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2017 SUBMITTED ABSTRACTS

ORAL PRESENTATIONS

ASTAXANTHIN PRODUCTION TECHNIQUE MATTERS: PRESENCE OF ENVIRONMENTALLY DERIVED CARCINOGENS, POLYCYCLIC ARYL HYDROCARBONS, IS COMMON IN OUTDOOR METHODS

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Background: Environmental chemicals, especially those arising from pollution, have the potential to enter our food supply and carry over into food products such as dietary supplements. Polycyclic Aryl Hydrocarbons (PAHs) are carcinogens that are common elements in air pollution and combustion waste. Plant based supplements are usually not tested for the presence of PAHs despite the potential for contamination when they arise from heavily polluted environments.

Purpose: To address this concern we tested astaxanthin produced from the algae H. pluvialis, for the presence of PAHs. Astaxanthin production techniques vary in sophistication. The indoor photobioreactor technology represents the system with the greatest environmental controls. In contrast, when algae are grown in open environments, either raceway ponds or outdoor tubular structures, interactions between the algae and the environment are more likely.

Methods: 23 samples of commercial astaxanthin from 11 companies were collected and shipped to a third-party testing company (Eurofins) and tested for the presence of 16 different PAHs, including benzo(a)pyrene, benzo(a)anthracene, benzo(b)fluoroanthene and chrysene. Collectively, these were designated PAH4, as they are widely recognized as the top four PAHs linked to health hazards.

Results: Of the 11 companies evaluated only 2 produced astaxanthin that was PAH free. In all 6 astaxanthin samples made with the indoor photobioreactor technique, originating from two countries, we failed to find any detectable amounts of any PAH. One sample produced with the outdoor tubular system was also negative for all PAHs. By contrast, in 16 astaxanthin samples from 9 companies, produced with outdoor techniques in either China or the USA, PAHs were readily detected. Samples that tested positive for the presence of PAHs, contained 6/16 – 16/16 varieties of PAHs. Of these positive samples, 75% contained amounts of either benzo(a)pyrene (2ug/kg) or the PAH4 total (10 ug/kg) that exceeded EU regulatory limits. In some cases the levels exceeded regulatory limits by 1500%.

Conclusion: Given that the outdoor algal production system for astaxanthin, by design, is sensitive to the environment and its associated pollutants, these production techniques pose the greatest risk for contamination. In all 17 samples derived from outdoor production systems only 1 was free of carcinogenic PAHs. It appears that this production technique poses a significant health risk to consumers. By contrast, when the environment is tightly controlled, as is the case with indoor photobioreactor systems, PAHs were undetectable in every sample. We conclude that it is in the public's best interest to monitor plant-based products for environmental carcinogens, especially if they are produced where the risk for contamination is high. We also conclude that while astaxanthin is a valuable and potent carotenoid with significant health benefits, only one production technique, indoor photobioreactors, offers routine assurance that the astaxanthin is free of environmental pollutants and carcinogens.

NUTRITION, MICROBIOME, AGING AND CANCER

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Given current demographic trends in our aging society and the high incidence of age-related illnesses including cancer, new strategies to counter such processes and decrease the risk and progression of debilitating and life threating conditions are being evaluated. Cancer is a multifactorial disease of the entire human body with complex underlying mechanisms. Intestinal microbiota impacts the immune system, and conversely, the immune system influences the composition of the microbiota. Age-related changes including immunesenescence, chronic systemic inflammation and the development of the frailty phenotype in the elderly appear to be affected by the microbiota and microbially produced metabolites.

Other factors, like changes in the intestinal permeability and consequently bacterial translocation, along with dormant microbiome and the biofilm are also contributing to the low chronic inflammation status characteristic for elderly. Potentially, dietary

intervention on microbiota and potentially on inflammation, could influence the risk and progression of some chronic diseases including cancer.

ZINC OREGANO COMPLEX NEGATIVELY REGULATES PANCREATIC CANCER CELLS

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Background: Pancreatic cancer is the fourth leading cause of cancer related mortality in the United States. Most current anticancer regimes do not effectively differentiate between cancerous and normal cells and frequently lead to systemic toxicity and adverse effects in normal tissues. Zinc, a second most abundant transitional metal in human, plays essential roles in cell proliferation, energy metabolism, cell signaling, and gene expression. In pancreatic cancer pathological samples, it was found a consistent major decrease in zinc concentration in the malignant cells compared with the normal/benign ductal and acini epithelial cells. Zinc-dependent physiological and pathological processes in pancreatic cancer cells remain elusive.
Purpose/objectives: We studied zinc organo complex zinc salicylate on pancreatic cancer functionality in vitro 3D model and in vivo animal models.

Methods: Using 3D culture system, we mimicked cancer cell at their competent growth and dormant phases to study the pancreatic cancer cell responses to the Zinc treatment on multiple cellular activities, including cell proliferation rate, ATP synthesis, mitochondria membrane potential, and tumoroid formation and disruption. The in vivo effect of Zinc complex treatment on tumor progression was studied by using xenograft tumor model in nude mice.

Results: Zn-salicylate complex (ZS) dose-dependently inhibited cell metabolism and proliferation in pancreatic cancer cells. ZS complex was necessary for the biological function and salicylic acid alone has no effect on cell inhibition. At the same concentration range, ZS spared normal fibroblast cells, showed no toxicity. ZS prevented cancer cell to form cluster and interrupted cell-cell interactions in tumoroids. ZS treatment changed mitochondrial membrane potential and regulated apoptosis and autophage pathways. ZS inhibited tumor progression tested in pancreatic xenograft mouse models.

Conclusion: Zinc uptake rate was enhanced in form of zinc salicylate which played important roles in pancreatic cancer cell functionalities. Zinc salicyate may be developed as an adjuvant agent or nutritional supplement to support cancer therapy.

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NATURAL ASTAXANTHIN IMPROVES MENTAL WELLNESS

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Introduction: Nutrition plays a major role in the pathophysiology of many "physical" disease states, including cardiovascular disease, cancer, obesity, and diabetes. The role of nutrition is less well-known with respect to "mental" disease states, including depression, anxiety, attention deficit disorder, psychological burnout and chronic pain. Diet-related changes in psychological mood state and mental wellness may be due to cellular, biochemical, and behavioral factors – and may be mediated by lifestyle factors including diet and exercise.

Purpose: Our objective was to assess changes in mental wellness by assessing psychological mood state in response to dietary supplementation with natural astaxanthin (12mg/day for 8 weeks). Marine microalgae is the predominant source of natural astaxanthin (NAX), a red-orange carotenoid with powerful antioxidant and anti-inflammatory properties. Studies in both rodents and humans suggest that NAX supplementation improves antioxidant capacity and reduces oxidative stress – effects which may be related to mental wellness.

Methods: Using a double-blind parallel design, 28 recreational runners (male = 14, female = 14, age = 42) were supplemented with NAX (Haematococcus pluvialis algal extract) or a placebo. Before and after the supplementation period, subjects completed the validated Profile of Mood States (POMS) survey to assess mental wellness parameters including global mood state (GM) and related subscales: Vigor (V), Tension (T), Depression (D), Anger (A), Fatigue (F), and Confusion (C).

Results & Conclusions: Significant changes (all, $p<0.05$) were found for improvements in positive mood state parameters: GM (+11%) & V (+5%); as well as reductions in negative mood state parameters: T (-20%), D (-57%), A (-12%), F (-36%), and C (-28%). Previous studies have shown astaxanthin supplementation to be associated with improvements in fatigue, attention, and memory – with suggestions that it may also play a role in prevention of dementia and age-related memory loss. These data are the first to suggest that astaxanthin supplementation improves mental wellness parameters associated with improvements in mood state and depression.

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ANTI -INFLAMMATORY AND ANTI -ARTHRITIC ACTIVITY OF CURCUMIN: IN VIVO MODEL

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Background: Existing treatments for rheumatoid arthritis (RA) provide pain relief and some anti-inflammatory effects, but no truly disease-modifying treatments are available for this disease. Curcuminoids are phenolic compounds have extensive biological activity as an antioxidant, neuroprotective, antitumor, anti-inflammatory, anti-acidogenic, radioprotective and arthritis. Injection of type II collagen leads to the development of severe polyarticular arthritis and associated with the immune system erosion of bone and cartilage leading to severe loss of joint function.

Purpose/Objectives: To assess curcumin effect on inflammatory markers and clinical scoring of arthritis in an in vivo model.

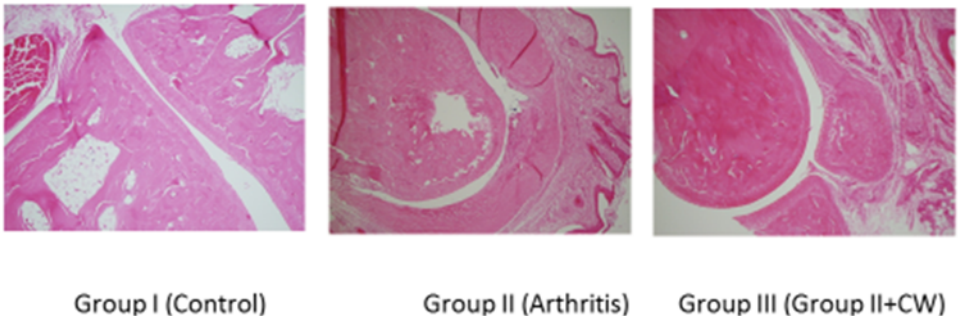
Methods: Female Wistar rats (n=7 in each group; 8 week-old; 180±20) were used and animals were reared at the temperature of (22 ±20C), humidity (55 ±5%) and a12/12 h light/dark cycle and food and water were provided ad libitum. The experiment was conducted under the protocol approved by the Firat University. Group I as a control group, Group II as an arthritic sham group, Group III as an arthritic sham group and

gavaged curcumin (CurcuWIN [CW], 10 mg/kg BW). Following the collagen injection, each rat was assessed on a daily basis for the development of arthritis. Clinical scoring of arthritis at 15th and 33rd day was performed on each back paws on a scale between 0 and 4 points. One back paw was fixed with 10 % formalin solution and was embedded in paraffin for histopathological examination, and the other back paw was stored immediately at −80 °C for Western blot analysis. Serum TNF-α, interleukin (IL)-17, obestatin, sclerostin, and Dickkopf-1 (DKK-1) levels were assessed by ELISA. Joint tissue samples were analyzed for the expression of TNF-α, nuclear factor kappa B, I-kB, cyclooxygenase-2 (COX-2), using the Western blot technique.

Results: A significant decrease in arthritis score was observed on 15th day ($p<0.077$), 33th day ($p<0.0001$), increased obestatin and sclerostin ($p<0.0001$) and decreased DKK-1 ($p<0.0001$). Serum IL-6, IL-17 and TNF-alpha decreased in CW and increased in arthritis group ($p<0.0001$). Histopathological changes were observed in Figure-1. The histopathological scoring of joint tissue samples showed a significant decrease in inflammation and destruction scores in Group III than Group II. Decreased IL6, COX 2, TNF-alpha, NFkB gene proteins were observed in joint tissues.

Conclusions: These results suggest that curcumin in treated group showed a higher statistical significant effect in the prevention of inflammation in an arthritis model.

Figure 1 Histopathological changes in different groups



USUAL CHOLINE INTAKES ARE ASSOCIATED WITH EGG AND PROTEIN FOOD CONSUMPTION IN THE UNITED STATES.

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Abstract: Choline is an essential nutrient with critical roles in several biological processes including neuronal development, cell signaling, nerve impulse transmission, and lipid transport and metabolism. The National Cancer Institute method was used to assess usual intakes of choline from foods according to data for participants enrolled in

the National Health and Nutrition Examination Survey 2009-2014 datasets and pregnant women in the 2005-2014 datasets. Suboptimal intakes of choline are present across many gender and life-stage subpopulations, as well as pregnant women in the U.S. Only 8.03 ± 0.56% of adults and 8.51 ± 2.89 pregnant women meet the AI for choline. Children 2-3 y were the most likely to meet their gender and life-stage specific AI, followed by children 4-8 y. Adults 19+ y who consume eggs were more likely to meet their gender and life-stage AI as compared to non-consumers (57.25 ± 1.45% and 2.43 ± 0.28%). Consumers of eggs had almost double the usual intake of choline as compared to non-consumers (524.62 ± 5.17 mg/d and 294.06 ± 1.98; $p<0.0001$). Protein food (meat, poultry and seafood) consumption also increased usual choline intakes compared to non-consumers (345.49 ± 2.21 mg/d and 235.02 ± 8.81; $p<0.0001$) to a lesser degree, but did not result in substantial increases in the percent of individuals meeting the AI. No subpopulation exceeded the UL for choline. This research illustrates that it is extremely difficult to achieve the AI for choline without consuming eggs or taking a dietary supplement.

Keywords: choline; NHANES; usual intake; adequate intake; tolerable upper intake level; dietary reference intake

PROANTHOCYANIDINS –RICH SALACIA CHINESIS EXTRACT (SCE) SUPPLEMENTATION REDUCES SERUM TRIGLYCERIDES WITH CHANGES IN BODY COMPOSITION: A RANDOMIZED PLACEBO-CONTROLLED PILOT TRIAL

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Background: Salacia chinensis (SC) has been extensively used in the treatment of diabetes in the ayurvedic system of Indian traditional medicine, little is known about the effects of SCE on obesity. Increased plasma lipid levels mainly total cholesterol, triglycerides and LDL along with decrease in HDL are known to cause hyperlipidemia that causes initiation and progression of atherosclerosis. Recent studies have shown the role of dietary polyphenols such as proanthocyanidin in the prevention of obesity and obesity-related chronic diseases. The present study is aimed to evaluate the effect of proanthocyanidins-rich SCE extract on lipid profile and body composition in overweight/obese pre-diabetes individuals.

Methods: A 2 month, randomized, double-blind, placebo-controlled study evaluated the efficacy and safety of proanthocyanidins-rich SCE extract on lipid profile and body composition in overweight/obese individuals (Pre-diabetes Asian Indian Population; N=24 completed; M/F; Age: 18-65y; BMI: 28.0 kg/m2 or above). Chronic disease conditions such as diabetes, CVD, Cancer, psychological disorders/conditions, HIV/AIDS and Cancer subjects were excluded. Subjects received either SCE (150mg

twice a day) or placebo (PLA, corn starch) for a period of 2 months. Efficacy was evaluated in terms of change in lipid profile, gut hormones and body composition. The safety and tolerability was evaluated by a physical examination and clinical laboratory evaluations.

Results: Treatment with SCE significantly decreased triglycerides levels (TG, SCE: 130.14 vs 111.5 and PLA: 126.8 vs 128.6 mg/dL $p<0.05$. Total cholesterol was reduced by 9.80%, VLDL by 13.04% and LDL by 4% from baseline values even if this reduction was not significant in SCE patient compared to placebo. A significant change in fat mass ($p=0.014$) and percent body fat ($p=0.016$) were also observed compared to baseline. These change from baseline in total fat mass and fat percentage were more pronounced in treatment group as there was a statistical significant ($p<0.05$) reduction in both the parameters from baseline to the end of the study as compared to placebo group. This change was associated with a significant reduction in waist circumference ($p=0.046$) as well as hip circumference ($p=0.017$) in Salacia treated group as compared to the baseline values. SCE treatment also affected hormones that promote satiety with significant changes in GLP-1 over baseline in SCE group at 2 months ($p=0.014$). Plasma levels of ghrelin and adiponectin also increased by 42.68% and 48.47% at 2 months. The plasma leptin, a hormone secreted by fat tissues that reduces food intake and suppress weight gain, was found to be reduced by 10.91% at 1 month and 1.82% at 2 months. There was a good reduction in free fatty acid by 10.11% as well as glycerol by 13.84% in SCE group. There were no notable changes in urine analysis parameters, vital signs, physical examination, and systemic examination.

