

Development of Synergistic Phyto-Metabolites as Health Promoting Dietary Systems

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Most food is considered functional in terms of providing nutrients and/or energy to sustain life but dietary systems that are able to prevent or remediate diseases are classified as functional foods or nutraceuticals (FFNs). In particular, diets rich in natural products (NP) that include vegetables, fruits, nuts, and legumes have been associated to lower risks of multiple chronic diseases (atherosclerosis, diabetes, aging, immune deficiency diseases, cardiovascular diseases, and arthritis) with secondary metabolites (phenolic acids, flavonoids, anthocyanins,) and other small molecules (lipids, amino acids, vitamins, and organic acids) playing a significant role. Increasing public awareness of the link between diet and health has propelled the consumption of health-promoting dietary sources to unprecedented levels. As an outcome, the functional food and nutraceutical (FFN) industry grew 3-4 times the rate of conventional foods and exceeded 30+ billion of the market share during the past decade. FFN are thus of significant value to the sustainability of agriculture and food industries. However, many of these products do not evoke their reported health benefits, or do so irregularly, and can even produce toxic side effects.

Similar to pharmaceutical drug development, potential health promoting dietary phyto-metabolites are typically identified based on their ability to perturb a single or combination of genes and/or proteins proposed to be involved in the etiology of the stress. Taking such a highly reductionist approach is thought to be one of the main failings in pharmaceutical discovery model resulting in shortage of new drugs entering the clinic. Additionally foods are not purified compounds acting on a single targets, but complex mixtures that may affect many

biochemical pathways. As such, the diverse milieu of phyto-metabolites that comprise a NP metabolome may act additively or synergistically to impart a greater biologic effect than can elicited by a component in isolation. Yet, a large majority of support for dietary therapeutics or interventions has and continues to focus on isolated agents (e.g., omega 3 from fish oil, tannins from cranberries, and catechins from green tea) or other marker components (isoflavones). Due to this approach, very little is known about the synergistic activity of phyto-metabolites when delivered in their original matrix (e.g., whole wheat or dry edible beans) or when transferred to another transport vehicle. These properties can further be impacted by effectors on the NP metabolome caused by farming applications, environmental conditions, post and pre harvesting practices, and food processing operations, which can either enhance or inhibit the active components.

Although often relegated as “look and see” research, these problems can only be solved by applying long-term (10-20 years) survey type approaches to thoroughly characterize the NP metabolome in response to production and processing factors. Survey type research is also needed to initially identify or link the likely and multiple biological targets (health promoting and toxic) exerted by the chemically complex and potentially synergistic phyto-metabolites. These preliminary data will then set the foundation for hypothesis driven studies that will provide a basic mechanistic understanding of the synergistic role of phyto-metabolites in maintaining health, which, in turn, will facilitate the development of consistently efficacious and safe FFN.

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Received June 27, 2012; **Accepted** June 28, 2012; **Published** June 30, 2012

Citation: Schlegel V (2012) Development of Synergistic Phyto-Metabolites as Health Promoting Dietary Systems. Metabolomics 2:e114. doi:10.4172/2153-0769.1000e114

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