“Myths and Facts about Caffeine: An Expert Evaluation of the Current Science”

International Food Information Council (IFIC)
Health Professional Webinar for Registered Dietitians
Tuesday, March 30, 2021
Today’s Presenters

Tony Flood, Moderator
Sr. Director Ingredient Communications
IFIC

Kris Sollid, RD
Sr. Director Nutrition Communications
IFIC

Candace Doepker, PhD
Practice Director
ToxStrategies’ Foods & Consumer Products
About IFIC

The International Food Information Council (IFIC) is a 501(c)(3) nonprofit educational organization with a mission to effectively communicate science-based information about health, nutrition, food safety and agriculture.

IFIC is supported primarily by the broad-based food, beverage and agricultural industries.

IFIC does not lobby and does not represent any company, industry or product.
Research and Resources

IFIC CONSUMER RESEARCH

HEALTH PROFESSIONAL RESOURCES
Not surprisingly, coffee, soft drinks and tea are the most common sources of caffeine consumption. Those who haven’t followed a diet in the past year are more likely than those who have to report that they consume coffee and soda.

Of those who consume caffeine, n=950:

- Coffee: 67%
- Soft drinks: 20%
- Tea: 40%
- Energy drinks: 60%
- Caffeine-containing treats: 80%
- Caffeine-containing dairy: 60%
- Caffeine-containing energy/breakfast bars: 40%
- Caffeine-containing candies or chewing gum: 20%
- Dietary supplements: 0%
- Caffeine pills and/or supplements: 0%
- Other: 0%

Type of Caffeine Product Consumed

67% of parents with children <18 who consume caffeine do so in multiple ways (vs. 55% without children).

Q61: Which of the following sources of caffeine do you consume? Select all that apply.

(Of those who consume caffeine, n=950)
Caffeine consumption differs by gender and for those with and without children

Men are much more likely than women to consume caffeine with a breakfast, while parents are much more likely to need caffeine with lunch.

Caffeine Consumption Schedule

- **When I wake up**
- **With breakfast**
- **Mid-morning**
- **Mid-afternoon**
- **With lunch**
- **After dinner**
- **With dinner**
- **Before exercising**
- **Avoid it, don’t consume caffeine, consume as…**
- **Other**

47% of consumers with less than a college degree who consume caffeine do so when they wake up (vs. 39% with a college degree)

47% of men who consume caffeine do so with breakfast (vs. 34% of women)

26% of parents with children under 18 who consume caffeine do so with lunch (vs. 15% without children)
Over the past 5 years consumers have trended towards believing that naturally-occurring and added caffeine have the same effect. Those in very good health are more likely than those in fair/poor health to believe that caffeine is naturally occurring. 

Knows the Amount of Caffeine in Foods and Beverages Consumed

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<tr>
<td>Strongly agree</td>
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<tr>
<td>Somewhat agree</td>
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<tr>
<td>Somewhat disagree</td>
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<tr>
<td>Strongly disagree</td>
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True/False: Caffeine that is naturally occurring has the same effect as caffeine that is added

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<tr>
<td>True</td>
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<tr>
<td>False</td>
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<td></td>
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<tr>
<td>Not sure</td>
<td></td>
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</table>

No change from 2019

40% of men indicate that the statement is true (vs. 28% of women)

Q58 (TREND): Please indicate how much you agree or disagree with the following statement: I know the amount of caffeine that is in the foods and beverages I consume. (Of those who consume caffeine, n=950)

Q59 (TREND): Please indicate whether the following statement is true or false: Caffeine that is naturally occurring in foods and beverages has the same effect as caffeine that is added to foods and beverages. (n=1,011)
Caffeine Calculator

https://foodinsight.org/caffeine-and-you/calculator.html

Calculate how to know if you’re having too much.
Dr. Candace Doepker

“Myths and Facts about Caffeine Safety: An Expert Evaluation of the Current Science”

Safety
Metabolism
Fact vs Fiction

Principal Scientist Dr. Candace Doepker is the Practice Director for ToxStrategies’ Foods & Consumer Products

