Tox Strategies

Systematic review of the potential adverse effects of caffeine consumption in healthy adults, pregnant women, adolescents, and children: **Overall Conclusions**

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> Innovative Solutions Sound Science

Overall Conclusions

Goal: update work of Health Canada

Approach:

- Systematic review (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.

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)



PK/PD - Approach and Findings

Evaluated contextually (systematically identified)

- ~100 studies combined from PK category as well as PK as part of an outcome
- 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

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.

Consistent observational evidence indicates that moderate coffee consumption is associated with reduced risk of type 2 diabetes and cardiovascular disease 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