Assessing bioavailability/bioaccessibility of the dietary supplement components

By

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FACT:

Nutrients/Toxins present in food system only represent the potential exposure

CHALLENGE:

How do we determine the true exposure of these biomolecule?
Bioavailability is an overarching term: “liberation”, “absorption”, “distribution”, “metabolism” and “elimination” phases

**Definition:**

- **Pharmacological point of view** - The rate and extent to which the therapeutic moiety is absorbed and becomes available at the organ site.

- **Nutritional point of view** - The fraction of the nutrient that is released from food matrix, thus available for physiological functions.

Fernández-García et al. (2009)
OVERVIEW

Processes required for the effective absorption of bioactive compounds:

- Release the from food matrix (Bioaccessibility),
- Incorporation into bile-salt micelles,
- Absorption by epithelial cells,
- Incorporation into the chylomicrons with secretion into lymphatic system.
THE PROCESS:

\[ F = F_L \times F_A \times F_D \times F_M \times F_E \]

- \( F_L \) = Fraction Liberated
- \( F_A \) = Fraction Absorbed
- \( F_D \) = Fraction Reaching Site of Action
- \( F_M \) = Fraction Not Metabolized
- \( F_E \) = Fraction Not Excreted

D. J. McClements and H Xiao · Food & Function 2014
Definition:

- **Bioaccessibility** is defined as the extent that a bioactive/nutrient is released from its matrix in the gastrointestinal tract, becoming available for absorption.

Intawongse & Dean, 2008; He et al., 2010
In Food/Dietary Supplement Formulations:

- Increased interest in those non-nutrient food components with bioactive properties that have value-added benefits in promoting health promotion and disease prevention.

- For bioactivity to be realized; compounds of interest, should withstand food processing conditions; be released from the food matrix post-ingestion and be bioaccessible in the gastrointestinal tract, undergo metabolism and reach the target tissue.

Intawongse & Dean, 2008; He et al., 2010
In Food/Dietary Supplement Formulations:

- Due to the complexity of food compounds, the many factors affecting their transition during digestion, unravelling the bioavailability of food constituents is challenging when compared with pharmaceutical drugs.

- Only by understanding the mechanisms of absorption of food derived compounds, can bioavailability be enhanced, and thus the potential for greater health benefits be realized.

Intawongse & Dean, 2008; He et al., 2010
In Mineral based Health Supplements

- Mineral clay products are widely used by consumers to relieve muscle soreness and to improve overall joint health and function.

- These products also include potentially harmful heavy metals (e.g., Arsenic, Cadmium, Lead).

- Depending on the ingestion dose, the level of these heavy metals could exceed the safe limit established by regulatory agencies.

- Some of these heavy metals are highly toxic and they could accumulate in humans.

- Hence, determining amounts accessible becomes important for safety consideration.

Evans et al., 2014; Miller et al., 2004, 2005; NHPD, 2015
BIOACCESSIBILITY METHODS

Methods most often employed to measure heavy metal bioaccessibility

• one-step USEPA method 1340;
• two-step methods that include the physiologically based extraction test (PBET) and the in vitro gastrointestinal method (IVG);
• three-step, Unified Bioaccessibility Research Group of Europe Method (UBM)

Wragg et al., 2009; Wragg et al., 2011; Ruby et al., 1996
BIOACCESSIBILITY METHODS

Unified BARGE Method (UBM)
- Developed by the Bioaccessibility Research Group of Europe (BARGE)
- Originally developed to test heavy metal toxicity in the soil matrix
- Also been used to determine metals available in fish and crab food sources
- The simulation consists of two phases, the gastric and gastro-intestinal phase

USEPA Method
- Initially established to measure Pb in soil samples
- Not tested for food and natural health products

Pelfrêne et al., 2012; Wragg et al., 2011; Beyer et al., 2016; Denys, 2006; Maulvault et al., 2011)
Points to consider.....

- Different test methods will likely result in different estimates of bioaccessibility, due to variables associated with medium pH, composition of digestion solution, sample to solution ratio, and digestion time;
- To establish accurate estimates of heavy metal bioaccessibility, it is advised to use one or two methods to include in the overall range of the results (Better Risk Assessments);
- If combining mineral clay products with other health supplements (curcumin, glucosamine), the bioaccessibility studies are important to conduct.
1. *In Vivo Approach*

2. *In-Vitro Approach*

- Cell culture (such as the Caco-2 cell) has proven to be effective in assessing bioavailability of heavy metal components in food products following gastrointestinal digestion.

Note: In vitro bioaccessibility assay for heavy metals has been reported to be linearly correlated with in vivo bioavailability data, hence strengthening its use to predict the exposure of heavy metals to humans.
Bioaccessibility (%) of Arsenic (As), Cadmium (Cd), and Lead (Pb) measured by UBM and USEPA methods

Chen et al., 2018 (in review)
OUR WORK

Bioavailability (%) of Arsenic (As), Cadmium (Cd), and Lead (Pb) measured by Caco-2 Permeability Assay

Chen et al., 2018 (in review)
CONCLUSIONS

D. J. McClements and H Xiao. *Food & Function* 2014
CONCLUSIONS

- With 2-step digestion, heavy metal bioaccessibility was “demonstrated to be approx. 1%”

- This was due to poor solubility of these metals at alkaline conditions (pH conditions ~7.5, used to mimic the gastrointestinal digestion).

- Results from USEPA were comparable to the UBM-G analysis

  - Reflects only the gastric digestion phase.

  - The limitations of using the USEPA method to predict heavy metal bioaccessibility from natural health products taken orally is its generic single-step extraction procedure;

- UBM-GI simulates digestion from gastric and gastrointestinal digestion.
CONCLUSIONS

- Complete UBM digestion produced bioaccessibility estimates, since it more closely mimics the conditions of the human GI tract.
  - Caco-2 cell culture assay revealed that all metals after correction for bioaccessibility exhibited very low to non-detectable permeability estimates.

- It can be concluded from these combined in-vitro bioaccessibility and bioavailability results:
  - There is very low probability of hazard associated with consumption of these mineral clays if the recommended usage specifications are followed.
THANK YOU!

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