Clinical investigations of dietary bean intake in children and adults

Metabolomics reveals cooked navy bean phytochemicals and their gut microbial metabolism

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Building Research and Education on Sustainable Foods for Enhanced Gut Health Across the lifespan
Health Promoting Properties of Dry Beans

(*Phaseolus vulgaris* L.)

- Dry cooked beans have unique nutrient profiles compared to corn and cereal grains.
- Consumption of common beans has been shown to alter chronic disease processes and risk factors.
  - Reduce inflammation
  - Promote weight loss
  - Inhibit tumor growth
  - Alter tumor metabolism
  - Reduce serum cholesterol
- Common dry beans are a promising staple food for chronic disease prevention.
Recommendations for Human Cancer Prevention

1. Be as lean as possible without becoming underweight.
2. Be physically active for at least 30 minutes every day.
3. Avoid sugary drinks. Limit consumption of energy-dense foods.
4. Eat more of a variety of vegetables, fruits, whole grains and legumes such as beans.
5. Limit consumption of red meats and avoid processed meats.
6. If consumed at all, limit alcoholic drinks to 2 for men and 1 for women per day.
7. Limit consumption of salty foods and foods processed with salt (sodium).
8. Don’t use supplements to protect against cancer.
9. *It is best for mother breastfeed exclusively for up to 6 months and then add other liquids and foods.
10. *After treatment, cancer survivors should follow the recommendations for cancer prevention.

*Special population recommendations

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Navy Bean Powder nutrient profile

Navy Bean
(35g=110kcal)

Fat
(1g)
- Saturated (g): 0.1
- Monounsaturated (g): 0.13
- Polyunsaturated (g): 0.45
- MFA 18:1, Oleic (g): 0.07
- PFA 18:2, Linoleic (g): 0.12

Protein
(9g)

CHO
(23g)
- Dietary Fiber, Total (g): 9
- Insoluble Fiber (g): 6
- Sugar, Total (g): 0.34

Ash
(1.2g)

Essential Amino Acids (mg)
- Histidine: 187
- Isoleucine: 352
- Leucine: 637
- Lysine: 473
- Methionine: 101
- Cystine: 69
- Phenylalanine: 429
- Tyrosine: 179
- Threonine: 263
- Tryptophan: 91
- Valine: 456

Non-Essential Amino Acids (mg)
- Alanine: 336
- Aspartic Acid: 961
- Glutamic Acid: 1146
- Glycine: 297
- Proline: 413
- Serine: 436
- Arginine: 378

Vitamins

- Sodium (mg): 0
- Potassium (mg): 354
- Phosphorus (mg): 131
- Magnesium (mg): 48
- Selenium (µg): 2.6
- Calcium (mg): 63
- Iron (mg): 2.2
- Alpha-Tocopherol (mg): 0.01
- Thiamin (mg): 0.22
- Niacin (mg): 0.6
- Pyridoxine (vitamin B6) (mg): 0.13
- Folate (total) (µg): 127
- Pantothenic Acid (mg): 0.24
- Vitamin K (µg): 0.5
COOKED NAVY BEAN POWDER METABOLOME REVEALS AMINO ACID PATHWAY

Leucine, Isoleucine, Valine
Lysine
Methionine, Cysteine, Taurine
Phenylalanine and Tyrosine
Polyamine
Tryptophan
Arginine, Proline
The Big Picture Vision

• ID America's favorite 20 crops
• Understand crop origins and breadth of each crop's genetic diversity
• Select cultivars from each crop for evaluation
• Identify the most cancer protective cultivars
• Define a cultivar-based diet of menus and recipes
• Evaluate in women at high risk for breast cancer or its recurrence
• Ultimate goal: a "certifiable disease prevention diet"

The “Omics” of Nutrition

Bioactive Food Component

Nutrigenomics

Nutrigenetics

RNA

DNA

Epigenetics

Nutritional Transcriptomics

Protein

Phenotype

Proteomics

Metabolomics

Metabolite

JA Milner: NCI Road Map 2005
Daniell and Ryan (2012). The Nutrigenome and Gut Microbiome: Chronic Disease Prevention with Crop Phytochemical Diversity
Healthy Weight Management

