THE EFFECT OF RAISINS ON ANTIOXIDANT CAPACITY AND CHOLESTEROL CONCENTRATIONS IN HUMAN SUBJECTS

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PROJECT SUMMARY

The putative cardioprotective effect of plant phenolics is hypothesized to result from their ability to modulate the processes of oxidation, inflammation, lipid regulation, and platelet activation. Due to the phenolic-rich nature of the raisin, it was reasonable to suggest that this fruit is particularly suited for conveying phenolic-mediated cardioprotective effect in humans. Therefore, the specific aim of this investigation was to determine the effect of consuming raisins (2, 3.5, and 5.5 oz/day) for 4 weeks on the following phenolic-sensitive parameters in healthy human subjects: (1) Plasma phenolic content (2) plasma antioxidant content (3) plasma lipid peroxide concentrations (4) blood lipid profiles. In addition, we assessed the impact of raisin consumption on platelet reactivity. No changes in phenolic content were detected in plasma drawn after overnight fasts at weeks 2 and 4 relative to week 0. As measured by the FRAP assay, but not the TRAP or DPPH assays, plasma antioxidant capacity increased in the high raisin treatment group at weeks 2 and 4 (relative to week 0). Total plasma lipid peroxide concentration was unchanged by treatment. However, circulating oxidized LDL, a useful marker for identifying patients with a high risk for coronary artery disease, was decreased in all treatment groups. Our assessment of platelet reactivity was also successful in its completion, but didn't show positive changes following raisin consumption. Collectively, these data illustrate how raisins can contribute as a healthy component of the 5 fruits/vegetables per day recommendation.

Currently, we foresee the preparation of this important scientific information for publication with the aim for submission to one of the leading nutrition journals. We suggest that potential follow-up experiments further delineate the ability of regular raisin consumption to influence risk factors for coronary artery disease such as circulating oxidized LDL, blood vessel reactivity, and potentially c-reactive protein in patients with cardiovascular disease.

Objective

To characterize the effects of consuming 2, 3.5, or 5.5 ounces of raisins, per day, for four weeks on plasma phenolics, antioxidant defense, oxidized lipids, cholesterol, and platelet function in 30 healthy human subjects. (Please note that the ounce dose was modified from the original proposed dose due to volume / weight conversion errors)

