Understanding Flavonoids and Their Role in Health

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John Erdman, PhD, University of Illinois
Barbara Lyle, PhD, ILSI North America, moderator

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This webinar was sponsored by the ILSI NA Technical Committee on Bioactives – Flavonoids, Polyphenols, and Carotenoids.

ILSI’s tri-partite structure creates a neutral forum for discussing scientific issues that impact the health of the public.

Dr. Eric Hentges, PhD, Executive Director
Dr. Barbara Lyle, PhD, Sr. Nutrition Advisor
## Disclosures for Johanna Dwyer

<table>
<thead>
<tr>
<th>AFFILIATION/FINANCIAL INTERESTS (within past 12 months)</th>
<th>CORPORATE ORGANIZATION</th>
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<tbody>
<tr>
<td>Grants/Research Support</td>
<td>none</td>
</tr>
<tr>
<td>Scientific Advisory Board/Consultant</td>
<td>Conagra, Bay State Milling, McCormick and Company</td>
</tr>
<tr>
<td>Speakers Bureau</td>
<td>none</td>
</tr>
<tr>
<td>Stock Shareholder</td>
<td>Several food and drug companies</td>
</tr>
<tr>
<td>Other</td>
<td>Until 1/2015 Public trustee, ILSI NA and member Flavonoids committee</td>
</tr>
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## Disclosures for John Erdman

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<td>Grants/Research Support</td>
<td>NIH; Center for Nutrition, Learning and Memory (Abbott Nutrition)</td>
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<tr>
<td>Scientific Advisory Board/Consultant</td>
<td>Soy Nutrition Institute; Mars Scientific Advisory Council</td>
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<tr>
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<tr>
<td>Stock Shareholder</td>
<td>None</td>
</tr>
<tr>
<td>Other</td>
<td>Pepsico – Sponsored travel to present talk on DRIs</td>
</tr>
</tbody>
</table>
Outline

- Definition, classification, and structure of flavonoids
- Possible health benefits by subclass
- Food sources
- Dietary recommendations

Objectives

Participants will be able to:

1. State what flavonoids are
2. State food sources of flavonoids
3. Describe the putative role of flavonoids in health
Overview

Flavonoids have always been around, but our understanding of them is in the early stages. Over 4,000 flavonoids have been identified in foods - occurring in fruit, vegetables, legumes and beverages.

1. New research and databases have allowed us to gain insight and expand application of knowledge
2. Still much work to ascertain absolute values for recommendations
3. Clarification is needed about how to make accurate claims by differentiating between whole foods and specific flavonoids

The Big Picture of Bioactives

• **Bioactives** are constituents in foods, other than those to meet basic nutritional needs, that are responsible for a change in human health.\(^*\)
  \(^*\)(Office of Disease Prevention & Health Promotion)

• Phenolics and their many derivatives are an example of one large group of these bioactives.

• Though often used interchangeably, there are important chemical differences between these groups of bioactive phenols and their safety.
Polyphenol Family

What are flavonoids?

Flavonoids are polyphenolic compounds that are ubiquitous in nature and are categorized, according to chemical structure into:

- Flavones
- Flavanones
- Isoflavones
- Flavonols
- Flavanols and Proanthocyanidins
- Anthocyanins

“Antioxidant Activities of Flavonoids” Department of Environmental and Molecular Toxicology, Oregon State University.
Classification of Flavonoids

Basic flavan ring structure

Subclass Structures

- Flavones
- Isoflavones
- Anthocyanidins
- Flavanones
- Flavonols
- Flavanols
Proanthocyanidins

**B-linked** proanthocyanidin
(grape, cocoa, apples, pears, blueberries)

**A-linked** proanthocyanidin
(cranberry, nuts and nut skins, cinnamon, plums)

Flavones
(Luteolin, apigenin)

- Found in Juniper berries, kumquats, oregano, parsley, celery seed, and thyme
- Epidemiological studies show consumption is associated inversely with inflammation and mortality

