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Risk Assessment

Protective Effects of Micronutrient Supplements, Phytochemicals and Phytochemical-Rich Beverages and Foods Against DNA Damage in Humans: A Systematic Review of Randomized Controlled Trials and Prospective Studies

Michael F Fenech, Caroline F Bull, B Jan-Willem Van Klinken. Adv Nutr. 2023 Nov;14(6):1337-1358. doi: 10.1016/j.advnut.2023.08.004. Article link

Significance: Supplementation with certain micronutrients and their combinations may reduce DNA damage and promote cellular health by improving the maintenance of genome integrity.

Accumulation of deoxyribonucleic acid (DNA) damage diminishes cellular health, increases risk of developmental and degenerative diseases, and accelerates aging. Optimizing nutrient intake can minimize accrual of DNA damage. The objectives of this review are to: 1) assemble and systematically analyze high-level evidence for the effect of supplementation with micronutrients and phytochemicals on baseline levels of DNA damage in humans, and 2) use this knowledge to identify which of these essential micronutrients or nonessential phytochemicals promote DNA integrity *in vivo* in humans. We conducted systematic literature searches of the PubMed database to identify interventional, prospective, cross-sectional, or in vitro studies that explored the association between nutrients and established biomarkers of DNA damage associated with developmental and degenerative disease risk. Biomarkers included lymphocyte chromosome aberrations, lymphocyte and buccal cell micronuclei, DNA methylation, lymphocyte/leukocyte DNA strand breaks, DNA oxidation, telomere length, telomerase activity, and mitochondrial DNA mutations. Only randomized, controlled interventions and uncontrolled longitudinal intervention studies conducted in humans were selected for evaluation and data extraction. These studies were ranked for the quality of their study design. In all, 96 of the 124 articles identified reported studies that achieved a quality assessment score ≥ 5 (from a maximum score of 7) and were included in the final review. Based on these studies, nutrients associated with protective effects included vitamin A and its precursor β-carotene, vitamins C, E, B1, B12, folate, minerals selenium and zinc, and phytochemicals such as curcumin (with piperine), lycopene, and proanthocyanidins. These findings highlight the importance of nutrients involved in (i) DNA metabolism and repair (folate, vitamin B12, and zinc) and (ii) prevention of oxidative stress and inflammation (vitamins A, C, E, lycopene, curcumin, proanthocyanidins, selenium, and zinc). Supplementation with certain micronutrients and their combinations may reduce DNA damage and promote cellular health by improving the maintenance of genome integrity.

Foodborne Pathogens

Impact of Vitamin B12 on Rhamnose Metabolism, Stress Defense and *in-vitro* Virulence of *Listeria monocytogenes*

Zhe Zeng, Lucas M Wijnands, Sjef Boeren, Eddy J Smid, Richard A Notebaart, Tjakko Abee. *Int J Food Microbiol.* 2023 Nov 16:410:110486. doi: 10.1016/j.ijfoodmicro.2023.110486. Article link

Significance: This study investigates the possible effects of Vitamin B12 on *L. monocytogenes* competitive fitness and virulence activation when utilizing rhamnose in anaerobic conditions encountered during digestion.