Conclusion: These results suggest pro-anthocyanidins-rich SCE extract was effective in reducing body fat, triglycerides (over placebo), and anthropometric measurements over baseline. There is evidence that a 5-10 percent weight loss results in a 20 percent decrease in triglycerides and the magnitude of decrease in triglycerides are directly related to the amount of weight loss. A meta-analysis has revealed that for every 1-mg/dL increase in HDL-C, there is an estimated 2% to 4% decrease in cardiovascular risk. SCE was safe and well-tolerated and may be beneficial in the management of mild to moderate hyperlipidemia. Further long term studies are warranted.

ASSOCIATION OF BRIGHT LIVER WITH I148M VARIANT OF THE PNPLA3 GENE IN HEALTHY TODDLERS

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Approved by the Bambino Gesù Ethical Committee

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Background: Given the epidemic obesity in the pediatric population, non-alcoholic fatty liver disease (NAFLD) has become the first cause of liver disease in young patients. Both genetics and in utero metabolic programming seem to influence the onset and the progression of the disease in young patients.

Purpose/Objectives: To identify early determinants of bright liver in toddlers and explore the interaction between common genetic variants and perinatal factors associated with increased risk of non-alcoholic fatty liver disease.

Methods: Cohort study of 505 mother-newborn dyads. Maternal intake of fatty acids during the pregnancy was estimated by profiling fatty acids on maternal erythrocytes at the end of pregnancy and on cord blood. Patatin-like phospholipase domain-containing 3 (PNPLA3) rs738409 C>G and transmembrane 6 superfamily member 2 (TM6SF2) rs58542926 C>T single nucleotide polymorphisms were genotyped. At 1 year of age, bright liver (BL+ v.s. BL-), thickness of subcutaneous (SAT) and epicardial adipose tissue (EAT) were estimated by ultrasonography.

Results: At 1 year, 505 toddlers underwent the follow-up visit. Genetic data were available in 391 out of 505 toddlers (77.4%); 374 of them were BL- and 17 BL+ . Body weight ($p < 0.01$) and body mass index (BMI) ($p < 0.05$) were higher in BL+ than in BL- children and the same was true for the pregnancy weight gain of their mothers ($p < 0.05$). No difference was found in birth weight, SAT and EAT values between BL+ and BL- children. No difference was found, as well, in maternal and fetal lipid profile on erythrocyte membranes. The odds of having the more severe PNPLA3 allele (GG vs. CG vs. CC) was higher among BL+ than BL- children (OR = 2.41, exact 95%CI 1.14 to 5.07, exact mid-p-value = 0.027, ordinal logistic regression). The odds of having the more severe TM6SF2 allele (CC vs. CT vs. TT) was similar among BL+ and BL- children (OR = 1.35, exact 95%CI 0.35 to 3.75, exact mid-p-value = 0.669, ordinal logistic regression).

Conclusions: Findings of the study demonstrates that liver brightness occurs in toddlers and carriers of the PNPLA3 I148M variant have an increased risk of presenting with this feature. BL+ toddlers had significantly higher body weight and body mass index than BL- toddlers. BL+ toddlers were born from mothers who gained significantly greater body weight during gestation.

INTRODUCTION AND MAINTENANCE OF EARLY ADAPTIVE TRAINING PROTEIN BLENDS IN SUPPORT OF INFANT NUTRITIONAL GOALS: SAFETY AND ACCEPTABILITY

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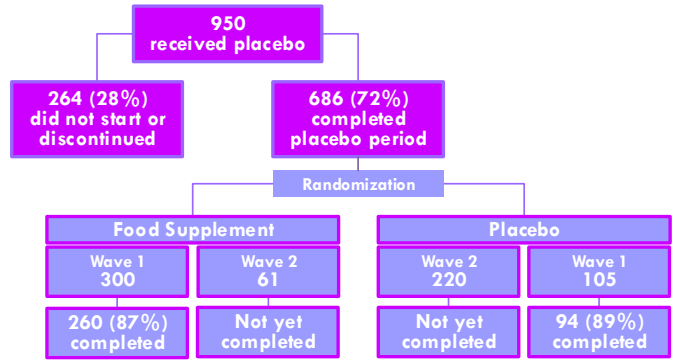
Background: Childhood food allergy affects about 8% of US children. Recent research has revealed protective effects of early dietary introduction of allergenic foods on the development of food allergy for infants, including those at elevated risk. , , Purpose/Objectives: The goal of this study was to evaluate the safety and acceptability of a blend of 16 common allergenic proteins (peanut, soy, almond, cashew, hazelnut, pecan, pistachio, walnut, wheat, oat, milk, egg, cod, shrimp, salmon, sesame) combined with 400 IU of Vitamin D into a food supplement powder.

Methods: All procedures were deemed exempt by the Northwestern University IRB. A national sample of healthy infants, 5-11 months of age, without severe eczema participated in a 28-day placebo period followed by a 28-day randomized, blinded, placebo-controlled period. Caregivers were instructed to to mix the powder into their infant's solid or liquid feeding once a day, observe their infant for 2 hours after ingestion, and record, in a web-based diary, any symptoms or allergic-type reaction including anaphylaxis occurring within 2 hours of ingestion and any reaction-related prescribed medication or medical care. Caregiver perceptions of the food supplement's smell, texture, and packaging, were also assessed.

Results: Figure 1 shows the enrollment and completion rates. Of the 19,208 placebo ingestions, 2% resulted in a reported symptom (e.g., cough diarrhea). Of the 8,827 food supplement ingestions to date, no infant had any allergic reaction, received any prescribed medication, or received medical care related to a reaction within 2-hours of ingestion and 1% had any reported symptoms. Final results will be available for the entire cohort in 2-weeks.

Figure 1. Enrollment and Completion Rates



Conclusions: This study strongly suggests that the food supplement is safe and feasible for infants to ingest. Future studies will assess the effect of the food supplement on immunologic responses to the allergenic proteins and on the longer-term incidence of food allergy.

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CLINICAL USE OF SUPPLEMENTAL BACTERIOPHAGE MIXTURES AND GASTROINTESTINAL HEALTH - THE PHAGE STUDY

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Background: Introduced in the early 1900's bacteriophage therapy is the application of bacteria-specific viruses to combat uncontrolled and/or undesired bacteria, such as those involved in infectious disease. Bacteriophages have been shown to be inherently non-toxic since they consist mostly of nucleic acids and proteins. Due to their host specificity, bacteriophages have a rare capacity to infect even relatively closely related bacterial genus' and have been shown not to impact the normal health-protecting GI microflora.

Purpose/Objectives: The Bacteriophage for Gastrointestinal Health (PHAGE) Study is a complex randomized, double-blind, placebo controlled cross-over trial designed to investigate the utility of four supplemental bacteriophage strains (LH01-Myoviridae, LL5-Siphoviridae, T4D-Myoviridae, and LL12-Myoviridae) to modulate the gut microbiome, and therefore ameliorate common gastrointestinal distress symptoms (e.g., gas, bloating, diarrhea, constipation, etc) experienced among healthy individuals.

Methods: 33 individuals not diagnosed with gastrointestinal disorders (e.g., Crohn's disease, irritable bowel disease, etc) but healthy individuals who reported significant gastrointestinal distress were enrolled into the study. The PHAGE Study is designed to evaluate shifts in the microbiome using 16S rRNA sequencing, changes in localized hs-CRP, fecal calprotectin, short-chain fatty acids, and systemic changes in 12 inflammatory mediators (e.g., TNF-a, IL-6, etc), total cholesterol, LDL-cholesterol, HDL-cholesterol, triglycerides, glucose, and metabolic safety markers (ALT, AST, etc).

Results: The bacteriophage cocktail was well tolerated, with no adverse events or differences in metabolic safety markers detected during the study. The treatment effectively modulated the microbiome, eliminating several pathogenic phyla, while improving LDL-cholesterol and some systemic inflammatory cytokines.

Conclusions: Bacteriophages seem to have a safe clinical application for eliminating problematic bacteria in the GI tract. Future studies designed to assess their lipid-lowering capacity as a primary endpoint are needed.

COGNIDIET®: A PRELIMINARY STUDY OF THE EFFECTS OF COGNITIVE-BEHAVIOR THERAPY AND MINDFULNESS TRAINING ON WEIGHT LOSS AND METABOLIC HEALTH

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Background and objectives: Poor adherence to diets and other weight-loss interventions is key to failure to achieve and maintain weight loss goals. We evaluated the effects of the CogniDiet® Program, a novel approach to weight loss and improved metabolic health.

Methods: Principles of cognitive-behavior therapy (CBT) and mindfulness-based stress reduction were taught over 12 weeks to help participants reframe thoughts and modify food-directed behaviors. No specific diet or calorie-counting regimen was imposed, although nutrition and exercise counseling were provided. Women ≥40 years of age who were chronic, unsuccessful dieters participated in this single-arm study. Primary outcomes were change from baseline at 12 weeks in body weight (BW), body fat mass (BFM), percent body fat (PBF), and waist-to-hip ratio (WHR). Blood lipoprotein analyses were also conducted. Paired t-tests were used to assess the change in study measures.

Results: Of the 40 women enrolled in the study, 34 completed all assessments and comprised the per protocol population, here reported on. Participants were largely white (76.5%), college-educated or higher (70.6%), engaged in no or infrequent exercise (67.5%), and had a mean age of 55.7 years. Mean baseline BW, BFM, PBF, and WHR were 200.9 (±35.7) lbs, 83.8 (±20.9) lbs, 41.3 (±3.6)%, and .95 (±.05), respectively. At 12 weeks, we observed a significant decrease in mean BW, to 188.9 (±35.7) lbs (mean difference, 12 [±7.5] lbs, $P < 0.05$), a significant improvement in all other anthropometric parameters (all $P < 0.05$), and significant decreases in total and low-density-lipoprotein cholesterol and in triglyceride levels (all $P < 0.05$). No difference was observed in A1C or high-density-lipoprotein cholesterol levels.

Conclusion: The results provide preliminary support for the efficacy of CBT and mindfulness training techniques, as employed in the CogniDiet® program, in promoting weight loss and improving metabolic parameters. The durability of the observed effects is under evaluation and will be reported at a later date.

Reference: Grossman P, Niemann L, Schmidt S, Walach H. Mindfulness-based stress reduction and health benefits. A meta-analysis. J Psychosom Res. 2004;57(1):35-43.

DOES AN ANTI-AGING DIET EXIST? DIETARY FACTORS AND THEIR IMPACT ON TELOMERE LENGTH – A REVIEW OF THE LITERATURE

Christina E. Kang, University of Western States

Abstract: Objective: To review the effects of dietary factors on telomere length (TL). Methods: PubMed database and Google Scholar were used to search for relevant articles between 2011 to present time. The specific search terms used in combination were "telomere" and "diet." Reference lists of all articles obtained from this search were used as sources for additional information. Discussion: The review discusses the positive and negative effects of dietary factors and the Mediterranean Diet (MD) on TL. Conclusion: This review determined that antioxidant status and MD show a positive association with TL, whereas processed meats and sugar shortened TL.

Keywords: Aging, anti-aging, telomere, telomerase, diet, Mediterranean

Introduction: In 2013, the median age of the US population was calculated at 37.6, with remaining life expectancy at 46.0 years. In 2098, the median age is forecasted to be 44.5, with remaining life expectancy forecasted to be 45.4 years.1 Even though lifespan is increasing, commensurate increases in the years without disease or disability, called healthspan, have not occurred. Accordingly, age-related healthspan interventions have become a public health priority.2

Aging is associated with functional decline due to an accumulation of detrimental changes at cellular and molecular levels.3 A primary hallmark of aging is TL attrition.4 Telomeres are repeats of DNA, specifically 5' TTAGGG 3' in tandem located at the ends of eukaryotic chromosomes.5 Telomeres are essential to prevent chromosomal ends from fusing together as would happen if the ends were recognized as DNA breaks.5 Telomeres also function to maintain cell viability, chromosome localization in the nucleus, chromosome segregation, recombination of homologous chromosomes in meiotic cells, and protect chromosome ends from unravelling, akin to the plastic caps at the end of shoelaces.6

Telomeres shorten after each cell division, with heritable genes partially dictating TL at conception.7 The rate of telomere shortening (TS) is 50–150 base pairs (bp) per somatic cell and is specific to cell types or tissue7. Tucker8 measured TS at a rate of 15.6 base pairs per year of age. With continued shortening, telomeres reach a point of

diminishment that triggers an uncapping signal, leading to cellular senescence.7 Cellular senescence is defined as permanent cessation of cell division due to cellular damage, including abnormal activation of onco-genes, telomere shortening, and macromolecule accumulation.9 Eventually, the cell will undergo apoptosis, or cell death, unless there is a disruption in the apoptotic mechanism.7 This may be due to either telomerase over-expression or telomerase-independent alternative telomere-lengthening mechanism, leading to cell immortality.7 Telomerase is a ribonucleoprotein comprised of two major components: protein reverse transcriptase (expression is the rate-limiting factor) and an RNA template5,10. Telomerase acts to counter telomere shortening by lengthening telomeres through reverse transcription.10
TS occurs independent of chronological age, inferring that telomere attrition is possibly a modifiable factor by lifestyle variables such diet, exercise, and adiposity.11 Although multiple lifestyle factors may contribute to telomere integrity in varying degrees, this review will focus on diet and its influence on telomere length.

Methods: PubMed database and Google Scholar were used to search for relevant articles between 2011 to present time. The specific search terms used in combination were “telomere” and “diet.” Reference lists of all articles obtained from this search were also examined for additional relevant articles.

Discussion:
Antioxidants and telomere length
Antioxidants (AOX) have been shown to play a pivotal role in determining telomere status. AOX reduce the burden of oxidative stress, thereby reducing inflammation.12 Telomeres are particularly rich in guanines which are more vulnerable to oxidation. In addition, reactive oxygen species (ROS) produce single strand breaks which are perfunctorily repaired in genomic DNA, however, telomeric DNA seems to be deficient in these repair systems. With telomeric DNA being more sensitive to oxidative damage, a cogent explanation is that AOX may mitigate telomere attrition.13,14
García-Calzón and Sonia et al15 found that AOX intake correlates with longer leukocyte telomere length (LTL), whereas diets comprised of white breads correlated with shorter telomeres. As a reciprocal relationship has been found between LTL and inflammation, AOX positively impacting LTL is logically supported.15
Seeds, nuts, legumes, and coffee intake have exhibited direct associations with LTL potentially due to their high content of AOX which have been found to delay the shortening rate of TL.16 A population cohort of 1,958 middle-aged and older Korean adults completed semi-quantitative food frequency questionnaires (FFQ) at baseline, between June 2001 to January 2003. Ten years later, LTL was assessed using real-time polymerase-chain reaction (PCR). The researchers divided results into two dietary patterns: “prudent dietary pattern” characterized by whole grains, seafood, legumes, vegetables, and seaweed and “western dietary pattern,” characterized by refined grains, red non-processed or processed meat, and sweetened sodas. After adjusting for age, sex, body mass index, and other potential confounding factors, the prudent dietary pattern,

containing high levels of AOX, correlated with longer LTL, mainly due to legumes, nuts, seaweed, fruits, dairy products, and reduced intake of red meat and sweetened sodas.16 Coffee consumption was examined in 4,780 women in the Nurses' Health Study (NHS) which began in 1976. Coffee intake was measured using validated FFQs and PCR measured LTL. The NHS found significant associations between higher intake of coffee and longer LTL after correcting for confounding variables (P-trend = 0.02), but not after adjusting for total coffee consumption (P-trend = .37). AOX content in coffee may likely explain the study's results.17

Fruits and vegetables have also been shown to positively impact LTL, again, most likely explained by the salutary actions of AOX. In the same population cohort of Korean adults discussed above, fruit consumption was positively correlated with LTL.16 Additionally, a case-control study of 300 gastric cancer patients and 416 age and gender-matched controls demonstrated a positive relationship between fruit consumption and LTL.18

