

Introduction

Workshop report

This workshop report constitutes the outcome of the workshop on “Naturally occurring and health compromising substances in plant-derived food: Do we have a problem” held in the European Parliament on May 15th 2008.

The workshop report includes a summary of each of the speakers’ presentation and a summary of the most important discussions and recommendations from the workshop. In the back of this document the workshop programme, cv’s of the speakers at the workshop and an attendance list is included.

The power point presentations made by the speakers are available on the STOA website and on the website of the Danish Board of Technology.

The workshop was commissioned by STOA and organised by The Danish Board of Technology on behalf of the European Technology Assessment Group (ETAG).

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Background information on the workshop

During the last decade, new knowledge has been accumulated on naturally occurring and health compromising substances in plant-derived food. Substances that are not added or taken in from pollution of the environment, but may be health compromising by their own nature, through, for example, toxic effects, allergenic effects or inhibition of nutrient assimilation.

The purpose of the workshop was to explore and debate new developments in basic research; industrial food processing; novel and functional food; and consumer knowledge and behaviour in order to determine whether problems can be identified which need to be dealt with by the European Union in the years to come:

- What are the problems?
- How big are they?
- Are they properly dealt with already?
- If not, how may they be better handled?

The workshop programme was divided into four sessions and a wrap-up session at the end, intended to sum up the conclusions of the workshop. Each session included 2-4 speakers and consisted of relatively short presentations followed by debate with questions from MEPs, other speakers and invited participants.

Conclusions reached at the workshop

1. Conclusions on Session :New knowledge and legal framework

- *Glucosinolates, polyphenols and phenolics at normal levels in foods are beneficial for health of the consumer.*

Glucosinolates, polyphenols and phenolics are naturally-occurring low molecular weight compounds found in plant-derived foods. **When consumed in adequate doses, these components can have a beneficial effect on human health.** They are an important part of the beneficial components making up the reason for the 5-a-day fruit and vegetable campaigns around the world. **The consumption of fruit and vegetables containing these compounds should be encouraged amongst EU consumers.** There are potential beneficial effects which include reducing the risk of certain cancers and cardiovascular diseases, including diabetes. **Thus continuation and even enhancement of the campaigns for increased consumption of fruit and vegetables is recommended in this area.**

- *Glucosinolates, polyphenols and phenolics at very high levels in supplements or in heavily fortified foods present a possible risk for health of the consumer which needs to be assessed.*

Concerns arise from the consumption of large doses of these naturally occurring compounds when extracted and concentrated from the original food and sold as supplements. Although in most cases there will not be a problem, research on purified glucosinolate breakdown products (the active form of glucosinolates formed on chewing, cutting and cooking) has shown some negative effects. High doses of these pure compounds have been shown, in animal studies, to exert negative effects on liver, kidneys, pancreas and thyroid. It is less clear if polyphenols and phenolic acids could have similar effects, but some negative effects at high doses could occur, such as inhibition of digestive enzymes and impaired iron absorption. **However, these problems are unlikely to arise from consumption of normal food. On the other hand, supplements, or heavily fortified foods, should be viewed more cautiously and the risks assessed.** In addition, very high doses of these compounds through supplements could **affect metabolism of some medical drugs**, and this also needs to be examined further. **These risks could be examined by the European Food Safety Authority (EFSA).**

- *Allergens in some plant-based foods are a high risk, but only to a small minority of the population.*

A completely different type of food issue is the presence of certain allergens, normally proteins, present in some plant foods giving an **undesired allergic reaction in a small proportion of the population.** These allergens are always undesirable, but only to a minority. However, the problem appears to be increasing, especially in the Western World. A way to support afflicted individuals **is through better labelling.** Additionally, the problem can be managed through improving knowledge on cross-reactivity with other plant derived proteins, and on reducing or eliminating cross-contamination. It is not feasible to remove these allergens from foods since they are naturally occurring proteins present in all foods containing that source. **The individual must ensure absence of the allergen in the diet,** since the potential allergenic protein is completely harmless to most individuals. However, labelling legislation is very slow to be introduced, and in addition, **restaurants and catering establishments often do not know exactly whether the allergens are present in the food served at these establishments.** In cases of emergency, crisis management is conducted through the Rapid Alert System for Food and Feed (RASFF).

The European Commission has adopted a proposal on labelling in January 2008 which is currently under discussion, and concerns pre-packed food and food served through catering establishments.