End Points

(1) Plasma Phenolic Content

(2) Ex-vivo Plasma Antioxidant Capacity

(3) Plasma Lipid Peroxide Concentrations

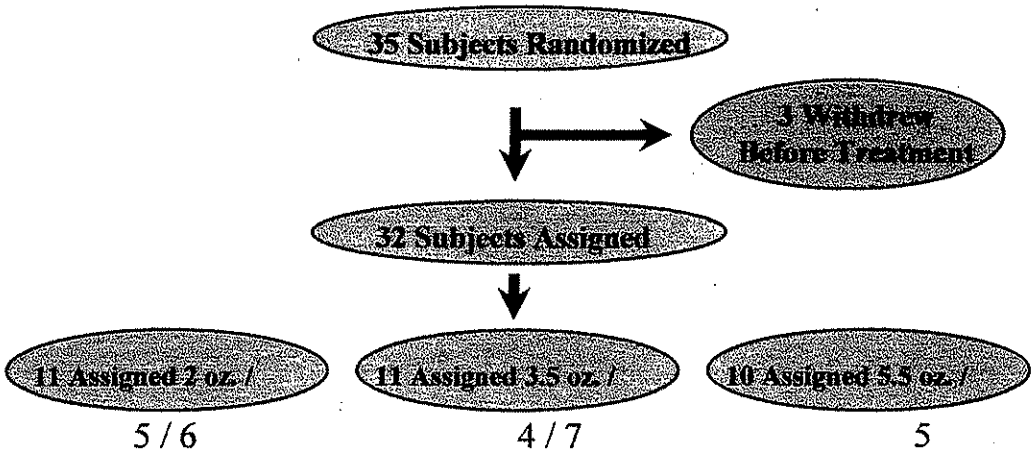
(4) Blood Lipid Profile

(5) Platelet Function Analysis

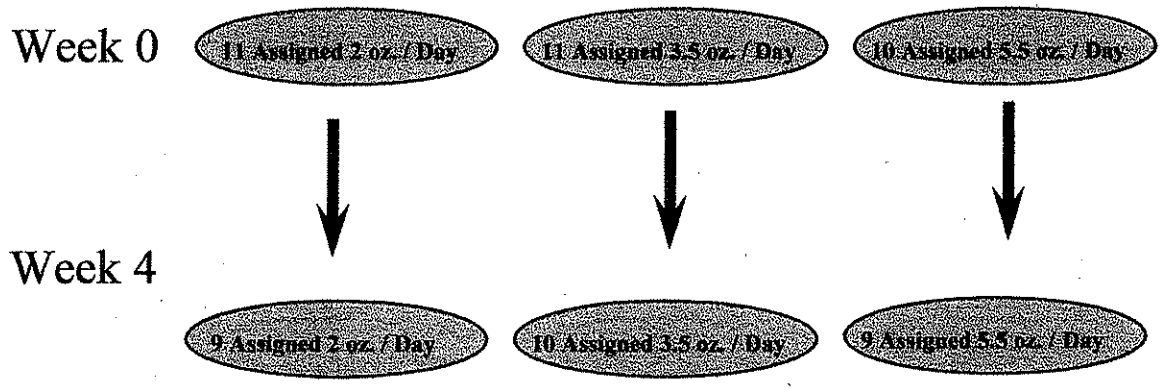
Data Analysis

The Tukey all pairwise comparison and Tukey-Kramer tests were used to identify differences between baseline, 2, and 4 weeks post raisin consumption. P-values ≤ 0.05 were considered statistically significant.

Recruitment Outline



Subjects were screened for a variety of factors including smoking, allergies, nutrient intake, polyphenol-rich food intake, medications, and ailments. Recruited subjects were between the age of 18 and 50, and instructed to avoid vitamins, and foods with grapes or grape derived substances for the two week period prior to and throughout the study, to avoid herbal products & NSAID drugs for three days prior to each blood draw, to avoid intentional exercise during the evening before and the morning of the blood draws, and to fast overnight prior to blood draws.



Select subjects withdrew citing personal reasons and scheduling conflicts.

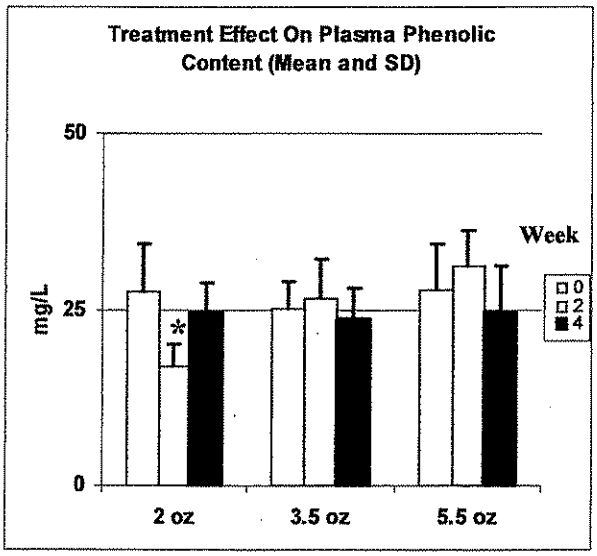
Characteristics of subjects who completed the experiment:

	2 oz / day	3.5 oz/day	5.5 oz/day
Male / Female Ratio	5 / 4	4 / 6	5 / 4
Weight (lb)	147	146	152
Height (in)	67	66	68
BMI	20.5	20.3	21.2

Tolerance: 10% of subjects reported toothache; 7% of subjects reported headaches. No differences were observed between treatment groups.

Raisin Consumption and Plasma Phenolic Content

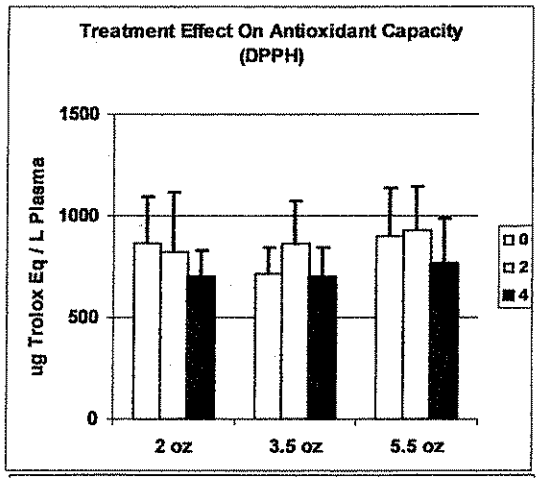
Immediately subsequent to the consumption of phenolic rich foods, plasma phenol content increases. However following phenolic rich food consumption and overnight fasts, this is observed less frequently. In this experiment, regular raisin consumption did not increase fasting plasma phenolic content. A significant reduction was observed with the low raisin treatment at wk 2.