In a cross-sectional study of a population aged 65 years and older, vegetable intake correlated with longer LTL.19 In addition, root vegetables, peppers, and carrots showed significant, positive associations with mean TL.20 In the Helsinki Birth Cohort Study enrolling 1,942 subjects aged 57–70 years, vegetable intake of women was positively associated with LTL (P=0.05).21

Mediterranean diet and telomere length

The Mediterranean diet (MD) has been recognized as the most salubrious dietary pattern for its outcomes related to reduced morbidity and mortality in cardiovascular disease and other chronic diseases.22 Increasing evidence is supporting MD as a longevity or healthy-aging diet.19,23 One study stratified 217 elderly subjects according to a Mediterranean diet score (MDS) and adherence level: low adherence (MDS 3), medium adherence (MDS 4–5) and high adherence (MDS 6). The highest adhering group showed longer LTL ($p = 0.003$) and higher telomerase activity (TA) ($p = 0.013$) compared to low and medium-adhering groups. After accounting for age, gender, and smoking habit, MDS was found to be independently associated with LTL ($p = 0.024$) and TA ($p = 0.006$). TA was also found to be independently associated with LTL ($p = 0.007$) and negatively impacted by oxidative stress and inflammation.24

Another study of twenty elderly subjects was performed to compare MD against a saturated fatty acid diet (SFA) and high-carbohydrate/low-polyunsaturated fat diet (CHO-ALA) in a randomized crossover design. Each patient's serum was supplied to umbilical endothelial cells and incubated to assess how each diet impacted ROS, cellular apoptosis (cell death), and telomere shortening. The MD was found to lower ROS production, apoptosis, and attenuate TS in comparison to SFA and CHO-ALA diets.25 Lastly, the NHS showed that women with higher adherence to MD had longer telomeres than less-adhering subjects, after adjusting for confounding variables.17

In contrast, some studies did not find an association of the MD with LTL. Nettleton et al26 surveyed 840 Caucasians, African Americans, and Hispanics in the Multi-Ethnic Study of Atherosclerosis (MESA) using 120-item FFQ completed at baseline and assigned a score of adherence to two dietary patterns, as defined by the predominating foods: 1) fats and processed meat and 2) whole grains and fruits (similar to the MD). The results did not show an association of the whole grains/fruits diet with LTL.26 Gu et al27 showed that MDS did not correlate with LTL in the overall study population, however, a significant association was seen amongst non-Hispanic Whites. Finally, a cross-sectional examination of 5,862 women within the NHS showed that while overall healthy living as characterized by physical activity, diet, non-smoking, BMI, and abstinence from alcohol was significantly associated with longer TL, diet alone was not.28

Processed meat and telomere length
The Strong Heart Family Study was comprised of 2,846 American Indians in a cross-sectional design to assess associations of processed meat and unprocessed red meat consumption with LTL. Subjects completed a 119-item block FFQ and LTL was measured with quantitative PCR. After adjusting for age, sex, education, smoking, alcohol intake, exercise, and other confounding variables, consumption of processed meats, but not unprocessed red meat was associated with shorter LTL.29
Nettleton et al26 study discussed above found an inverse relationship between a diet predominating in fats and processed meats and TL. This result corroborated the larger MESA study of 5,089 nondiabetic subjects which showed a dietary pattern loaded with fats and processed meats to be associated with inflammation.30

Sugar and telomere length
A study of 556 Chinese subjects were screened for diabetes, then grouped into diabetic, non-diabetic, and pre-diabetic groups. Their LTL and hemoglobin A1c (HbA1c) were measured. After adjusting for age, the results showed that newly diagnosed diabetic subjects with HbA1c < 7 % had longer LTL than in the group with HbA1c ≥ 7 %.31
A study including 5,309 healthy American adults, aged 20 to 65 years, from the National Health and Nutrition Examination Surveys 1999-2002 (NHANES) was conducted. After adjusting for sociodemographic and health-related variables, sugar-sweetened carbonated beverage consumption correlated with shorter telomeres (b = −0.010; 95% confidence interval [CI] = −0.020, −0.001; P = .04).31 However, the smaller MESA study discussed above did not find such a correlation.25

Limitations: This study had several potential limitations. First, studies included in this literature review were mostly cross-sectional, thereby incapable of establishing a temporal relationship between lifestyle factors and TL. Second, most studies measured LTL, thus extrapolation to other tissues may not be viable. Third, measurement error in TL may occur during long-term storage as DNA may oxidize or degrade. Fourth, since most studies administered self-reported dietary intake questionnaires, the chance of

measurement error exists. Fifth, most studies examined specific populations such as women, making it difficult to generalize to other groups. Lastly, residual confounding variables may still exist despite noble attempts to control for them.

Conclusion: Many chronic diseases and age-related decline have been explained by the deleterious effects of inflammation and oxidative stress. Since telomere status has been recognized as a biomarker of aging, it follows that inflammation and oxidative stress also compromise telomere integrity. Dietary factors and patterns that reduce inflammation have been hypothesized to benefit TL, creating an opportunity for this review. AOX and the MD have been shown to be positively associated with TL and even though the evidence is robust, a few studies found null results in select groups. Studies on processed meats have a united front in showing a negative association (i.e., shortening) with TL and sugar appears damaging as well. More research is warranted to unveil the role of these and other dietary factors and patterns in preventing, maintaining, or even lengthening telomeres, which may translate into not only a longer lifespan, but more importantly, a commensurate healthspan.

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TARGETING ZINC METABOLISM IN SKELETAL MUSCLE DURING INFLAMMATION

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Zinc is an essential trace mineral and has important roles on growth, development, and immune function. Insufficient intake of zinc or impairment of zinc metabolism contribute to zinc deficiency. The zinc-deficient state results in growth retardation, weakened immune function, and chronic inflammation. Inflammation increases the risks of metabolic diseases and conditions such as atrophy of skeletal muscle. Skeletal muscle, the largest organ in human body, comprises approximately 60% of body zinc and secretes multiple cytokine molecules during inflammation. Therefore, the prevention of inflammation is critical. Using a mouse model, we identified that zinc transporter Zip14 (slc39a14) showed greater upregulation in skeletal muscle of wild type (WT) mice treated by LPS (endotoxin) to mimic acute inflammation. However, the role(s) of ZIP14 in skeletal muscle in response to inflammation needs to be investigated. The aim of this study was to determine muscle ZIP14 expression and inflammatory cytokine expression during both acute inflammation induced by LPS injection and chronic inflammation induced by a high-fat diet (HFD) in skeletal muscle of WT and Zip14-/- (KO) mice. Our results demonstrated that Zip14 KO mice exhibited growth abnormalities with reduced hind leg length and greater atrophic muscle fibers. Following LPS stimulation, ZIP14 was upregulated and an increase in zinc concentrations were observed in muscle of WT mice. However, this increase was not observed in Zip14 KO mice, suggesting impaired zinc uptake in this genotype. Interestingly, Zip14 KO mice exhibited greater interleukin-6 (IL-6) production in

muscle than WT mice after LPS administration, which was coincident with greater inflammatory NF-κB activation. This suggests that ZIP14-mediated zinc uptake in muscle may reduce inflammatory signaling activation. Elevation of IL-6 may contribute to induce muscle-wasting cachexia via regulation of inflammatory signaling and protein degradation pathways. Consistent with the LPS model, ZIP14 expression also increased in muscle of WT mice during chronic inflammation induced by the HFD treatment for 16 weeks. In conclusion, muscle ZIP14-mediated cellular zinc uptake reduces inflammatory responses and this may partially explain the protective effects of muscle zinc in chronic inflammatory diseases of muscle and immune function. This study will provide a better understanding of mammalian zinc metabolism in systemic inflammation-induced muscle diseases such as sepsis, sarcopenia and cancer-associated cachexia.

POSTER PRESENTATIONS

WHAT'S IN YOUR DIETARY FIBER SUPPLEMENT? AN UPDATED LOOK AT THE NIH DIETARY SUPPLEMENT LABEL DATABASE (DSLD) FOR DETERMINING TOTAL DIETARY FIBER CONSUMPTION IN COMMUNITY ONCOLOGY HEALTH CARE PRACTICES.

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Keywords: dietary supplements, dietary fiber, colon health, colon cancer, supplement facts panel, community health care, oncology

Background: Over 50% of U.S. adults consume dietary supplements (DS) to promote health and well-being contributing to an estimated $41.2 billion in sales in 2016. 26-77% of cancer patients and long-term survivors report using any type of DS after cancer diagnosis. Dietary fiber-containing supplements are often recommended by oncology health care professionals, and others in the oncology community to promote bowel health and reduce disease risks, including risk of colorectal cancer. DS can greatly contribute greatly to total nutrient intake and may go underreported in clinical care. Dynamic product entry and exit from the U.S. marketplace, combined with increasing product variations and reformulations, pose considerable challenges for health care providers and others needing accurate nutrient consumption data for individuals ingesting these supplemental products. We examined the National Institutes of Health dietary supplement label database (NIH DSLD), a web-based interface containing over 66,400 U.S. commercially available DS products, to assess amounts and types of fiber-containing DS per manufacturers' supplement label panels.

Methods: The NIH DSLD database (Version 6.5.3) was queried for all currently available products using search terms “fiber”, “dietary fiber”, “soluble fiber”, “insoluble fiber”, “resistant starch”, “colon cleanse” and “colon health” as either product name, dietary ingredient, brand name, or label element.

Results: DSLD yielded a total of 5,799 DS products containing the term “fiber” anywhere on the product label. A total of 220 products contained ingredients classified as “fiber” and 254 products contained “fiber” in the product name. 4,267 products contained “dietary fiber” anywhere on the label and 7 contained “dietary fiber” in the dietary ingredient name. 577 contained “soluble fiber” anywhere on the label. Of the 8 products that contained “soluble fiber” in the product name, only 3 products contained “soluble fiber” in the ingredient names. Similarly, of the 238 products that contained “insoluble fiber” anywhere on the label, 1 product contained “insoluble fiber” as a dietary ingredient name. “Resistant starch” appeared anywhere on 20 product labels and by dietary ingredient name in 2 dietary supplements.
120 products contained “colon cleanse” anywhere on the product label; 61 contained “colon cleanse” on in the product name; and one contained “colon cleanse” in the dietary ingredient name. Finally, 265 products contained “colon health” anywhere on the label, and 5 contained “colon health” in the product name. DSLD can also be used in some cases to determine the type(s) of fiber claimed as present in each product, providing the potential for assessment of fiber intake. This federal government-supported database may assist the oncology community in differentiating fiber intake into soluble vs insoluble fiber categories, as well as in assessing total fiber intake.

Conclusion: DSLD serves as an online resource supplying a broad range of users, including oncology practitioners, with relevant DS information for research and clinical use. Funding: National Cancer Institute, Office of Dietary Supplements and the National Library of Medicine, National Institutes of Health.

ASSOCIATION BETWEEN DIETARY FAT INTAKE AND COLORECTAL ADENOMA IN KOREAN ADULTS
A CROSS-SECTIONAL STUDY

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The incidence of colorectal cancer is rapidly increasing in South Korea. It is important to clarify the association between colorectal cancer and diet, being one of the main modifiable risk factors, as such studies in the Korean population are lacking.

A cross-sectional study was performed using data from participants who had undergone a screening colonoscopy and a nutritional assessment during a routine health check-up from January 2008 to December 2011. Dietary intake data were derived from 1-day food records; colorectal adenoma was histopathologically confirmed by biopsy during colonoscopy. Eventually, 2604 participants were included in the analysis. The risk of colorectal adenoma by quintile of dietary fat intake was analyzed using logistic regression. Subgroup analyses by degree of risk and by location of colorectal adenoma were additionally performed.

In men, total fat intake was not associated with risk of colorectal adenoma. However, risk of colorectal adenoma increased with higher saturated fatty acid (SFA) intake. The adjusted odds ratio in the highest quintile was 1.71 (95% confidence interval, 1.01–2.91) compared with that in the lowest quintile. There was no significant association between fat intake and risk of colorectal adenoma characterized by subsite. In female participants, total fat and specific fatty acid intake were not associated with risk of colorectal adenoma.

These data support that high SFA intake is associated with risk of colorectal adenoma in Korean men.

SERUM 25-HYDROXYVITAMIN D CONCENTRATIONS ≥60 NG/ML ARE ASSOCIATED WITH 70% LOWER CANCER RISK AMONG OLDER WOMEN: POOLED ANALYSIS OF TWO RANDOMIZED TRIALS AND PROSPECTIVE COHORT STUDY

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Background: Serum 25-hydroxyvitamin D [25(OH)D] concentrations have been associated with a lower risk of all cancers between ~10-40 ng/ml [1].

Objectives: To investigate whether 25(OH)D concentrations ≥40 ng/ml may provide additional reduction in risk among women aged 55 years and older.

Methods: Data from three cohorts representing different median 25(OH)D concentrations were pooled to afford a broader range of 25(OH)D concentrations and improved statistical power: the 2007 Lappe RCT cohort (N=1,169, median 25(OH)D=30

ng/ml) [2], the 2016 Lappe RCT cohort (N=2198, median 25(OH)D=36 ng/ml) [3] and the prospective GrassrootsHealth cohort (N=1713, median 25(OH)D=49 ng/ml). The outcome of interest was the diagnosis of any invasive non-skin cancer during the multi-year observation period (median: 4.0 years). Kaplan-Meier plots were developed and the association between 25(OH)D and cancer risk was examined with multivariate Cox regression using time-varying 25(OH)D measurements and spline functions.

Results: Within the pooled cohort (N=5080), 176 women were diagnosed with cancer during the observation periods. Age-adjusted cancer incidence across the pooled cohort was 1118 cases per 100,000 person-years (1048 per 100,000 person-years in the 2007 Lappe cohort, 1354 per 100,000 person-years in the 2016 Lappe cohort and 791 per 100,000 person-years in the GrassrootsHealth cohort). Kaplan-Meier curves for women <20, 20-39, 40-59 and ≥60 ng/ml were significantly different (P=0.01), with the highest proportion cancer-free at 4 years in the ≥60 ng/ml group (98.2%) and the lowest proportion cancer-free in the <20 ng/ml group (93.6%) (Figure 1). Women with 25(OH)D concentrations ≥60 ng/ml had a 70% lower risk of cancer than women with concentrations <20 ng/ml (HR=0.30, P=0.009) (HR=0.69, P=0.18 for 20-39 vs. <20 ng/ml; HR=0.62, P=0.10 for 40-59 vs. <20 ng/ml). After adjusting for age, smoking status and calcium intake, this lower risk remained (HR=0.35, P=0.03). Spline regression revealed a decrease in cancer risk with increasing 25(OH)D with tight confidence bands between ~20-70 ng/ml (Figure 2).

Conclusions: Increasing 25(OH)D concentrations to ≥60 ng/ml could substantially reduce cancer incidence and associated mortality.

Figure 1.

