Nutritional Translation Blended With Food Science: 21st Century Applications

Mario G. Ferruzzi, Devin G. Peterson, R. Paul Singh, Steven J. Schwartz, and Marjorie R. Freedman

ABSTRACT

This paper, based on the symposium “Real-World Nutritional Translation Blended With Food Science,” describes how an integrated “farm-to-cell” approach would create the framework necessary to address pressing public health issues. The paper describes current research that examines chemical reactions that may influence food flavor (and ultimately food consumption) and posits how these reactions can be used in health promotion; it explains how mechanical engineering and computer modeling can study digestive processes and provide better understanding of how physical properties of food influence nutrient bioavailability and posits how this research can also be used in the fight against obesity and diabetes; and it illustrates how an interdisciplinary scientific collaboration led to the development of a novel functional food that may be used clinically in the prevention and treatment of prostate cancer. Adv. Nutr. 3: 813–819, 2012.

Introduction

Chronic diseases accounted for nearly 75% of the $2.6 trillion in US health care expenditures and 70% of US deaths in 2010 (1,2). These chronic diseases (which include obesity, diabetes, and cancer) are modifiable by diet (3,4). Addressing these public health issues will require the continued development and promotion of a safe and healthful food supply (5). This food supply must also meet consumer demands for palatability, convenience, and affordability (6).

Traditionally, food and nutrition scientists have had divergent roles in the context of food. Food scientists have helped bring “farm to fork” by working on the technical and sensory aspects of food composition, processing, and consumption (5). Nutrition scientists, by contrast, have focused on the “fork-to-cell” phase, researching the metabolic and physiological responses to food and nutrients after consumption and applying that research to improve public health (7).

The current public health crisis calls for a new paradigm in which food and nutrition scientists align their efforts and approaches to generate novel research aimed at improving human health (8,9). This work must also include translating basic nutritional research findings into practical food-based applications. Development of such an integrated “farm-to-cell” health-promoting food system would create the framework to address pressing public health issues (10) by providing an innovative food supply that translates cutting edge nutrition research into consumer-friendly foods. With the promise to effect positive dietary changes, this concept is thus an important public health strategy (8,11) (Fig. 1).

One integral component of this new paradigm will be to develop “functional foods,” defined as foods and food components that can provide a health benefit beyond basic nutrition and can promote health and reduce disease risk (12). In the context of this paper, functional foods include conventional processed foods (such as cereals, breads, yogurt, snacks, and beverages); fortified, enriched, or enhanced foods; and dietary supplements.

A majority of consumers believe that they have some control over their health and identify foods and nutrition as playing an important role in health maintenance (13). Functional foods merge consumers’ desire for healthful eating and health promotion with their demand for convenience (14). In 1994, the Institute of Medicine noted: “functional foods are the wave of the future” (10). Indeed,
the functional food and beverage industry, with 2010 sales of ~$40 billion, is outpacing sales of traditional foods and beverages (15,16).

In this context, this paper discusses current cutting-edge translational research at the interface of food and nutrition sciences. First, using the example of whole wheat bread, this paper describes the process by which chemical reactions may influence flavor (a key concern in consumer acceptability of healthful food products) and posits how these chemical flavor reactions can be used in health promotion. Second, this paper explains how computer modeling and mechanical engineering are being used to study digestive processes to better understand how the physical properties of food influence nutrient bioavailability. Food scientists may someday translate this research to formulate foods that slow the rate of stomach emptying—a critical step in the digestive process that is important in obesity and diabetes management. The final section illustrates how a model collaboration among horticulturists and crop scientists, food and nutrition scientists, and clinicians led to the development of a novel functional food that may be used clinically in the prevention and treatment of cancer.