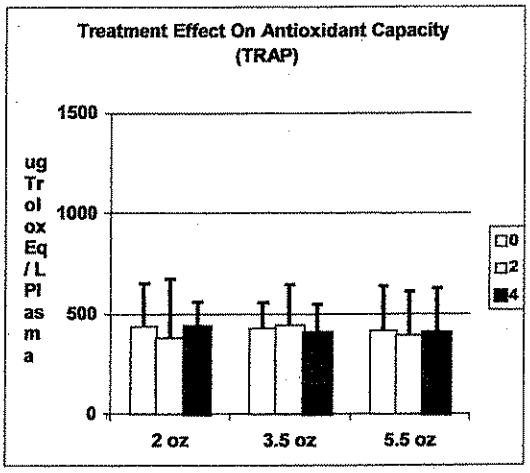


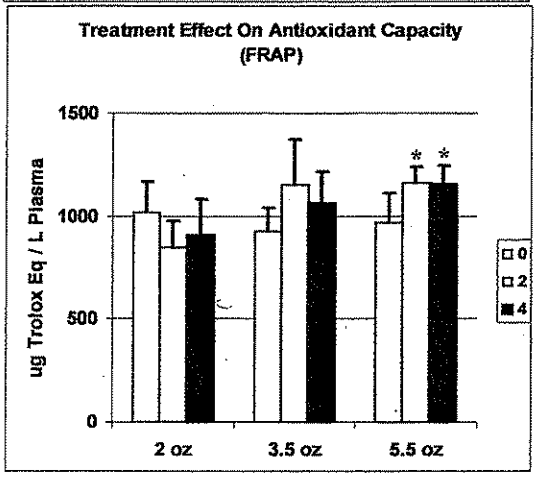
HPLC analysis in an effort to assess for specific phenolics was not conducted due to a lack of evidence of positive phenolic changes and the absence of phenolic antioxidants with high lipid solubility.

Raisin Consumption and Plasma Antioxidant Capacity

As with plasma phenolic content, plasma antioxidant content can be observed to increase following the consumption of phenolic rich foods. However, as with plasma phenolic content, these changes are commonly transient unless the phenolic antioxidants have a high lipid solubility (e.g. soy isoflavones). Therefore, they are seldom observed following overnight fast. In this experiment, regular consumption of 5.5 oz raisins / day did increase antioxidant capacity based on the FRAP assay. No other significant changes were detected.



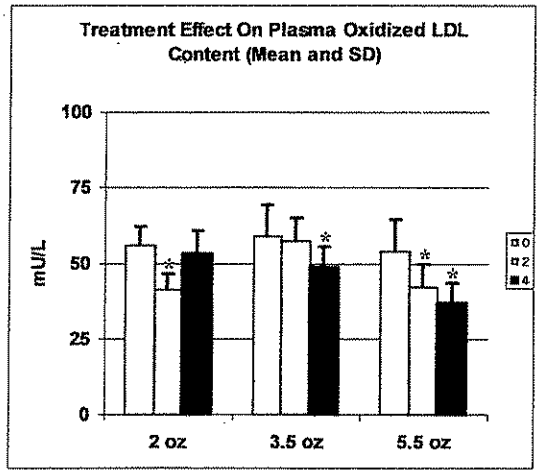


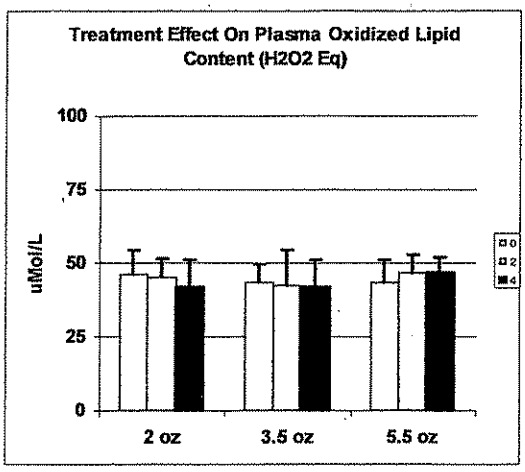


Raisin Consumption and Plasma Lipid Peroxides

In contrast to the relatively transient measures of oxidative stress discussed above, some measures of lipid peroxides are long term indicators of oxidative stress. Circulating lipid peroxides can provide a measure of tissue damage and be a useful marker for identifying patients with a high risk for coronary artery disease. The effect of raisin consumption on plasma lipid peroxides was assessed in terms of H_2O_2 equivalents and circulating oxidized LDL. Circulating oxidized LDL is a particularly useful measure since ninety-four percent of the subjects with high circulating oxidized LDL have cardiovascular disease.

Regular raisin consumption did not affect plasma lipid peroxides based on the Fox assay. However, circulating oxidized LDL, a long-term marker for oxidative stress, was reduced by all three raisin treatments.