**Intervention studies show:**

- Improved lipid profiles, antioxidant status and endothelial function in patients with mild hyperlipidemia
- Improved levels of blood antioxidant enzymes
**Flavones – Sources and Levels**

<table>
<thead>
<tr>
<th>Food</th>
<th>Per 100 g/100ml</th>
<th>Per std. serving</th>
</tr>
</thead>
<tbody>
<tr>
<td>Celery Seed</td>
<td>• 900 mg</td>
<td>• 36 mg/tsp</td>
</tr>
<tr>
<td>Oregano (fresh)</td>
<td>• 3-4 mg</td>
<td>• 0.1-0.2 mg/tsp</td>
</tr>
<tr>
<td>Oregano (dried)</td>
<td>• 1100 mg</td>
<td>• 40-45 mg/tsp</td>
</tr>
<tr>
<td>Parsley (dried)</td>
<td>• 4500 mg</td>
<td>• 150-200 mg/tsp</td>
</tr>
<tr>
<td>Thyme (fresh)</td>
<td>• 45 mg</td>
<td>• 2 mg/tsp</td>
</tr>
<tr>
<td>Sage (fresh)</td>
<td>• 15 mg</td>
<td>• 0.5 mg/tsp</td>
</tr>
</tbody>
</table>

**Flavanones**  
**(Hesperetin, Naringenin)**

- Found in citrus fruits, such as oranges, and their juices
- Epidemiological studies show association between consumption and reduced risk of CHD, ischemic stroke, acute coronary events, and improved lipid profiles

**Intervention studies show:**

- A significant increase in HDL-C and improved LDL:HDL ratio
- Sweetie juice (a hybrid of pummelo and grapefruit) reduced systolic blood pressure in individuals with Stage I hypertension; reduced total, LDL-C and triglycerides in individuals with existing CVD
- Improved flow mediated dilation, improved inflammatory markers, total cholesterol, and increased HDL in individuals with metabolic syndrome
- Chronic daily consumption of flavanone-rich 100% orange juice over 8 week was beneficial for cognitive function in healthy older adults.
### Flavanones - Sources and Levels

<table>
<thead>
<tr>
<th>Food</th>
<th>Per 100 g/100ml</th>
<th>Per std. serving</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grapefruit (whole)</td>
<td>• 20-50 mg</td>
<td>• 30-75 mg/average size (150 g)</td>
</tr>
<tr>
<td>Grapefruit juice</td>
<td>• 15-20 mg</td>
<td>• 35-50 mg/8 oz.</td>
</tr>
<tr>
<td>Orange</td>
<td>• 40-45 mg</td>
<td>• 35-40 mg/small orange (96 g)</td>
</tr>
<tr>
<td>Orange juice</td>
<td>• 15-30 mg</td>
<td>• 35-75 mg/8 oz.</td>
</tr>
<tr>
<td>Lemon</td>
<td>• 50 mg</td>
<td>• 3 mg/wedge</td>
</tr>
<tr>
<td>Tangelo juice</td>
<td>• 100-125 mg</td>
<td>• 240-300 mg/8 oz.</td>
</tr>
</tbody>
</table>

### Isoflavones (Daidzein, Genistein)

- Found in soybeans; small amounts in chickpeas, fava beans, pistachios, peanuts & other fruits and nuts
- Epidemiological studies show an association with improved cardiovascular and women’s health

Intervention studies show:
- Bind weakly to estrogen receptors and can have estrogenic & anti-estrogenic effects
- May reduce incidence of hot flashes in postmenopausal women
- Modest effects on maintaining bone density
- May slow progression of plaque in artery walls
- Improved blood vessel function
- Some may slow cancer cell growth in animals
### Isoflavones – Sources and Levels