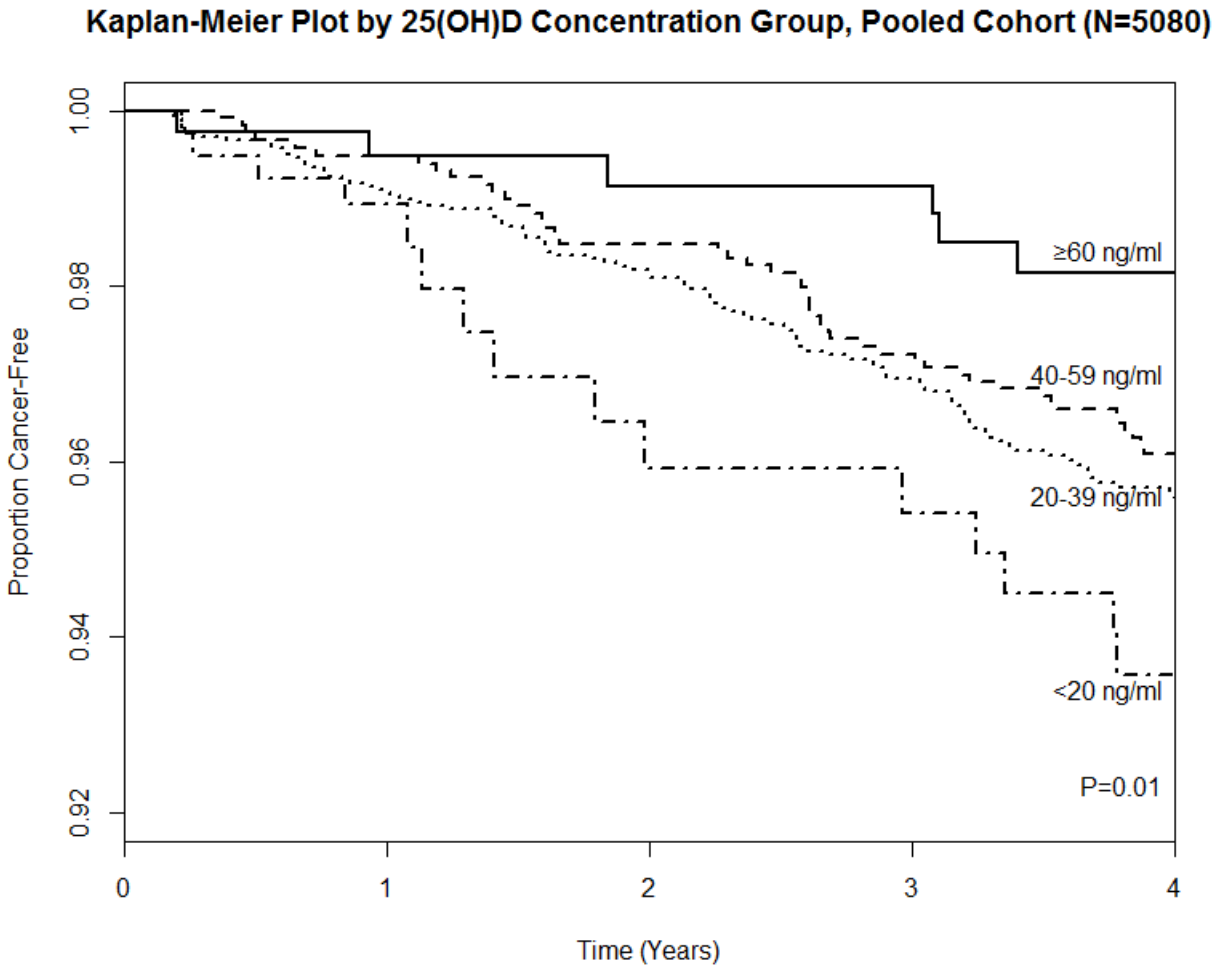

Fig 1. Kaplan-Meier plot comparing the proportion of cancer-free participants by 25(OH)D concentration (allowing for participants switching groups), pooled cohort (N=5080).

Figure 2.

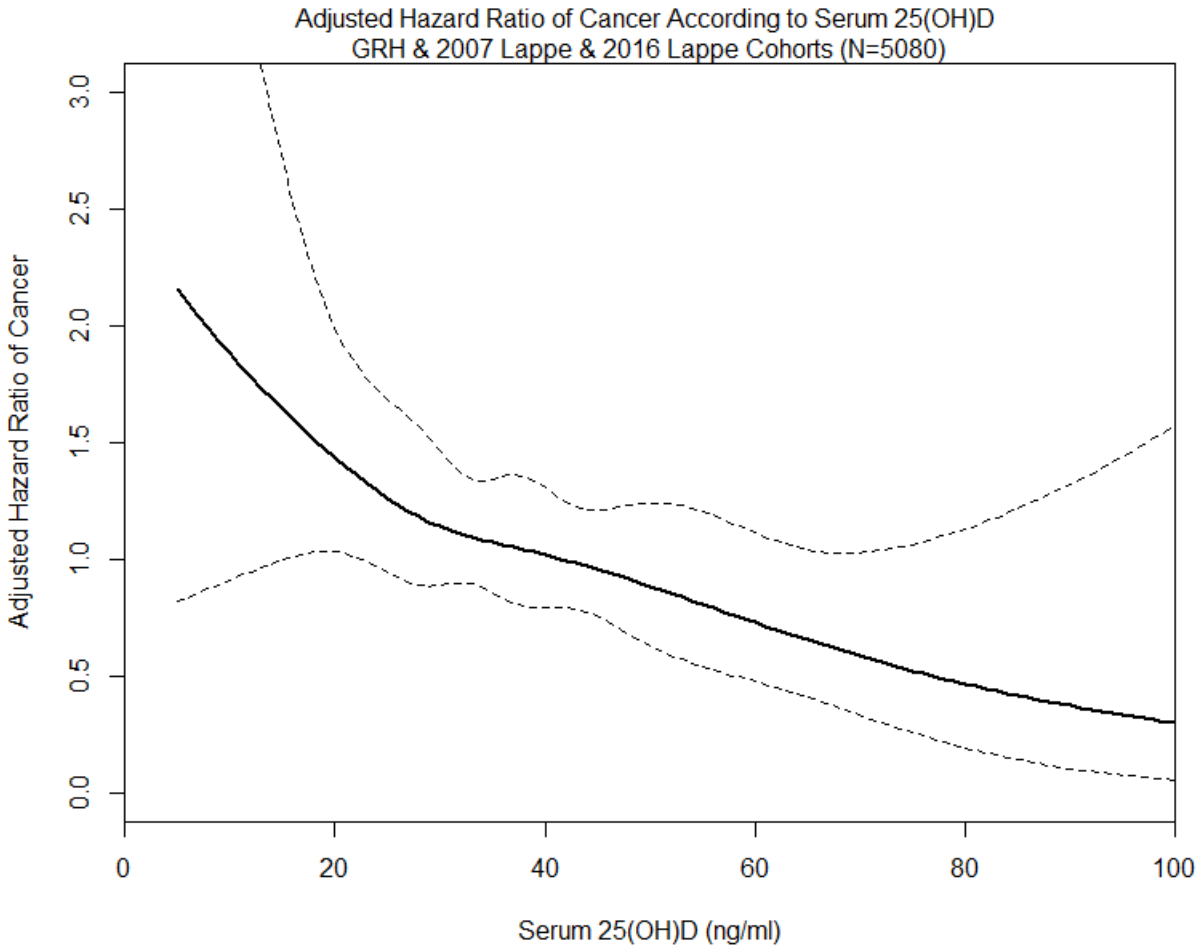

Figure 2. Association between serum 25(OH)D and risk of cancer adjusted for age, smoking status, and calcium supplement intake in the range of ≤100 ng/ml, pooled cohort (N=5080). Solid black line represents the estimated hazard ratio for the Cox regression model with restricted cubic splines with 5 knots and dashed lines represent the 95% confidence interval of the estimate.

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EVALUATION OF THE HEALTH EFFECTS OF A MULTIVITAMIN MINERAL HERBAL ESSENTIAL OIL-INFUSED SUPPLEMENT: A PILOT TRIAL

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Short Title: Clinical trial of a multi-component supplement

Abstract: This study was designed to quantitatively evaluate the health effects of a multivitamin mineral herbal essential oil-infused supplement using serum biomarkers. We also qualitatively evaluated the health effects of this supplement using a survey. Sixteen participants were recruited to take the supplement as directed for two months. The levels of the following serum components were measured in the participants: total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, triglycerides, lipoprotein(a), LDL/HDL cholesterol ratio, total/HDL cholesterol ratio, ferritin, fibrinogen, c-reactive protein, insulin, testosterone, sex hormone binding globulin, free androgen index, red blood cell magnesium, homocysteine, coenzyme Q10, lipid peroxides, alpha-tocopherol, gamma-tocopherol, cardiovascular index, eicosapentaenoic acid (EPA), arachidonic acid (AA), and the AA/EPA ratio. The following markers were significantly improved ($p < 0.05$) after two months of supplementation: HDL cholesterol, LDL/HDL cholesterol ratio, fasting insulin, homocysteine, serum vitamin E, EPA, and the AA/EPA ratio. These findings demonstrate that the supplementation had significant positive effects on biochemical indicators of cardiovascular health, antioxidant status, inflammation, and blood glucose regulation. All of the outcomes in the 16-item qualitative survey were improved after two months of supplementation. Twelve of these outcomes were significantly improved. The participants reported more mental clarity, energy, motivation, control, balance, and happiness, while reporting less back pain, muscle pain, cold and flu incidence, anxiety, frustration, and irritation at the end of the two-month supplementation period. Though

definite clinical efficacy remains elusive, these results suggest that the supplement may provide a broad range of health benefits for users in a short period.

Keywords: cardiovascular health, blood glucose, energy, immunity, anti-inflammation, mental health

COMPARATIVE STUDY OF THE THERAPEUTIC EFFECTS OF NOPAL EXTRACT AND ALOE VERA GEL EXTRACT ON HEMATOLOGICAL, ANTI-INFLAMMATORY AND OXIDATIVE STRESS INDICES IN STREPTOZOTOCIN- INDUCED DIABETIC RATS.

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1. Background: Diabetes is a complex and multifarious group of disorders characterized by hyperglycaemia, that has reached epidemic proportions in the present century. Although insulin treatment and other chemical therapies can control the disease to various extents, the complications are very common, whose pathologic base is microangiopathy. and thus, searching for a new class of compounds is essential to overcome these problems. [1]

Several herbal medicines have been reported to show preventive and treatment effects on diabetes mellitus.

Of those, Opuntia ficus indica, also known as nopal or prickly pear cactus, is widely consumed and used as a traditional medicine in the treatment of metabolic diseases such as diabetes and hypercholesterolemia . Nopal is high in dietary fiber and polyphenols, and is regarded as a functional food due to its low glycemic index and high antioxidant properties [2].

Aloe Vera (Aloe barbadensis) is a succulent plant that has been used for many years for its healing properties. The plant has been used medicinally for treatment of stomach ache, wrinkles, and burn treatments. The class of compounds of interest in the Aloe Vera plant and other succulent plants that possess antioxidant activity are known as polyphenols [3].

2. Aim of the work: The present study was conducted to investigate the effects of oral supplementation of Nopal extract (NPE) and Aloe vera extract (AVE) on hematological, anti-inflammatory and Oxidative Stress indices in streptozotocin- induced diabetic rats

3. Materials and methods:
3.2. Chemicals and Reagents.

Streptozotocin(STZ) was purchased from Sigma-Aldrich. All chemicals and solvents, were guaranteed reagent grade and purchased from Sigma-Aldrich Chemical Co.

3.2. Plant Materials.

3.2. 1. Preparation of Nopal extract (NPE):
Dried Opuntia cus-indica stem (for which the general name is Nopal"NP") purchased and was identified. The stems and distilled water were put into an ultrahigh-speed low-temperature vacuum extractor, which was maintained at 80–90◦C for 3 h to produce water extract powder of fresh NP stem (NPE). Extract was filtered, distilled, and put into a washed container, which was then frozen in a deep freezer set to −70◦C, put into a freeze dryer, and dried. The dosing 100mg/ kg body weight schedule was once per day.[4]
3.2. 2. Preparation of Aloe vera extract:
Mature, healthy and fresh leaves of Aloe vera were washed with fresh water. They were cut transversely into pieces. The thick epidermis of leaf was selectively removed and the semi solid gel in the centre was homogenized. The resulting mucilaginous, thick and straw colour homogenate was lyophilized using 95% ethanol. The filtrate was collected and evaporated to dryness under reduced pressure in rotary evaporator.
The residue was stored in dry sterilized small containers at 4°C until further used. An aqueous suspension was prepared fresh each time and administered by intra gastric route. The dosing 300mg/ kg body weight schedule was once per day. [6]

3.3. Animals:

Forty healthy male Wistar rats were purchased from breeding unit of Medical Research Center (Faculty of Medicine, Ain Shams University). The rats were housed individually under a controlled condition of temperature (25 ±5 °C) humidity (50% ±10%) and acclimatized to 12 hr light/dark. The experimental period was 25 days on which food and water were provided ad libitum. Animal's experiment was conducted according to the guidelines of the institutional animal ethical committee. Diet: Basal diet was based on AIN-93 recommendations Reeves et al. (1993)[7].

3.4 Induction of experimental diabetes

After fasting, diabetes was induced by intraperitoneal (ip) injection of STZ (Sigma, St. Louis, Mo., USA) dissolved in 0.1 M cold sodium citrate buffer, pH 4.5, at a dose of 55 mg/kg [44]. The control rats received the vehicle alone. The animals were allowed to drink 5% glucose solution overnight to overcome the drug- induced hypoglycemia. After

a week time for the development of diabetes, the rats with moderate diabetes having glycosuria and hyperglycemia (blood glucose range of above 250 mg/dl) were considered as diabetic rats and used for the experiment.

3.5 Experimental protocol

Forty healthy male Wistar rats were randomized into 4 groups (n=10 per group). All international and local rules and regulation for handling animals in experiments were followed. The experimental groups illustrated as follows:

Group I: Normal Healthy control rats.

Group II: STZ-induced diabetic control rats

Group III: Diabetic rats given Aloe vera leaf gel extract (300 mg/kg) daily using an intragastric tube for 21 days

Group IV: Diabetic rats given Nopal extract (100 mg/kg) n daily using an intragastric tube for 21 days.

At the end of the experiment (21 days), the animals were anesthetized with diethyl ether after 12 hours fasting and whole blood samples were taken from a hepatic portal vein. The blood samples were divided into two tubes, the first tube contained EDTA for determination of hemoglobin and glycosylated hemoglobin and other hematological parameters. The second tube contained left for 15 minutes at 37°C for serum separation, then centrifuged at 3000 rpm for 20 minutes, then serum was separated and kept in plastic vials at 200C until analyses of anti-inflammatory and Oxidative Stress indices.

Liver was removed, rinsed with cold saline and dried with filter paper and kept frozen until biochemical assays.

3.6. Statistical analysis

The data were analyzed using one-way ANO- VA (SPSS 17). Differences among the groups were determined by Duncan's multiple range test. Differences were considered significant at $P < 0.05$.

4. Results: There was a significant elevation in blood glucose, glycosylated hemoglobin and thiobarbituric acid reactive substances while the level of total hemoglobin decreased in STZ induced- diabetic group when compared with corresponding control group.

oral supplementation of Nopal extract (NPE) or Aloe vera extract (AVE) significantly tended to bring the values to near normal and the effect was more pronounced in the group of rats treated with Aloe vera gel extract.

During diabetes, there was a significant reduction in the activities of SOD, CAT, GPx, GST and GSH in liver tissues. Treatment with of Nopal extract (NPE) or Aloe vera extract (AVE) significantly increased the activity of SOD, CAT, GPx and GST and GSH levels and the effect was more pronounced in the group of rats treated with Aloe vera gel extarct.

In addition, the results of this study have indicated that mean corpuscular haemoglobin (MCH), mean corpuscular volume (MCV) and lymphocytes for the diabetic group are significantly ($p<0.05$) lower than the values of control group. supplementation of (NPE) and (AVE) significantly increase (<0.05) (MCH), (MCV) and lymphocytes and decrease neutrophils. and the effect was more pronounced in the group of rats treated with Aloe vera gel extract.

The results also revealed that (NPE) and (AVE) application for 21 days in streptozotocin-induced diabetic rats resulted in decreasing levels of pro-in flammatory cytokines including interleukin 1-beta (IL-1β), tumor necrosis factor-alpha (TNF-α) and C-Reactive Protein (C-RP).

5. Conclusion: Results of this study concluded that (NPE) and (AVE) supplementation has hematopoietic, anti-inflammatory, antihyperglycemic and antioxidant effects; thus (NPE) and (AVE) can be used as an alternative remedy for treatment/management of diabetes mellitus.

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EXAMINING THE EFFECTS OF POWERFUL TOOLS FOR CAREGIVERS, A GROUP PSYCHOEDUCATIONAL SKILL-BUILDING INTERVENTION FOR CAREGIVERS.

