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Viewpoint

An integrated systems-based model for substantiation of health claims in functional food development

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There is a pressing need for new innovative models to boost functional food production processes. However, it is not clear how the food industry can technologically transform its traditional NPD model into a modern, integrated NPD pipeline that can satisfy regulatory and consumer demands, on one hand, and enhance the capacity for innovation and competition, on the other hand.

We provide a new perspective on how systems-based approaches may practically enable the food industry to support substantiation of health claims for their innovative functional products and to reduce the time and cost of risky decisions associated with clinical trials.

Introduction

Functional food represents the fast growing category in the US food market with an annual rate of 8.6–20 percent (Smith & Charter, 2011). Although, in the absence of a controlled vocabulary or standard terminology, there is no universal definition for "functional food" and "nutraceutical" and these two terms have been often used interchangeably, a 'nutraceutical' has been defined as "*a food or part of a food that provides medical or health benefits, including the prevention and/or treatment of a disease*" (Brower, 1998). Doyon and Labrecque (2008) performed an exhaustive analysis on 26 proposed definitions for 'functional food' in literature and generated the following working definition: "*A functional food is, or appears similar to, a conventional food. It is part of a standard diet and is consumed on a regular basis, in normal quantities. It has proven health benefits that reduce the risk of specific chronic diseases or beneficially affect target functions beyond its basic nutritional functions.*" Based on these definitions, both functional foods and nutraceuticals aim at strengthening physiological functions (health promotion) through enhancement of mental and physiological performance, reduction of the disease risk, and treatment of health problems (Andlauer & Furst, 2002).

Historically, the concept of "food as medicine" was first suggested by medieval Persian practitioners such as Avicenna and Rhazes who developed scientific guidelines on the use of natural products for treatment of diseases and health problems (Nikaein, Zargaran, & Mehdizadeh, 2012). This concept was shadowed by the advent of modern drug development technology but, for two main reasons, the important role of functional food in health promotion has again gained increasing attention: first, the current "one size fits all" paradigm with synthesized drugs in pharmaceutical industry has been greatly challenged by incompatibility of new drug candidates with the complex natural system of the human body, leading to toxicities and side-effects (safety issue); second, increasing attrition rates in drug development pipelines, on one hand, and inability of current diagnostic and therapeutic strategies to diagnose and intervene early in progressive cascade of the chronic diseases such as dementia or cancer, on the other hand (efficacy issues), has encouraged both pharmaceutical and food industries to focus on the disease prevention and treatment using functional, natural compounds (Sharma & Tan, 2013).

Currently a convergence between the food and pharmaceutical industries is witnessed due to a paradigm shift from traditional food NPD to functional food NPD so that boundaries between the two industries are blurring in terms

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of technologies and demand structures (Bröring, Martin Cloutier, & Leker, 2006). However, R&D competencies between the two sectors are different, and in this regard, we agree with the roadmap proposed by Khan, Grigor, Winger, and Win (2013) in their recent review where they highlight the need for the food industry to evolve from traditional NPD toward an integrative and innovative NPD portfolio. This roadmap draws on established technological capabilities of the pharmaceutical industry in terms of "knowledge generation activities" to support safety and efficacy of novel bioactive ingredients. In contrast to Khan and colleagues who focused on the organizational requirements, we draw the attention to technological development required for generation of knowledge and extend on their roadmap for functional food NPD from a technological perspective.

Shifting trend in functional food product development

Tackling the complex biology of human chronic diseases, which has been the focus of the pharma industry for many years, poses a new challenge to the food industry if safety and efficacy of the functional food products are to be shown. The pressure on food manufacturers is increasing to cope with stringent regulatory demands required for substantiation of health claims for functional products. For example, the Food and Drug Administration (FDA) – responsible for protecting public health through the regulation of food safety in the U.S. – does not recognize functional food as a food category and accordingly, food and beverage products with health claims are considered to be drugs and must meet the FDA's regulatory requirements, including proof of safety and efficacy. In Europe, any statement advertising effect of nutrients on disease risk reduction and treatment is strictly regulated under article 14.1a of the health claims regulation (http://www.efsa.europa.eu/en/topics/topic/nutrition.htm?utm_source=%20homepage&utm_medium=infocus&utm_campaign=healthclaimshttp://www.efsa.europa.eu/en/topics/topic/nutrition.htm?utm_source=homepage&utm_medium=infocus&utm_campaign=healthclaims). Recently, the European Food Safety Authority (EFSA) – the risk assessment authority for food and feed safety in the European Union – has released guidelines on scientific assessment of health claims, which enforces food manufacturers to show the quality, relevance and adequacy of studies supporting the health claim (Vero & Gasbarrini, 2012). Currently efforts are underway to set best practice guidelines for health claim dossiers in Europe, for example through the EU funded BACCHUS project, which is specifically funded to provide good quality evidence for health claims on polyphenols, bioactive peptides and cardiovascular outcomes (www.bacchus-fp7.eu).

In contrast to these challenges, however, significant opportunities for the food industry emerge that can not be ignored. Disease prevention through healthy nutrition is a priority on the political agenda of many countries and this is a clear opportunity for the food industry to claim more market share than the pharma industry in this area. Food and beverage companies that seek to enter the market of functional foods for health and wellness recognize the need for investment in new research and development (R&D) competencies. The food industry has been traditionally regarded as a sector with low R&D-to-research ratio and little innovation (Bigliardi *et al.*, 2013). But, with the introduction of high-throughput technologies – primarily nutrigenomics – to food research, the situation has changed and now the grand challenge is integration of findings across multiple research disciplines in food science (Khoo & Knorr, 2014). For instance, the giant food company Nestlé has established its own "Institute of Health Sciences" in 2011 with focus on "integrated systems science". However, most of food and beverage companies – particularly small and middle size manufacturers-need R&D strategies that can support substantiation of health claims associated to bioactive ingredients in an integrative manner. The food industry can take advantage of valuable experiences that the pharma industry has gained during years of heavy investment in technology development and scientific research for tackling complexity of human diseases. Of course, due to differences between a drug (with an immediate health effect) and a functional food ingredient (with a long-term health effect), this does not mean that pharmaceutical standards should be directly applied to the food industry. Nevertheless, considerable similarities between pharmaceutical and nutraceutical production pipelines in terms of addressing purity, safety and efficacy imply that already existing and tested technological platforms in the pharmaceutical sector could be – at least partially – adopted and tailored to the needs of the food industry (Hardy, Hardy, & McElroy, 2002). For example, knowledge management and systems modeling technologies, which have been extensively used – in an integrated manner – across all levels of pharmaceutical production pipeline, could play a similar role in support of knowledge generation for development of new functional food products.

Unlike the pharmaceutical industry that has established a firmly strong technological infrastructure to deal with the complexities stemming from the drug–disease relations, the food industry appears to lag behind such advancements when it comes to exploring diet–disease relation and proving safety and efficacy of functional ingredients. This is because food – compared to drug – comprises of a large spectrum of molecules that elicit numerous physiological responses and, due to this complexity, nutritional science has been long lagging behind advances in pharmacology (Vergères, 2013). The pharmaceutical industry has witnessed a gradual transformation from a manufacturing-based to a knowledge-based industry, highlighting the increasingly important role of knowledge-driven systems biology in support of time- and cost-effective decision making (Butcher, Berg, & Kunkel, 2004). Systems biology approaches in the pharmaceutical R&D attempt to model and predict drug safety and efficacy across multiple biological scales – from molecules to cells, tissues and organs – by