CV Available in the “Reference” Section
Caffeine

Important foundations, learnings from a systematic review and commonly misunderstood topics

Candace Doepker, PhD.
Principal & Practice Leader
Food and Consumer Products, ToxStrategies
IFIC, 2021
Topics for Today

• Qualifications, Transparency & Personal Perspective
  • Caffeine Landscape
  • Need to know basics

• Key Learnings from our 2017 Systematic Review
  • The value and challenges of “systematic review”
  • General guidance on intake
  • Corroboration of authoritative body positions

• Common Misperceptions
Qualifications & Transparency

• PhD Toxicology
• Chaired the IFIC Caffeine committee – worked on “Everything you Need to Know…”
• Have been involved in studying caffeine or working on caffeine related issues since ~2004
  • Caffeine in cough drops in Europe
  • Previously worked for Folgers Coffee
  • Current Scientific Advisor to National Coffee Association
• Co-Author of one of the largest systematic reviews conducted on Caffeine safety
  • Funding from ILSI and NCA
  • Disclaimer- it takes an army of experts!
Keep in mind: “The dose makes the poison” ~ Paracelsus

This is true for all chemicals including water
Caffeine Landscape - personal perspective

• ~2004 – cough drop project
  • Foreseeable misuse
  • Energy Drinks emerged
  • Pressure on caffeine labels

• ~2006 – started work on Folgers Coffee. What is a cup?
  • Decaff- small market by comparison
  • People want caffeine
  • Billion cups of coffee/day

• ~2013 – IOM workshop
  • congressional pressure
  • This led to SR work – Health Canada old position foundational
Caffeine overview—basic facts that are important to know
Caffeine – 1,3,7-trimethylxanthine

Sources:
- Naturally occurring = plant insecticide (1984)
- Decaffeination by-product
- Synthesized – rare!

Purity:
- Food Chemical Codex (Food Grade)
- USP (Drug Grade)

Consumer choices are Abundant!
Pharmacokinetics (how our bodies handle caffeine)

- We absorb it = Rapidly and completely
  - 95% within 45 minutes
  - Peak plasma within 30-60 minutes
  - Saliva or blood concentrations = common measures
    - ~3mg/L following 2 cups of coffee in plasma
      - Saliva is generally 65-85% of plasma
  - Half life = 4-6 hours
  - Follows first order linear PK up to 750 mg
    - children PK similar to adults, if not more rapid
    - Unchanged caffeine = excreted in urine
Pharmacokinetics (how our bodies handle caffeine’ con’td)

- **Metabolism & Distribution**
  - Nearly all enters liver and is metabolized by P450 enzymes
    - CYP1A2
    - Enzyme activity does not generally vary with age but does with:
      - Smoking (faster)
      - Pregnancy (slower)
      - Liver disease
      - Oral contraceptives
      - Antibiotics
      - Grapefruit juice

- **Caffeine is rapidly distributed**
  - Crosses blood-brain barrier
  - Crosses placental barrier
  - Crosses blood testicular barrier
Pharmacodynamics (what caffeine does to our bodies)

• Chemically similar to adenosine
• Adenosine blocks the arousal response
• Caffeine = Adenosine blocker = non-specific binding to G-protein coupled adenosine receptors
• Heightens arousal response
  • Receptors found throughout the body
    • Cardiovascular
    • Respiratory
    • Renal
    • Central nervous system
Emerging interest in genetic make-up

• Recent research focusing on how one’s own genetic makeup leads to inter-individual differences in how caffeine is handled by the body
  – SNPs and metabolism and/or consumption practices
  – Example: ADORA2A gene polymorphisms as they relate to differences in anxiogenic responses

• Data are beginning to provide insight into potential epigenetic trends or effects

• PK/PD considerations likely to be important in characterizing sensitive individuals/effects in the future
Very common question – how much is in......