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Background: Care providers consistently report negative consequences to their mental health as a direct result of their caregiving responsibilities. Specifically, they describe higher levels of distress, mental health problems, and depressive symptoms compared to their non-caregiving matched controls. Powerful Tools for Caregivers (PTC) is a national program that aims to empower caregivers to better care for themselves and enhance their self-efficacy.

Purpose: The purpose of the present study was to determine and quantify the effectiveness of the PTC program through pre/post data analysis.
Methods: PTC intervention was evaluated using a quasi-experimental design that had two questionnaire time points: pre-PTC and post-PTC between June 30, 2004 and Oct 16, 2013 (n = 1038).

Results: PTC significantly increased caregivers' self-care behaviors (13.9 - 28.9%, $p < 0.05$), self-efficacy (21.6 - 57.0%, $p < 0.05$), management of emotions (25.7 - 43.5%, $p < 0.05$), and use of community resources (46.9 - 70.2%, $p < 0.05$). Additionally, approximately half of the caregivers (45.7%) reported eating poorly prior to PTC without significant improvement post-PTC (39.4%, n = 409, SE = 0.033, $p = 0.07$).

Conclusion: PTC results in caregivers taking better care of themselves, reacting to their emotions in a healthier manner, gaining more confidence in their caregiving abilities and coping skills, and becoming more knowledgeable about receiving assistance from community resources. Caregivers may additionally benefit from interventions that focus on nutrition. Diet may help to improve the health status of chronically stressed caregivers who have elevated susceptibility to high calorie "comfort" foods, or who do not have the time to cook and eat sufficient quantities of nutritious foods.

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HEPATOPROTECTIVE AND RENOPROTECTIVE EFFECTS OF ARTICHOKE LEAF EXTRACT VERSUS ROSEMARY EXTRACT AGAINST ACETAMINOPHEN INDUCED TOXICITY IN ADULT ALBINO RATS

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1. Introduction

Acetaminophen (APAP) has been widely used as an analgesic and antipyretic drug for many years. [1]

The pathogenesis of APAP- induced hepatotoxicity begins by the cytochrome P450-catalysed formation of the reactive metabolite N-acetyl-p-benzoquinone imine (NAPQI) that directly trigger oxidative stress, mitochondrial damage and hepatocellular injury [2].

Hence, the use of herbal medicine approach can be a promising alternative due to its multipronged mechanisms of action [6–8].

Therefore, natural compounds as medicinal herbs could be used for alternative treatments of paracetamol toxicity and to decrease its side effects due to their antioxidant activity.

Among these medicinal herbs is Artichoke (Cynara scolymus) is a plant rich in natural antioxidants and thus is used as herbal drug. Based on recent basic and clinical investigations, the extract of artichoke leaf has been revealed to be used for hepatoprotective [3], antimicrobial [4], and cholesterol reducing purposes [5].

artichoke, has multiple pharmacological actions. It was shown to have antitoxic activity antiulcero- genic activity and glycemia-lowering effect It helped in the management of mild hypercholesterolaemia and was protective against hepatocellular carcinoma and human breast cancer [6].

Rosmarinus officinalis, a common spice used worldwide for culinary and medicinal purposes. Various pharmacological studies demonstrated the analgesic, antiinflammatory, antioxidative, antitumor, antibacterial, and hepatoprotective properties of rosemary [7].

Therefore, the current research has been conducted to investigate the protective effect of artichoke leaf extract versus rosemary extract against acetaminophen Induced nephrotoxicity and hepatotoxicity in adult male albino rats.

2. Materials and Methods

2.1. Chemicals

Paracetamol (produced by EL Nasr Pharmaceutical Che- micals Co. 'ADWIC', Abu-Zaabal, Egypt) was purchased from a local pharmacy. All other chemicals used for the investigation were of analytical grade.

2.2. Extraction of plant material:

2.2.1. Artichoke leaves extract preparation

Artichoke (Cynara scolymus L.) was purchased from local market (Cairo, Egypt). The plant material was authenticated. Fresh leaves were separated and cleaned (weighed 2000 gm), it mechanically blended with 2000 ml distilled water then filtered through two-layer of cheese cloth, and the resultant residue was re-dissolved in 1000 ml distilled water by using magnetic stirrer for 1h. The later aqueous extract was added to the first one. The combined aqueous extract was condensed in rotary evaporator under vacuum then lyophilized and stored at 4°C until further use. Lyophilization was conducted by using Freeze-Dryer Lyophilizer, Virtis, USA in KFCMR. The method of extraction was carried out according to [8]

2.2.2. Rosemary leaves extract preparation

Rosemary was purchased from local market (Cairo, Egypt). The plant material was authenticated .The dried rosemary (R. officinalis L.) leaves were purchased from a local supermarket in Cairo (Egypt). Leaves were cleaned, shade dried, powdered, and extracted. The extract was prepared by refluxing leaves with bidistilled H2O for 36h (12h 3). The cooled liquid extract was then transformed to powder by evaporating water. The powder was redissolved in bidistilled water just before oral administration [9].

2.3. Doses and treatment

The dose of paracetamol used in this study was 1000 mg/kg body weight. This dose was previously reported to induce hepatotoxicity in rats [10]. This dose was dissolved in distilled H2O according to Yousef et al. [11] and given orally by gastric tube one time per 2 days for 4 weeks. Artichock leaves extract dose was 1.5 g/kg body weight according to [12] The chosen dose of rosemary extract was 125 mg/kg body weight. This dose was given by gastric tube for 4 weeks.

2.4. Experimental design

Animals were divided into four groups comprising ten animals each designed as the following:

Group 1 was regarded as the control group, which received distilled water.

Group 2 was administered paracetamol orally at a dose level of 1000 mg/kg/ every other day for 4 weeks.

Group 3 (administered Artichoke and paracetamol) was given artichoke at a dose level of 1.5 g/kg body weight and paracetamol for 4 weeks.

Group 4 (administered rosemary and paracetamol) was given rosemary at a dose level of 125 mg/kg body weight and paracetamol for 4weeks.

At the end of the experimental period, all animals were then sacrificed. The kidneys and liver were rapidly removed and washed in ice-cold saline in all groups. The organs were labelled and stored at 80 C until the biochemical analyses were conducted. Cardiac blood samples were collected immediately and the sera were obtained to determine biochemical parameters.

2.5. Biochemical analysis: Indices of liver damage (serum alanine aminotransferase and aspartate aminotransferase), alkaline phosphatase (ALP), c-glutamyltransferase (GGT) , and lactate dehydrogenase (LDH) activities were measured. Liver and kidney homogenates were analyzed for oxidative stress biomarkers malondialdehyde (MDA);, superoxide dismutase activity (SOD);, reduced glutathione (GSH), glutathione reductase (GR), and utilization glutathione-S-transferase (GST).
Renal function also was estimated by measuring serum Albumin, total protein, and creatinine and urea.

2.6. Histopathological examination
Kidney sections were fixed immediately in 10% formalin and prepared for examined microscopically.

2.7. Statistical analysis
Data analyzed statistically by SPSS using L.S.D. test, one way ANOVA, post hoc multiple comparisons.

3. Results
paracetamol produced a significant increase in serum activities of aminotransferases (AST & ALT), alkaline phosphatase (ALP), c-glutamyltransferase (GGT) , and lactate dehydrogenase (LDH) activities as compared with normal control. The treatment of paracetamol- administered rats with artichoke leaf extract and rosemary extract induced

a significant decrease in serum AST, ALP, and GST activities and a significant decrease in serum ALT and LDH activities as compared with the paracetamol group.
Administration of paracetamol-to male albino rats produced a significant increase in the levels of serum urea, creatinine and potassium when compared with normal rats. On the other hand, paracetamol administration caused a significant decrease in sodium concentration when compared with normal control rats. The treatment of paracetamol-administered rats with artichoke leaf extract and rosemary extract resulted in a significant decrease in serum urea, creatinine, and potassium and a significant increase in the sodium concentration in comparison with paracetamol-treated rats.
The results of the current study demonstrated that, there was a significant decrease in hepatic and renal glutathione (GSH) contents and GST, GPx, and SOD activities and a significant increase in lipid peroxidation in paracetamol administered rats as compared to control rats. Supplementation of ALE and RE significantly increased glutathione contents and GPx, GST and SOD activities (in the liver and kidney) as compared with paracetamol-treated rats.

4. Conclusion:
From the results of the present investigation we can conclude that, treatment with artichoke leaf extract (ALE) and Rosemary extract (RE) produced a potential protection of the liver and kidney against biochemical and histological alterations and oxidative stress induced by paracetamol.

5. Ethics approval and consent to participate
All experimental procedures conformed to the guidelines provided by the CPCSEA for studies and the ARVO resolution on the use of animals in research and to institutional guidelines. The study performed according to the recommendations of Faculty of Medicine, Ain Shams University Research Ethical Committee, (FMASU REC) No. FWA000017585. This study was an animal study and consent to participate and for publication was not applicable.

The protocol was approved by the Research Council and Ethical Committee.

6. Competing Interests

The authors have no competing interests.

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DEVELOPMENT OF A RAPID, AFFORDABLE, CONSUMER-FOCUSED MICROBIOME TRACKER

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Background: Interest in and knowledge of the gut microbiome has increased exponentially in the past decade. This once overlooked component of the gastrointestinal tract is now implicated in multiple aspects of human health, including mental wellness (e.g. depression, anxiety, stress), metabolic (e.g. diabetes, obesity),

neurologic (e.g. Alzheimer's, autism), gastrointestinal (e.g. irritable bowel syndrome, Crohn's), and immunologic (e.g. inflammation, cancer), among others.

Purpose/Objectives: Currently, most laboratory methods to test the microbiome rely on 16S ribosomal RNA sequencing. This testing method has several drawbacks, including: slow turnaround time, inconclusive quantification of low abundance species, labor intensive library preparation, and relatively high cost. Furthermore, the output is generally geared toward the scientific community, and are not particularly intuitive for the general public (e.g. consumers, patients).

Methods: Herein, we have developed a consumer-facing microbiome test and scoring system (BiomeTracker) that provides an attractive alternative to 16S rRNA-based testing services. This system allows samples to be processed quickly at low cost, and provides an easy to understand score for bacterial composition and health.

Results: BiomeTracker analysis was performed in parallel with 16S sequencing for human fecal samples, with similar abundance quantification for major phyla through families of bacteria. As a proof of concept, patient baseline and final samples following microbiome intervention (diet and supplementation) were tested, and BiomeTracker was able to accurately assess changes of low abundant species known to function in a healthy gut.

Conclusions: We envision that this system can be used by scientists and consumers alike to more quickly and easily evaluate the efficacy of dietary interventions on microbial composition and function.

THE EFFECTS OF VELOSITOL ON EXERCISED-INDUCED MYOKINES

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Velositol is a novel nutritional compound comprised of a modified-release chromium complex and a specialized form of amylopectin. This compound has been clinically shown to double exercise-induced muscle protein synthesis when added to a whey protein supplement. One mechanism of action is believed to be via increased skeletal muscle insulin sensitivity and improved amino acid metabolism leading to increased mTor activation and muscle protein synthesis. Another potential mechanism of action may be via enhanced myokines. Myokines (e.g., musclin and fractalkine) are cytokines released by muscle during exercise that lead to muscle protein synthesis and hypertrophy. To evaluate if myokines are affected by Velositol, the following preclinical and clinical studies were conducted.

In a preclinical study, 8-week old male Wistar rats weighing approximately 250 – 300g were reared at 22 ± 2oC in a 12/12 hour light/dark cycle and randomized into exercise

control, exercise + whey protein, and exercise + whey protein + Velositol treatment groups. Doses of whey protein increased from 6 – 40g equivalents. All rats completed a 10-day treadmill acclimation schedule that gradually increased in speed and duration up to 26 m/min for 15 minutes. On the day of the single-dose experiment, rats were exercised at 26 m/min for 2 hours and then administered by gavage study product or water, immediately after exercise. Study results showed that all active treatment groups significantly increased musclin serum levels compared to the exercise control group ($p<0.05$). However, all groups supplemented with Velositol + whey protein had significantly higher musclin levels compared to whey protein alone ($p<0.05$). The increases in musclin levels, seen in the Velositol + whey protein treatment group, were significantly correlated ($p<0.0001$) with increases in muscle protein synthesis ($r2=0.921$).

In a clinical study, blood samples were collected from four subjects for pharmacokinetic analysis of myokines. These subjects participated in a double-blind, cross-over design study, where they consumed a beverage containing 6g whey protein or 6g whey protein + 2g of Velositol and then completed 8 sets of bilateral isotonic leg extension at 80% of their estimated 1-RM. Blood samples were collected over a 4-hour period and analyzed for cytokines (musclin, fractalkine, GRO, IL-10, IL-15, IL-1RA, IL-6, MCP-1, MIP-1a, MIP-1b, and VEGF). Study results showed that cytokine levels were highest in Velositol + whey protein treated subjects. Of particular interest were the increases in musclin and fractalkine, both being exercise-responsive myokines involved in muscle growth and endurance.

In conclusion, preclinical and clinical data support the beneficial effects of the addition of Velositol to whey protein on enhancing levels of various myokines after exercise. These data present a novel mechanism by which Velositol exerts its beneficial effects on increasing muscle protein synthesis.

THE EFFECTS WHEY AND SOY PROTEIN SUPPLEMENTATION ON SERUM TESTOSTERONE AND CORTISOL CONCENTRATIONS WITH LONG TERM RESISTANCE TRAINING

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Background: Protein supplementation has been observed to support changes the adaptive response to resistance training. More specifically, whey protein has gained the most attention due to the multiplicity of biological actions related to its composition. Prior research in our laboratory on these compounds have found that daily supplementation with whey was more effective than soy protein or isocaloric

carbohydrate control treatment conditions in promoting gains in lean body mass (Volek et al., 2013). Testosterone and cortisol represent anabolic and catabolic signals, respectively, to muscle and have been shown to be involved with the adaptational changes in skeletal muscle and other tissues.

Purpose/Objectives: The purpose of this study was to examine the resting and acute exercise changes in with different protein supplementation protocols over a 9 month resistance training program.

Methods: Healthy recreationally active men were recruited and then randomly placed into one of three experimental groups, carbohydrate control (CC) (n =8, age 23.7±2.1yrs), whey protein (WP) (n =13, age 22.6±3.6 yrs.) and soy protein (SP) (n =8, 23.7±3.7 yrs.) with no differences in subject characteristics. All subjects performed periodized resistance training program that was supervised and testing included strength (1RMs), body composition (DEXA) and determination of serum concentration of testosterone and cortisol at baseline, and after 32 (~3 months), 64 (~6 months), and 96 (~9 months) workouts. An acute resistance exercise test at baseline and at 9 months was used to evaluate exercise-induced concentrations of the hormones before and after performing 6 sets of 10 repetitions in that squat at 80% of their 1 repetition maximum (1 RM) with 2 minutes rest between sets with blood collected at rest and then post-exercise at 0, 15, 30 and 60 minutes. Nutrient composition for the supplements were tested by and independent laboratory carbohydrate (maltodextrin), whey protein concentrate, and soy isolate (isoflavone free). Packets were given to subjects with instructions to mix the contents in 240 mL of water. Subjects were provided a 2-week supply with instructions to consume the supplement in the morning with breakfast on non-training days and immediately after exercise on training days. Subjects also recorded the date and time of supplement ingestion on log sheets. Empty packets were returned and counted at the end of each 2-week period. In addition, all supplements were spiked with 200 mg of para-aminobenzoic acid (PABA). Unannounced urine samples were collected from each subject during a training session approximately one time a month.

