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INTRODUCTION

Many compounds contained in the diet have been proposed as having anticarcinogenic properties. These compounds are found in foods of many different types, although plant-based foods appear to be the richest source. The degree to which these compounds are present in plant tissue can vary markedly and be dependent on the plant variety, the growth conditions and other factors. The microbial flora in the gut also plays an important role in their action and composition through bioconversion and the release of various bioactive dietary components. There is thus a need for more knowledge on the supply of different anticarcinogenetic compounds from different sources.

A deeper understanding of the mechanisms underlying the protective effects that various food components can have against carcinogenesis is also needed. Considering the links to the susceptibility the individual has inherited is becoming increasingly important too. At the same time it is often difficult to single out the mediating components in the protective food patterns emerging from epidemiological studies diet–cancer relationships. It is important, therefore, to identify the compounds that are most active in different experimental systems, and to study variations in their activity when they are ingested as a part of different foods, together with the combinatorial effects of phytochemicals and other food components. There is also much uncertainty regarding the relevance of observed in vitro or short-term effects in humans in relation to the long-term effects documented in chemopreventative human studies.

A growing number of in vitro and in vivo studies indicate that combinations of dietary chemopreventative agents can sometimes result in significant levels of activity at concentrations at which any single agent is inactive. This may explain why some food items or diets may show cancer preventive effects that cannot be explained on the basis of the individual bioactive ingredients alone. The development of ideas regarding this has also been stimulated by findings that dietary supplements of only a single compound, often taken at high doses, may have negative effects. Although our understanding of the molecular mechanisms behind the observed combinational effects is still limited, it appears that many combinations of complementary modes of action may be involved. Much hope is attached in this connection to the powerful techniques available today within the field of nutritional genomics.

An understanding of the mechanisms involved is also a necessary basis for the development and validation of new biomarkers of nutritional status. Biomarkers are a key tool for assessing nutritional status and dietary exposure to specific substances. Markers differ considerably in their characteristics, some of them mainly reflecting recent dietary intake and others indicating more the individual's long-term nutritional status, which to a large extent reflects the kinetics of metabolism and transport, and pool sizes of the substance in question. Also, the confounding factors affecting a given biomarker vary appreciably for different dietary components as well as in terms of the body fluid or tissue considered suitable for sampling. The area of biomarkers has progressed markedly with the advent of new analytical technology and the emergence of data showing that hitherto neglected food components may have important health effects and can be of strong interest. Nutritional biomarkers are essential for studies of the links between dietary intake and the risk of cancer, which is a very complex field indeed in view of the large number of cancer diseases, pathogenetic mechanisms, food components and food preparation methods involved.

Environmental Cancer Risk, Nutrition and Individual Susceptibility (ECNIS; http://www.ecnis.org) is a FP 6 Network of Excellence running for 5 years (May 2005–April 2010). One of its aims is to identify nutritional and lifestyle factors that modulate environmental and occupational cancer risks. The present series of articles was written as a part of this work and the major aim was to summarize the state-of-the-art in use of biomarkers for some anticarcinogenic food components and to identify knowledge gaps. The important links found between use of a substance as a biomarker and its mechanisms of action led to a further aim, that of reviewing the mechanisms of action of some of the most promising anticarcinogenic compounds.

The present review focuses on two major groups of food components, vitamins and selenium on one hand, and bioactive compounds, on the other. In the former part, Lars Dragsted reviews the knowledge of the biomarkers of exposure to several vitamins used as antioxidants and makes a thorough summary of the available data on the effects of vitamins A, C and E on different markers of lipid and protein oxidation. The antioxidant vitamins have also been studied very much in relation to risk of cancer, using oxidative DNA damage as a biomarker. Steffen Loft and his colleagues summarize the large amount of data available and point out some of the difficulties in assessing the effects of diet in this context. They also state that in the future greater attention should also be

EJN 2002

European Journal of Nutrition (2008) Vol. 47, Supplement 2

directed at alternative chemopreventive mechanisms such as up-regulation of DNA repair systems and the chemopreventive effects of antioxidants on non-lymphatic tissue. Selenium is a promising nutrient for having anticarcinogenetic effects, and several positive intervention trials have been performed although additional confirmatory data are needed. Gromadzinska et al. also summarize the recent discoveries of 25 specific selenoproteins in the human genome giving the basis for a much wider action of selenium in the body. It is also clear that many cellular actions of different selenium compounds have been documented but as yet there is no consensus regarding the main anticarcinogenetic mechanisms of selenium.

Concerning the bioactive components in foods there is a need to develop and validate new biomarkers reflecting their intake and body stores. Jakob Linseisen and Sabine Rohrmann show that an impressive number of flavonoids and phenolic acids can be measured in human body fluids. For several polyphenols, the data on the epidemiologic validity encourages their future use in epidemiological studies but at present the integration of these biomarkers in such studies is very limited. Another important aspect is the mechanism of action of combinations of bioactive compounds. De Kok et al. discuss the molecular mechanisms that are likely to be involved in cancer chemoprevention and summarize the most important findings of the studies reporting synergistic chemopreventive effects of dietary compounds. An interesting example of a food containing a mixture of bioactive compounds is olive oil, and Sotiroudis and Kyrtopoulos review the mechanisms of action of some of its constituents. Another interesting group of compounds regarding anticarcinogenetic effects is the glucosinolates and their breakdown products, and Hayes et al. review the mechanisms by which glucosinolate breakdown products are thought to inhibit carcinogenesis. They show that some of the compounds can induce cytoprotective genes, mediated by different transcription factors whereas some compounds also can affect cell cycle arrest and stimulate apoptosis. The mechanisms responsible for these antiproliferative responses are discussed.

It is clear from the chapters in the present volume that much progress has been made in the unravelling of mechanisms of action of a number of dietary components and also concerning the use of different biomarkers of nutritional status and dietary intake of different components in different settings. Still much more knowledge is needed before the knowledge can form the basis for formulating new advice and policies within the public health field.

B. Åkesson (✉)
Biomedical Nutrition
Pure and Applied Biochemistry
Lund University
Lund, Sweden
E-Mail: bjorn.akesson@tbiokem.lth.se

B. Åkesson
Dept. of Clinical Nutrition
Lund University Hospital
Lund, Sweden

S.A. Kyrtopoulos
Institute of Biological Research and Biotechnology
National Hellenic Research Foundation
48, Vassileos Constantinou Avenue
11635 Athens, Greece