The interplay between flavor reactions and mechanisms of health promotion

Flavor research is important because the acceptability of food is related to chemical stimuli that evoke taste and smell, collectively known as flavor compounds, and, consequently, flavor quality affects food choice, nutritional status, and eventually health and disease risk (6,17–19). Flavor is a complex sensation that is influenced not only by chemical stimuli (aroma, taste) but also by other attributes such as, mouthfeel, sight, sound, and temperature (20–22). Clusters of receptor cells (e.g., taste buds, olfactory membrane) mediate the chemical sense of flavor (23). Evolutionarily, taste-sensing systems in the mouth served 2 important survival functions: the taste categories of sweet and umami helped animals to consume more energy-dense nutrients (24) and bitter taste detection helped them avoid consuming toxic substances (25,26). Although bitterness is associated with toxicity, there is not a necessary correlation between bitterness and toxicity (27). Many fruits and vegetables contain phytochemicals that are both bitter tasting and health promoting (28). Unfortunately, many consumers generally reject bitter-tasting foods (27,28). This poses a dilemma both for the food industry, which seeks to develop functional foods with health-promoting effects, and for the consumer, who desires healthful foods that taste good. By identifying the chemical processes that create unpleasant flavor profiles, food scientists may be able to develop food-processing techniques that remove or mask these unpleasant flavors or promote the formation of more desirable flavors and thereby improve the palatability and consumption of health-promoting foods.

The Dietary Guidelines for Americans 2010 recommends that half of daily grain intake be composed of whole grains...
Whole grains contain important nutrients (e.g., iron, magnesium, selenium, B vitamins, and dietary fiber), and consumption of whole grains is associated with decreased risk of cardiovascular disease, type 2 diabetes, and obesity (29). Despite these health benefits and the wide variety of whole-grain products available in the marketplace, daily intake of whole grains is only 20% of what is recommended (4). Notably, a negative “bitter” flavor profile associated with whole-wheat bread leads to consumer preference for the less bitter refined wheat bread, even when all other ingredients are equivalent (30). Purported healthful intrinsic phenol compounds in whole grains have been suggested to be the cause of this negative flavor profile (31).

Researchers at the Flavor Research and Education Center at the University of Minnesota (32) seek to better understand flavor profiles of whole-grain products so that they can develop strategies to alter these profiles, resulting in increased consumer acceptance. A central focus of this research has been on a series of reactions described by chemist Louis-Camille Maillard in 1912 (33). The Maillard reaction is classified as a nonenzymatic browning reaction that results when the carbonyl group of a sugar reacts with the amino group of amino acids, which are accelerated during cooking at higher temperatures (e.g., >250°F/120°C). In bread, the Maillard reaction produces melanoidin compounds that impart the characteristic brown color to the crust (34). Although the Maillard reaction is defined in terms of its influence on the color characteristics of a product, it is equally known for its important role in the development of the odor and flavor properties of baked products (35).

One intermediate product of the Maillard reaction is the Amadori product (1-amino-1-deoxy-2-ketose), which can be transformed by different chemical pathways depending on the conditions (e.g., time, temperature, reactants, pH). Dehydration reactions can transform the Amadori product to the characteristic brown-colored melanoidin compounds. However, both dehydration and fragmentation reactions may result in compounds that interact with Strecker degradation products to form potent flavor compounds, including pyrazines, pyrrols, oxazoles, and thiophenes (36). Flavor research thus aims to understand the conditions that could alter these chemical pathways to influence flavor in the final baked product.

Researchers at the Flavor Research and Education Center used isotopic-labeling studies to determine whether the presence of hydroxycinnamic acids (phenolic compounds present in whole grains) influenced the Maillard reaction (37). Hydroxycinnamic acids were tagged and applied to a simple glucose/glycine baking reaction model (providing the sugar and amino acid necessary for the Maillard reaction). By identifying reaction products having both a phenolic moiety and a glucose and/or glycine moiety, researchers identified 2 main compounds resulting from the interaction between hydroxycinnamic acids and Maillard reaction precursors. These hydroxycinnamic acid–Maillard reaction products indicate how the intrinsic phenolic compounds in whole-wheat flour can alter the mechanisms of the Maillard reaction during baking, a critical pathway related to a less desirable flavor development. Isolating these reaction products allows researchers to study their chemical structure for clues as to what precursors and chemical pathways were involved and consequently provides novel insight into whole grain chemistry. One goal might be to control these chemical reactions to promote the formation of desirable flavors and thereby improve the palatability and consumption of healthful whole-grain products.

