Interview

U. Schlemmer (left)
W. v. Dokkum (middle)
S. Knasmüller (right)

Impact of new technologies on the health benefits and safety of bioactive plant compounds

Interview with Professor Wim van Dokkum, TNO Quality of Life, Zeist, The Netherlands, Dr. Ulrich Schlemmer, Max Rubner-Institut, Federal Research Institute of Nutrition and Food, Karlsruhe, Germany and Professor Siegfried Knasmüller, Institute of Cancer Research, Medical University Vienna, Austria.

The interviewees are national delegates of the COST Action 926 from the Netherlands, Germany and Austria and coordinators of the Focus Group-2, Working Group-3 and Working Group-4 (for further information see http://www.ueb.cas.cz/COST926).

The COST Action 926 focuses on a central field in current nutrition research. It covers the effects of bioactive plant food compounds on human health and their possible role in disease prevention. It encompasses not only the highly topical field of gene regulation by selected bioactive compounds but also problems regarding the bioavailability of these compounds, a pivotal factor in the development of their beneficial activity in humans. For these reasons MNF wanted to gain more information on the concept of this COST action and on any outcomes which might be of special interest to the broad scientific public.

MNF:
What are the basic considerations of the COST Action 926?

Answer:
We all know that it is generally agreed that consuming an ample amount of fruits, vegetables and whole grain products can reduce the risk of cancer and heart diseases. We think that there are many bioactive components (phytochemicals) in these foods which may be partly responsible for this health benefit.

MNF:
Which bioactive components did the COST action focus on?

Answer:
The members of this COST action focussed on carotenoids, polyphenols (including flavonoids and tannins), phytoestrogens, especially isoflavones, glucosinolates and phytates. Moreover, many other compounds from each substance class or group have been discussed in detail.

MNF:
What is the COST Action 926 and why is it necessary to have such a project?

Answer:
Most scientists working in the field of bioactive compounds are specialists in only a few classes or a small number of bioactive components. It is, therefore, important that scientists from different disciplines share their knowledge in order to understand the different activities of these compounds. The European Union has encouraged this process through the COST programme which provides a scientific platform for meetings to exchange experience and expertise between various European countries. COST Action 926 is one such platform involving scientists from 19 countries across the EU who have been focusing their attention on whether the new ‚omics' technologies can be used to provide supporting evidence of the beneficial effects of an increased consumption of fruits, vegetables and whole grain products on human health (www.ueb.cas.cz/COST926/).

MNF:
Can you give examples for the use of -omics technologies for the identification of plant components with beneficial health effects?

Answer:
The evaluation of this issue was one of the key topics of the action. Omics-approaches are high throughput techniques which enable the simultaneous detection of transcription alterations of thousands of genes as well as changes in protein patterns as a consequence of consumption of specific dietary factors. A large number of data show that phytochemicals affect the risk of diabetes II, cardiovascular disease, neural functions, and oxidative damage related disorders. Several valuable reviews concerning this topic emerged as a consequence of the activities of the scientists involved in the action.

MNF:
Will the new technologies replace conventional approaches?

Answer:
This is definitely not the case. For example, it is not possible to establish a common "signature" of alterations of gene expressions due to antioxidant properties of a given phytochemical. Therefore it is not possible to detect putative protective effects solely on the basis of the new methods. Their value lies in the combination with disease-related endpoints. For example it was shown by German researchers that the consumption of isoflavones causes reversion of genetic changes which are characteristic of cardiovascular diseases. Omics-techniques can also substantially contribute to the search for mechanistic explanations for specific phenomena. For example, the antioxidant effects of Brussels sprouts in humans could be explained by induction of protective enzymes, as detected using a proteomic approach. "Nutrigenomics" is not, as many believe, a new field of science, but rather designates a collection of various new tools which will hopefully provide additional valuable information.

MNF:
Can you give us some more details about this new way of thinking?

Answer:
According to current thinking, bioactive components can not only neutralise free radicals, they can also affect gene expression, cell signalling, the activation of transcription factors and the process of DNA translation into functional proteins. Indeed, recent findings indicate that the activation of transcription factors that regulate genes involved in antioxidant defence is an important pathway for phytochemical activity. Such processes cannot be adequately studied in cell culture. However, modern ‚omics' techniques such as genomics, transcriptomics, proteomics and metabolomics offer alternative approaches and a means to improve the scientific basis for health claims. Their application makes it feasible to monitor patterns of gene expression in humans *in vivo*, and to provide essential molecular biomarkers of early disease. By combining such data with knowledge of dietary exposure and bioavailability, it will be possible to predict the most effective dietary sources and to evaluate the potential role of bioactive components in clinical nutrition.