2. Conclusions on Session : New developments in industrial food processing

- *New processing methods offer a potential way to improve the quality of products made from fruits and vegetables.*

Some conventional processes for industrial food processing can lead to the loss of certain nutrients. These include vitamins such as vitamin C, but also the naturally occurring compounds such as glucosinolates, polyphenols and phenolics discussed above. For example, highly processed and filtered apple juices contain a much lower content of potentially beneficial polyphenols (proanthocyanidins) compared to the original fruit. New processes such as High Pressure and High Intensity Electric Field Pulses may overcome some of these problems, and **ensure more of the beneficial components and nutrients from the original food are retained**. Problems are not likely to arise, but some risk assessment is necessary for these new processes, especially since these new processing methods will also better preserve potentially harmful substances as well as the beneficial ones. **Research into the positive and negative aspects of new processing methods is required**, including gentle or minimal processing. This may provide a **good opportunity to increase the healthiness of processed foods in the European Union** and should not be ignored. In addition, it seems that consumers would like products, which are more natural, which implies minimal and gentle processing to retain the beneficial compounds of the original fruit or vegetable.

3. Conclusions on Session: New developments in novel and functional foods

- *Functional foods based on naturally occurring plant compounds offer potential to improve the health of the European population. However, the risks of too-high doses need to be considered.*

There is a consumer demand for healthy foods, and food products claimed to affect mood, increase beauty, help weight management and facilitate healthy snacking are becoming more prevalent. In addition, **functional foods are already available claiming to affect many health outcomes**. Legislation should ensure that these new and existing products are acting appropriately but are treated as foods, not drugs. The distinction between the food and drug industries is important. Health benefits from food imply long term benefits to reduce the risk of disease, not to cure disease. For all nutrients, and also **for many naturally occurring substances in food, the risk-benefit is complicated and follows a U shaped curve**. A definite research need is for more information to define the dietary intakes of the U-shaped curve in humans. It needs to be ensured that supplements or fortified foods do not increase the intake above that of the second upper limb of the U shaped curve. It is unlikely that existing fruits and vegetables could provide this overdose. It is, in fact, likely that the general intake of naturally occurring plant low molecular weight compounds, such as polyphenols, glucosinolates and phenolic acids, is actually too low. New processing methods, as described above, could help this situation by increasing the intake of these desirable natural products. On the other hand, supplements and very highly fortified foods would need monitoring and some legal framework as provided by EFSA.

- *The exact doses of naturally occurring plant compounds necessary to provide a benefit or which could cause a risk is not yet clearly defined.*

The optimal dose of naturally occurring substances necessary to exert their optimal beneficial effects is not yet known, and more research is required in this area. As observed and reported for vitamins, the **requirements are likely to vary for different groups of the population**, such as children, adults, and elderly. Although it is desirable to have information on the needs of each group, it is first necessary for all consumers to obtain basic information.

- *Labelling of foods to indicate the content of the naturally occurring substances relative to the original plant is required.*

Labelling of (functional) foods could, for example, include information to **show how much of the original naturally occurring beneficial substances remained in the food after processing**. A higher percentage value could be readily understood by the consumer as more desirable than a low value. In addition, a simple system is needed to indicate on the label the amount of naturally occurring substances that are in supplements. This could be clearly indicated on the label. This could be coupled with **better and further education of consumers into food and health in general**.

- *Novel functional foods should not increase the risk of allergy.*

Another type of naturally occurring functional food ingredient is plant seed proteins, which are used to enhance the protein content of foods. The information on the safety of these additives is scarce, and would require risk assessment as provided by EFSA. In addition, the **allergenicity of these and any novel food proteins would need to be carefully tested and monitored**.

- *Better tools to establish the healthiness of individuals in studies on foods are needed.*

Potential health benefits and risks from functional food products require more experimentation and studies on humans, although these should not necessarily be randomised clinical studies. It cannot be too highly emphasised that **better biomarkers to indicate health status of the population**, and how this might be affected by food consumed chronically, **are very definitely required**.

4. Conclusions on Session: Consumer knowledge and behaviour

- *The information needed by the consumer to make food choices based on health is very complex.*

Information that consumers would require to make informed choices is quite extensive. A balanced diet with no overwhelming emphasis on one particular food is good advice, but the nature of the balance changes with time once new scientific discoveries are published. In addition, there is a tendency for more developed countries to eat more meat, whereas poorer ones eat mostly plant foods. The correct balance needs to be communicated to consumers, since increasing the proportion of plant based food in the diet to ensure optimal intake of naturally occurring compounds would have a benefit for health. **Consumers perceive most plant based foods as good for health**, and have the **baseline expectation that foods will be safe to consume**. Thus the U-shaped curve is difficult to communicate since it means that most dietary constituents can be both good or bad, depending on the dose. Many consumers know this intuitively for fat, for example, but the link to naturally occurring plant substances is not so obvious. Care should be taken to ensure that any messages on the negative effects of naturally occurring plant components at high doses are not confused with messages on the beneficial effects of the same components at low doses.