However, a dilemma could arise if this research leads to altering the Maillard reaction in ways that would eliminate the chemical products of the reaction that have been implicated in health-promoting physiological processes (38). Maillard reaction products have been shown to have antioxidant and antiproliferative effects that help prevent chronic disease and cancer cell growth (39). It is possible that the hydroxycinnamic acid–Maillard reaction products, which create the negative flavor attribute, may be the same compounds that are responsible for the health-promoting effects of whole grains.

To determine whether this novel phenolic–Maillard chemistry identified in whole-grain food also could potentionally provide health benefits, researchers at the Flavor Center measured the bioactivity of the hydroxycinnamic acid–Maillard reaction products previously identified (37). Both compounds were found to suppress, in macrophages, the expression of the proinflammatory genes inducible nitric oxide synthase and cyclooxygenase (37). Because the inflammatory process is implicated in the pathophysiology of many chronic diseases, these compounds may supply some of the health benefits associated with the consumption of whole grains.

Current food-processing strategies used to mask unpleasant flavors generally involve the addition of salt, sugar, or fat (28,40). These ingredients and foods are already consumed at higher than recommended levels (4), underscoring the need for new, innovative strategies to make healthful foods, especially whole grains, more palatable. Consequently, food scientists hope to use technology to overcome the negative sensory perception (flavor) while maintaining the healthful compounds found in whole-grain products, indicating the complexity of food chemistry and the need for more comprehensive research strategies. In the process, efforts will be made to ensure the safety of food components. In this way, flavor research and food technology can significantly contribute to the development of a healthful, safe, and palatable food supply, acceptable to the consumer.

**Modeling gastric digestion of foods characterized by their material properties**

The current emphasis on health promotion and disease prevention, coupled with consumer demand for a palatable, healthful, convenient, and affordable food supply, provides opportunities for food scientists to develop functional foods that reduce disease risk and meet consumer needs. Communication of the health benefits of functional foods occurs via health claims on food labels (41). Before claim approval, the FDA requires substantial scientific evidence quantifying the relationship between a food component and reduced risk of a disease or health-related condition (41). Developing
specific and scientifically supported health claims will require an accurate understanding of how the putative health-promoting components in functional food products are digested, absorbed, and subsequently metabolized and/or otherwise used by the body (42). Unfortunately, the human digestive system involves a complex series of organs, glands, and chemical and mechanical processes that remain poorly understood.

The stomach is the major digestive system organ responsible for breaking down food into small particles through a combination of chemical (acids and enzymes), physical (rubbing and grinding, temperature), and mechanical (peristaltic contractions) processes (42). This disintegration of food particles releases nutrients and bioactive compounds for absorption and thus is an important focus of functional-food research (42). However, an understanding of gastric digestion has been limited for several reasons. First, it has proved difficult to reproduce, using commonly applied in vitro digestion models, the complexities of stomach physiology, especially the peristaltic movements of the stomach wall that produce both mechanical and hydrodynamic forces that affect the rate of food disintegration. Second, studies have shown that the physical properties of a particular food (such as its microstructure or food matrix) influence the bioavailability of the food’s nutrients (42). Researchers at the Departments of Food Science and Technology, and Biological and Agricultural Engineering at the University of California, Davis (43,44) developed a series of gastric models that could bridge these gaps in scientific knowledge.