Reduced Chronic Disease

- Gut Hormones
- Lipid and Carbohydrate Metabolism
- Antitumorigenesis & Apoptosis
- Liver Metabolism and Excretion
- Inflammation
- Oxidative Stress
- Gut Microflora Metabolism
Carnitine Metabolism, **Monohydroxy** fatty acids, Inositol, Lysolipid, Medium Chain, Phosphatidylcholine, Sterol
Multi platform strategy to assess disease fighting and health promoting properties of foods

- Human clinical trials
- Immune modulation/infectious disease
- Cancer prevention and control
- Cellular and Molecular Assays-Metabolomics, Phytochemical fractionation: mechanisms of action and cultivar variation
- Gnotobiotic neonatal pigs- human rotavirus infection
- Probiotic fermentation
- Canine Phytokinetics/bioavailability, nutrient digestibility, weight loss, cancer chemoprevention and control

Healthy Hearts with Rice Bran and Beans

http://clinicaltrials.gov/ct2/show/NCT01911390
http://clinicaltrials.gov/show/NCT01929122
Community-Academic Partnerships in Northern Colorado

Healthy Hearts
- Improve lipid & carbohydrate metabolism in children at risk for hypercholesteremia with dietary interventions

Beans/Bran Enriching Nutritional Eating For Intestinal health Trial
- Enhance gut & immune health in cancer survivors

Colorectal cancer control & chemoprevention
- Establish biomarkers for reduced gut inflammation and colorectal cancer prevention

Sooper Staples
- Educate & empower community on whole grains and legumes at point of purchase
Goal: Advance evidence-based dietary chemoprevention research through increased navy bean and rice bran consumption

Investigate changes in the stool microbiome and metabolome following dietary intervention (NCT01929122).

Examine effects of stool extracts following diet intervention on killing of cancer cells.

Current project: Utilize blood, urine, stool and saliva samples from trial to identify dietary biomarkers of navy bean and rice bran intake.
Flow diagram of BENEFIT participants

**Enrollment**
- Assessed for eligibility (n=92)
  - Excluded (n=55)
    - Not meeting inclusion criteria (n=14)
    - Declined to participate (n=35)
    - Other reasons (n=6)
- Randomized (sex, BMI, caloric intake) (n=37)

**Allocation**
- Control diet (n=10)
  - Received intervention (n=10)
  - Withdrawn from study (n=0)
- Navy bean diet (n=12)
  - Received intervention (n=10)
  - Withdrawn from study (n=2)
- Rice bran diet (n=15)
  - Received intervention (n=9)
  - Withdrawn from study (n=6)

**Analysis**
- Baseline, week 2, and week 4 study visits
  - Collected blood, urine, stool, saliva samples
  - Recorded height and weight
  - Completed weekly dietary food logs and study questionnaires
- Reasons for Withdrawal
  - Noncompliant to study protocol (n=4)
  - Family emergency (n=1)
  - Other (n=3)
Recipe Development

- Control: no bean or bran
- Bean Powder: 35 grams
- Rice Bran: 30 grams

**Seven Meals**
- Baked Pasta Marinara
- Cream of Tomato Basil Soup
- Homemade Chili
- Mexican Chicken Bake
- Pizza Dough
- Roasted Pear and Butternut Squash Soup
- Tuna Cheddar Bake

**Six Snacks**
- Banana Nut Muffin
- Blackberry Cobbler
- Caraway Crackers
- Cranberry Apple Granola
- Energy Date Bites
- Strawberry Pineapple Smoothie

- Combination of one meal and one snack provides 100% of daily intervention dose.
- All meals were designed by a Registered Dietitian.
Consumption levels in colorectal cancer survivors that showed chemoprevention in animal studies

![Bar graph showing consumption levels of dry bean or rice bran intake from total calories across different study groups and time points.]

Participants by study diet group


Protective Effects of Rice Bran on Chemically Induced Colon Tumorigenesis may be Due to Synergistic/Additive Properties of Bioactive Components. International Journal of Cancer Research (2009) 5: (4), 153-166
No gastrointestinal health changes across groups over 4 weeks after consuming study diets
Percent change from baseline to week 4 across diet groups
No major shifts in Stool microbial composition at the phyla level following navy bean intake in colon cancer survivors
Shifts in Stool microbial richness and diversity following navy bean intake in colon cancer survivors

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BENEFIT CRC Survivors Navy Bean Group – Stool Metabolites Significantly Different between 4 Weeks and Baseline
BENEFIT CRC Survivors Navy Bean and Control Group – Metabolites Significantly Different at 4 Weeks
Diagram of colon tissue and stool metabolites distinguished by microbial or mammalian production.