- *There is a danger of losing silent or hidden knowledge on food processing.*

For handling of food, **there is substantial “silent knowledge” which is in danger of disappearing**, and this may need to be carefully monitored and retained. In addition, many consumers are not interested in potential negative effects of high doses of naturally occurring substances from supplements or heavily fortified foods. Consumers only pay attention to the information that they are interested in, and often ask questions on how the food should be prepared or eaten. As a summary, the information given to consumers needs to be simple, but **informative enough to allow consumers to make their own choice**. The option of mandatory labelling is currently being explored in the European Community.

- *Multi-interest cooperation and collaboration is important to maximise benefits and minimise risks.*

It would be beneficial for the consumer if there was **more cooperation and collaboration** between research scientists, policy makers, industry and stakeholders when dealing with naturally occurring plant substances in foods.

Presentations

1. Food Group: Cruciferous vegetables; cabbage, broccoli, cauliflower etc.

Toxic and anti-nutritional substances: glucosinolates and glucosinolate derived compounds, by Gary Williamson

Glucosinolates occur in Cruciferous plants. On damage to the plant (which would include food processing, chewing, cooking and others) the glucosinolates breakdown into a variety of products. These products are highly bioactive, and also have sensory properties, giving rise to the distinct tastes of wasabi, mustard and horseradish. The breakdown products are isothiocyanates, nitriles, epithionitriles and thiocyanates. Several decades ago, glucosinolate breakdown products were considered only as natural toxicants. Indeed, oil seed rape contained a high level of progoitrin, a glucosinolate which exhibited some toxic properties when given in high amounts to farm animals. This led to the development of varieties of oil seed rape low in glucosinolates (and also erucic acid). However, the situation for glucosinolates changed in 1992 with a report from Talalay's group which reported the identification and purification of sulforaphane, a breakdown product from a glucosinolate called glucoraphanin, which showed anticarcinogenic properties. Substantial research effort has now confirmed this, at least in vitro and in animal models. This highlights the dual nature of many naturally occurring compounds in plants, but the concept is not new to nutrition. Daily Recommended Intake (DRI) values exist for vitamins and minerals, and provide a guideline on how much is required to avoid deficiency or toxicity. Even well known vitamins such as vitamin A and D and minerals such as selenium may have toxicity at very low levels, but of course are essential. Thus the U shaped dose-response curve is now a commonly accepted concept in nutrition and toxicity, and builds on the well known comment from Paracelsus from more than 400 years ago that the dose makes the poison. This implies that all substances which are biologically active – whether from food, drugs or other chemicals – can have possible toxicity, but this depends on the dose. This applies equally to vitamins, minerals, and naturally occurring plant products. The U shaped curve indicates that compounds are actually beneficial to health at optimum, often dietary doses, and only present a health risk at very high concentrations. The high amounts are generally not achievable through normal dietary means such as food, but can only be obtained from heavily fortified foods or “mega-dose” supplements.

Intake of glucosinolates: Daily intake of two glucosinolates, glucobrassicin and neoglucobrassicin, was 5.0 and 0.5 mg/capita/day in the Danish and 2.5 and 0.3 mg/day in the Finnish population populations respectively¹. These average values might be very different in individuals, who favour Brassica vegetables or who dislike and thus avoid Brassicas because of their distinct flavour. In the Potsdam region of Germany, the average daily cabbage consumption was 54 g/capita/day, mainly white cabbage, cauliflower and red cabbage, with consumption increasing with age². The intake was slightly higher in the winter compared to the summer. The uptake of progoitrin was relatively low with only 3 and 2 mg/capita/day in winter and summer, respectively³.

¹ Vang O, Dragsted LO. III. Indoles. Naturally occurring antitumourigens. Nordic Council of Ministers; 1996.

² Pfaff G, Georg T, Mueller W, Seppelt B, Boing H, Lange R. Der Kohlgemueseverzehr in Deutschland - Ergebnisse einer repraesentativen Erhebung in der Region Potsdam. Ernahrungsforschung 1994; 39:139-149.

³ Glucosinolates in Cruciferous vegetables - Natural Toxicant or protective factors 8341. 1994.

Beneficial effect of Cruciferous vegetables: Isothiocyanates are potent inducers of Phase II detoxification enzymes, and increase the metabolism and detoxification of chemical carcinogens *in vitro* and in animal models. Some inhibit mitosis and stimulate apoptosis in tumour cells by blocking DNA damage, thus inhibiting the growth of tumour cells after initiation by chemical carcinogens.