A realistic computer-aided model of the human stomach was designed to simulate the motility pattern of the stomach during digestion to characterize the fluid–mechanical forces that aid food breakdown (45). Results of the computational model both confirmed and challenged current understandings of gastric digestion characteristics. Stronger fluid dynamics were observed in the distal portion of the stomach, which supports previous descriptions of stomach function in which the proximal portion acts as a reservoir while the distal portion is responsible for mechanical mixing (46). The computational model demonstrated 2 main flow patterns that have been proposed as primary mechanisms of gastric digestion (47–49). The computer model showed that a retropulsive-jet pattern was created as contraction waves moved toward the distal stomach, pushing back gastric contents, and an eddy pattern (characterized by the circular motion of gastric contents) was also created between 2 consecutive contraction waves. Finally, the model demonstrated that higher viscosity food significantly diminished the formation of both of these gastric flow patterns. This finding challenges the conventional idea that meals are rapidly and completely homogenized in the stomach, indicating instead that highly viscous meals may in fact be poorly mixed.

Next, a model stomach system was developed to identify disintegration characteristics of specific foods (50,51). To compare digestion characteristics among categories of foods, researchers analyzed samples of meat products, nuts, fruits, baked products, and fried products. The model stomach system suggested 2 mechanical forces responsible for food disintegration: fragmentation, which resulted from high forces breaking samples into several large particulates, and erosion, which resulted from normal forces wearing away the food surface. The prevailing mode of disintegration was associated with a food’s texture, with fragmentation being the primary force in digestion of baked products and meat products and erosion being the primary force in digestion of carrot and nuts.

Additionally, researchers analyzed the mass retention of food samples over time, which resulted in the characterization of 3 distinct disintegration profiles. Ham and fried dough followed an exponential disintegration profile, with a linear decrease in mass over time. Carrots followed a sigmoidal disintegration profile, characterized by an initial lag phase in which mass remained relatively stable and then was followed by a linear decrease. Finally, beef jerky, almonds, and peanuts followed a delayed-sigmoidal profile, in which the mass initially increased, likely as a result of initial absorption of gastric fluid exceeding the mass lost from disintegration. The practical application of this research is related to the rate of gastric emptying. Foods with an exponential disintegration are broken down and released from the stomach quickly. Controlling gastric emptying may prove to be an important future focus of the functional application of food processing due to the effect that gastric emptying has on satiety. Determining which foods and food combinations break down more slowly, and thus have a higher satiety value, might be useful information in the fight against obesity. Depending on caloric value, individuals could be counseled to consume foods with a high satiety value. This might decrease the total amount of food (and energy) that they consume (42).

In addition to comparing disintegration profiles of various food categories, researchers compared disintegration profiles of single foods to determine how the level of processing may influence food disintegration. Raw carrots demonstrated a sigmoidal profile with a significantly longer total disintegration time, whereas cooked carrots had an exponential profile. As the length of cooking time increased, the time required for disintegration decreased. These results may be applied functionally to the study of nutrient bioavailability, which is dependent on food disintegration. In practical application, this research supports the observation that cooked carrots, compared with raw carrots, have increased bioavailability of select nutrients such as beta-carotene (52). This remains an important area of research because there currently is no differentiation in the communication of nutrition content of foods (through food labeling) based on the actual nutrient bioavailability from a particular food. For example, a package of 20 raw carrots would have the same Nutrition Facts label as a can containing 20 cooked carrots, even though, as this and previous research shows, the nutrients in 20 cooked carrots may be more bioavailable.

Researchers also developed an advanced in vitro system: the Human Gastric Simulator (HGS) (53). Unlike previous
models, the HGS replicated peristaltic waves to simulate the mechanical forces important in food disintegration. The model also simulated gastric secretion of enzymes and hydrochloric acid and incorporated a gastric-emptying system and temperature control to closely mimic in vivo conditions. Researchers evaluated the effects of peristaltic contraction forces on digestion by comparing results of digestion in the HGS model with those of a traditional in vitro model that uses a shaking bath to mix gastric juices and food to simulate gastric digestion. The HGS resulted in a digesta with significantly smaller particle size and confirmed the significance of the unique flow patterns on the mechanical breakdown of food during gastric digestion.

