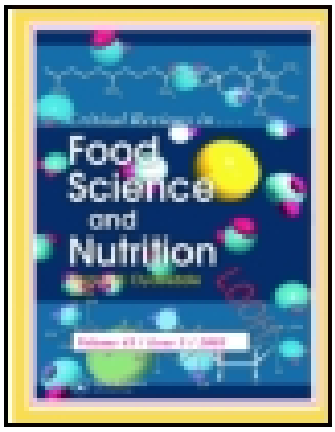

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Evaluating Bioactive Food Components in Obesity and Cancer Prevention

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Evaluating Bioactive Food Components in Obesity and Cancer Prevention

Kristi M. Crowe, PhD, RD[1*] and David Allison, PhD[2*], for the Bioactive Food Compounds Components Speakers[3].

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Word Count: 1850 (abstract: 116, manuscript: 1655, references: 79)

[3]Speakers: Mario Ferruzi, Yao-Wen Huang, Michael Lefevre, Shengmin Sang, Elizabeth Jeffery, Susanne Talcott, Stephen Anton, Jason Locasale, Ralphenia Pace, Kristi Crowe, Agnes Rimando, Naima Moustaid-Moussa, David Allison, Johanna Lampe, Esther Guzman, Ben de Lumen, Wendy Demark-Wahnefried, Balakrishna Lokeshwar, Jim Kaput, Stephen Zeisel, Leonard Williams

Abstract

Research into bioactive food compounds (BFC) continues to evolve albeit with shared challenges among scientists in the fields of obesity and cancer treatment and prevention. Given the diversity of scientific disciplines involved in evaluating BFC, multi-disciplinary conferences provide opportunities to update the state of the science and critically discuss conceptual and methodological challenges encountered in studying BFC in both pre-clinical and clinical trials. This overview is an introduction to presentations given at a conference sponsored by the National Cancer Institute of the National Institutes of Health and the University of Alabama at Birmingham which convened a multi-disciplinary group of researchers evaluating BFC in obesity and cancer prevention. Full presentations can be viewed in video format at http://www.norc.uab.edu/courses/conferences/conference2013.

Conference Overview

Widespread consumer focus on bioactive components in foods and supplements in health promotion and disease prevention is of great public health interest. While food has long been known to influence and improve human health, recent scientific advances have aided the investigation of bioactive food components (BFC) in reducing cancer risk factors among obese and normal weight individuals. In light of the relationship between obesity and cancer risk, assessing the shared opportunities and challenges in obesity and cancer research in studying BFC demands an ongoing dialogue among cross-disciplinary researchers in the areas of food science and nutritional biochemistry, nutrigenomics, molecular biology, pharmacology, and medicine. Such dialogue is critical to thoroughly and practically addressing the short- and long-term efficacy of pre-clinical and clinical trial testing of BFC in weight reduction and cancer prevention.

In a recent publication by the National Cancer Institute (NCI) on Obesity and Cancer Risk, an additional 500,000 new cases of cancer among obese individuals is projected by the year 2030 based on existing trends in obesity.[1] A multidisciplinary group of researchers assembled in 2013 with the support of the NCI and Nutrition Obesity Research Center at the University of Alabama at Birmingham to address the state-of-the-science on BFC research in obesity and cancer. The following presentations highlight the influence of BFC in obesity and cancer prevention/treatment as well as the methodological challenges in testing and developing functional foods with BFC.

Mario Ferruzi, PhD, from Purdue University addressed the unresolved challenges in characterizing the benefit of BFC including the lack of standards for the various metabolites resulting from a parent compound of interest. He emphasized the need for identifying and quantifying these metabolites while calling for a better understanding of the impact of the gut microbiome on BFC metabolism.

Yao-Wen Huang, PhD, from University of Georgia addressed the concept of dysfunctional foods. He challenged the attendees to consider the term "dysfunctional" and whether a food can be called dysfunctional in and of itself, or if rather, any food or BFC can be dysfunctional if consumed in excess. He focused his point by discussing trends in food consumption which showed a pattern of dysfunctional dieting or excessive intake of compounds considered by some to be dysfunctional including caffeine, sugar, sodium, etc.

Michael Lefevre, PhD, from Utah State University spoke on the need for valid endpoints or outcome biomarkers for determining BFC efficacy. He emphasized the importance of considering background diet when evaluating BFC and the differences in metabolism of BFC in normal weight versus obese patients, possibly due to gene modification.

Shengmin Sang, PhD, from North Carolina A&T State University addressed the use of cellular models for assessing activities of BFC. He emphasized the importance of cell cultures to provide an understanding of BFC effect and highlighted the differences in compound stability and bioavailability *in vitro* and *in vivo*.

Elizabeth Jeffery, PhD, from University of Illinois at Urbana-Champaign spoke on the differences in bioavailability of phytochemical BFC. She illustrated her point by discussing the impact of molecular structure on metabolism as well as the role of the microbiome in BFC bioavailability.

Susanne Talcott, PhD, from Texas A&M University addressed the impact of polyphenols on intestinal inflammation. She illustrated her points by discussing research on rats with inflammatory bowel disease fed human equivalent doses of gallic acid equivalents, which showed that mango polyphenols may be a potential therapeutic agent for treating colitis.

Stephen Anton, PhD, from University of Florida addressed the design of clinical studies evaluating BFC. He focused primarily on important considerations related to the use of parallel versus crossover designs and also highlighted the importance of understanding potential regulatory hurdles in phase I and phase 2 clinical trials.

Jason Locasale, PhD, from Cornell University spoke on the use of metabolomics in nutrition assessment and monitoring of cancer patients. He illustrated his points by discussing the heterogeneity of metabolism across a variety of colon cancer cells which showed a need for untargeted and targeted metabolomic screening to investigate cancer metabolism.