Listeria monocytogenes is a facultative anaerobe which can cause a severe food-borne infection known as listeriosis. *L. monocytogenes* is capable of utilizing various nutrient sources including rhamnose, a naturally occurring deoxy sugar abundant in foods. *L. monocytogenes* can degrade rhamnose into lactate, acetate and 1,2-propanediol. Our previous study showed that addition of vitamin B12 stimulated anaerobic growth of *L. monocytogenes* on rhamnose due to the activation of bacterial microcompartments for 1,2-propanediol utilization (pdu BMC) with concomitant production of propionate and propanol. Notably, anaerobic 1,2-propanediol metabolism has been linked to virulence of enteric pathogens including *Salmonella* spp. and *L. monocytogenes*. In this study we investigated the impact of B12 and BMC activation on i) aerobic and anerobic growth of *L. monocytogenes* on rhamnose and ii) the level of virulence. We observed B12-induced pdu BMC activation and growth stimulation only in anaerobically grown cells. Comparative Caco-2 virulence assays showed that these pdu BMC-induced cells have significantly higher translocation efficiency compared to non-induced cells (anaerobic growth without B12; aerobic growth with or without B12), while adhesion and invasion capacity is similar for all cells. Comparative proteome analysis showed specific and overlapping responses linked to metabolic shifts, activation of stress defense proteins and virulence factors, with RNA polymerase sigma factor SigL, teichoic acid export ATP-binding protein TagH, DNA repair and protection proteins, RadA and DPS, and glutathione synthase GshAB, previously linked to activation of virulence response in *L. monocytogenes*, uniquely upregulated in anaerobically rhamnose grown pdu-induced cells. Our results shed light on possible effects of B12 on *L. monocytogenes* competitive fitness and virulence activation when utilizing rhamnose in anaerobic conditions encountered during transmission and the human intestine.

740 15th Street NW
Washington, DC
20005

Tel: 202.659.0184, Ext. 135
Fax: 202.659.3859
iafns@iafns.org

Foodborne Illness

Restaurant and Staff Characteristics Related to Practices that Could Contribute to Cross-Contamination

E Rickamer Hoover, Matthew Masters, Jona Johnson, Wendy McKelvey, Nicole Hedeen, Danny Ripley, Laura Brown. *J Food Prot*. 2023 Dec;86(12):100182. doi: 10.1016/j.jfp.2023.100182. Article link

Significance: Given that potential contamination actions were greater in independent restaurants that do not have strong food safety practices, the food service industry and food safety officials can consider encouraging strong food safety training and policies, particularly concerning hand hygiene.

Foodborne illness is a persistent public health concern in the U.S.; over 800 foodborne illness outbreaks are reported to the Centers for Disease Control and Prevention (CDC) annually. Most of these outbreaks (60%) are linked with restaurants. Contamination of food with foodborne pathogens during preparation and storage is a significant contributing factor to many of these outbreaks. The CDC's Environmental Health Specialists Network (EHS-Net) collected data to identify restaurant characteristics, policies, and practices associated with contamination prevention practices. Data collectors interviewed managers and conducted kitchen observations in 312 restaurants across six EHS-Net sites in five states. Data collectors observed at least one food worker action that could lead to contamination in 63.1% of restaurants. The most frequently observed action that could lead to contamination was bare-hand or dirty glove contact with ready-to-eat food (35.9%). The estimated mean number of observed potential contamination actions was greater in restaurants that were independently owned (does not share a name and operations with other restaurants), did not require managers to be certified in food safety, did not have workers trained in food safety, did not have a handwashing policy, did not have a policy minimizing bare-hand contact with ready-to-eat foods, and had a manager with more than two years of experience at their current restaurant. These results suggest that to improve contamination prevention, the foodservice industry and food safety officials can consider supporting and encouraging strong food safety training and policies, particularly concerning hand hygiene, and targeting interventions to independent restaurants.

Mycotoxins

Biotechnological and Biocontrol Approaches for Mitigating Postharvest Diseases Caused by Fungal Pathogens and Their Mycotoxins in Fruits: A Review

Esa Abiso Godana, Qiya Yang, Xiaoyun Zhang, Lina Zhao, Kaili Wang, Solairaj Dhanasekaran, Teame Gereziher Mehari. *J Agric Food Chem*. 2023 Nov 22;71(46):17584-17596. doi: 10.1021/acs.jafc.3c06448. Article link

Significance: An overview of major postharvest diseases caused by fungal pathogens and the potential of biotechnological approaches in controlling these diseases.