Next, researchers applied the HGS model to study the influence of physical characteristics of a food product on gastric digestion by comparing white and brown rice (54). This research was performed in the context of determining a possible relationship between the functional properties of brown rice and its health benefits. White rice is manufactured by removing the bran covering from brown rice kernels, resulting in a product with significantly reduced amounts of insoluble fiber, fat, protein, vitamins, minerals, and phenolic compounds (55). Although the chemical compounds in brown rice undoubtedly play a role in health promotion, the physical characteristic of the bran surrounding the kernel has also been suggested to play an important role (56). Results of the HGS model confirmed significant differences in the digestion of white and brown rice and provided insights into its health-promoting properties.

Evaluation included measurement of soluble solids (which include starch and sugars among other compounds), particle size, and viscosity of white rice compared with brown rice digesta. Comparing the release of soluble solids revealed both a lower and steadier rate of starch hydrolysis in brown rice. Evaluating rice particle size after 3 h of digestion showed that particles of brown rice were significantly larger than those of white rice. Analysis of the viscosity of the gastric digesta showed that brown rice created a more viscous product. Researchers were able to attribute these results to the bran by using a soaking test that demonstrated that the bran layer inhibited absorption of gastric juices, slowing the textural softening and thereby delaying the disintegration of the brown rice particles.

These results help confirm the proposed relationship between the functional and physical properties of brown rice and its health-promoting abilities. The steady rate of starch hydrolysis explains the reduced glycemic response observed after digestion of brown rice, which is important because higher glycemic loads are associated with an increased risk of several chronic diseases (57). The research additionally helped to quantify the effects of a food’s physical properties on its digestion, and that quantification may be used in the scientific formulation of functional foods. For example, scientists may be interested in replicating the physical barrier of the bran layer to control nutrient release.

Finally, in vivo feeding trials using pigs functioned to validate the previous computational and in vitro model results and provide further quantitative information to update models for future research. Pigs were euthanized at 0, 60, 120, 180, or 300 min after consuming white compared with brown rice or raw compared with roasted almonds. Outcome measurements included texture, viscosity, pH, moisture content, and particle size distribution of digesta samples taken from both the proximal and distal regions of the stomach. Results indicated that the level of processing, digestion time, and location in the stomach from which samples were drawn influenced outcome measures. A linear relationship between gastric emptying and digestion time was noted for the more processed foods (white rice and roasted almonds), suggesting that delayed gastric emptying and lengthened satiety were correlated with consumption of the less processed counterparts. Evaluation of viscosity and particle size of samples taken in the proximal and distal regions of the stomach confirmed greater mechanical forces in the distal region resulting in greater food disintegration. Adding titanium dioxide and chromium oxide markers to food allowed for the development of a quantitative mixing index that may be applied to future models to further simulate in vivo gastric digestion conditions. Continued research will help elucidate the nutritional ramifications of gastrointestinal mechanical processes and their potential application in health promotion and disease reduction.

Food-based clinical interventions toward cancer prevention

The Center for Advanced Functional Foods Research and Entrepreneurship at The Ohio State University is a multidisciplinary functional foods research center whose aim is to enhance collaboration among investigators from such diverse disciplines as horticulture and crop science, food and nutrition sciences, and medicine (58). By such collective efforts, the Center for Advanced Functional Foods Research and Entrepreneurship seeks to develop functional food products useful for disease prevention and control and then research the efficacy and safety of these new functional foods in a “crops-to-clinic” program. A new functional food product (a soy-fortified, high-lycopene tomato juice product possibly useful in preventing prostate cancer) was described from conception and design to researching its safety and the actual bioavailability of the presumptive active ingredients.