<table>
<thead>
<tr>
<th>Item</th>
<th>Typical</th>
<th>Range notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coffee (Brew/Brewed, dry brew)</td>
<td>95</td>
<td>75-165</td>
</tr>
<tr>
<td>Instant coffee</td>
<td>35</td>
<td>50-80</td>
</tr>
<tr>
<td>Decaf</td>
<td>2</td>
<td>2-4</td>
</tr>
<tr>
<td>Espresso</td>
<td>60</td>
<td>40-70</td>
</tr>
<tr>
<td>Tea (Black/Decaf)</td>
<td>47</td>
<td>14-70</td>
</tr>
<tr>
<td>Green tea</td>
<td>25</td>
<td>26-41</td>
</tr>
<tr>
<td>White tea</td>
<td>25</td>
<td>15</td>
</tr>
<tr>
<td>Instant tea</td>
<td>36</td>
<td>11-47</td>
</tr>
<tr>
<td>Iced tea</td>
<td>25</td>
<td>9-58</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Caffeine Source</th>
<th>mg Caffeine per 8 oz</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soft Drink (cola)</td>
<td>24</td>
</tr>
<tr>
<td>Tea (green)</td>
<td>24.8</td>
</tr>
<tr>
<td>Soft Drink (citrus)</td>
<td>36.8</td>
</tr>
<tr>
<td>Tea (black)</td>
<td>47.2</td>
</tr>
<tr>
<td>Energy Drink</td>
<td>80</td>
</tr>
<tr>
<td>Coffee</td>
<td>95</td>
</tr>
</tbody>
</table>
Effects of caffeine on human health

P. Nawrot1, J. Jordan, Z. Eaveswood, J. Rotteria, A. Hugheboul and M. Finley
Toxicological Prevention Service, Canadian Health Hazard Assessment
Program, Bureau of Chemical Safety, Food Directorate, Health Canada, Toronto’s Pantry, P.O. Box 2560, Ottawa, Ontario, Canada K1Y 4E1

(Manuscript received 23 October 2001; revised 17 June 2002; accepted 18 June 2002)

Caffeine is probably the most frequently ingested pharmacologically active substance in the world. It is found in common beverages (coffee, tea, soft drinks), in products containing cocoa or chocolate, and in medications. Because of its wide consumption at different levels by most segments of the population, the public health implications remain uncertain as to the potential for caffeine to produce adverse effects on human health. The possibility that caffeine ingestion adversely affects human health may be assessed based on reviews of (largely) published human studies obtained through a comprehensive literature search. Based on the data reviewed, it is concluded that for the healthy adult population, moderate daily caffeine intake of up to 400 mg/day (7 or less cups of coffee/day) is safe. This is also the current acceptable daily intake established by the World Health Organization. However, the results of this assessment are summarized here.

Introduction

Caffeine (1,3,7-trimethylxanthine) is a natural alkaloid found in coffee beans, tea leaves, cocoa beans, cola nuts and other plants. It is probably the most frequently ingested pharmacologically active substance in the world, found in common beverages (coffee, tea, soft drinks), products containing cocoa or chocolate, and medications, including headache or pain remedies and over-the-counter stimulants (Murphy and Benjamin 1981; DRAC 1993; Drago and Bruckner 1992; entertí and Bentéé 1996).

The possibility that caffeine consumption may have adverse effects on human health was assessed based on the results of (largely) published human studies obtained through a comprehensive literature search. The results of this assessment are summarized here.

Sources and prevalence of caffeine consumption

In North America, coffee (68-75%) and tea (15-30%) are the major sources of caffeine in the adult diet. Certain ethnic and geographic groups may have a higher intake of caffeine. Coffee is also the primary source of caffeine in the diet of children. Total caffeine intake is highest in Europe, with Southern Europe consuming more caffeine than Northern Europe. The intake of caffeine is highest among women, who are exposed to higher levels of caffeine than men.

