Effect of Pulses on Blood Vessel Function and Atherosclerosis—Preventing Hormones

Peter Zahradka

University of Manitoba
and
Canadian Centre for Agri-food Research in Health and Medicine

Pulse Food Symposium
Toronto, 2008
The Canadian Approach to Good Nutrition
Food for Health Concept

• Cardiovascular disease is the number one killer in developed countries (35.2% of deaths in US)
• The incidence of CVD is not declining because the prevalence of diabetes is increasing
• But, you can reduce your risk of cardiovascular disease by consuming:
  – Low glycemic index foods: better metabolic control
  – Fibre: lowers blood cholesterol levels
  – Flavonoids: improve blood vessel function directly
Why Pulses?

- low glycemic index, high in fibre and flavonoids
- components may aid disease prevention and management
  - Body weight management/obesity
  - Metabolic syndrome; cardiovascular disease
  - Gut health and prebiotics
- but clinical trials investigating health-related benefits of pulses are lacking
• **Hypothesis:** A diet containing at least one serving of pulses per day provides flavonoid compounds that will improve cardiovascular health by increasing the levels of serum adiponectin.

  **Participants:** Peripheral Artery Disease (PAD)

• **Main Outcomes:**
  - Blood vessel function & biochemical markers of cardiovascular disease
  - Blood concentrations of flavonoids
  - Subset of samples for gene expression profile (nutrigenomics)
Stage 1: Selection of 14 Recipes

Recipes from the Pulses (Bean) Study

Soups
Dill Green Pea Soup
Pinto Bean Hamburger Soup
Ham Pea Soup
Lemony Parsley Lentil Soup
Chickpea and Spinach Soup

Main Dishes with Meat
Snow White Turkey Chili
Beef Chili
Apricot Chicken with Lentils
Baked Stuffed Sole
Bean and Beef Lasagna
Italian Sausage and Pasta Casserole

Meatless Main Dishes
Chickpea Curry
Sautéed Asian Yellow Peas
Bistro Beans
Refried Bean Burrito & Refried Beans
Black Bean Quesadilla & Mexican Baked Beans
Baked Beans
Sweet Potato Chickpea Wrap
Zucchini Bean Casserole
Chickpeas with Tomatoes and Rice

Desserts
Chickpea Lemon Cake
Raspberry Chews
Lentil Muffins
Oatmeal Chocolate Chip Lentil Cookies
Study Design

0 week

25-30 Participants:
mild Peripheral Artery Disease (PAD)

Blood Vessel Function
(Pulse Wave Analyses)
Clinical Assessments
Fasting Blood Sample

8 weeks

Blood Vessel Function
(Pulse Wave Analyses)
Clinical Assessments
Fasting Blood Sample
Study Design

0 week

Daily ½ cup serving of locally grown beans (pinto, kidney, navy, black), peas (whole green, yellow), lentils (green, red) or chickpeas

8 weeks

Informed Consent

Food Frequency Questionnaire
& 3 Day Food Record:
Usual pulse consumption and background diet

3 Day Food Record:
Background Diet
(other changes?)
Fasting Blood Sample

- Blood lipids (cholesterol/triglycerides)
- Blood glucose levels (diabetes)
- Markers of inflammation and vascular disease
- Blood adiponectin levels
- Blood flavonoid levels
- Isolate RNA from white blood cells to identify changes in expression profile
Other Clinical Assessments

- Age, gender, alcohol usage, smoking, exercise habits, medications, family history of chronic diseases
- Height and weight to calculate body mass index (BMI)
- Blood pressure
Primary Target: Peripheral Vascular Disease

• Symptom of systemic atherosclerosis
• Indicates high risk of heart attack and stroke
• Leads to claudication (painful to walk long distances) and gangrene (limb amputation)
• Easy to diagnose (ankle-brachial index)
• Exercise and healthy diet (fish oil, flaxseed, walnuts, soybeans, canola oil) recommended for self-help management of early-stage disease by Mayo Clinic
Endothelial Dysfunction: Precursor to PAD
Measuring Vascular Elasticity

(Elasticity of the arteries)

Pulse Wave Analysis
Insulin Resistance Impairs Vascular Contractility

from Wiernsperger et al. (2007) Microcirculation 14:403-38
Vascular Effects of Flavonoids

- Antioxidants
- Cholesterol lowering properties
- Inhibitors of platelet aggregation
- Improve vascular reactivity
- Modulators of gene activity
Flavonoids in Pulses

• Formononetin (present in peas, beans and chickpeas) improves arterial stiffness and reduces hypercholesterolemia

• Pterocarpans prevent proliferation of vascular smooth muscle cells, a process closely linked to the onset and progression of atherosclerosis

• Anthocyanins, a family of isoflavones found at high concentrations in the common bean (*Phaseolus vulgaris*), stimulate adipocytes to secrete adiponectin, a cardioprotective hormone
What is the Contribution of Adipose Tissue?