Toxicological data: Glucosinolate breakdown products at high levels alter organ mass, and cause renal dysfunction or thyroid-toxicity in animal experiments⁴. Whereas the anti-thyroid effects of certain isothiocyanates are based on interference with the synthesis of thyroid hormones, thiocyanates compete with iodine and thus inhibit iodine uptake by the thyroid gland. Beside the thyroid gland, liver, kidney, and pancreas are the main target organs. In rats, toxic effects were observed with daily doses higher than 10 - 50 mg/kg body weight. At such high concentrations, certain isothiocyanates and nitriles may initiate mutagenic, cytotoxic, and carcinogenic processes⁵⁻¹². Glucosinolate breakdown products induced genetic mutations in both bacterial and mammalian cells¹³. *In vivo* animal studies with benzyl isothiocyanate, allyl isothiocyanate, and phenethyl isothiocyanate have the potential to be genotoxic and probably carcinogenic, in their own right^{14 15}. The post-initiation effects of phenethyl isothiocyanate and butyl isothiocyanate on hepato-carcinogenesis and urinary bladder carcinogenesis in rats pre-treated with diethylnitrosamine and N-butyl-N-(4-hydroxybutyl)nitrosamine confers a strong promoter activity for both compounds¹⁶.

⁴ Heaney RK, Fenwick GR. Natural toxins and protective factors in brassica species, including rapeseed. *Nat Toxins* 1995; 3(4):233-237.

⁵⁻¹² Fenwick GR, Heaney RK, Mawson R. Glucosinolates. *Toxicants of Plant Origins* 1997.

(6) Mawson R, Heaney RK, Zdunczyk Z, Kozłowska H. Rapeseed meal-glucosinolates and their antinutritional effects. Part 6. Taint in end-products. *Nahrung* 1995; 39(1):21-31.

(7) Mawson R, Heaney RK, Zdunczyk Z, Kozłowska H. Rapeseed meal-glucosinolates and their antinutritional effects. Part 5. Animal reproduction. *Nahrung* 1994; 38(6):588-598.

(8) Mawson R, Heaney RK, Zdunczyk Z, Kozłowska H. Rapeseed meal-glucosinolates and their antinutritional effects. Part 4. Goitrogenicity and internal organs abnormalities in animals. *Nahrung* 1994; 38(2):178-191.

(9) Bjerg B, Eggum BO, Jacobsen I, Otte J, Sorensen H. Antinutritional and toxic effects in rats of individual glucosinolates (+/- Myrosinases) Added to a standard diet .2. *Journal of Animal Physiology and Animal Nutrition-Zeitschrift fur Tierphysiologie Tierernahrung und Futtermittelkunde* 1989; 61:227-244.

(10) Vermorel M, Heaney RK, Fenwick GR. Antinutritional effects of the rapeseed meals, darmor and jet neuf, and progoitrin together with myrosinase, in the growing-rat. *Journal of the Science of Food and Agriculture* 1988; 44:321-334.

(11) Fenwick GR, Heaney RK, Mullin WJ. Glucosinolates and their breakdown products in food and food plants. *CRC crit rev Food Sci Nutr* 1983; 18:123-201.

(12) Stoewsand GS. Bioactive organosulfur phytochemicals in brassica oleracea vegetables - a review. *Food Chem Toxicol* 1995; 33:537-543.

¹³ Kassie F, Parzefall W, Musk S, Johnson I, Lamprecht G, Sontag G et al. Genotoxic effects of crude juices from Brassica vegetables and juices and extracts from phytopharmaceutical preparations and spices of cruciferous plants origin in bacterial and mammalian cells. *Chem Biol Interact* 1996; 102:1-16.

¹⁴ Kassie F, Pool-Zobel B, Parzefall W, Knasmuller S. Genotoxic effects of benzyl isothiocyanate, a natural chemopreventive agent. *Mutagenesis* 1999; 14(6):595-604.

¹⁵ Kassie F, Knasmuller S. Genotoxic effects of allyl isothiocyanate (AITC) and phenethyl isothiocyanate (PEITC). *Chem Biol Interact* 2000; 127(2):163-180.

¹⁶ Hirose M, Yamaguchi T, Kimoto N, Ogawa K, Futakuchi M, Sano M et al. Strong promoting activity of phenylethyl isothiocyanate and benzyl isothiocyanate on urinary bladder carcinogenesis in F344 male rats. *Int J Cancer* 1998; 77(5):773-777.

Epidemiological data: Despite some evidence of toxicity at high doses, the study of populations (epidemiology) has overwhelmingly shown a positive effect on health in human populations. These studies on Brassica vegetable consumption and cancer risk was summarised by van Poppel et al. (6 cohort studies and 74 case-control studies). High Brassica consumption was correlated with a decreased risk of cancer of the lung, stomach, colon, and rectum, and least consistent for prostatic, endometrial, and ovarian cancers¹⁷. The Karolinska Institute compared the diets of 2,832 women aged 50 to 74 years and diagnosed with invasive breast cancer with the diet of 2,650 women of the same age with no history of breast cancer. While there was no correlation between total fruit and vegetable consumption and breast cancer risk, postmenopausal women consuming 1 to 2 servings of Brassica vegetables daily had a 20 to 40 % decreased risk of breast cancer¹⁸. A follow-up of the 'Health Professionals' study followed over 47,000 men for 6.3 years and compiled food intake data for 8 years. They observed that Brassica vegetable consumption was related to a 51 % reduction in the risk of bladder cancer¹⁹. However, there are also human studies that failed to show any link between Brassica vegetable intake and markers of disease risk, or even a positive association²⁰. Thus, the 'pooled analysis of cohort studies' conducted by Smith-Warner et al. failed to show any correlation between the Brassica consumption and the risk of cancer²¹.