<table>
<thead>
<tr>
<th>Food</th>
<th>Per 100 g/100ml</th>
<th>Per std. serving</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soybeans (edamame)</td>
<td>80-150 mg</td>
<td>50-100 mg per ½ cup</td>
</tr>
<tr>
<td>Soymilk</td>
<td>7-11 mg</td>
<td>18-28 mg/8 oz.</td>
</tr>
<tr>
<td>Veggie Patty/Burger</td>
<td>4-6 mg</td>
<td>3-4 mg/patty</td>
</tr>
<tr>
<td>Soy Sauce</td>
<td>1-2 mg</td>
<td>&lt;0.3 mg/Tbsp.</td>
</tr>
<tr>
<td>Tofu, cooked</td>
<td>20-40 mg</td>
<td>22-45 mg/4 oz.</td>
</tr>
<tr>
<td>Soy cheese (mozzarella, swiss)</td>
<td>6-8 mg</td>
<td>2-3 mg per 1 oz.</td>
</tr>
</tbody>
</table>

### Flavonols (Quercetin, Isorhamnetin, Kaempferol, Myricetin)

- Found in almost every plant based food at some level, including onions, cranberries, tea, beans, & greens
- Epidemiological studies show mixed results; some evidence shows consumption associated inversely with risk of CVD and stroke

**Intervention studies show:**
- Inhibited platelet aggregation and thrombus formation
- Lowered systolic blood pressure and plasma oxidized LDL concentrations in overweight individuals with a high CVD risk
### Flavonols* Sources and Levels

<table>
<thead>
<tr>
<th>Food</th>
<th>Per 100 g/100ml</th>
<th>Per std. serving</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tea</td>
<td>3-5 mg</td>
<td>8-13 mg/8 oz. cup</td>
</tr>
<tr>
<td>Apples</td>
<td>5-10 mg</td>
<td>9-18 mg/med. apple (180 g)</td>
</tr>
<tr>
<td>Cranberry juice</td>
<td>1-4 mg</td>
<td>4-10 mg/8 oz. glass</td>
</tr>
<tr>
<td>Onions</td>
<td>10-40 mg</td>
<td>1-4 mg/1 Tbsp. (10g)</td>
</tr>
<tr>
<td>Blueberries</td>
<td>10-12 mg</td>
<td>15-18 mg/1 c. (148 g)</td>
</tr>
<tr>
<td>Tomato (fresh &amp; raw)</td>
<td>1 mg</td>
<td>1-2 mg/med. tomato (123 g)</td>
</tr>
</tbody>
</table>

* Widely distributed in foods; found in nearly all plant-based foods

### Flavanols & Proanthocyanidins*

- Found in cocoa, tea, grape products (juice, wine), and berries (including cranberries)
- Epidemiological studies show consumption associated inversely with risk of cardiovascular disease and stroke

**Intervention studies show:**

- Improved nitric oxide-dependent vascular function
- Inhibition of platelet aggregation
- Improved blood pressure
- Improved lipid profiles
- Improved cognitive function
- Type A proanthocyanidins in cranberry reduced adhesion of pathogenic bacteria and demonstrated of reduced occurrence of urinary tract infections

*(polymeric form of flavanols)*
Flavanols & Proanthocyanidins – Sources and Levels

