British Journal of Nutrition (2008), **99**, E-Suppl. 1, ES1–ES2 doi:10.1017/S0007114508965740

Genomic effects of phytochemicals and their implication in the maintenance of health

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A large variety of phytochemicals are found in vegetables, fruits, spices and staple plant foods(1,2). These compounds have often accumulated in specific species along the evolution to protect plants against herbivores, pathogens, UV light, etc. or in the case of pigments and sapid agents to facilitate recognition by animals. It is realized today, that many of these compounds, when ingested with the diet, influence human metabolism and different functions in the body, with possible consequences on health. It is highly probable that some phytochemicals, at doses compatible with their common dietary intake, may protect against major chronic diseases(3). For example, polyphenols may protect against cardiovascular diseases(4), cancers of the gastrointestinal tract(5), or improve brain function(6); isoflavones may prevent prostate and breast cancers(7), and different antioxidants type 2 diabetes(8) as discussed in the present volume.

However, apart from some rare exceptions, no clear recommendations on either the daily level of intake of phytochemicals, or their optimal contents in foods have yet been made. This is largely due to (i) the lack of suitable markers describing their effects relevant for the maintenance of health or the prevention of diseases and (ii) the limited understanding of their mechanisms of action. The exploration of the biological effects of phytochemicals has often relied on a limited number of specific markers, chosen either on the basis of putative mechanisms of action and/or on their links with health or diseases. However, the strength of the associations between phytochemical intake and the level of these markers are often not firmly established nor are the effects fully consistent(4).

These inconsistencies appear to be derived, at least in part, on the choice of a marker based on a non-validated mechanistic hypotheses. The problems concerning antioxidants are particularly enlightening as discussed in one of the papers in this supplement issue(9). Various reducing (in a chemical sense) dietary compounds (for example polyphenols and carotenoids) were shown to scavenge free radicals in *in vitro* models and were therefore suggested to protect the body against oxidative stress insults and associated diseases. Their effects on oxidative stress markers have therefore been explored in a large number of human studies. However, no health claims could be derived from these studies, even after 20 years of intensive research. New markers of effects for phytochemicals need to be identified and this requires a re-examination of their mechanisms of action.

The effects of various phytochemicals on gene expression are reviewed in this volume. Modern molecular biological tools have shown that the expression of various genes can be affected by phytochemicals, some of these genes being key players in the physiopathological processes leading to diseases. Phytochemicals may thus influence human physiology through cell-mediated effects (e.g. via induction of transcription factors), rather than by directly interacting with free radicals or with some key enzyme as often thought in what appears today as an inspiring but somewhat naive vision. It became clear that the dose applied appears to be particularly critical to determine both, the nature of the genes affected and also the magnitude of the effects. These issues are therefore critically discussed in the light of our present knowledge on the bioavailability of phytochemicals(7).

The identification of the genes affected by phytochemicals may also lead to the elucidation of the signalling pathways involved and ultimately to the identification of their molecular targets. Apart from phytoestrogens known to interact with estrogen receptors, the primary molecular targets of phytochemicals remain largely unknown. Their putative identity is discussed in the papers of this supplement issue.

The recent application of nutrigenomics approaches to characterize the biological effects of some phytochemicals has also unravelled the complexity of their effects on the human metabolism. The achievements made so far will allow to formulate new hypotheses on their mechanisms of action. Most recent studies on phytochemicals using either transcriptomic, proteomic or metabolomic techniques are also discussed in this volume and the perspectives opened by these high-throughput techniques, as well as the different animal or cell models used to explore the biological effects of phytochemicals are presented(10,11).

The reviews contained in this special issue result from discussions within the European Co-operation in the field of Scientific and Technical (COST) Research Action 926 entitled 'Impact of new technologies on the health benefits

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and safety of bioactive plant compounds' (2004–2008; http://www.ueb.cas.cz/COST926/). The authors and the guest editors are grateful to COST for supporting this publication.

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