CAN EVALUATION OF BIOACTIVES FIT THE CURRENT DRI (NRV) FRAMEWORK?

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Disclosures

• Member, Food and Nutrition Board, Institute of Medicine
• Member, National Academy of Medicine
Working Definitions

• **Bioactive.** A substance, obtained from food, that promotes a beneficial physiological effect in humans and is not an essential nutrient.

• **Essential Nutrient.** A substance, obtained from food, that promotes a beneficial physiological effect in humans and must be obtained from the diet.
Focus of the Talk

• Rationale for having a DRI/NRV process for bioactives?

• Is the current DRI process compatible with determining intake values for bioactives?

• What are the major obstacles to having a DRI-like process for bioactives?

• Where do we go next?
Focus of the Talk

- Rationale for having a DRI/NRV process for bioactives?
Why is it important to have a Framework for setting intake values for Bioactives?

• They are important to human health. There is a substantial scientific database on beneficial physiological effects of certain classes of bioactives.
  • Curcuminoids
  • Prenylated flavonoids
  • Carotenoids
  • Flavanols
  • Polyphenols
  • Omega 3 fatty acids (EPA and DHA)

• Research on bioactives is a significant part of Government, University and Food Manufacturer research portfolios.

• The quality of research would likely be enhanced if bioactives were subjected to the same standards as have the essential nutrients.
Learning from the DRI
Proposed Criteria for the Evaluation of bioactives by a DRI-like process

- **Criteria for assessing the potential role of a bioactive [non-essential nutrient] in the context of chronic disease endpoints**
  - A clear and commonly accepted definition/nomenclature of the bioactive
  - Well established and accredited methods of analysis
    - AOAC accredited or equivalent
    - Comprehensive food-content data bases;
  - Epidemiological Data
    - Population-based data on the habitual dietary intake;
    - Prospective investigations of intake & disease risk;
  - Comprehensive Safety Data
    - Upper Lever [UL]?
    - inter-individual differences based on sex, age, genetics, etc.?
  - Comprehensive Understanding of the ADME in humans
    - inter/intra-subject variations?
    - adverse nutrient-nutrient- or nutrient-drug interactions?
  - Meta-analyses; Systematic-and Evidence-based Reviews
  - A plausible explanation for the mechanism of action that underlies the observed effects?
  - Efficacy data from adequate clinical dietary interventions
    - in healthy populations;
    - long-term, large-scale?
    - ‘dose-response’?

Learning from the DRI
Proposed Criteria for the Evaluation of bioactives by a DRI-like process

- Understanding of impact of food manufacture and processing on final bioactive content;
- Focus bioactive-preserving food processing technologies

- A clear and commonly accepted definition/nomenclature of the bioactive
- Well established and accredited methods of analysis
  - AOAC accredited or equivalent
  - Comprehensive food-content data bases;
- Epidemiological Data
  - Population-based data on the habitual dietary intake;
  - Prospective investigations of intake & disease risk;

- Comprehensive Safety Data
  - Upper Lever [UL]?
  - inter-individual differences based on sex, age, genetics, etc.?
- Comprehensive Understanding of the ADME in humans
  - inter/intra-subject variations?
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- Efficacy data from adequate clinical dietary interventions
  - in healthy populations;
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  - ‘dose-response’?

A plausible explanation for the mechanism of action that underlies the observed effects?

Learning from the DRI
Proposed Criteria for the Evaluation of bioactives by a DRI-like process

- A clear and commonly accepted definition/nomenclature of the bioactive
- Meta-analyses; Systematic- and Evidence-based Reviews
- A plausible explanation for the mechanism of action that underlies the observed effects?
- Development of sustainable, secure, and safe supply chains
- Comprehensive Understanding of the ADME in humans
  - inter/intra-subject variations?
  - adverse nutrient-nutrient- or nutrient-drug interactions?
- Comprehensive Safety Data
  - Upper Lever [UL]?
  - inter-individual differences based on sex, age, genetics, etc.?
- Epidemiological Data
  - Population-based data on the habitual dietary intake;
  - Prospective investigations of intake & disease risk;
- Well established and accredited methods of analysis
  - AOAC accredited or equivalent
  - Comprehensive food-content data bases;
- Efficacy data from adequate clinical dietary interventions
  - in healthy populations;
  - long-term, large-scale?
  - ‘dose-response’?

Ref.:
Schroeter et al. 2010, JMAM;
Why is it important to have a Framework for setting intake values for Bioactives?