Keywords: behaviour, breast, caffeine, infants, hair, hypertension, heart rate, heart rate variability, hysteresis, infant growth, maternal smoking, memory, nutrition, oral contraceptives, pantography, pregnancy, smoking, smoking cessation, tea, weight gain, women

Food Additives and Contaminants 2003, Vol. 20, No. 1, 1-10

Another common question – how much is safe?

Highly cited reference: Nawrot et al., 2003

Authors from Health Canada

Review of multiple endpoints

Guidance on “safe” level

• 400 mg/day in healthy adults

• Format is easy to follow for the reader

• But……is it still relevant?
Highlights of the Caffeine Systematic Review
Motivation for work in 2015

- Evaluate if work of Health Canada (that seemed to be pointed to the most) was still relevant
- Systematic Review Approach was emerging and would be an excellent approach
- Existing Government documents difficult to follow approach.
The Basics of a Systematic Review

- Establishing a Team and Protocol Development
  - IOM Framework
  - Scientific Team
  - Protocol
- Study Screening and Selection
  - Literature search and screen
- Individual Study Assessment
  - Data extraction
- Body of Evidence Assessment
  - Internal and External Validity
  - Risk of Bias
  - Synthesis
IOM Standard 2 Components (see IOM for detail)

BOX S-2
Recommended Standards for Initiating a Systematic Review

Standard 2.1 Establish a team with appropriate expertise and experience to conduct the systematic review
Required elements:
2.1.1 Include expertise in the pertinent clinical content areas
2.1.2 Include expertise in systematic review methods
2.1.3 Include expertise in searching for relevant evidence
2.1.4 Include expertise in qualitative methods
2.1.5 Include other expertise as appropriate

Standard 2.2 Manage bias and conflict of interest (COI) of the team conducting the systematic review
Required elements:
2.2.1 Require each team member to disclose potential COI and professional or intellectual bias
2.2.2 Exclude individuals with a clear financial conflict
2.2.3 Exclude individuals whose professional or intellectual bias would diminish the credibility of the review in the eyes of the intended users

Standard 2.3 Ensure user and stakeholder input as the review is designed and conducted
Required elements:
2.3.1 Protect the independence of the review team to make the final decisions about the design, analysis, and reporting of the review

Standard 2.4 Manage bias and COI for individuals providing input into the systematic review
Required elements:
2.4.1 Require individuals to disclose potential COI and professional or intellectual bias
2.4.2 Exclude input from individuals whose COI or bias would diminish the credibility of the review in the eyes of the intended users

Standard 2.5 Formulate the topic for the systematic review
Required elements:
2.5.1 Confirm the need for a new review

2.6.2 Develop a systematic review protocol
Required elements:
2.6.1 Describe the context and rationale for the review from both a decision-making and research perspective
2.6.2 Describe the study screening and selection criteria (inclusion/exclusion criteria)
2.6.3 Describe precisely which outcome measures, time points, interventions, and comparison groups will be addressed
2.6.4 Describe the search strategy for identifying relevant evidence
2.6.5 Describe the procedures for study selection
2.6.6 Describe the data extraction strategy
2.6.7 Describe the process for identifying and resolving disagreement between reviewers in study selection and data extraction decisions
2.6.8 Describe the approach to critically appraising individual studies
2.6.9 Describe the method for evaluating the body of evidence, including the quantitative and qualitative synthesis strategies
2.6.10 Describe and justify any planned analyses of differential treatment effects according to patient subgroups, how an intervention is delivered, or how an outcome is measured
2.6.11 Describe the proposed timetable for conducting the review

Standard 2.7 Submit the protocol for peer review
Required elements:
2.7.1 Provide a public comment period for the protocol and publicly report on disposition of comments

Standard 2.8 Make the final protocol publicly available, and add any amendments to the protocol in a timely fashion
### Scientific Advisory Board