¹⁷ van Poppel G, Verhoeven DTH, Verhagen H, Goldbohm RA. Brassica vegetables and cancer prevention - Epidemiology and mechanisms. *Advances in Experimental Medicine and Biology* 1999; 472:159-168.

¹⁸ Terry P, Wolk A, Persson I, Magnusson C. Brassica vegetables and breast cancer risk. *JAMA* 2001; 285(23):2975-2977.

¹⁹ Voorrips LE, Goldbohm RA, van Poppel G, Sturmans F, Hermus RJ, van den Brandt PA. Vegetable and fruit consumption and risks of colon and rectal cancer in a prospective cohort study: The Netherlands Cohort Study on Diet and Cancer. *Am J Epidemiol* 2000; 152(11):1081-1092.

²⁰ Verhoeven DT, Goldbohm RA, van Poppel G, Verhagen H, van den Brandt PA. Epidemiological studies on brassica vegetables and cancer risk 3. *Cancer Epidemiol Biomarkers Prev* 1996; 5(9):733-748.

²¹ Smith-Warner SA, Spiegelman D, Yaun SS, Adami HO, Beeson WL, van den Brandt PA et al. Intake of fruits and vegetables and risk of breast cancer: a pooled analysis of cohort studies. *JAMA* 2001; 285(6):769-776.

2. Food group: All plant-derived food

Toxic and anti-nutritional substances: Phenolics and antioxidants

By Mariusz K. Piskula

The conclusions following from the epidemiological studies on large populations show a direct relation between the diet and the incidence of chronic diseases. Nutritional factors may be involved in preventing or slowing down the development of diseases commonly called diet-related such as coronary heart disease, stroke, diabetes, obesity, hypertension, osteoporosis, certain cancers or gastrointestinal disorders, the cause of which may be consuming large amounts of fruit and vegetables. There are indications that disturbing the balance of oxidation-reduction processes, which are essential life processes, induce the development of the above mentioned diseases as well as aging. It occurs when the human organism is not able to cope with excessive production of free radicals, i.e. highly active species ready to immediately react with the surrounding biomolecules. This means that as long as the complex system of human antioxidative protection works efficiently, the changes do not proceed. But although slow and gradual, with time they become the cause of aging and age-related diseases.

About 15 years ago attention was drawn to antioxidants present in plant-derived food, especially polyphenolics which as a group of food components with in vitro antioxidative potential might be responsible for the observed positive correlation between the consumption of fruit and vegetables and the incidence of chronic diseases. It was a come-back to a great interest in these compounds and their beneficial health promoting action from the 1930s when Szent-Gyorgyi observed a positive relation between their consumption and decrease in blood vessels permeability. It was even postulated to give polyphenolics a vitamin status (vitamin P).

Phenolic compounds are widespread in the Plant Kingdom and occur in all plant parts; therefore, they make a significant part of the human diet. The average daily intake of these compounds in the western diet is about 1 g and depends on dietary habits of the population. In general, their function in plants is similar to that which is assumed to occur in humans after consumption of plant-derived food - the protection against environmental stress generating excess of free radicals. Presently, there is a common agreement that habitual consumption of vegetable- and fruit-rich diet lowers the risk of coronary heart disease and certain cancers, the reflection of which is a wide-ranging action promoting consumption of five servings of fruit and vegetables a day. This triggered human intervention studies aimed at demonstrating that supplementation with antioxidants can be a way to suppress the development of certain diseases. Surprisingly, trials with high doses of dietary antioxidants such as beta-carotene, ascorbic acid, vitamin E, selenium and zinc over a long period have not confirmed this expected beneficial effect; moreover, some of them proved to be harmful when taken in high doses.

The message that polyphenolics are good for health resulted in the immediate appearance on the market of an array of dietary supplements labelled with 'health claims' without sound scientific evidence but attracting potential health-conscious consumers to their health beneficial action. At the moment it seems that the situation has almost run out of control since it is easy to buy supplements equivalent to cases of fruit and vegetables, or litres of wine or tea, each claiming miracle effects. Such health-focused behaviour propagated by media may cause that consumers can do themselves more harm than benefit via excessive supplementation as the anti-nutritional and toxic nature of polyphenolics may take over the beneficial one.