Results: Expected significant ($P \leq 0.05$) increases in 1 RM squat and bench press performances were observed for all groups with no treatment differences observed. Fat-free mass of the WP group as noted before in our prior research was significantly ($P \leq 0.05$) greater than the other two treatment groups. There were no differences between the groups for changes in resting serum testosterone (nmol/L) (CC: To 24.2±6.1;T3 23.4±5.1;T6 24.6±4.9;T9 24.3±5.2)(WP: To 25.2±5.1;T3 24.4±6.1;T6 26.6±3.9;T9 24.8±4.2) SP: To 23.2±6.5;T3 22.4±6.1;T6 25.6±4.3;T9 23.3±4.2). In response to the acute resistance exercise stress all groups demonstrated significant ($P \leq 0.05$) increases following exercise at 0, 15, 30 minutes. Again for serum cortisol (nmol/L) there no significant differences between the groups (CC: To 402±150; T3 455±188; T6 404±188;T9 403±177) (WP To 366±170; T3 415±168;T6 424±168;T9 373±187) (SP To

412±170; T3 425±178;T6 394±178;T9 413±167). Again in response to the acute resistance exercise stress all groups demonstrated significant (P ≤0.05) increases following exercise at 0, 15, 30 minutes.

Conclusions: These data indicate that testosterone and cortisol as dynamic hormonal signaling molecules do not change at resting homeostatic conditions over 9 months irrespective of the nutritional intervention. This may be due to optimal training programs and supervision allowing adequate rest and recovery along with dietetic supervision. How the acute signaling consequent to elevations of testosterone and cortisol with resistance exercise stress impact lean body mass remains to be determined.

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HERBALS AND NEUTRACEUTICALS AS ADJUVANT THERAPY IN ACUTE EXACERBATIONS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background: Chronic obstructive pulmonary disease (COPD) continues to be a major medical problem and is the third leading cause of death in the United States behind cancer and heart disease. Acute exacerbation of COPD is associated with upper and lower airway inflammation, as well as with systemic inflammation. Exacerbations in COPD are recognized as heterogeneous events, and different interventions may impact on different exacerbation drivers, depending on their mechanism. Thus, combined interventions with distinct actions of herbs and nutraceuticals to maximize the potential for exacerbation should be attempted.

Objective: To investigate the effectiveness of a herbal and nutritional supplement as an adjuvant therapy for managing acute exacerbations of COPD compared to conventional therapy alone.

Methods: This was a prospective, randomized, open-label, controlled trial in 60 patients presenting with acute exacerbation of COPD. Patients were randomized into two groups, the Control and the Experimental groups. The Control group was treated with the standard therapeutic protocol (Antimicrobial + Corticosteroids + Bronchodilator + Mucolytic drugs). The Experimental group, besides standard therapeutic protocol, patients were given a Test Supplement, a unique combination of natural herbal ingredients including Sophora flavescens, Dracaena cambodiana, Reynoutria japonica extract, Calotropis gigantea extract, together with L-carnitine, fumarate, alpha lipoic acid, and magnesium. The treatment outcomes including clinical and para-clinical parameters of exacerbation of COPD were compared between the experimental group and the control group at day 15 and day 30. This study was conducted according to protocol: 01.2014-HTNCKH.

Results: The results showed a significant reduction of major COPD exacerbation symptoms in Experimental group. The favorable progresses in mMRC scale and CAT score before and after treatment, between Experimental group and Control group were statistically different. Symptom control such as cough, copious sputum secretion and bacterial infection was 90% effective (very good 50.0%, good 40.0%) in Experimental group compared to 50% (very good 20%, good 30.0%) in Control group. No adverse side effects were observed in Experimental group.

Conclusions: nutritional supplement could be an effective and safe adjuvant therapy in acute exacerbations of COPD.

MAKING NUTRITION RELEVANT TO CURRENT HEALTH CARE PROTOCOLS: A SYSTEMIC REVIEW OF NUTRITION COST-EFFECTIVENESS FOR INTEGRATIVE AND FUNCTIONAL HEALTH CARE

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Purpose: Nutrition plays a critical role in one's health. Not only do humans rely on the food supply for energy, health, and connection, it is an epigenetic form of communication via a modifier of gene expression. Nutritional interventions offer value for money in different healthcare settings and among different populations with beneficial outcomes, but lacks support due to more rigid guidelines in comparison to traditional healthcare funding and reimbursement. While national bodies and scientific organizational and health care decision makers at all levels create protocols based on the best evidence available, evidence-based nutrition is more challenging due to its complex multidisciplinary nature and pharmaceutical competitors.

Objective: 1) Review current research on the cost-effectiveness of nutrition therapies/interventions; 2) provide support for aligning paradigm shift of nutrition economics for health reimbursement policy-makers

Method: This review of literature of the last five years will look at evidence-based acute, chronic, and preventative care medical nutrition intervention studies. This study follows the PICO search protocol, summarizing the value for money of nutrition intervention/therapy. Validity is provided through Drummond's checklist and the AMSTAR checklist.

Results: A PICO summary chart provides the results from the inclusionary sample of 30 free full text articles. Traditional health economic methodology plus additional factors for nutrition economic evaluation are discussed.

Conclusion: Nutrition economics is a critical multi-faceted component to integrative and functional healthcare. Research alignment to the paradigm shift from sick care to patient-centered preventative/pro-health care is evolving. A patient's perspective and personalized care must be represented when formulating cost-effectiveness of nutrition. A PICO summary chart provides the results from the inclusionary sample of 30 free full text articles. Traditional health economic methodology plus additional factors for nutrition economic evaluation were discussed. There is a growing body of research to support the necessary shifts in determining the economic value of nutrition for national bodies and scientific organizational and health care decision-makers that is relevant to current health care protocols. This accumulation of evidence is needed to demonstrate the health and economic benefits of quality nutrition therapy, intervention, and education, as it plays as a critical integrative and functional role across the continuum of care.

A UNIQUE SYSTEM FOR STUDYING OF THE ANTIOXIDANT PROPERTIES OF RESVERATROL AND GLUTATHIONE

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Biomolecular and cellular damage caused by natural free radical production can be significant, having been implicated in Alzheimer's disease, autisms, Down's syndrome, atherosclerosis, and some forms of cancer, despite the presence of antioxidants obtained from the diet and from cellular metabolism. However, these antioxidants do afford the cell significant protection against free radical-induced damage. Thus, we have utilized a unique chemical model system, developed by our research group that utilizes a multistep, 0.1% hydrogen peroxide-initiated luminol reaction. In this reaction, a diradical intermediate is produced that results in chemiluminescence, quantifiable by luminometry. Because the chemiluminescence is proportional to the radical production, we have evaluated the antioxidant action of resveratrol and glutathione individually and combined for their ability to inhibit the radical-induced chemiluminescence. All reactions were run in triplicate, utilizing a 7.2 pH sodium phosphate buffer containing

112 μM luminol. The buffer also contained 0, 21, 42, and 85 μM glutathione, respectively, or 0, 21, 2.1, 0.2 μM resveratrol, respectively, or various concentrations of both. For each antioxidant, separate dose-responses curves for the highly significant inhibition of chemiluminescence were obtained. When combined, the significant inhibitory effect of both antioxidants was additive. Thus, these data validate the use of our chemical model system to evaluate the relative efficacy of a variety of antioxidants. Finally, spectrophotometric studies are being carried out to demonstrate the actual release of hydrogen during the antioxidant-induced inhibition reactions.

VITAMIN D STATUS AND JUMP HEIGHT IN FIGURE SKATERS

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Background: Historically, vitamin D is best known for its role in bone health by maintaining serum calcium levels via intestinal calcium absorption (Lovell, 2008). However, recent evidence demonstrates it is a complex fat-soluble hormone involved in a wide range of metabolic functions including immune system support, calcium homeostasis, and muscle function (Wolman et al., 2013). Vitamin D is thought to directly impact neuromuscular function via the existence of vitamin D receptors in muscle tissue and deficiency can result in sarcopenia, muscle weakness, and pain (Flueck, Schlaepfer, & Perret, 2016). Muscle growth and cell differentiation are both influenced by vitamin D, as well as muscle contractility (Flueck et al., 2016)

Vitamin D is most effectively obtained through skin exposure to ultraviolet B rays of the sun, with minimal amounts obtained from the diet. However, lack of sun exposure through sunscreen use, latitude, seasonal variation, and indoor training causes a reduction in serum vitamin D status
(Hildebrand, Miller, Warren, Hildebrand, & Smith, 2016). Athletes in sports such as figure skating, gymnastics, and dance spend the majority of their training sessions indoors. Indoor training has been associated with low vitamin D status compared to those training outdoors (Wyon, Koutedakis, Wolman, Nevill, & Allen, 2014). For these indoor athletes, living in northern latitudes may also have a negative impact due to the major reduction in sun exposure during winter months. For example, a study of professional ballet dancers showed that all dancers were either insufficient or deficient in the winter months, with only 3 out of the 19 dancers reaching normal status at the end of the summer (Wyon et al., 2014). However, it is difficult to assess status of athletes and the general population based on these studies since different serum marker levels are used to determine insufficiency, deficiency, and sufficiency. The effects of vitamin D status on muscular performance have been assessed in multiple studies, some within specific athletic populations, and some within the general, healthy population. One such test used to measure muscular performance is a jump height test.

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Problem: Figure skating is a sport that requires multiple hours per day of indoor training. For many of these athletes, they also live in northern latitudes where the sun does not get to a high enough angle to provide sufficient UVB radiation in the winter months (Jastrzebska, Kaczmarczyk, & Jastrzebski, 2016). Because Vitamin D plays a contributing role in the health of muscles and musculoskeletal performance, many figure skaters are at risk of decreased performance based on musculoskeletal strength measures. Figure skaters need muscular strength and power to perform many of the difficult jumps and skills
(Ziegler, Nelson, & Jonnalagadda, 1999). In order to compete at the top level, skaters are now required to complete triple and quadruple jumps. In order to do this successfully, a skater must generate enough vertical velocity at takeoff to complete the rotations cleanly (King, 2005). According to Ziegler et al.
(1999), the majority of male and female figure skaters have low dietary intake of vitamin D, with vitamin D intake status at 35% RDA. The combination of low dietary vitamin D intake and limited sun exposure, especially in the winter, puts figure skaters at increased risk of decreased musculoskeletal performance.

Hypothesis: Supplementation with Vitamin D3 during the winter months improves lower body muscle power in figure skaters as measured by jump height tests.

Methodology: A search was conducted on PubMed within the University of Western States library database using the following search terms: Vitamin D AND Jump Height; Vitamin D AND athletes; Vitamin D AND muscle function; Vitamin D AND muscle performance; Vitamin D AND performance; Vitamin D AND sports; Vitamin D AND figure skating. Exclusion criteria were based on relevance, publication date, full text availability, and English language. Articles were examined thoroughly for the associations between vitamin D status and jump height, as well as the methodologies and test parameters.

Results: In 2013, Close et al. conducted a placebo controlled trial examining the effects of vitamin D3 supplementation of 5000 IU per day for 8 weeks. Participants included 61 male athletes training or competing 6 days per week and 30 male healthy non-athletic controls. Both athletes and controls were living in the British Isles of the UK at latitude of 53° N and were not taking supplements at the time. This particular location typically experiences extreme cloud cover. All blood samples of total serum 25(OH)D were taken in the winter months (November – January) following an overnight fast. Capsules of vitamin D were given as a daily supplement of 5000 IU in a double blind design. While they used multiple tests to study the effects of D3 supplementation on musculoskeletal performance, the vertical jump test was used to determine the maximum power of the lower limbs using an electronic jump mat. Hands were placed on the hips to emphasize lower leg strength measures only. At baseline, there were no significant differences in performance measurements between the placebo and control groups. Significant improvements were seen for the vitamin D group in regards to vertical jump height,

while the placebo group showed no significant improvements. The studied concluded that musculoskeletal performance, as measured by jump height, improved with vitamin D3 supplementation (Close et al., 2013).

A controlled prospective study published in 2014 looked at the effects of supplementation with 2000 IU per day of Vitamin D3 on muscle function in elite ballet dancers. Twenty-four elite ballet dancers were recruited for the study, with 17 in the intervention group, and 7 in the control group. These dancers primarily train indoors. Serum 25(OH)D was taken during the previous year monitoring the dancers during the summer and winter months. While 15% of the dancers reached normal levels of serum 25(OH)D at the end of summer, all dancers were found to be insufficient (10-30ng/ml) or deficient (<10 ng/ml) during the winter. Oral supplementation of 2000 IU per day in tablet form was given to the intervention group for 4 months. Lower body muscular power was assessed using a standing vertical jump on a jump meter. This jump test was different than the previous study in that athletes assumed the dance 1st position, starting with heels together and hips rotated externally. All jumps were performed on a jump meter with the dancers starting in a half-squat then jumping as high as possible with heels together and arms remaining at their sides. Jumps were repeated 3 times. Results showed significant improvements in isometric quadriceps strength for the intervention group, while the control group stayed the same. Even though the study had some limitations such as small sample size and the inability to randomize, the authors concluded that vitamin D3 should be considered for athletes training indoors, especially in the winter months (Wyon et al., 2014).

A study published in 2016 looked at the effects of vitamin D status on muscle strength and power in a group of 113 male and female NCAA collegiate athletes. All athletes were located in the southern United States with latitudes ranging from 35.3° to 36.12° N. Data was collected in the months of September and October, with a few in November. Serum 25(OH)D was collected on all participants and vitamin D status was determined using the World Health Organization standards of sufficient (>75 nmol/L), insufficient (72.5-50 nmol/L), and deficient (<50 nmol/L). Samples were collected over 2 years and athletes were categorized as deficient (8.9%), insufficient (22.7%), and sufficient (68.3%). Vertical jump height was measured using the TENDO Weightlifting Analyzer and contact mat. Athletes performed 3 jumps with hands on their hips and the average of the 3 jumps was used for the maximum jump height total. Based on their results, the authors concluded lower vitamin D status resulted in a decrease of 15% for the vertical jump test. Therefore, as serum 25(OH)D decreases, indicators of muscle strength and power decrease as well (Hildebrand et al., 2016).

Another study examined the results of vitamin D status and exercise performance in 67 professional soccer players in Crete, Greece (latitude of 35.9° N). Baseline measurements were taken in May, and follow-up testing was completed in July. These tests included serum 25(OH)D levels taken in the morning followed by measures of

muscle strength which included jump height testing (squat jump and countermovement jump). Athletes were instructed to abstain from vitamin D or performance enhancing supplementation and to avoid any exercise training 2 days prior to the tests. Vitamin D levels were defined as severely deficient (<10 ng/ml), deficient (between 10 – 20 ng/ml) and insufficient (between 20 – 30 ng/ml). A jumping mat was used to assess the squat jumps and countermovement jumps. The results showed an association between vitamin D levels and neuromuscular performance and power in this group of professional soccer players (Koundourakis, Androulakis, Malliaraki, & Margioris, 2014).

A double-blind, placebo-controlled study published in 2016 examined the effect of 8 weeks of vitamin D3 supplementation from January to March in 36 well-trained football players in Poland. Sunlight during this time was very low. Athletes were divided into either the experimental group supplemented with 5000 IU vitamin D3 per day (n = 20), or placebo group (n = 16). All athletes were involved in high intensity interval training (HIIT) and serum 25(OH)D was collected pre- and post- experiment. Vertical jumps of squat jump and countermovement jump were used to assess explosive power. All subjects lived on campus and were fed the same meals. Supplementation was given using droplets in the morning while the placebo group received sunflower oil in identical form. Serum 25(OH)D levels were not different between the groups at baseline. There were also no significant differences in power tests between groups at baseline as well. For the jump test, athletes performed a 20 minute warm-up of 5 vertical jumps followed by a test of 2 squat jumps without arm swings and 2 countermovement jumps with arm swings. The authors found that both groups improved significantly in response to HIIT training adaptation, and no significant differences were seen in the power-related parameters in the supplemented vs. placebo groups. The authors also suggest that according to the most current research, significant strength gains may not be seen in athletes unless they are deficient to begin with (Jastrzebska et al., 2016).