<table>
<thead>
<tr>
<th>Food</th>
<th>Per 100g/100ml</th>
<th>Per std. serving</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apples (whole w. skin)</td>
<td>• 40-80 mg</td>
<td>• 70-145 mg per med. apple (180 g)</td>
</tr>
<tr>
<td>Apple juice</td>
<td>• 12-15 mg</td>
<td>• 20-30 mg per 6 oz.</td>
</tr>
<tr>
<td>Blueberries</td>
<td>• 100-150 mg</td>
<td>• 80-120 mg per 1 cup</td>
</tr>
<tr>
<td>Cranberry juice</td>
<td>• 15 mg</td>
<td>• 30 mg per 6 oz.</td>
</tr>
<tr>
<td>Grapes (red w. skin)</td>
<td>• 15-20 mg</td>
<td>• 14-18 mg per cup (92 g)</td>
</tr>
<tr>
<td>Red Wine</td>
<td>• 10-20 mg</td>
<td>• 14-30 mg per 5 fl. oz.</td>
</tr>
<tr>
<td>Natural Cocoa Powder</td>
<td>• 1300 mg</td>
<td>• 65 mg per 1 Tbsp.</td>
</tr>
<tr>
<td>Dark Chocolate</td>
<td>• 230 mg</td>
<td>• 90 mg per 40-g bar</td>
</tr>
<tr>
<td>Brewed Tea (black/green)</td>
<td>• 60-120 mg</td>
<td>• 110-230 mg per 6 oz.</td>
</tr>
<tr>
<td>Peanut Butter</td>
<td>• 10-15 mg</td>
<td>• 3-5 mg per 2 Tbsp.</td>
</tr>
</tbody>
</table>

Anthocyanidins—Cyanidin, Delphinidin, Malvidin, Pelargonidin

- Found in berries, grapes, cherries, purple carrots, and red cabbage
- Epidemiological studies show consumption associated with improved cardiovascular health outcomes, stroke, as well as, cognitive outcomes (including those related to declines with aging)

Intervention studies show:

- Improved lipid metabolism
- Improved insulin resistance
- Improved vascular function
- Lowering of markers of inflammation
- Improved cognitive function
Anthocyanidins: Sources and Levels

<table>
<thead>
<tr>
<th>Food</th>
<th>Per 100 g/100ml</th>
<th>Per std. serving</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blackberries</td>
<td>20-50 mg</td>
<td>30-70 mg/1 cup</td>
</tr>
<tr>
<td>Blueberries</td>
<td>300-350 mg</td>
<td>220-260 mg/1 cup</td>
</tr>
<tr>
<td>Pear</td>
<td>10-12 mg</td>
<td>18-22 mg/med fruit</td>
</tr>
<tr>
<td>Strawberries</td>
<td>30-40 mg</td>
<td>40-60 mg/1 cup</td>
</tr>
<tr>
<td>Cranberries</td>
<td>90-100 mg</td>
<td>90-100 mg/1 cup</td>
</tr>
<tr>
<td>Raspberries</td>
<td>40-50 mg</td>
<td>50-60 mg/1 cup</td>
</tr>
<tr>
<td>Red cabbage</td>
<td>70-80 mg</td>
<td>100-125 mg/1 cup</td>
</tr>
<tr>
<td>Plums</td>
<td>10-12 mg</td>
<td>7-8 mg/sm. plum</td>
</tr>
</tbody>
</table>

Sample Menu

Breakfast
- 1 small whole-wheat bagel 1
- 2 tablespoons peanut butter 2
- 1 medium orange 43
- 1 cup fat-free milk 280
- 1 cup black tea 55
- Arugula salad made with:
  - 4 cups of fresh arugula leaves 32
  - 1 sliced pear 18
  - 1/2 cup canned mandarin orange sections 18
  - 1/3 cup unsalted peanuts 1
  - 1 tablespoons reduced-fat red wine vinaigrette 1
- Herb-crusted baked cod, 3 ounces (blend of 1 tsp parsley, oregano, and celery seed) 100
- 2 reduced-sodium wheat crackers 32
- 1/2 cup fat-free milk 1
- 1/2 cup brown rice pilaf 180
- 1 small sourdough roll 18
- 1 teaspoon trans fat-free margarine 58
- 1 cup fresh sweet cherries (with pits) 350
- Brewed white iced tea (2c) 2

Snack (anytime)
- 1 cup low-fat yogurt 45
- 1 oz dark chocolate 45

Total 1178
Summary

• Flavonoids are naturally occurring and present in a wide variety of plant-based foods.

• Different types of foods contain different types of flavonoids
  – No two foods exactly the same
  – Diet diversity diversifies flavonoid intakes

• Flavonoids are demonstrated bioactive compounds in foods.