MNF:
What role does bioavailability play in the efficacy of bioactive compounds in the organism?

Answer:
Bioavailability plays a key role in the effectiveness of bioactive compounds. If food is rich in bioactive components, it does not necessarily mean that they are bioavailable and can be utilized. There are many factors contributing towards a reduction or improvement of the bioavailability of bioactive compounds such as industrial processing, storage, home preparation, enzymatic degradation, content of antinutrients in foods, and interactions among food compounds during digestion in the gut. All these factors ultimately affect the activity of bioactive components in the body. Bioavailability gives the essential information to what extent food components are available to the body. In nutrition it is defined as the proportion of a food compound in a given chemical form in the diet, which can be liberated from the food matrix, absorbed in the gut and transported to organs and cells, where it fulfils its physiological functions.

MNF:
Can you give some more information about the different classes of bioactive components the COST Action 926 was dealing with?

Answer:
The group of glucosinolates are found in brassica (or cruciferous) vegetables. Examples of these sources include cabbage, Brussels sprouts, broccoli, cauliflower and various root vegetables (*e.g.* radishes and turnips) and leaf vegetables (*e.g.* rocket salad). The concentration and composition of the glucosinolates in different plants, but also within a single plant (*e.g.* in the seeds, roots or leaves), can vary greatly and change during plant development. A number of epidemiological studies have identified an inverse association between consumption of these vegetables and the risk of colon and rectal cancer. Glutathione-S transferases (GSTs) are a family of enzymes responsible for the elimination of activated carcinogens from the body and it has been shown that levels of these enzymes can be increased by consumption of brassica vegetables. While the consumption of the brassica vegetables has the potential to reduce the risk of colon cancer, increasing the consumption of isothiocyanates *via* supplements may not be beneficial and thus, is still under controversial discussion. Industrial processing and consumer preparation of glucosinolate-containing vegetables are important factors affect their bioavailability.

Flavonoids are found in almost all fruits and vegetables but amounts vary enormously. In Europe the average intake is around 25 mg/day, but this varies with individual food habits. Onions are an important source (30-40 mg *per* 100 grams), and tea drinkers can consume around 80 mg *per* 100 ml. Substantial concentrations are found in oranges, orange juice, apples and red wine. However, the content in white wine is much lower due to the separation of the juice from the skins before fermentation. Flavonoids are found predominantly in the outer layers of fruits and vegetables, thus removal of the peel reduces intake. Oranges are however an exception as flavonoids are found predominantly in the pulp. Heating may reduce the flavonoid content signifi-

cantly but, when bound to sugars, they tend to be stable during cooking. There is now substantial evidence from animal studies and cell culture to support the hypothesis that flavonoids in particular are protective against cancers of the gut, particularly of the oesophagus and the large bowel.

Tannins are polyphenolic compounds that are widely distributed in nature, and are present in almost all plant foods and some beverages. Major sources of tannins in Western diets are berries, legumes, cocoa and beverages like wine, beer and tea. The average daily intake is much higher than that of many other bioactive components. The bioavailability of tannins**,** however, is generally very poor and varies between different food groups. Small molecules appear to be absorbed to a limited extent in the small intestine. Larger molecules show a very low absorption and are readily fermented by the colonic microflora on reaching the colon. Tannin content is reduced during storage, soaking and thermal processing. In grains, it is also reduced significantly by dehulling, since tannins are mainly located in the seed coats. Tannins are often the active components of 'medicinal plants' and their intake with respect to potential disease prevention has been studied with particular interest. Many tannins have antimicrobial properties and show antioxidant activities as radical-scavenges.

Carotenoids are a group of fat-soluble pigments widely distributed in nature. They are especially abundant in yellow-orange fruits and vegetables and dark green, leafy vegetables. Of the more than 700 naturally occurring carotenoids identified thus far, as many as 50 are present in the human diet and can be absorbed and metabolized by the human body. However, only six (β-carotene, β-cryptoxanthin, α-carotene, lycopene, lutein and zeaxanthin) represent more than 95% of total blood carotenoids. Estimated intakes vary widely both on an individual and regional level. There are also significant seasonal variations in several countries. For example total carotenoid intake in Europe is around 12 mg/day, ranging from 8 mg/day in Sweden to 20 mg/day in Greece. Both increased thermal processing and lengthened storage times reduce carotenoid bioavailability, and stability is decreased when oxygen is present during drying as well as during storage of fresh, dry and frozen products. Several papers have demonstrated a variety of beneficial effects of carotenoids, for example against cardiovascular diseases and cancer. Recent studies have also shown that lutein, an antioxidant found in leafy green vegetables, has interesting biological properties useful for the prevention of macular degeneration.