Ralphenia Pace, PhD, RD, LD, from Tuskegee University highlighted the importance of evaluating BFC within foods of cultural relevance. She pointed out the phytochemical profile of foods commonly consumed by specific population groups along with discussing results of animal studies in which vegetable greens rich in polyphenols were evaluated for potential impact on cardiometabolic measures.

Kristi Crowe, PhD, RD, LD, from University of Alabama addressed the need for understanding the primary food matrix housing BFC in order to optimize BFC delivery in developed functional foods. She illustrated her point on lessons learned from the primary matrix by discussing research on fruit polyphenols and the impact of food processing on the bioactivity of these compounds in processed fruit products.

Agnes Rimando, PhD, with the United States Department of Agriculture, Agricultural Research Service, Natural Products Utilization Research Unit spoke on the potential role of phytochemicals in the treatment of metabolic syndrome. Specifically, she discussed the hypolipidemic and hypoglycemic effects of pterostilbene a phenolic compound which has been identified in blueberry skins.

Naima Moustaid-Moussa, PhD, from Texas Tech University highlighted the anti-inflammatory effects of eicosapentaenoic acid (EPA), an omega-3 fatty acid. She focused her points by discussing research on the role of EPA in preventing diet-induced excessive weight gain, glucose intolerance, and insulin resistance as well as the reduction in adipose tissue inflammation in male mice fed high fat diets supplemented with EPA.

David Allison, PhD, from University of Alabama at Birmingham spoke on the design of weight loss trials evaluating BFC effectiveness. He illustrated the various methods of handling missing data points in clinical research and the comprehensive nature of the multiple imputation model of analysis for thoroughly assessing clinical trial data.

Johanna Lampe, PhD, RD, from the Fred Hutchinson Cancer Research Center discussed the potential chemopreventative effects of food phytochemicals. She highlighted signal

transduction pathways important to cancer development along with the functionality of BFC to modulate these pathways while also underscoring the importance of the whole diet rather than isolated compounds to reduce cancer risk.

Esther Guzman, PhD, from Florida Atlantic University spoke on the cancer preventing effects of bioactive compounds isolated from marine organisms. She pointed out the various methods of screening these secondary metabolites for bioactivity as well as the results of research investigating marine natural products for inhibiting mast cell migration and degranulation.

Wendy Demark-Wahnefried, PhD, RD, from University of Alabama at Birmingham highlighted the complexities of using functional foods in clinical trials. She illustrated her points by discussing research from a Phase II randomized controlled trial of flaxseed supplementation among prostate cancer patients which showed that dietary inclusion of flaxseed is associated with reduced prostate cancer growth.[2, 3]

Ben de Lumen, PhD, from University of California at Berkeley presented research on the cancer preventive effects of lunasin, a seed peptide abundant in soybeans, wheat, barley, rice and other seeds used as major crops. He discussed the potential mechanisms of action of lunasin in tumor suppression and the bioavailability of this compound in humans.

Balakrishna Lokeshwar, PhD, from University of Miami spoke on the chemo-preventative effects of BFC within herbs and spices such as turmeric and allspice. He accentuated the anticancer efficacy of bioactive compounds within allspice by discussing its efficacy both *in vitro* and *in vivo*. He demonstrated that the BFC present in allspice extracts kill

human prostate cancer cells in vitro and by oral administration in transgenic animal models by their inhibition of androgen receptor activity and induction of apoptosis.

Jim Kaput, PhD, from Nestlé Health Sciences, described an emerging conceptual and experimental approach for human research studies that accounts for the known genetic, nutritional, and physiological differences between individuals. Differences in response due to genotype or lifestyle may produce varied responses to bioactive food components that are consumed in small amounts and often require a threshold to produce observable effects. Hence, comparing physiological responses before and after long-term exposure may be necessary to determine the action of BFC. Dr. Kaput described the Delta Vitamin Obesity project, which analyzed blood levels of vitamins A, D, E, riboflavin, thiamin, pyridoxal, pyridoxine, folate, homocysteine, and erythrocyte levels of S-adenosylmethionine and S-adenosylhomocysteine and conducted detailed multivariate analyses to assess patterns of relations among metabolites. This approach or others which aim to account for heterogeneity in biological responses among individuals may have value in assessing the efficacy of BFC.

Steven Zeisel, MD, PhD, from University of North Carolina, Chapel Hill spoke on the use of metabolomic profiling in identifying compound bioactivity and teasing apart responders and non-responders in clinical research. His discussion focused on metabolomic changes caused by choline deficiency across the lifespan.

Leonard Williams, PhD, from North Carolina A&T University concluded the session on emerging approaches for utilizing BFC by discussing the effect of various compounds on the

survival and virulence of food-borne pathogens. He emphasized his point by presenting research on the encapsulation of BFC and use of these nano-particles in the packaging of fresh produce.

While research on BFC in obesity and cancer prevention holds promise, several existing challenges were deliberated upon during panel discussions which need to be addressed in order to scientifically justify the integration of these compounds into the diet. Such challenges include the validity of experimental models and the need for a defined testing plan moving from *in vitro* to *in vivo* studies using isolated compounds as well as functional foods formulated with these compounds. Dose considerations for testing were also discussed as a major challenge for researchers due to the dual application of use of BFC – prevention and treatment. Additionally, testing considerations with single compounds, mixtures of compounds, or mixtures of compounds and metabolites remained a topic of focus. Overall, overcoming such challenges in BFC research demands a greater understanding of the multiplicity of interactions among food components and the governance of these interactions by the matrix of delivery. As such, additional research taking into consideration the aforementioned challenges is needed to better characterize the potential efficacy of BFC to treat or prevent obesity and cancer.

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