Published in 2015, a cross-sectional study examined 53 junior and collegiate hockey players training near Minneapolis, Minnesota (latitude of 44.9° N) during the months of May through June (off-season). The authors investigated the association between serum 25(OH)D levels and maximal-intensity exercise performance, with one of the measurements being vertical jump performance. No athletes were deficient (<20 ng/ml) at baseline measurements. The athletes were assessed at 2 different sessions, minimally separated by 2 days, with second tests completed by day 9. Vertical jump was measured using mechanography and a Vertec with a force plate located below the Vertec. The athletes completed a 5 minute treadmill warm-up followed by the squat jump. Arm swing was not allowed and best performance determined jump height. Results showed that serum 25(OH)D levels affected measures of upper-body strength, but failed to show an association with lower body strength and power measures. The authors suggested that this might be due to the fact that deficient vitamin D status below 20 ng/ml might be needed to see any significant changes (Fitzgerald, Peterson, Warpeha, Johnson, & Ingraham, 2015).

A double-blind, randomized, placebo-controlled study of healthy male and female Gaelic soccer players was performed to assess the effects of oral spray solution of vitamin D3 supplementation on exercise performance outcomes. The study included 18 males and 24 females living near Coleraine at latitude of 55°N. Vitamin D3 supplementation of 3000 IU was administered as an oral spray solution for 12 weeks. The placebo group received the same oral spray solution without the vitamin D3. All participants (subjects and researchers) were blinded to the allocations. Fasting blood levels were taken. Vertical jump height was measured using a countermovement jump on a calibrated electronic jump mat. A total of 3 jumps was allowed with 10 seconds rest between jumps. The best height was recorded, rather than an average. While supplementation did correct deficiencies in these athletes, it did not improve the aspects of physical performance, such as jump height (Todd et al., 2016).

Another randomized, double-blind, placebo-controlled trial examined the effects of vitamin D3 supplementation on measures of muscle strength in ethnic minority immigrant adults in Oslo, Norway. A group of 251 healthy adult males and females were assigned to 3 supplementation groups of 1000 IU vitamin D3, 400 IU vitamin D3, or placebo all in identical tablet form for 16 weeks. Jump heights were measured at baseline and post-intervention. Baseline assessments were measured between January and March with follow ups at 16 weeks of intervention. Using a platform, countermovement jump tests were used to assess jump height. All jumps were performed with hands on their hips and a total of 5 jumps were performed. The average of the 2 highest jumps was then used in the data pool. Results showed no significant different between the 3 groups in regards to jump height. The authors suggested one limitation to their study was that the levels of vitamin D3 supplementation were not enough to raise serum 25(OH)D levels above 50 nmol/L in the majority of the participants that were deficient at baseline (Knutsen et al., 2014).

A retrospective study examined the difference between serum 25(OH)D3 and 1,25(OH)D3 on measures of lower body strength, which included jump height. A total of 79 women, and 37 men were included in the study and serum vitamin D status of multiple metabolites was performed. Deficiency was defined as <20 ng/ml, insufficiency was 20 - 30 ng/ml, and normal was >30 ng/ml. 58% of the group was deficient, while only 14% had normal levels. Jump height was measured using a ground force reaction plate but the study failed to mention the exact parameters of the jump mechanics. Results conclude that the active form of vitamin D3, 1,25(OH)2D3 are better correlated with jump height than the inactive form of vitamin D3, 25(OH)D3. No significant correlations were seen between the other vitamin D metabolites and jump height. This particular study was interesting because it pointed out that many previous studies have failed to show a significant correlation between vitamin D3 status and jump height possibly because they have all focused on the inactive form of 25(OH)D3 in circulation (Hassan-Smith et al., 2017).

A double-blind, randomized controlled trial examined the effect of high doses of vitamin D2 in 69 postmenarchal females over the course of 1 year. All participants had baseline levels of serum 25(OH)D less than 37.5 nmol/liter and were attending the same school in Manchester, United Kingdom at a latitude of 53.4° N. Participants were given either placebo or 4 doses of 150,000 IU for 1 year (once every 3 months). Jump height was tested using a Leonard Mechanograph Ground Reaction Force Platform. Participants were encouraged to jump as high as possible using Two-footed jumps performed using countermovement with no restrictions on arm movements. Supplementation resulted in an increase to 56.0 nmol/L in the treated group vs. 15.7 nmol/L in the placebo group. However, the authors concluded that jump height only improved marginally and therefore was not significant or supportive of their hypothesis. The authors did recognize that one limitation to their study design could have been their decision to use ergocalciferol (D2) over cholecalciferol (D3). However, their decision to use the plant form of D2 was necessary for the religious beliefs of the girls participating in the study (Ward et al., 2010).

Conclusion: Based on the above research study analysis, the evidence is mixed in regards to vitamin D3 supplementation for improvements in lower body musculoskeletal performance as measured by jump height. The limited number of studies, as well as the differences between deficiency versus sufficiency measures limited the ability to relate all studies. The majority of the randomized, double-blinded, placebo-controlled studies reported findings that did not support the hypothesis of this paper, while the majority of the smaller studies did. Variations in measurements of jump height protocol could also have an impact on the results above. In addition, some studies tested athletes during the winter months, and some in the summer which might also result in different outcomes. The research points to musculoskeletal improvements only in those athletes that are severely deficient. More studies are needed to assess the serum 25(OH)D levels of figure skaters to see if they are deficient and to see if supplementation will affect lower limb muscle power as assessed by jump height. Overall, more studies are needed to assess the role of vitamin D and jump height

Suggestions for future research include:

1. Assessing serum vitamin D status using both the active 1,25(OH)2D3 form, and inactive 25(OH)D3 form on jump height in larger studies of athletic populations.
2. Assessing serum vitamin D status with the markers in #1 during the US Figure Skating S.T.A.R.S. combine. The combine occurs multiple times each year and it assesses jump height and other measures of musculoskeletal strength for figure skaters all over the United States.
3. Standardizing the vertical height measures as well as the levels of vitamin D status will help to compare future studies.

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MICRONUTRIENT VARIATION BETWEEN FRUIT AND VEGETABLES

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Background: Diets that incorporate fruit and vegetables are beneficial, and their consumption not only promotes bone health (1-3), but is also protective against excess

adiposity (4), diabetes (5), cardiovascular and cerebrovascular disease (6, 7), and some forms of cancer (8, 9). The need for incorporating nutrient-rich fruit and vegetables in our diets is apparent. However, the general consensus of what is considered fruit or vegetable is misleading.

Purpose/Objectives: Our study aims to examine how do botanical fruit and vegetables differ in micronutrient content, and whether in the US, people who are eating what they perceive as a vegetable, actually are eating botanical fruit. Finally, we aim to analyze whether this misperception matters in terms of nutrient intake. We hypothesized that there is a high micronutrient variation within the individual groups of fruit and vegetable, and between fruits and vegetables.

Methods: A list of the most commonly eaten fruit and vegetables in the USA, and their per-capita consumption, was compiled. In total, 22 botanical fruit and 20 botanical vegetables were included in the study. Each item was individually searched in the USDA's National Nutrient Database. Data was further normalized in milligrams per Calorie (mg/kcal) for all micronutrients. IBM SPSS was used to run the statistical analyses. The significance level was set at 5%. A 2-tailed Mann-Whitney test was used to determine the p-values. Descriptive statistics were used to determine the mean and standard deviation, and coefficient of variation and the inter- and intra-variability of nutrients among items was determined. Using Top/Bottom rules in Excel, for each micronutrient, we identified the above average, top 10% and bottom 10% of produce containing the specified micronutrient.

Results: On average, 22 out of 28 micronutrients were statistically significant. The majority was significantly higher in vegetables than in fruit, except cryptoxanthin, which was higher in fruit compared to vegetables. Botanical vegetables were on average higher in calcium, sodium and selenium. Conversely, perceived vegetables were on average higher in alpha carotene. There was a higher variability of micronutrient content within the vegetables group than within the fruit group. Likewise, there was a higher variability within the botanical vegetables than within the perceived vegetables. Spinach, asparagus and endive lead in the micronutrient content per Calorie. Among the least micronutrient dense per Calorie were onion and sweet potato.

Conclusions: With this study, we aimed to investigate what are the most commonly eaten fruit and vegetables, and evaluate their nutrient content per Calorie, and how this differs across groups. Our findings suggest that vegetables as a group have a higher micronutrient content per Calorie than fruit. However, vegetables also have a higher within group variability. In general, we noticed that the most consumed fruit and vegetables in the US have some of the lowest micronutrient content and variety. In terms of perceived and botanical vegetables, we noticed that botanical vegetables are higher in calcium, selenium and sodium. In conclusion, understanding the

micronutrient content in many of the commonly eaten fruit and vegetables, will help consumers make more informed decisions about their choice of diet.

Table 1: Micronutrient content (mg/kcal) difference between fruit and vegetables

	Fruit (N=16)			Vegetables (N=20)			
Micronutrient	**M**	**SD**	**CV (%)**	**M**	**SD**	**CV (%)**	**p-value**
Calcium	0.3847	0.3300	85.7738	2.0283	2.7513	135.6468	0.0001
Iron	0.0067	0.0060	89.5447	0.0363	0.0333	91.6553	0.0001
Magnesium	0.2303	0.0915	39.7507	0.8258	0.6930	83.9107	0.0001
Phosphorous	0.3660	0.1749	47.7964	1.5006	0.6261	41.7187	0.0001
Potassium	3.6407	1.5462	42.4698	10.6100	5.4345	51.2201	0.0001
Sodium	0.0555	0.1124	202.7872	1.1798	1.2326	104.4815	0.0001
Zinc	0.0026	0.0014	55.5410	0.0129	0.0095	74.0344	0.0001
Copper	0.0013	0.0005	39.1738	0.0045	0.0063	140.8888	0.0020
Manganese	0.0034	0.0054	157.2817	0.0109	0.0092	84.5120	0.0001
Selenium	0.0001	0.0001	82.1797	0.0003	0.0003	89.6549	0.0001
Thiamin	0.0009	0.0004	49.8925	0.0026	0.0018	68.3816	0.0001
Riboflavin	0.0007	0.0001	20.6103	0.0029	0.0020	70.8903	0.0001
Niacin	0.0089	0.0056	63.3382	0.0203	0.0101	49.7732	0.0010
Pantothenic acid	0.0045	0.0026	57.7776	0.0110	0.0108	98.5289	0.0040
B6	0.0017	0.0009	51.0382	0.0049	0.0019	38.6650	0.0001
Folate	0.0035	0.0024	69.5901	0.0257	0.0267	103.6892	0.0001
Choline	0.1449	0.0518	35.7488	0.5126	0.3978	77.6092	0.0010
Betaine	0.0036	0.0029	80.8670	0.5051	1.4834	293.6813	0.0250
Cryptoxanthin	0.0099	0.0199	200.3937	0.0019	0.0050	257.8034	0.0040
Lutein + zeaxanthin	0.0092	0.0090	98.3676	0.6472	1.2059	186.3318	0.0340
Vitamin E	0.0058	0.0054	94.5583	0.0225	0.0269	119.7406	0.0500
Vitamin K	0.0494	0.0597	120.8866	4.8786	6.1345	125.7418	0.0001

M = mean, SD = standard deviation, CV = coefficient of variance

Table 2: Micronutrient content (mg/kcal) difference between perceived- and botanical vegetables

	Perceived vegetables (N=6)			Botanical vegetables (N=20)			
Micronutrient	**M**	**SD**	**CV (%)**	**M**	**SD**	**CV (%)**	**p-value**
Calcium, Ca (mg)	0.7978	0.3562	44.6478	2.0282	1.6307	80.4013	0.0290
Sodium, Na (mg)	0.1495	0.0800	53.5072	1.1798	1.2326	104.4815	0.0070
Selenium, Se (mg)	0.0111	0.0082	73.6897	0.0325	0.0291	89.6549	0.0310
Carotene, alpha (mg)	0.0277	0.0620	224.1725	0.0043	0.0185	430.2326	0.0160

M = mean, SD = standard deviation, CV = coefficient of variance

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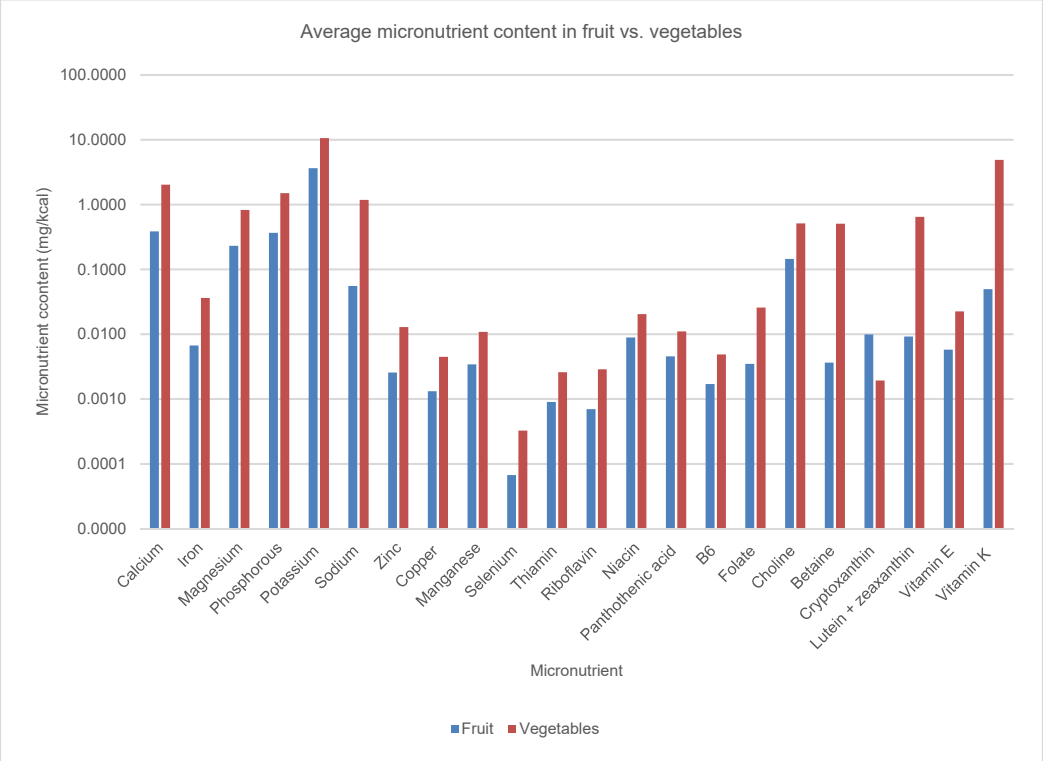

Figure 1: Average micronutrient content in fruit compared to vegetables1
1Only statistically different micronutrients are included in the graph

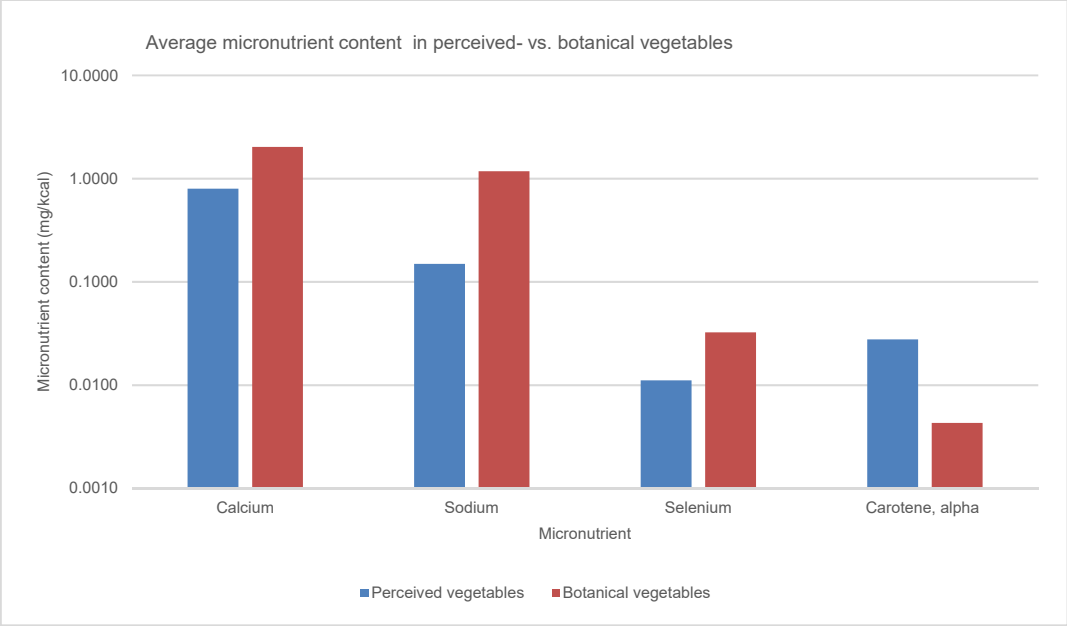

Figure 2: Average micronutrient content in perceived vegetables compared to botanical vegetables1
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THE EFFECT OF SIMPLE CARBOHYDRATE CONSUMPTION ON MARKERS OF METABOLIC HEALTH IN FIREFIGHTERS

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Background: Consumption of simple carbohydrates (sCHO) is associated with increased markers of cardiometabolic disease, chronic inflammation, cognitive decline,

and cancer risk1-4. However, physical activity has been shown to play a protective role against the deleterious effects induced by inflammatory markers5.