The new soy-tomato juice product has its genesis in the 1995 paper by Giovannucci et al. (59) that reported an inverse association between prostate cancer and the intake of certain tomato-based products, positing that lycopene was the main active component in the tomato. In light of other research suggesting that soy isoflavones may also have beneficial effects on prostate cancer (60,61), a soy-fortified tomato juice was chosen as a test product for clinical evaluation. Scientists from the Department of Horticulture and Crop Science at Ohio State bred tomatoes containing up to 5 times the lycopene content of comparable control tomatoes, with the hope of developing tomato-based products, positing that lycopene was the main active component in the tomato. In light of other research suggesting that soy isoflavones may also have beneficial effects on prostate cancer (60,61), a soy-fortified tomato juice was chosen as a test product for clinical evaluation. Scientists from the Department of Horticulture and Crop Science at Ohio State bred tomatoes containing up to 5 times the lycopene concentration of typical red tomatoes (62). This high-carotenoid tomato variety FG99–218 has excellent juice-producing properties and grows successfully in Ohio (63). The soy-fortified tomato juice was developed and produced at The Ohio State University.
State University pilot plant of the Food Science and Technology Department (63).

An initial clinical nutritional intervention involved feeding the soy-tomato juice product (300 mL/d) to 18 healthy subjects for 8 wk, with no adverse effects (63). At the end of 8 wk, plasma lycopene concentrations doubled and 50% of soy isoflavones were recovered. Juice consumption also significantly improved blood lipid status and lipoprotein resistance to oxidation. This initial trial showed excellent patient compliance and absorption of the biologically active phytochemicals from the soy-tomato juice product.

A subsequent pilot trial was conducted among 32 prostate cancer patients, randomized to groups of 8 who consumed V8 juice, tomato soup, tomato sauce, or soy protein for 3 wk before surgery. Analysis of blood and prostate tissue samples revealed that after this short intervention, lycopene levels in both plasma and prostate samples increased for all 3 groups who consumed the tomato products compared with the soy-only group.

Thereafter followed a 4-wk clinical trial with 60 prostate cancer patients, evenly divided into 3 groups. Group 1 (controls) did not consume any soy-tomato juice, whereas groups 2 and 3 consumed 5 or 10 oz (148 or 296 mL)/d, respectively, of soy-tomato juice boosted with 1% olive oil. Olive oil was added because previous research had shown that the bioavailability of the ingested lycopene and carotenoids was dependent on co-consumption with fat or oil (64). Plasma lycopene concentrations decreased in control group 1, but increased in groups 2 and 3. Further examination of plasma carotenoids revealed a large number of lycopene metabolites (apo-lycopenals) whose biological activity is being examined (65). Data from the mean change in the percentage of prostate-specific antigen from the start of the intervention to the end are currently being compiled.

This research illustrates the power of a transdisciplinary research team comprising food technologists, cancer biologists, and clinical translational investigators, with crucial support from such diverse disciplines as horticulture and crop science to create and test the safety and efficacy of a new functional food product that may be useful in the prevention and treatment of disease.

Conclusion

The research described in this paper provides 3 examples of the new paradigm in which food and nutrition scientists are engaged in cutting-edge collaborative research aimed at improving human health and preventing disease. Research findings can be applied to translate fundamental nutritional discoveries to consumer products that meet the demand for palatability. Findings can help us understand how consumers can achieve optimal nutrition if foods are processed or developed to provide nutrients in their most bioavailable form. Finally, these approaches can show us the life-saving possibilities when we unlock and apply the powerful substances inherent in natural foods to fight disease. In the past, food supply issues centered on food safety and preservation, and food scientists were instrumental in creating a safe, appealing, and abundant food supply. As we improve our understanding of the dietary impacts on health and the importance of the food environment in influencing people's ability to make dietary changes, a central focus of food and nutrition scientists must be to work collaboratively to improve our understanding and consumption of health-promoting foods.

Acknowledgments

The authors acknowledge the ASN Nutrition Transition RIS for help in planning and coordinating this symposium, and Miranda Westfall for her help with research and manuscript preparation. All authors have read and approved the final manuscript.

Literature Cited

57. The Ohio State University. Center for Advanced Functional Foods Research and Entrepreneurship (CAFFRE) [Internet]. [Cited 2012 Aug 15]. Available from: http://fst.osu.edu/caffre/