Indeed, there is also the other face of polyphenolics which recently has been almost forgotten. For years polyphenolics have been counted to the group of anti-nutritional compounds and in some cases even as mutagenic or toxic. The most important and complex anti-nutritional effects of polyphenols are those resulting from their interactions with proteins, which can clearly reduce nutrients digestibility through inhibition of proteolytic, lipolytic and glycolytic enzymes leading to lowering nutrients assimilation. This is the case of populations where legume seeds are staple food and the presence of polyphenols is a serious anti-nutritional factor. Moreover, the observed problems with minerals deficiency in humans consuming plant type diet is related to the formation of complexes between polyphenols and metal cations which interferes with metals intestinal absorption, especially for iron, calcium and zinc bioavailability.

When food is concerned, it is necessary to remember of its sensory properties like colour and taste. Polyphenols can bring a variety of pigmentation to food as one of their functions in plants is to attract insects necessary for pollination through palette of colours during flowering. However, in certain conditions they are the reason for food colour deterioration. Oxidation of polyphenols during food storage and processing results in product browning which can be suppressed by addition of inhibitors of this process. Bitter and astringent taste of plants serves them as predator repellent and it results from a high level of certain polyphenols which are transferred to food, which is also regarded as anti-nutritional factor since it limits plant food consumption. However, this drawback can be handled via application of taste masking food additives. Finally, their highly regarded antioxidative activity attributed to their health beneficial feature is not stable, as polyphenols have the potential to act as prooxidants under certain conditions, for instance in the presence of Al, Zn, Ca, Mg and Cd, which can be easily achieved in the dietary tract where these food components can meet thus generating all sorts of health problems related to free radicals. Still, summing up the data on at least certain groups of polyphenolics, they are regarded as health promoting plant food components.

Polyphenols potential toxicity has not yet been fully recognized and was ignored for years. From the nutritional point of view, polyphenolics are xenobiotics and once ingested are efficiently metabolised and eliminated from the organism as in 'normal dietary situation'. The picture is different when excessive use of polyphenols containing supplements is considered. The Recommended Daily Intake (RDI) for polyphenolics is still lacking and it seems to be rather impossible to elaborate a uniform one. There is a vast number of different phenolic compounds divided into several classes forming the group called "polyphenolics" and they exhibit different biological activities at different concentrations. They cannot be unified also because of their toxicity or adverse actions. For instance, grape seed proanthocyanidins, even when ingested in dietary unrealistically high doses (gram level), obtained a NOAEL grade (no-observed-adverse effect level). Consumption of milligram doses of soy isoflavones sold under the name phytoestrogens is still under discussion because of potentially adverse effects and their use as "natural" alternative to hormone replacement therapy, protection against hormone-related cancers or presence in infant formulas, remains controversial. Moreover, quercetin, probably one the most studied flavonoids attributed with a number of properties positive to health, is still sold by chemical companies as a pure compound labelled "hazardous".

Another serious safety issue is polyphenols interaction with therapeutic drugs. Simultaneous intake of flavonoids and drugs can cause serious complications by modulating drug absorption and metabolism. In other words, it may result in decline of drug therapeutic effect through its low absorption or, just the opposite, cause its increase to levels that might be toxic to a patient.

The potential nutritional significance of polyphenols expressed on the systemic level depends on their behaviour in the digestive tract. Particular polyphenols classes are absorbed from food in different extent and their systemic action differs substantially. Numerous studies demonstrate that these compounds are rather low bioavailable and are intensively metabolised during absorption, which in most cases results in a substantial loss of their antioxidative activities. Polyphenols unabsorbed in the upper part of the digestive tract become the subject to microbial metabolism. In some cases deleterious to health products of microbial metabolism might be formed. Moreover, when their intensive microbial degradation in the colon and the lack of support from human intervention studies with high doses of dietary antioxidants are considered, it becomes increasingly convincing that polyphenols health promoting action is not necessarily related to their antioxidative activity. Recently, they and their metabolites have become dietary candidates for molecules with the potential of influencing metabolic pathways on other than antioxidative mechanisms.

One has to keep in mind that polyphenols, which are one of the dietary supplements sold in concentrated form alone or even in combinations with other components aiming at mimicking a certain type of food, are in fact only a minute representation of compounds which are normally consumed with food. Plant-type diet is usually composed of diverse palette of vegetables and fruits prepared for consumption in ways sometimes unique for certain populations. Therefore, all that is generally understood as a dietary habit and is associated with the protective action of plant-derived food for certain populations includes both the traditional way of food preparation and the kind of plant material used. Moreover, the health promoting effect of certain diets, single plants or their components are usually observed over a long period of exposure and it is still only a presumption.

Polyphenols are consumed in relatively low doses along with other accompanying compounds which may be still underestimated dietary factors. In the case of coronary heart disease, the suggestion coming from an epidemiological study is that people with a very low intake of flavonoids have higher risk of coronary heart disease rather than that a high intake of polyphenols provides protection. It is clear that there exist potential safety issues if mega doses of polyphenols are consumed daily. Their overconsumption may, among others, yield in generation of free radicals which are cytotoxic, hepatotoxic, co-oxidize unsaturated lipids, may cause dangerous drug-flavonoid interactions or inhibit or induce drug metabolizing enzymes and hence adverse effects may take over the beneficial ones.