Postharvest diseases caused by fungal pathogens are significant contributors to the postharvest losses of fruits. Moreover, some fungal pathogens produce mycotoxins, which further compromise the safety and quality of fruits. In this review, the potential of biotechnological and biocontrol approaches for mitigating postharvest diseases and mycotoxins in fruits is explored. The review begins by discussing the impact of postharvest diseases on fruit quality and postharvest losses. Next, it provides an overview of major postharvest diseases caused by fungal pathogens. Subsequently, it delves into the role of biotechnological approaches in controlling these diseases. The review also explored the application of biocontrol agents, such as antagonistic yeasts, bacteria, and fungi, which can suppress pathogen growth. Furthermore, future trends and challenges in these two approaches are discussed in detail. Overall, this review can provide insights into promising biotechnological and biocontrol strategies for managing postharvest diseases and mycotoxins in fruits.

Heavy Metals

Molecular-Assisted Breeding of Cadmium Pollution-Safe Cultivars

Wen-Juan Ni, Samavia Mubeen, Xiao-Min Leng, Chuntao He, Zhongyi Yang. *J Agric Food Chem*. 2023 Nov 3. doi: 10.1021/acs.jafc.3c04967. Article link

Significance: This review summarizes the recent progress in the research on low-Cadmium accumulation traits of pollution-safe cultivars in different crops and provides the potential future for breeding Cd-PSC using modern molecular technologies.

Cadmium (Cd) contamination in edible agricultural products, especially in crops intended for consumption, has raised worldwide concerns regarding food safety. Breeding of Cd pollution-safe cultivars (Cd-PSCs) is an effective solution to preventing the entry of Cd into the food chain from contaminated agricultural soil. Molecular-assisted breeding methods, based on molecular mechanisms for cultivar-dependent Cd accumulation and bioinformatic tools, have been developed to accelerate and facilitate the breeding of Cd-PSCs. This review summarizes the recent progress in the research of the low Cd accumulation traits of Cd-PSCs in different crops. Furthermore, the application of molecular-assisted breeding methods, including transgenic approaches, genome editing, marker-assisted selection, whole genome-wide association analysis, and transcriptome, has been highlighted to outline the breeding of Cd-PSCs by identifying critical genes and molecular biomarkers. This review provides a comprehensive overview of the development of Cd-PSCs and the potential future for breeding Cd-PSC using modern molecular technologies.

Food Packaging

Phytochemicals and Bioactive Constituents in Food Packaging - A Systematic Review

Shahida Anusha Siddiqui, Sipper Khan, Mohammad Mehdizadeh, Nur Alim Bahmid, Danung Nur Adli, Tony R Walker, Rosa Perestrelo, José S Câmara. *Heliyon*. 2023 Nov 24;9(11):e21196. doi: 10.1016/j.heliyon.2023.e21196. Article link

Significance: Consumer preferences for natural bioactive agents over synthetic compounds have increased and are becoming essential in food packaging planning.

Designing and manufacturing functional bioactive ingredients and pharmaceuticals have grown worldwide. Consumers demand for safe ingredients and concerns over harmful synthetic additives have prompted food manufacturers to seek safer and sustainable alternative solutions. In recent years the preference by consumers to natural bioactive agents over synthetic compounds increased exponentially, and consequently, naturally derived phytochemicals and bioactive compounds, with antimicrobial and antioxidant properties, becoming essential in food packaging field. In response to societal needs, packaging needs to be developed based on sustainable manufacturing practices, marketing strategies, consumer behaviour, environmental concerns, and the emergence of new technologies, particularly bio- and nanotechnology. This critical systematic review assessed the role of antioxidant and antimicrobial compounds from natural resources in food packaging and consumer behaviour patterns in relation to phytochemical and biologically active substances used in the development of food packaging. The use of phytochemicals and bioactive compounds inside packaging materials used in food industry could generate unpleasant odours derived from the diffusion of the most volatile compounds from the packaging material to the food and food environment.

Chemical Contaminants

Linking Prenatal Environmental Exposures to Lifetime Health with Epigenome-Wide Association Studies: State-of-the-Science Review and Future Recommendations

Kelly M Bakulski, Freida Blostein, Stephanie J London. *Environ Health Perspect*. 2023 Dec;131(12):126001. doi: 10.1289/EHP12956. Article link

Significance: Better powered Epigenome-Wide Association Studies could identify methylation exposure signatures across many exposures and enable comprehensive biomarker development.