<table>
<thead>
<tr>
<th>Name</th>
<th>Affiliation</th>
<th>Expertise</th>
<th>General Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dr. Jeffrey Goldberger</td>
<td>University of Miami Miller School of Medicine</td>
<td>Cardiovascular health and toxicity</td>
<td>SAB member</td>
</tr>
<tr>
<td>Dr. Harris Lieberman</td>
<td>U.S. Army Research Institute of Environmental Medicine</td>
<td>Physical performance; behavioral effects</td>
<td>SAB member, Caffeine Working Group Government Liaison</td>
</tr>
<tr>
<td>Dr. Esther Myers</td>
<td>EF Myers Consulting</td>
<td>Systematic evidence-based reviews</td>
<td>SAB member</td>
</tr>
<tr>
<td>Dr. Charles O’Brien</td>
<td>Department of Psychiatry, University of Pennsylvania</td>
<td>Effects of caffeine on human behavior</td>
<td>SAB member</td>
</tr>
<tr>
<td>Dr. Jennifer Peck</td>
<td>University of Oklahoma Health Sciences Center</td>
<td>Reproductive and developmental toxicity</td>
<td>SAB member, Caffeine Working Group Science Advisor</td>
</tr>
<tr>
<td>Dr. Milton Tenenbein</td>
<td>University of Manitoba</td>
<td>Pharmacokinetics</td>
<td>SAB member</td>
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<tr>
<td>Dr. Connie Weaver</td>
<td>Department of Nutrition Science, Purdue University</td>
<td>Bone and calcium</td>
<td>SAB member</td>
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</table>

- Assembled a SAB with expertise in each of the key Outcome areas.
- SAB provided guidance and feedback throughout the process to scientists from ToxStrategies
Background

“Systematic review of the potential adverse effects of caffeine consumption in healthy adults, pregnant women, adolescents, and children”

Goal: update work of Health Canada (Nawrot et al., 2003)

Approach:

• Systematic review of literature
  • (2001-2015) - 5 outcomes, 4 populations
  • Weight of evidence conclusion incorporated findings of evidence base along with study quality, relevance, consistency, level of adversity, etc.
• PECO – based on updating Nawrot et al 2003:
  - For [population], is caffeine intake above [dose], compared to intakes [dose] or less, associated with adverse effects on [endpoint]?
• For PK, the objective is to generally characterize the current understanding of caffeine PK and critically review anything that advances the science, particularly with respect differences/similarities between our populations of interest, characterization of PK in non-adult populations of interest, and characterization of PK (particularly fast/slow phenotypes) in context of our endpoints of interest. (Contextual topic)
For [population], is caffeine intake above [dose/exposure], compared to intakes [dose/comparator] or less, associated with adverse effects on [outcome]?

<table>
<thead>
<tr>
<th>Population</th>
<th>Healthy Adults</th>
<th>Pregnant Women</th>
<th>Adolescents</th>
<th>Children</th>
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<tbody>
<tr>
<td><strong>Exposure</strong></td>
<td>&gt; 400 mg/day</td>
<td>&gt; 300 mg/day</td>
<td>&gt; 2.5 mg/kg-day</td>
<td>&gt; 2.5 mg/kg-day</td>
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<tr>
<td><strong>Comparator</strong></td>
<td>≤ 400 mg/day</td>
<td>≤ 300 mg/day</td>
<td>&gt; 2.5 mg/kg-day</td>
<td>≤ 2.5 mg/kg-day</td>
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<tr>
<td><strong>Outcome</strong></td>
<td>Acute, Reproductive and Developmental, Cardiovascular, Behavior, Bone and Calcium</td>
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Study Screening and Selection – Inclusion/Exclusion

- Quantitate estimate of caffeine exposure
  - e.g. Coffee, tea, cola, energy drink, supplements
- Must have reported an effect for an Outcome of interest
- Healthy population only
  - i.e. not having been hospitalized or diagnosed with disease and/or receiving medical treatment for a disease at the time of the study
- Caffeine must have been studied alone, or in one of the approved forms
  - Mixtures with alcohol, nicotine, acetaminophen, or other drugs were excluded
- Available in English
- Case reports included for Acute only
- Must present original data; reviews excluded
  - Exception: Meta-analyses were included
Process of Screening