Objective: We examined the effects of sCHO on metabolic health parameters between active (PA) and sedentary (S) firefighters.

Methods: As part of a nutritional wellness assessment and lifestyle program, eighty-nine active duty male firefighters age 42 ± 15 y volunteered for the study. Physical activity level (PAL), daily energy expenditure divided by resting metabolic rate, was used to categorize firefighters into two groups: 1) S (PAL < 1.5, n = 27) and 2) PA (PAL >1.5, n = 62). Their sCHO intake was classified using plate-sized volumes per week as: Low (0-1), Moderate (1-2), High (3-4), and Very High (>5). Systolic blood pressure (SBP), body fat percentage (BF%), and waist circumference (WC) were analyzed across groups.

Results: As anticipated, subjects who consumed Very High sCHO had higher SBP than those who consumed Low amounts, 138 mmHg ± 3.6 vs. 126 mmHg ± 2.8 ($p < 0.05$). However, SBP was not different ($p > 0.05$) between S (130.6 mmHg ± 15.8) and PA (127.8 mmHg ± 12.6).
Waist circumference of S (39.4 ± 5.3) and PA (39.3 ± 5.4), and body fat percentage of S (26.8 ± 8.7) and PA (24.5 ± 8.2) were similar among groups ($p > 0.05$).

Conclusion: High intake of sCHO exerted unfavorable effects on SBP in male firefighters regardless of physical activity level. Thus, exercise alone may not be sufficient to combat the cardiometabolic disease risks associated with sCHO consumption in firefighters. More research is warranted to evaluate the benefits of dietary change and other lifestyle factors to reduce health risks in this population.

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DO RESTRICTIVE DIETS LEAD TO IODINE DEFICIENCY?

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Iodine deficiency is one of the most common and preventable causes of mental retardation and thyroid dysfunction in the world, and has been associated with various other health complications and diseases, even in countries with sufficient iodine intake. The rise in popularity of restrictive diets, such as the Paleo Diet is cause for concern due to the avoidance of common foods containing iodine such as grains, dairy, processed foods, and added salt.
These restrictive diets prove beneficial for many people; however, people following these restrictive diets should have their iodine levels monitored closely to ensure healthy iodine status.

Iodine is an essential trace element, required by humans for normal thyroid function, growth, and development. Although only a small amount is required, iodine must be obtained through exogenous sources as it plays an important role in thyroid hormone synthesis of thyroxine (T4) and triiodothyronine (T3), as well as lipid metabolism (Lee, Shin, Cho, & Song, 2016; Lee, Shin, & Song, 2016). Adults have about 15–20 mg of circulating iodine and roughly 70%–80% is stored in the thyroid (Zimmermann, Jooste, & Pandav, 2008) with the remaining iodine found in the eye, and mucosa of the gastrointestinal, mammary, and salivary glands (Ahad, & Ganie, 2010). Iodine accumulates in the breast to be used during lactation and is important for the development of infants. Additionally iodine may have antioxidant properties and play a role in immune function. (Ahad, & Ganie, 2010).

The US Department of Agriculture (USDA) percentage daily value of iodine is set at 150 µg (100% DV) for US adults 18 years and older, with increasing levels for pregnant (220 µg/day) or lactating females (290 µg/day) (United States Department of Agriculture (USDA), n.d.)

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Iodine Deficiency Dysfunction (IDD) is used to describe an array of conditions and diseases that are associated with iodine deficiency (Kapil, 2007; Kopp, 2004). Iodine deficiency is the most common endocrinopathy and remains the leading cause of preventable mental retardation globally (Patrick, 2008; Pearce, Andersson, & Zimmermann, 2013). Two major factors for IDD are inadequate iodine intake (associated with low consumption of iodine-containing foods), and inadequate iodine utilization (associated with intake of goitrogens) (Ahad & Ganie, 2010). As of 2013, the global iodine status showed one-third of the world's population remains iodine deficient (Pearce et al., 2013). Even in countries with sufficient iodine status, it has been reported that some groups such as vegans, vegetarians, and those avoiding iodized salt by choice may actually be deficient (Pearce et al., 2013). Adults deficient in iodine have low energy, reduced cognitive function and a reduction in work performance (Ahad & Ganie, 2010). Deficiency can also lead to hypothyroidism, goiter, and is associated with dyslipidemia (Lee, Shin, & Song, 2016; Pfeiffer, Sternberg, Caldwell, & Pan, 2013).

The most recognized and well-documented sign of iodine deficiency is endemic goiter, but there are several other manifestations that can occur. Some of the most common include hearing loss, learning disabilities, brain damage, and myelination disorders that occur in infants and children due to maternal iodine deficiency. Pregnancy and lactation also increase iodine loss, increasing the risk for goiter and possibly hypothyroidism. Women who are iodine deficient can also experience overt hypothyroidism, infertility, and miscarriage (Patrick, 2008).

Additionally, iodine deficiency may be associated with increased risk of certain cancers, such as reproductive, prostate, endometrial, ovarian, and breast cancers (Patrick, 2008; Stadel, 1976). With mild iodine deficiency, normal thyroid hormone levels may still be present, but there will be thyroid enlargement. Studies have shown mild hypothyroidism as a result of iodine deficiency during pregnancy can lead to lower IQ and cognitive defects in children (de Escobar, Obregón, & del Rey, 2007; Patrick, 2008).

The prevalence of iodine deficiency in North America is less severe than other parts of the world. However, according to the National Health and Nutrition Survey (NHANES), US adult median urinary iodine levels dropped from 320 mcg/L between 1971-1974 down to 145 mcg/L between 1988-1994, representing a 50 percent decrease in iodine intake, but in 2007-2008 levels median levels increased slightly to 164 mcg/L (Caldwell, Makhmudov, Ely, Jones, & Wang, 2011)

The Centers for Disease Control (CDC) reports that in the United States (U.S.), over 1/3 of women of childbearing age are iodine insufficient as defined by urinary iodine levels below 100 mcg/L, which could lead to complications with their pregnancies, or the development of their children (Patrick, 2008).

Dietary iodine is found in food, water, and in fortification, as seen in iodized salt. Naturally occurring iodine can be found in the ocean and soil, with higher concentrations near coastal areas and decreasing levels in the soil due to erosion (Leung, Braverman, & Pearce,
2012). Iodine food sources include seaweed, cod, dairy, processed breads and noodles, eggs and iodized salt (Zimmermann et al., 2008; National Institutes of Health (NIH), 2011). However, organic milk is found to have lower levels of iodine than conventional, possibly because of the reduced use of iodine-containing feed and the practice of teat dipping in iodine solution in conventional milking (Flachowsky, Franke, Meyer, Leiterer, & Schone, 2014). Due to these food sources and iodized salt (used by about 70% households in the U.S.), iodine deficiency is rare in the U.S. In food processing where iodized salt was previously used, the majority of the salt now used in processed foods is not iodized (Fuge & Johnson, 2015). Iodine content in some common foods can be seen in Table 1 below.

Iodine content of food

Food	Iodine (µg)
Salt, iodized, 1 teaspoonful	400
Haddock, 75g	104 – 145
Bread, regular process, 1 slice	35
Cheese, cottage, 2% fat, 1/2 cup	26 – 71
Shrimp, 75g	21 – 37
Egg, 1	18 – 26
Cheese, cheddar, 30g	5 – 23
Ground beef, 75g, cooked	8

Table 1
Source: (Kapil, 2007)

In addition to the prevalence of insufficient iodine in U.S. women, the rise in popularity of the restricted diets like the Paleolithic Diet and vegan diets raises concerns over the restrictive nature of the diet and possible further iodine deficiency (Leung et al., 2011). Restricted diets, such as the paleo diet, do not include dairy and other foods that are fortified with iodine. These diets are high in the consumption of foods rich in goitrogens, such as brassica vegetables which inhibit iodine binding in the thyroid (NIH, 2011). These factors could possibly contribute to increasing the risk of iodine deficiency for individuals following a restricted diet. Food labels are not required to include iodine as

an ingredient, making it unclear the amount of iodine included in a specific food (Leung et al., 2011).

The paleo diet has grown in popularity over the years for its perceived health benefits (Manheimer, van Zuuren, Fedorowicz, & Pijl, 2015). The idea was first developed by gastroenterologist Walter Voegtlin in 1975, and later the term 'Paleo Diet' was trademarked by Loren Cordain (Genoni, Lyons-Wall, Lo, & Devine, 2016). According to Cordain, consumption of fruits, vegetables, lean meats, eggs, and nuts are encouraged, while any products of modern agricultural origin are excluded such as grains, legumes, and dairy (Genoni et al., 2016). Because of the restrictive nature of the Paleo Diet, men and women following this popular diet may be at risk of developing iodine deficiency.

Hypothesis: It is unclear whether following a restrictive diet eliminating grains and dairy leads to iodine deficiency in healthy adults living in the United States. Therefore, we will longitudinally examine the association between restrictive diets and iodine status in adults for 1 year to test the hypothesis that adults who eat restricted diets eliminating grains and dairy are at higher risk of developing iodine deficiency than adults on non-restricted diets.

Proposed Study Design: We propose a prospective cohort design with a population base of 1000 subjects ranging in age from 18 to 55 years old selected from 10,000 CrossFit and fitness gyms, as well as colleges and medical facilities in the United States and recruitment measures using social media. Groups will be stratified by age and zip code, and they will be observed for 1 year.

Case Definition: We plan to investigate whether eating a strict Paleo Diet has a more detrimental impact on urinary iodine levels than eating a less restrictive diet as defined by iodine insufficiency and deficiency. In healthy non-pregnant and non-lactating adults, iodine deficiency is defined as
<100 mcg/L of urinary iodine with varying levels of deficiency as labeled in Table 2.

Table 2: Criteria for assessing iodine status based on urinary iodine concentrations

MEDIAN URINARY IODINE (µg/L)	IODINE INTAKE	IODINE STATUS
<20	Insufficient	Severe Iodine Deficiency
20-49	Insufficient	Moderate Iodine Deficiency
50-99	Insufficient	Mild Iodine Deficiency
100-199	Adequate	Adequate Iodine Nutrition
200-299	Above Requirements	Likely to provide adequate intake for pregnant/lactating women, but may pose a slight risk of more than adequate intake in the overall population
≥300	Excessive	Risk of adverse health consequences (iodine-induced hyperthyroidism, autoimmune thyroid diseases)

Source: Table adapted from (Andersson, Karumbunathan, & Zimmermann, 2012).

Proposed Population: The study includes healthy adults in the United States between age 18 and 55 who are following a Paleo diet according to the study guidelines. The subjects will be recruited via a survey at crossfit gyms, health clubs, medical facilities, and colleges around the U.S., and via Facebook and Instagram targeting the specific age group listed above. The subjects will be randomized and stratified based on demographics and age, since age affects iodine status, and geographically iodine levels may be different.

A complete history will be taken of the subject's age, ethnicity, gender, demographics, duration of Paleo diet if currently on one, medical history, iodine levels, thyroid history (including family thyroid history), food history, drugs and supplements. Each subject will have a physical examination by a medical doctor to ensure subjects are free from thyroid conditions. This assessment will include assessing urinary iodine concentration, goiter, TSH and serum thyroglobulin. Subjects must have access to the internet for use of dietary record apps either via computer or phone.

Exclusion criteria include pregnancy, current diagnosis of thyroid disorder, autoimmune disease, infection, gastrointestinal absorption issues, iodine status below 100 mcg/L, or genetic disease. Subjects should also be free from taking any therapeutic drugs, thyroid hormone, birth control pills, or supplements containing iodine for 6 months.

Over the years, the paleo diet has developed into many variations on the type of foods included and excluded. This study will use the following dietary allowances and restrictions (Manheimer et al., 2015; Jonsson, Granfeld, Lindeberg, & Hallberg, 2013):

- Allowances:

    - Vegetables, including root vegetables
    - Fruit, including fruit oils
    - Olive oil, coconut oil and palm oil
    - Nuts, seeds, unprocessed meat, eggs
- Exclusions:
    - Dairy, grains, legumes
    - Canola, vegetable oil, refined fats
    - Refined carbohydrates, added sugars, and beer
    - Nutritional products containing supplemental iodine

Each subject will be provided a detailed list of foods that are included and excluded from the diet. In order to participate, the subjects do not have to be following a paleo diet at onset, but if they are, they should have been following the diet for no more than six months.

Proposed Measures: Dietary records, spot checks with random 24-hour recalls, and measurement of iodine status using median urinary iodine will be used to measure iodine status. We will be using Cronometer record keeping app to track food. The Nutrition Coordinating Center (NCC) Food and Nutrient Database will be used to validate iodine amounts within foods.

Subjects will be provided a checklist of foods they are allowed and not allowed to eat. They will be required to track any additional items they choose to eat that are not on the list. We will be conducting 24-hour recalls randomly once per week for different subjects throughout the year.

Subjects will be instructed to visit their assigned local lab once every month for median urinary iodine tests. Subjects will also have 24-hour urinary measurements taken at baseline, 6 months, and 1 year.

Possible Confounding Factors: We will control for perchlorate and thiocyanate foods, goitrogen foods, and cigarette smoke (urinary cotinine levels) (Leung et al., 2011). In addition, we must control for how long they've been on a paleo diet. Prolonged profuse sweating can cause iodine depletion in individuals, regardless of diet (Mao, Chen, & Ko, 2001), so we must therefore control for subjects who may be working in environments with extreme temperatures, such as outdoors or in factories, and patients who play sports at the elite level in hot environments. Additionally, we will stratify by age group (18 – 25, 26 – 40, and 41 – 55), zip code and gender since iodine and thyroid hormone interact with estrogen. Female subjects will also be stratified into pre-menopausal and post-menopausal groups.

Limitations: As an observational study we cannot show a causal relationship. Since we are looking at specific age groups 18 – 55, we cannot generalize our findings to other age

groups. We also cannot generalize our findings to other populations not included in our study population such as pregnant and lactating females, or those with disease. Other limitations to our study include:

- Lack of valid data on amounts of iodine in foods
- Other factors that might influence iodine levels, such as deficiency in vitamin A (Zimmerman et al., 2007), bromine used in cooking (Pavelka, 2004), and other environmental toxins
- Lack of information on iodine levels in drinking water
- Consumption of seaweed and seafood
- Possible differences in urinary iodine measurements and pre-study physicals between facilities and physicians

Finally, we cannot say that because an individual becomes iodine deficient, they will develop one of the diseases associated with iodine deficiency.

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