular follow-up studies should be conducted to observe any changes in diet and biomarkers over time, determine whether there is a sustained association, and randomised dietary trials need to be carried out to ascertain if increasing the consumption of flavonoid-rich food can reduce inflammation in the body. Further studies should also examine the different origins of flavonoids in food and determine whether the associations vary with age, overweight status, metabolic syndrome, etc. The above data can help us know what functions dietary flavonoids have in managing chronic diseases.

References

[1] Al-Khayri, J. M., Sahana, G. R., Nagella, P., Joseph, B. V., Alessa, F. M., & Al-Mssallem, M. Q. (2022). Flavonoids as potential anti-inflammatory molecules: A review. *Molecules, 27*(9), 2901. https://doi.org/10.3390/molecules27092901

[2] Rakha, A., Umar, N., Rabail, R., Butt, M. S., Kieliszek, M., Hassoun, A., & Aadil, R. M. (2022). Anti-inflammatory and anti-allergic potential of dietary flavonoids: A review. *Biomedicine & Pharmacotherapy, 156*, 113945. https://doi.org/10.1016/j.biopha.2022.113945

[3] Chun, O. K., Chung, S.-J., Claycombe, K. J., & Song, W. O. (2008). Serum C-reactive protein concentrations are inversely associated with dietary flavonoid intake in U.S. adults. *The Journal of Nutrition, 138*(4), 753-760. https://doi.org/10.1093/jn/138.4.753

[4] Vernarelli, J. A., & Lambert, J. D. (2017). Flavonoid intake is inversely associated with obesity and C-reactive protein, a marker for inflammation, in U.S. adults. *Nutrition & Diabetes, 7*(5), e276. https://doi.org/10.1038/nutd.2017.22

[5] Rohrmann, S., Shvetsov, Y. B., Morimoto, Y., Wilkens, L. R., Monroe, K. R., Le Marchand, L., Franke, A. A., Kolonel, L. N., & Maskarinec, G. (2018). Self-reported dietary flavonoid intake and serum markers of inflammation: The Multiethnic Cohort. *Cancer Causes & Control, 29*(6), 601-607. https://doi.org/10.1007/s10552-018-1034-z

DOI: 10.54254/2753-8818/2027.MB39325

[6] Mohammadi, S., Hosseinikia, M., Ghaffarian-Bahraman, A., Clark, C. C. T., Davies, G. I., Yousefi Rad, E., & Saboori, S. (2023). Dietary inflammatory index and elevated serum C-reactive protein: A systematic review and meta-analysis. *Food Science & Nutrition, 11*(10), 5786-5798. https://doi.org/10.1002/fsn3.3553

[7] Li, H., Zeng, Y., Zi, J., Hu, Y., Ma, G., Wang, X., Shan, S., Cheng, G., & Xiong, J. (2024). Dietary flavonoids consumption and health: An umbrella review. *Molecular Nutrition & Food Research, 68*(12), e2300727. https://doi.org/10.1002/mnfr.202300727

[8] Jiang, F., Zheng, T., & Li, Y. J. (2025). The mediating role of C-reactive protein (CRP) in the dietary intake of flavonoids and the risk of albuminuria. *Food & Function, 16*(2), 452-460. https://doi.org/10.1039/D4FO03589E

[9] Sebastian, R. S., Martin, C. L., Goldman, J. D., & Moshfegh, A. J. (2022). Flavonoid values for USDA survey foods and beverages 2017-2018. U.S. Department of Agriculture, Agricultural Research Service, Food Surveys Research Group. https://www.ars.usda.gov/nea/bhnrc/fsrg

[10] National Center for Health Statistics. (2020). High-sensitivity C-reactive protein (HSCRP_J): NHANES 2017-2018 data documentation, codebook, and frequencies. Centers for Disease Control and Prevention. https://wwwn.cdc.gov/Nchs/Data/Nhanes/Public/2017/DataFiles/HSCRP_J.htm