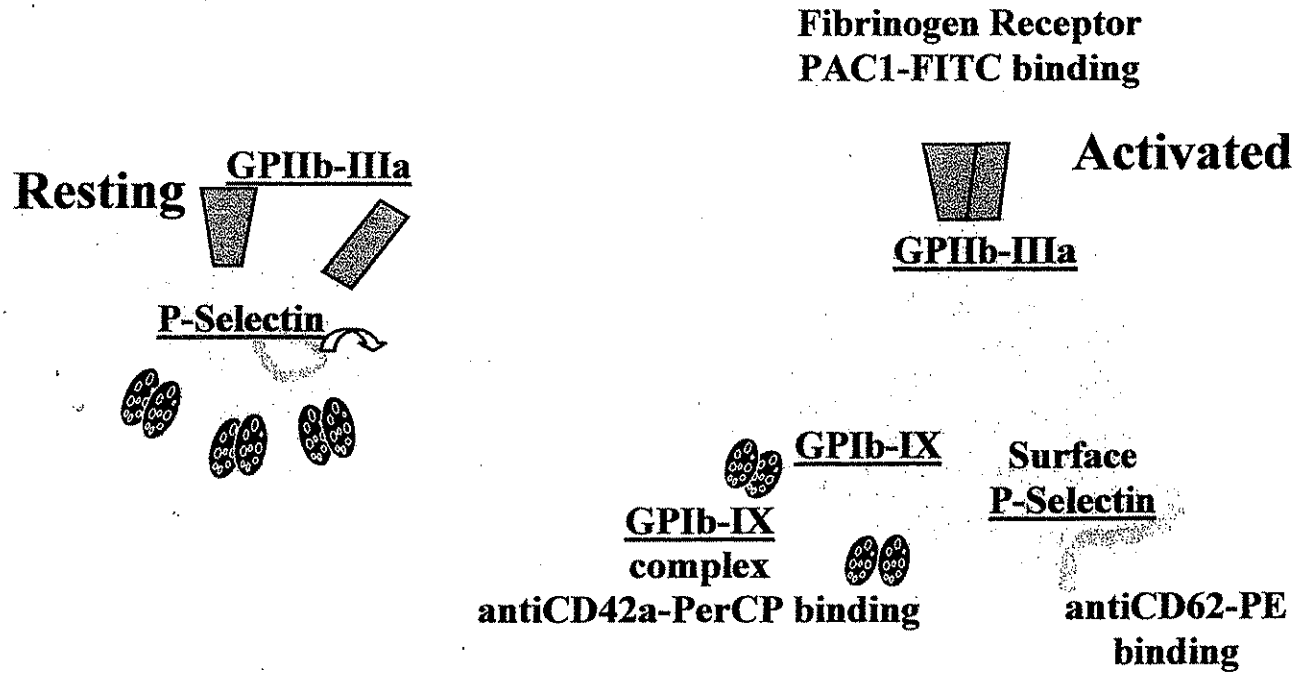


*** Plasma LDL, HDL, and total cholesterol are currently being assessed at the UCD medical center.**

Raisin Consumption and Platelet Reactivity

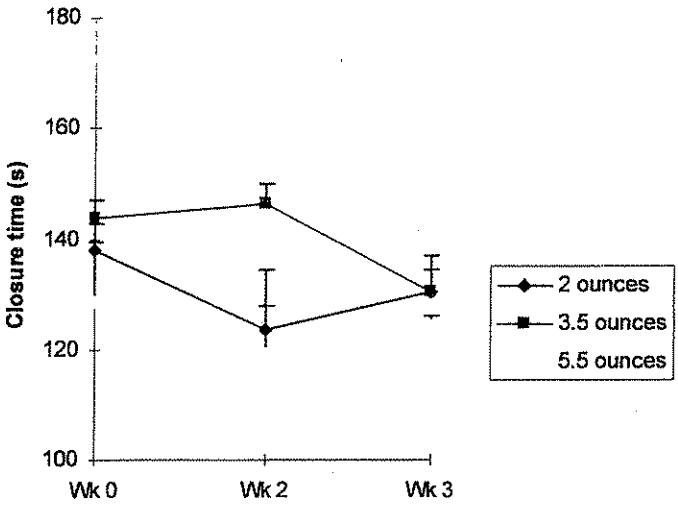
Plant phenolics are known to inhibit platelet reactivity by preventing glycoprotein IIb-IIIa expression, H2O2 generation, and cyclo-oxygenase activity.

Phenolics & Platelet Activity



In the assays below, an increase in seconds (s) would have indicated protective effects. However, as shown below our results do not indicate any cardioprotective effect of regular raisin consumption.

PFA - Epi / Collagen



PFA - ADP / Collagen