Background: The prenatal environment influences lifetime health; epigenetic mechanisms likely predominate. In 2016, the first international consortium paper on cigarette smoking during pregnancy and offspring DNA methylation identified extensive, reproducible exposure signals. This finding raised expectations for epigenome-wide association studies (EWAS) of other exposures. **Objective:** We review the current state-of-the-science for DNA methylation associations across prenatal exposures in humans and provide future recommendations. **Methods:** We reviewed 134 prenatal environmental EWAS of DNA methylation in newborns, focusing on 51 epidemiological studies with meta-analysis or replication testing. Exposures spanned cigarette smoking, alcohol consumption, air pollution, dietary factors, psychosocial stress, metals, other chemicals, and other exogenous factors. Of the reproducible DNA methylation signatures, we examined implementation as exposure biomarkers. **Results:** Only 19 (14%) of these prenatal EWAS were conducted in cohorts of 1,000 or more individuals, reflecting the still early stage of the field. To date, the largest perinatal EWAS sample size was 6,685 participants. For comparison, the most recent genome-wide association study for birth weight included more than 300,000 individuals. Replication, at some level, was successful with exposures to cigarette smoking, folate, dietary glycemic index, particulate matter with aerodynamic diameter < 10μ m and < 2.5μ m, nitrogen dioxide, mercury, cadmium, arsenic, electronic waste, PFAS, and DDT. Reproducible effects of a more limited set of prenatal exposures (smoking, folate) enabled robust methylation biomarker creation. **Discussion:** Current evidence demonstrates the scientific premise for reproducible DNA methylation exposure signatures. Better powered EWAS could identify signatures across many exposures and enable comprehensive biomarker development. Whether methylation biomarkers of exposures themselves cause health effects remains unclear. We expect that larger EWAS with enhanced coverage of epigenome and exposome, along with improved single-cell technologies and evolving methods for integrative multi-omics analyses and causal inference, will expand mechanistic understanding of causal links between environmental exposures, the epigenome, and health outcomes throughout the life course.

Caffeine

Inverse Association between Caffeine Intake and Albuminuria in US adults: An Analysis of NHANES 2005-2016

Qiqi Ma, Shuaihua Song, Gaosi Xu. *Acta Clin Belg*. 2023 Dec;78(6):438-445. doi: 10.1080/17843286.2023.2222243. Article link

Significance: This study confirms the potentially protective effects of caffeine on the kidney by demonstrating an inverse correlation between caffeine intake and albuminuria — a significant biomarker of kidney disease.

Objectives: Albuminuria is a significant biomarker of various kidney diseases and is associated with renal outcome. Recently, caffeine intake has shown potential renoprotective effects. However, the relationship between caffeine intake and albuminuria remains profoundly elusive.

Methods: We conducted a cross-sectional study aimed to explore the association between caffeine intake and albuminuria in the American adult population using the data acquired from the National Health and Nutrition Examination Survey (NHANES) 2005-2016. Caffeine intake was assessed by 24-h dietary recalls, and albuminuria was assessed by albumin-to-creatinine ratio. Multivariate logistic regression was performed to explore the independent association between caffeine intake and albuminuria. Subgroup analysis and interaction tests were also conducted. **Results:** Among 23,060 participants, 11.8% of the individuals exhibited albuminuria, and the prevalence of albuminuria decreased with higher caffeine intake tertiles (Tertile 1: 13%; Tertile 2: 11.9%; Tertile 3: 10.5%; P < 0.001). After adjusted potential confounders, the results of logistic regression indicated that a higher caffeine intake was associated with a decreased risk of albuminuria (OR = 0.903; 95% CI: 0.84, 0.97; P = 0.007), especially in females and the participants aged <60 years and chronic kidney disease stage II. **Conclusion:** The present study first indicated an inverse correlation between caffeine intake and albuminuria, which further confirmed the potentially protective effects of caffeine on the kidney.