Phytate, the salt of inositol hexaphosphate, is widely distributed in the plant kingdom. As a storage form of phosphorus and minerals, phytate is present in a wide variety of plant seeds. In cereals, phytate is located in the bran and germ, while in legume seeds it is found in the protein bodies in the endosperm. The daily intake of phytate and other inositol phosphates has been estimated to vary from ~0.3 to ~3 g depending on the diet consumed. For decades phytate was regarded as an antinutrient due to its ability to inhibit the absorption of essential trace elements and minerals during the passage through the gastro-intestinal tract, and can, under certain circumstances, cause marked calcium, iron and zinc deficiencies. Over the past 15 years, however, phytate has also shown beneficial properties such as antioxidant and anticarcinogen activities. Moreover, it has been shown that phytate may also contribute to lower blood glucose and blood lipid levels and prevent renal stone formation. If phytate shows all these beneficial activities in humans and not just in *in vitro* systems or animal models then it should no longer be regarded as an antinutrient but should be very welcome in our daily diet.

Phytoestrogens comprise two subclasses of polyphenols: isoflavones and lignans. Both have estrogen-like effects comparable to the human hormone estradiol, whose properties they can mimic. Phytoestrogens have been identified in more than 800 plants. Soybean and red clover are the major sources of isoflavones, but sunflower seeds, sesame seeds and various nuts are also rich in isoflavones. Other good sources are berries, broccoli, garlic and carrots. Plant lignans are an important subclass of phytoestrogens, and are present in many cereals, grains, fruits and vegetables. Rye grains contain relatively high amounts of lignans compared to other cereals. In Nordic countries, such as Finland, rye contributes significantly to the daily lignan intake. It is estimated that the Asian population has a daily isoflavone intake of 20-50 mg, based on the relatively high consumption of soybean (products) there. By contrast, the average western European consumer ingests at most only a few mg *per* day. It has been suggested that isoflavones might have a protective role in cardiovascular disease, cancer, osteoporosis and menopausal symptoms. However evidence from *in vitro*, animal and human studies has been somewhat confusing, although nutrigenomics offers a new approach. An inverse relationship between soybean intake and rates of breast cancer has been demonstrated in Asian women, but no such association has been shown for Caucasian women.

MNF:
What is the best way to increase the intake of the bioactive components you have been working on?

Answer:
There are several possibilities to increase the intake of the bioactive components. One is to enhance the consumption of plant food in the daily diet, especially of fruits and vegetables, containing most of these bioactive components. Another possibility is to use supplements or ‚preparations'. It should be pointed out, however, that the majority of scientists in this COST action strongly recommend increasing the fruit and vegetable content of the daily diet and thus

enhancing the intake of bioactive components! Epidemiological studies have provided good evidence for ill-health prevention by diets rich in plant food and high bioactive components rather than by supplements, which have actually rarely been evaluated in human intervention trials and their beneficial effects are often just concluded from *in vitro* or animal studies.

MNF:
What are the main conclusions from the COST 926 programme?

Answer:
The conclusions are based on a 4-year cooperation programme involving more than 30 scientists from some 19 European countries. Details of the work have been published or will be published in respected international journals. We can summarize the conclusions as follows:

The consensus reached is that a range of bioactive phytochemicals, present in many plant foods, show promise as health promoting components.

The original theory regarding the mechanism governing the effect of phytochemicals has shifted from their direct antioxidant capacity to their effects at the molecular level, affecting gene expression and cell signalling.

It is not easy to extrapolate from the observed effects of individual bioactive components on antioxidant capacity and gene expression to their effects when part of the whole diet. COST 926 emphasizes the importance of foods rather than supplements as sources of bioactive components, both for the consumer and for further scientific studies.

Final concentrations of bioactive compounds in consumed food are not only affected by original concentrations in the plants but also by both commercial and domestic processing.

MNF:
What will be the follow up of the COST 926 programme?

Answer:
We hope that the results will eventually reach the consumer, food technologists, nutrition policy makers and health professionals. Apart from some 15 scientific papers published in the international literature, two position papers have been written. One for *Nutrition Bulletin*, which is a consumer-oriented journal and one for *Trends in Food Science and Technology* which will reach food scientists and food technologists. It is up to the various categories of people mentioned to further ‚translate' the results into appropriate levels of understanding.

Moreover, we think that our COST programme has stimulated our fellow scientists to continue their research on bioactive components. The strong cooperation between the scientists from many countries evident within this programme will make it easy to exchange new research plans and results in the coming years.