It was also shown that a substantial increase in consumer exposure to dietary polyphenols can be achieved through recipes and instructions on how food should be prepared proving that dietary modifications can be as effective as taking supplements. It is also possible to provide consumers with diverse in composition and properly balanced polyphenolics load through agricultural practices and proper processing and storage. It does not mean that dietary supplementation is always wrong. In some cases consumer can benefit from the compounds which are not delivered via habitual diet. However, the health claim and recommended dose must be properly scientifically substantiated.

The problem of scientifically not supported health claims appearing on food and dietary supplements labels has been already noticed by the European Food Safety Authority and respective regulations should soon be effective; however, it does not mean that the demand for polyphenolics and antioxidants containing supplements will drop dramatically or that they will disappear from the market. Thus, potential toxicities including interactions with drugs will still be the case.

3. Food group: Plant Proteins

Toxic and anti-nutritional substances: Allergens

By Hanne Frøkjær

A substantial number of proteins in plants possess allergenic properties, and these proteins largely constitute what is called food allergens. Although food allergens are found in most plant families, their presence is particularly prevalent in certain plant families, e.g. legumes, tree nuts, and oily seeds (sesame, sunflower and mustard seeds) and, in these plant families some members are in particular serious allergy provokers.

The far most common form for allergy is IgE mediated allergy. In allergic individuals, the allergenic food gives rise to an increased level of IgE antibodies against one or several proteins present in the food and, by subsequent encounters with the allergen, the allergenic proteins bind to IgE molecules present on the surface of the mast cells, causing release of histamine and other substances responsible for the immediate symptoms experienced upon ingestion of the allergenic food.

Although the mechanisms behind most of the allergic symptoms experienced in food allergy are well-established, understanding of how in particular the allergenic foods in the first round evoke the allergy in a limited number of individuals is limited. It is, though, well-accepted that properties of the allergenic food as well as predisposition of the sensitized individual are factors required to provoke the allergy. Importantly, many cases of allergy to fruit and treenut are caused by inhalation of pollen from the respective trees. Thus, a high proportion of food allergy is induced by inhaled pollen protein with homology to the proteins present in the fruits and nuts. Whether this is the case for the majority of plant food allergies remains to be established, but there is a clear geographical prevalence of the various types of allergies, e.g. apples and hazelnuts in the Northern Europe and peach and almond allergy in the Mediterranean countries.

The symptoms evoked by food allergens are quite diverse, ranging from mild irritation in the mouth and throat over diarrhoea and eczema to severe life threatening anaphylactic shock. In order to rank the problem with food allergens, it is, therefore, necessary to regard the severity of symptoms generally evoked by a group of allergens. Peanuts and tree nuts are by far the most severe allergenic food of plant origin, while serious life threatening or life quality reducing effects may also in fewer cases be caused by soybean, celery and sesame. Many fruits (e.g. apples, peaches, apricots, mango) also have the capacity to elicit allergic reactions, but these are generally milder.

Moreover, it is difficult to set a safety limit of the allergenic food proteins in a food, as sensitized individuals respond very differently to various doses of the allergenic proteins. For example in the case of peanuts some allergic individuals react to as little as 0.1 mg proteins, while others can tolerate up to 1 g before they experience allergic symptoms.

Peanut and treenut (e.g. almonds, brazilnut, hazelnuts and walnuts) allergy is an important condition because it starts at an early age, is lifelong and can be fatal. These allergenic foods can give rise to symptoms even with minimal contact through intact skin or by inhalation. In its mildest form, treenuts allergy can be limited to a rash, sickness and headache to swelling of the tongue and lips, whereas both treenuts and peanuts allergy in its extreme form it can cause anaphylactic shock. The potential severity of the symptoms of allergic reaction to nuts dictates that sufferers have to avoid carefully any contact with nuts and to carry adrenaline (to counteract the severe allergic reaction) at all times.

Although the reactions to the various food allergens are caused by the same mechanisms, the plant food allergenic proteins constitute a diverse group of proteins. Some allergenic proteins are readily denatured by cooking and food processing, and this destroys in most cases the allergenic capacity of the protein. Other food allergens are, however, highly resistant towards denaturing and resist even extensive food processing, and few proteins are allergenic also in the denatured state.

What is the problem?

Food allergy actually constitutes two separate problems that must be addressed and handled in different ways:

- *How do we avoid allergic reactions in individuals already suffering of food allergy to one or more foods?*

As described above, the adverse health effects of food allergens are well-established. Although food allergy only concerns a minor part of the population, it has to be handled seriously. Most allergenic consumers can overcome their allergy by simply avoiding the allergenic food and many only have to avoid the non-processed food, e.g. raw apples and nut in order to escape allergic symptoms.