1. Piloting
2. Conduct Search
3. Remove Duplicates

- Initial Screen (Titles and Abstracts)
  - QA, Committee Review
  - Subject Expert Review

- Full-Text Screen
  - Subject Expert Review
  - Included Studies
Literature Search and Screening (all Outcomes)

**Identification**
- Pubmed: n = 5191
- Embase: n = 539
- Duplicates: n = 24

**Initial Screening**
- Quality Control: n = 573 (10%)
- Committee Review: n = ~277 (~5%)
- Excl. not relevant: n = 4809

**Subject Expert Review**
- n = 894
- Excl. not relevant or adverse: n = 154

**Full-text Review and Extraction**
- n = 740

**Literature search dates:**
January 1, 2001 and June 8, 2015

**Common exclusions:**
Outcomes not relevant, unhealthy populations, co-exposures, benefit studies, in vitro

**Common exclusions:**
No quantitative estimate, unhealthy populations
Did author conduct analysis or report based on caffeine? If no, we normalized
### Synthesize Evidence and Rate Confidence

<table>
<thead>
<tr>
<th>Initial Confidence by Key Features of Study Design</th>
<th>Factors Decreasing Confidence</th>
<th>Factors Increasing Confidence</th>
<th>Confidence in the Body of Evidence</th>
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<tbody>
<tr>
<td>High (++++) 4 Features</td>
<td>Risk of Bias</td>
<td>Large Magnitude of Effect</td>
<td>High (++++)</td>
</tr>
<tr>
<td>Moderate (+++) 3 Features</td>
<td>Unexplained Inconsistency</td>
<td>Dose Response</td>
<td>Moderate (+++)</td>
</tr>
<tr>
<td>Low (++) 2 Features</td>
<td>Indirectness</td>
<td>Residual Confounding</td>
<td>Low (+)</td>
</tr>
<tr>
<td>Very Low (+) ≤1 Features</td>
<td>Imprecision</td>
<td>Consistency</td>
<td>Very Low (+)</td>
</tr>
<tr>
<td>Features</td>
<td>Publication Bias</td>
<td>Other</td>
<td></td>
</tr>
<tr>
<td>- Controlled exposure</td>
<td>- Across animal models or species</td>
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<tr>
<td>- Exposure prior to outcome</td>
<td>- Across dissimilar populations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Individual outcome data</td>
<td>- Across study design types</td>
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<td></td>
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<tr>
<td>- Comparison group used</td>
<td>- e.g., particularly rare outcomes</td>
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</tbody>
</table>

![Cardiovascular Studies (A-B) - Risk of Bias](chart.png)

- Ader-Nielsen et al., 2012
- Addicott et al., 2009
- Addis et al., 2012
- Andreia et al., 2011
- Aherne et al., 2007
- Aherne et al., 2007
- Ajayi and Uwadie, 2001
- Akopov et al., 2008
- Anwar et al., 2001
- Azzurro et al., 2007
- Azzurro et al., 2008
- Azzurro et al., 2011
- Azzurro et al., 2012
- Azzurro et al., 2012
- Azzurro et al., 2015
- Azzurro et al., 2015
- Azzurro et al., 2016
- Bagott et al., 2013
- Barry et al., 2015
- Barry et al., 2017
### Summary by outcome

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Count</th>
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</thead>
<tbody>
<tr>
<td>Acute</td>
<td>44</td>
</tr>
<tr>
<td>Behavior</td>
<td>226</td>
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<tr>
<td>Bone and Calcium</td>
<td>40</td>
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<tr>
<td>Cardiovascular</td>
<td>282</td>
</tr>
<tr>
<td>Pharmacokinetics</td>
<td>76</td>
</tr>
<tr>
<td>Reproductive and Developmental</td>
<td>107</td>
</tr>
</tbody>
</table>

Total title/abstracts included: 739

For perspective, EFSA only carried 142 forward…
How Results Were Visualized in Plots

• Plots were created for each of the major endpoints within each outcome

• Effect levels were identified for each endpoint within a study (i.e. NOEL or LOEL)
  – Most refined result presented
  – Levels were point estimates and ranges

• Color, size, and shape of symbols were used to capture information on the type of effect and risk of bias

Some unique endpoints were not included on the graphs (see AHRQ and supplemental material for more information)

Plots do not show all data from every study (see AHRQ for more information)
The evidence demonstrates that in adolescents and adults, deaths occurred at doses mostly > 10g/day.