• Although studied for over two decades, the science on the benefits of flavonoids to health is promising, but still emerging.

Summary

• Research suggests that these dietary bioactive components may have a role in supporting improved health, including
  – cardiovascular-related benefits
  – anti-cancer benefits
  – cognitive
  – gastrointestinal and urinary tract health
  – anti-inflammatory benefits

• Despite the emerging science, there is not yet today a quantified recommended intake level for flavonoids, or for any specific sub-class of flavonoids.
Where do these foods fit?

Because many flavonoid-rich foods (like fruits, vegetables, legumes) are also nutrient-rich, including a range of plant-based foods means getting vitamins, minerals, and fiber, along with flavonoids!

Consumers are increasingly hearing about the benefits of flavonoids, so you can use their interest to reinforce the benefits of including a range of plant-based foods in their diet to get these phytochemicals they want, plus the essential nutrients they need to support good health.

Focus on Dietary Guidelines

Flavonoids are becoming increasingly recognized as an important beneficial dietary component, as noted several times by the Dietary Guidelines Advisory Committee in 2010:

• “It is possible that ... nutrients are most beneficial to health when they are consumed in their natural form and in combination with each other, such as in vegetables (including cooked dry beans and peas), fruits, and whole grains. These foods contain not only the essential vitamins and minerals that are often targeted in nutrient supplement pills, but also hundreds of naturally-occurring phytonutrients and other substances, including...flavonoids.” p.125
• “Beneficial effects of chocolate have been attributed to polyphenolic compounds, in particular flavonoids.” P.244
• “High-flavanol chocolate or cocoa significantly lowered systolic and diastolic BP” p.244
What you can recommend

Takeaway messages:

- There is currently no recommended level of intake for flavonoids (including sub-classes of flavonoids), but there is emerging science to suggest that the inclusion of a range of flavonoids in the diet can support overall health.

- Eat a mixed diet with nutrient-rich fruit, vegetables, legumes, and whole grains in order to get the essential nutrients that your body needs, as well as a range of flavonoids, that can help support your overall health.

- Don’t forget to include herbs and spices like parsley, oregano, cinnamon, and thyme as a regular part of the diet – simple and tasty ways to get more flavonoids in your diet.

- Many real fruit juices, red wine, and even dark chocolate contain flavonoids – all tasty options for getting some flavonoids – but do so in moderation as part of a balanced diet.

Many Thanks

ILSI NA thanks Drs. Catherine Kwik-Uribe, Mars, Incorporated & Doug Balentine, Unilever, along with the ILSI NA committee scientists for collaborating with Drs. Dwyer and Erdman in developing this webinar

This slide deck, webinar and reference recommendations are available on the ILSI NA website.
Questions & Answers

Please submit your questions via the “questions box” on your screen.

Useful Resources

Recommendations on reporting requirements for flavonoids in research$^{1,2,3}$

Douglas A Balentine, Johanna T Dwyer, John W Erdman Jr., Mario G Ferruzzi, P Courtney Gaine, James M Harnly, and Catherine L Kwik-Uribe


http://ajcn.nutrition.org/content/early/2015/04/08/ajcn.113.071274.abstract
Useful Resources

1. USDA-Iowa State University Database on the Isoflavone Content of Foods, Release 2.0 – 2008
   http://www.ars.usda.gov/News/docs.htm?docid=6382

   http://www.ars.usda.gov/News/docs.htm?docid=6231

   http://www.ars.usda.gov/News/docs.htm?docid=5843

4. Phenol-Explorer database, v 3.6
   http://phenol-explorer.eu/

Selected References

FLAVONOIDS:

FLAVONES
Selected References

**FLAVANONES**

**ISOFLAVONES**
Selected References

FLAVONOLS


FLAVANOLS & PROANTHOCYANIDINS
Selected References

ANTHOCYANINS


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