- Consumers are interested in bioactives and are purchasing foods containing them.
- Food is now viewed as a source of substances to provide optimal health rather than just to protect against nutrient deficiency diseases.
- It’s important to provide consumers with information as to
  - How strong the science is behind purported benefits
  - How much they would need to eat to achieve these benefits
  - How much is too much
Focus of the Talk

• Rationale for having a DRI/NRV process for bioactives

• Is the current DRI process compatible with determining intake values for bioactives?
Three Key National Academies Press Publications

• IOM. 1994. *How should the Recommended Dietary Allowances be revised?*

A conclusion was: “Reduction in risk of chronic disease is a concept that should be included in the formulation of future RDAs where sufficient data for efficacy and safety exist.”
Applying the DRI framework to chronic disease endpoints

- Affected how nutrients were grouped for review
  - Calcium and related nutrients together because of their role in bone health and general health
  - Antioxidants and potential role in reduction of risk of cancer and CHD
  - Electrolytes (blood pressure and hypertension)
- …”A guiding principle conveyed to the DRI study committees was to review the evidence on chronic disease first in setting a DRI”
There are two DRI intake values

- RDA
  - Derived from the EAR
- AI (Adequate Intake)
Would setting an intake value for a bioactive fit the DRI paradigm?

Recommended Dietary Allowance (RDA)

- The average daily dietary nutrient intake level sufficient to meet the nutrient requirement of nearly all (97-98%) healthy individuals in a particular life stage and gender group.
Characteristics of an AI (Adequate intake)

- **Definition**: “The recommended average daily intake level based on observed or experimentally determined approximations or estimates of nutrient intake by a group (or groups) of apparently healthy people that are assumed to be adequate – used when an RDA cannot be determined”.

- “For adults, the AI may be based on data from a single experiment, on estimated dietary intakes in apparently healthy population groups, or on a review of data from different approaches that, when considered alone, do not permit a reasonably confident estimate of an EAR.”
DRIs Established and Published as Nutrient Groups 1997-2005

Credit Dr. Linda Meyers
Basing DRI values on chronic disease endpoints

- Five, based on chronic disease, all were AIs.
  - Calcium and vitamin D (osteoporosis and fractures, also balance data)
  - Fluoride (dental caries)
- Fiber (CHD)
- Potassium (risk for hypertension, kidney stones, and blood pressure)
Focus of the Talk

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Applying the DRI framework to chronic disease endpoints

  - [http://nap.edu/catalog/12086.html](http://nap.edu/catalog/12086.html)
  - Dr. Paula Trumbo
The absence of a specific bioactive in the diet does not result in a deficiency disease

- The absence of an essential nutrient does result in a deficiency disease
  - Vitamin C
    - Scurvy
  - Thiamin
    - Beriberi
  - Iron
    - Microcytic Anemia

- The absence of a specific bioactive in the diet does not result in a deficiency disease
  - Bioactives need a different type of “endpoint.”
    - Decreased risk of chronic disease
    - Optimal health
    - A beneficial physiological effect

Ben Van Ommen
Cesar Fraga
Issues with applying the EAR to bioactives

- A nutrient specific indicator is not being applied.
  - Microcytic anemia vs CHD
- Endpoints of inadequacy assumed ALL individuals are at risk of inadequacy for essential nutrients.
  - Not true for bioactives and chronic disease
- Chronic diseases are not nutrient specific, but multifactorial
  - The absolute risk of most chronic diseases applies to only a portion of the population
  - Not likely that a bioactive would account for 50% of the risk reduction
Calcium and Vitamin D revisited 2011
The Vitamin D/Calcium Report
(two goals were described)

• 1) The framework should ensure and foster transparency of the decision making process.

• 2) The framework should anticipate the need to make decisions in the face of limited data and the interest in protecting public health and the reality that “no decision is not an option”—that is, a science-based judgment is more useful than no recommendation at all. In other words, the framework must operate under conditions of uncertainties.
The Vitamin D/Calcium Report

- Is the only report that has come out after “Lessons Learned” Report.
- It characterizes setting DRIs as a “risk assessment process”
- It benefitted from a thorough evidence based review
Summary

- There are multiple reasons why a framework for the evaluation of bioactives should be considered.
- The primary reason is to promote public health
  - What is an efficacious amount
  - How strong is the science
  - What are potential toxic effects
- Would setting an intake value for a bioactive fit the DRI paradigm?
  - A definite “maybe”
  - Probably not for an RDA value, but “yes” for an AI
- Where is the evaluative process for bioactives headed?
Using chronic disease as an endpoint for intake values

- Committee from Canada and the USA
- Chair is Bert Garza, MD, PhD
NIH VideoCasting and Podcasting

- Joint Canadian-US DRI Working Group
- You need to know the dates, March 10, 11, 2015
Closing remarks from Dr. Bert Garza
Chair of the Committee on Options for Consideration of Chronic Disease Endpoints for DRIs
Chair of the Food and Nutrition Board, IOM

• …”not having enough data will always be an issue, but we need to do the best we can at synthesizing what we have, for if we don’t – not doing so inevitably invites less rigorously derived guidance to fill perceived vacuums.”