Most exposures were suicidal gestures.

Adverse effects in non-fatal cases included nausea, vomiting, and cardiovascular events.

Exposure characterization was poor.

Very low to low level of confidence in the body of evidence.
Bone: Risk of Fracture and Fall

- The majority, although not all, of the data demonstrate a lack of effects of caffeine consumption at levels both above (up to 760 mg/day) and below 400 mg/day
  - Effects <400 were of low magnitude (RR = <1.2) or were reported in analyses that did not consistently control for calcium intake
- Moderate confidence: findings generally consistent, most studies controlled for calcium intake
Overall Conclusions based on WOE

- Bone and Calcium
- Behavior
- Cardiovascular
- Repro/Developmental
- Acute

Are Nawrot et al. (2003) conclusions supported?
Conclusion: intake levels remain acceptable

- 400 mg/day in healthy adults
- 300 mg/day in healthy pregnant women
- 2.5 mg/kg-day in healthy children and adolescents (limited data)
Findings Relative to Other Recent Assessments

Adults: Caffeine intakes from all sources up to 400 mg per day (about 5.7 mg/kg bw per day for a 70-kg adult) consumed throughout the day do not give rise to safety concerns for healthy adults in the general population.

Pregnant Women: Caffeine intakes from all sources up to 200 mg per day consumed throughout the day by pregnant women in the general population do not give rise to safety concerns for the fetus.

Children: Single doses of caffeine of no concern derived for adults (3 mg/kg bw per day for a 70-kg adult) may also apply to children.

Strong and consistent evidence shows that consumption of coffee within the moderate range (3 to 5 cups/d or up to 400 mg/d caffeine) is not associated with increased risk of major chronic diseases, such as cardiovascular disease (CVD) and cancer and premature death in healthy adults.
Collective Impact

Anticipated utility for health professionals and consumers
Identification of future research areas

Shift in caffeine research may be warranted
• Sensitive populations
• Interindividual variability
• Co-exposures
• Subpopulations (e.g., unhealthy)

Application of SR in field of toxicology
• Demonstrates need to further develop tools
PAPER OF THE YEAR!

Re: Best Paper of the Year (2017) published in FOOD CHEM TOXICOL

Daniele Wikoff
José L. Domingo-Roig; Food and Chemical Toxicology (ELS); Mirkina, Jagna (ELS-AMS); Candace Doepker
Monday, June 11, 2018 at 7:18 AM

To: Daniele Staskal-Wikoff <dwikoff@toxstrategies.com>
Cc: “Food and Chemical Toxicology (ELS) <<tct@elsevier.com>>, “Mirkina, Jagna (ELS-AMS) <<J.Miriska@elsevier.com>>
Subject: Best Paper of the Year (2017) published in FOOD CHEM TOXICOL

Dear Dr Wikoff,

I am contacting you as the first and the corresponding author of the paper published in 2017 in Food Chem Toxicol:


As Editor-In-Chief of the Journal, and on behalf of the Editorial Board, I am very pleased to announce you that your article has been selected as the BEST PAPER OF THE YEAR (2017) published in Food Chem Toxicol. The co-Editors made a first preselection of 8 articles, which was ‘in turn’ submitted to the vote of all our Associate Editors. I am pleased to inform you that your paper has been the winner.

My most sincere congratulations!

Kind regards,

Jose L. Domingo
EIC
Common Misperceptions
Evergreen topics that are NOT supported by data

• Pregnant women should avoid caffeine
• Caffeine is dehydrating
• Caffeine is associated with increased risk of heart disease
Caffeine and Pregnancy – alarming headlines

• Results from Health Canada, 2003; Wikoff et al., 2017, FDA position, EFSA position are not consistent with the need to AVOID caffeine.