- Modulates blood lipid levels
- Regulates food intake
- Production of:
  - inflammatory mediators
  - blood pressure hormones
  - hormones that affect vascular elasticity
  - hormones that confer resistance to atherosclerosis (adiponectin)
Normal adipocyte

- Adiponectin
  - Insulin sensitive
  - Anti-atherosclerotic
  - Anti-inflammatory

Dysfunctional adipocyte

- Altered phenotype affects metabolic & endocrine properties
- Adiponectin
  - Insulin resistance
  - Atherosclerosis
  - Inflammation

Overnutrition

Diet/exercise & other interventions
DIET

Blood Vessel Function

direct effects

Adipose Tissue

indirect effects
Anticipated Outcomes

• Dietary pulse consumption will positively affect cardiovascular function in relation to atherosclerotic disease
  – Daily consumption for 8 weeks in individuals with peripheral artery disease
  – Functional, biochemical and genetic markers

• Flavonoid compounds will contribute to the beneficial effects
  – Relate blood flavonoid concentrations with functional and biochemical markers
Anticipated Outcomes

• Determine whether the mechanism of action involves alteration in adiponectin
  – Relationship between obesity and cardiovascular function

• Initial survey of changes in gene expression induced by dietary pulse consumption
  – Nutrigenomics approach; relate flavonoid concentrations in blood with changes in gene expression
Preliminary Results

• Pulse enriched diet lowers body-mass index, total cholesterol, LDL cholesterol over 8 weeks

• Diet has no effect on triglycerides, HDL, cholesterol/HDL ratio, blood pressure or glycated hemoglobin
Note: *improvement in BMI due to 0.5 kg decline in weight!*
Study Reveals Doubt on Drug for Cholesterol

“Doctors generally believe that the amount by which cholesterol is lowered, not the method of lowering it, is what matters…In the last 13 months, however, the failures of two important clinical trials have thrown that hypothesis into question.”

“Because the link between excessive LDL cholesterol and cardiovascular disease has been so widely accepted, the Food and Drug Administration generally has not required drug companies to prove that cholesterol medicines actually reduce heart attacks before approval.”

“They have not had to conduct so-called outcome or events trials beforehand, which are expensive studies that involve thousands of patients and track whether episodes like heart attacks are reduced.”

“So far, proof that a drug lowers LDL cholesterol has generally been enough to lead to approval. Only then does the drug’s maker begin an events trial. And until the results of that trial are available, a process that can take several years, doctors and patients must accept the medicine’s benefits largely on faith.”
Next Stages

- A more comprehensive study
  - More participants
  - Individual pulses
  - Longer study period
- Animal studies to examine mechanism(s) of action and confirm identity of the active component(s) in pulses
- Screen to identify pulse varieties with highest amount of active component
Food Preparation & Nutrition

• Carla Taylor
  – Professor, Human Nutritional Sciences
Clinical Component

• Randy Guzman
  – Head, Vascular Surgery Program, WRHA
  – Patients served as pool for study
Acknowledgements

• Funding:
  – Pulse Canada
  – Manitoba government: Science, Technology, Energy and Mines

• Assistants
  – Alanna Baldwin (Study Coordinator),
  – Wendy Weighall (Research Nurse),
  – Sherif Louis (Technician),
  – Connie Malgalhaes, Francine St.-Hillaire (Food preparation),
  – Angela Hubbard, Erin Kotyk (Food deliveries)

• The 28 study participants
THE SIMPLIFIED HEALTH CARE PROGRAM...
Natural Health Protectorate Branch

• Claims of risk reduction by foods are regulated by Health Canada under their Natural Health Products policy for
  – Diagnosis, treatment or prevention of disease
  – Restoring or correcting organic functions in humans
  – Modifying organic functions in humans to maintain or promote health
• A health claim is any representation that states, suggests or implies that a relationship exists between a food or a constituent of that food and health.

• Standards of evidence that must be met include:
  – A description of the characteristics of the diet associated with reduced risk of disease.
  – A description of the composition of the food that makes it suitable for the diet.