Metabolites that are colored in red are produced exclusively or mainly through bacterial metabolism. Both mammalian cells and bacteria produce metabolites that are colored in blue. Metabolites denoted with a $^1$ were detected in colon tumor or adjacent mucosa tissue and a $^2$ indicates detection in stool. Metabolites without a denotation were detected in both matrices.
Healthy hearts with rice bran and navy beans

- Objective: To determine the effect of increasing consumption of cooked dry bean powder or dietary rice bran or a combination on serum cholesterol levels in children.

  1) Establish feasibility for dietary intake of cooked dry bean powder, dietary rice bran or a combination in 8-12 yr children’s daily diet for one month.

  2) Does cooked bean powder/rice bran consumption separately or together improve lipid profiles after a 4-week intervention?

(NCT01911390)
Healthy Hearts Participant flow

Enrollment

Assessed for eligibility (n=3350 4th graders)

Eligibility pool (n=1146)

Consented/Assented (n=50)

Excluded (n=2204)
- Not meeting inclusion criteria (n=2179)
- Declined to participate (n=19)
- Other reasons (n=6)

Randomization

Randomized (sex) (n=50)

Allocation

Allocated to Control Diet (n=11)
- Received intervention (n=9)
- Withdrawn from study (n=2)

Allocated to Navy Bean Diet (n=15)
- Received intervention (n=10)
- Withdrawn from study (n=5)

Allocated to Rice Bran Diet (n=13)
- Received intervention (n=9)
- Withdrawn from study (n=4)

Allocated to Combination Diet (n=11)
- Received intervention (n=10)
- Withdrawn from study (n=1)

Reasons for Withdrawal
- Noncompliant to study protocol (n=5)
- Declined to participate (n=5)
- Gastrointestinal issues (n=1)
Nutrient comparisons of study intervention snacks

<table>
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<tr>
<th></th>
<th>Banana Nut Muffin</th>
<th>Control</th>
<th>Navy Bean Powder (17.5 g/day)</th>
<th>Rice Bran (15 g/day)</th>
<th>Combination (9 NBP &amp; 8 RB g/day)</th>
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<tbody>
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<td>Sodium (mg)</td>
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<td>127</td>
<td>220</td>
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No differences across groups in GI symptoms over time
Basic Summary

• Established tolerance and feasibility of increasing intake of navy bean powder and/or rice bran in children.
• Only lipid parameter to see significant change at 4 weeks was HDL-cholesterol in Navy Bean Powder group.
• A total of 17 children (45%) did not have elevated or borderline high cholesterol levels at week 4.
• Increases in total dietary fiber and certain micronutrients in intervention groups
Food Metabolomics for Identifications of Biomarkers of Rice Bran and Bean Intake in children and Adults
Locally grown rice bran

Provide nutritionally dense foods to at-risk infants

Community-based dietary interventions & clinical trials

Global R&D of rice bran/bean based foods to reduce diarrheal disease, malnutrition, and growth stunting
Complex Interactions to determine the health benefits of plant foods
Translational and Cross Disciplinary Research Partnerships for Sustainable Food and Health Trials

Agriculture/Plant Sciences
Veterinary medicines
Biomedical Sciences
Microbiology/Immunology
Environmental Health
Global Social Sustainable Enterprise
Global Public Health Nutrition and Food Systems
School of Global Environment and Sustainability

http://clinicaltrials.gov/ct2/show/NCT01911390
http://clinicaltrials.gov/show/NCT01929122
A. Poor Sanitation
   - Bacterial pathogens
   - Parasites/Viruses
   - Contaminated Water (Microbial or Chemical)

B. Dietary Exposure
   - Antigens in food
   - Preservatives in food
   - Microbial metabolites

C. Environmental Toxicants
   - Heavy Metals
   - Aerosols
   - Pesticides

Environmental Enteric Dysfunction (EED)

- Transient
  - Occurs in healthy individuals in EED conditions
  - Reversed when environment is changed

- Chronic
  - Persistent
    - EED develops in Infancy and Childhood
  - No change even if the environment is changed