YET........
What drives this perpetuated misunderstanding?

• This is a well known and documented phenomenon called the **pregnancy signal** which confounds the studies of most common source of caffeine in pregnant women…coffee

• **What is the Pregnancy signal?**
  – In early pregnancy when high hormone levels exist (reflecting a healthy pregnancy) there is a frequent aversion to strong odors (coffee is an example);
  – This aversion does not occur when low hormone levels (reflecting an unhealthy pregnancy) are present.
  – This phenomenon led to a misperception of the researchers that caffeine was the causative agent when the pregnancy was already doomed.
  – First documented in 2004
Supporting Data for the Pregnancy Signal & Safety

• Comprehensive review of literature in 2010¹
  –“Weight of evidence does not support a positive relationship between caffeine consumption and adverse reproductive or perinatal outcomes.”
  • Moderate = 1-2 cups/day
Caffeine and dehydration

- Caffeine does have a mild diuretic effect = increased urine output
- Research suggests consumption of caffeine will NOT cause dehydration
- Some researchers in this area.....

Caffeine and exercise: metabolism, endowment, and performance

T. Grade 1

Affiliation: e-mail

PMID: 17593074 DOI: 10.1212/JN.0b013e3181c7f69c

Abstract

Caffeine is a common substance in the diet of most athletes and it is now appearing in many new products, including energy drinks, sport gels, caffeinated beverages and diet aids. It can be a powerful ergogenic aid at levels that are considerably lower than the acceptable limit of the International Olympic Committee and could not improve measured oxygen capacity.

In summary, research suggests caffeine will not cause dehydration.

Fluid, electrolyte, and renal indices during 11 days of controlled caffeine intake

Lindon C. Armstrong, MD, JD, AP, F investm, W. Hi, Dan; Davis; C. O, Balun, Sultan; Douglas; J. C.; Marsh, H.

Affiliation: e-mail

PMID: 19178558 DOI: 10.1213/01.jnci.0000339956.93021.0f

Abstract

This investigation determined if 3 levels of controlled caffeine intake affected electrolyte balance and renal function differently. Healthy males (n = 27) consumed 3 mg caffeine/kg/d, 75% of caffeine, and 75% of caffeine during 11 days of treatment phase, subjects consumed

No significant differences in NV were found between conditions, although a modest positive effect was observed within NV (14.1 ± 3.9 kg vs. 20.5 ± 1.0 kg). Our data show that there were no significant differences across a wide range of hematological and electrolyte variables between both trials. These data suggest that caffeine, when consumed in moderation, can have beneficial effects on hydration status.
Caffeine and heart health

- This has been a traditionally recognized “concern”
- Research of late has continued to support that caffeine intake does not increase risk of CVD
- Ding; Bravi; Poole et al., have done large reviews
Toxicologist’s Mantra

Everything in Moderation
In Summary

Caffeine remains one of the most researched ingredient in today’s marketplace.

- Occurs naturally; it can also be added to foods and beverages.
- Naturally occurring caffeine has the same effect of caffeine that is added – there is no difference in the effect

- Moderate caffeine consumption is not a concern;
- Up to 400mg is considered moderate;
- 200mg for pregnant women

Understand the various sources and amounts in each product

Visit IFIC’s Caffeine website and check out the Caffeine Calculator and understand the caffeine content from various sources.
Acknowledgements/References

TODAY’S WEBINAR TEAM

Dr. Candace Doepker, ToxStrategies
Kris Sollid, RD, IFIC
Will Whitman, IFIC
Tony Flood, IFIC

LINKS/REFERENCES

www.foodinsight.org/caffeine
https://foodinsight.org/caffeine-and-you/calculator.html
2020 Food & Health Survey
Candace Doepker, Speaker CV
Thank you

flood@ific.org
cdoepker@toxstrategies.com