Food Allergens

IgE to Common Food Allergens is Associated with Cardiovascular Mortality in the National Health and Examination Survey and the Multi-Ethnic Study of Atherosclerosis

Corinne Keet, Emily C McGowan, David Jacobs, Wendy S Post, Nathan E Richards, Lisa J Workman, et. al. *J Allergy Clin Immunol*. 2023 Nov 2:S0091-6749(23)01251-4. doi: 10.1016/j.jaci.2023.09.038. Article link

Significance: The finding that food sensitization is associated with increased risk of cardiovascular mortality challenges the current paradigm that sensitization without overt allergy is benign.

Background: In individuals without symptomatic food allergy, food-specific IgE is considered clinically irrelevant. However, recent studies have suggested that galactose-α-1,3-galactose (alpha-gal) IgE is associated with cardiovascular (CV) disease. **Objective:** We sought to determine whether sensitization to common food allergens is associated with CV mortality. **Methods:** The association between IgE sensitization to foods and CV mortality ascertained to 2019 was examined in the National Health and Examination Survey (NHANES) 2005-2006 and the Wake Forest site of the Multi-Ethnic Study of Atherosclerosis (MESA) cohort; MESA enrolled adults without baseline clinical CV diseases between 2000 and 2002. Total and specific IgE was measured to cow's milk, egg, peanut, shrimp, and a panel of aeroallergens (NHANES), and to cow's milk, alpha-gal, peanut, dust mite, and timothy grass (MESA). Cox proportional hazard models were constructed, adjusting for sex, age, race/ethnicity, smoking, education, and asthma. **Results:** A total of 4414 adults from NHANES (229 CV deaths) and 960 from MESA (56 CV deaths) were included. In NHANES, sensitization to at least 1 food was associated with higher CV mortality (hazard ratio [HR], 1.7 [95% confidence interval (CI), 1.2-2.4], P = .005). Milk sensitization was particularly associated (HR, 2.0 [95% CI, 1.1-3.8], P = .026), a finding replicated in MESA (HR, 3.8 [95% CI, 1.6-9.1], P = .003). Restricting analyses in NHANES to consumers of the relevant allergen strengthened food sensitization relationships, unmasking shrimp and peanut sensitization as additional risk factors for CV mortality. **Conclusions:** The finding that food sensitization is associated with increased risk of CV mortality challenges the current paradigm that sensitization without overt allergy is benign. Further research is needed to clarify mechanisms of this association.

Emerging Science Areas

Emerging Areas Food Safety –Stem-Based Cultivated Meat

Stem Cell-Based Strategies and Challenges for Production of Cultivated Meat

T. C. Jara, K. Park, P. Vahmani, A. L. Van Eenennaam, L. R. Smith & A. C. Denicol .*Nature Food* volume 4, Oct 16, p841–853 (2023). Article link

Significance: This study explores the challenges for industrial scale-up, including differentiation and culture protocols, as well as genetic modification options for stem cell immortalization and controlled differentiation.

Cultivated meat scale-up and industrial production will require multiple stable cell lines from different species to recreate the organoleptic and nutritional properties of meat from livestock. In this Review, we explore the potential of stem cells to create the major cellular components of cultivated meat. By using developments in the fields of tissue engineering and biomedicine, we explore the advantages and disadvantages of strategies involving primary adult and pluripotent stem cells for generating cell sources that can be grown at scale. These myogenic, adipogenic or extracellular matrix-producing adult stem cells as well as embryonic or inducible pluripotent stem cells are discussed for their proliferative and differentiation capacity, necessary for cultivated meat. We examine the challenges for industrial scale-up, including differentiation and culture protocols, as well as genetic modification options for stem cell immortalization and controlled differentiation. Finally, we discuss stem cell-related safety and regulatory challenges for bringing cultivated meat to the marketplace.

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