The major problems exist for those individuals that also react towards processed food. Newer processing techniques, such as high-pressure treatment of foods, fermentation and enzyme treatment, can help to reduce the allergenicity of some food proteins, but still reactivity is often seen in the most sensitive individuals. Moreover, allergens can be removed from oils by refining. Some of the unresolved problems of food allergy are concerned with the presence of low amounts of a given allergen in processed foods or recipe dishes served out of home.

Another major problem is cross-reactivity with proteins from other plant sources. If an individual has allergy to hazelnuts, it is most likely that he also reacts to other nuts, as plants within the same families often contain proteins with high homology, but he may also react to apples and other fruits as these plants contain proteins highly homogeneous to proteins in nuts. Accordingly avoidance is necessary, not only as regards nuts, but also a number of fruits. In some food allergies these interrelationships are not easily foreseen and, therefore, the allergic person may experience bad surprises, when eating plant food not considered to be related to the plant food he is allergic to.

- *How do we avoid that new foods –e.g. crops that have not previously been used for human nutrition or new processing methods for food preparation – gives rise to new incidences of allergy?*

The current knowledge of why some but not other relatively similar plant foods are strong provokers of food allergy is limited. For example, peanuts is known as a strong food allergy provoker, while many other legumes less frequently give rise to food allergy, but it is currently not known, what makes peanut such a strong allergy provoker.

Such lack of knowledge regarding which properties of a food that confers it its allergy provoking capabilities makes it very difficult to envisage whether introduction of new plant foods or new processing methods will pose increased risk of food allergy for the consumers.

How are the problems currently being handled?

In order to give the allergic consumer the best possibilities to avoid food containing the offending allergen(s), the EU legislation has been changed, so even minor amounts of an allergenic food must be declared. Until 2003, when the Directive 2000/13/EC was amended, the rule was that if a compound food (e.g. batter in deep fried vegetables) made up less than 25% of the final food, there was no legal requirement for listing all the ingredients used in that compound food. Accordingly the allergic consumer had a high risk for ingestion of allergens in amount sufficient to elicit an allergic reaction.

The directive 2003/89/EC, which came into effect in November 2004, amends directive 2000/13/EC and establishes a list of allergenic food ingredients that must be included on the label, if they are used in food pre-packed in Europe independently of the amount present. Moreover, these rules require that the source are indicated for all allergenic compounds on the list, e.g. if peanut oil has been used it has to be specified whereas in the past, peanut oil could be declared as 'vegetable oil'.

Accordingly, the currently rules give the consumers suffering from food allergy a high protection, although the allergic individual is still at risk for allergenic provocation, in certain cases:

- *Contamination of food products not intended to contain the food allergen.*

This is often caused by the use of the same production plan for production of different food products. This risk is often prevented by labeling all products from the production plant with 'may contain traces of..' or similar declarations

- *Cross-reactivities between the food allergen and other plant foods.*

Precisely which cross-reactivity the allergic individual experiences varies. Accordingly it is not strait forward to establish labeling for possible cross-reacting food allergens. Rather the consumers should have easy access to all relevant knowledge concerning crossreactivities, e.g. through easily accessible web-sites addressing the consumer, and which are regularly being updated with new knowledge.

With respect to novel food and novel processing methods concerns regarding the risk of introducing food allergy in a consumer segment should be addressed. Although rules for risk assessment in relation to introduction of such new foods have been established, which seek to envisage the allergenic risks, e.g. by assessment of cross reactivity and other similarities with known allergenic food, the current knowledge is still too limited to ensure prevention of introduction of new allergenic foods on the marked.

4. Legal framework for food safety in the European Community

By Helen Lee

The basic framework regulation on food and feed safety in the European Community is Regulation No. (EC) 178/2002¹ which concerns general food law. This Regulation provides a framework to ensure a coherent approach in the development of food legislation covering all stages of food/feed production and distribution. To achieve this goal:

- it establishes the European Food Safety Authority (EFSA)
- it lays down the over-arching definitions, principles and requirements on which all EC food legislation is based.

In particular, the Regulation establishes:

- the principles of risk analysis in relation to food and establishes the structures and mechanisms for the scientific and technical evaluations which are undertaken by the EFSA;
- the Precautionary Principle as an option open to risk managers when decisions have to be made to protect health but scientific information concerning the risk is inconclusive or incomplete in some way;
- the basic principle that the primary responsibility for ensuring compliance with food law, and in particular the safety of food, rests with the food business.

An example where legislation has been specifically enacted in relation to naturally occurring toxicants is regarding spices and herbs and other source materials that are used for the production of flavourings. Council Directive 88/388/EC² lays down maximum limits for food and beverages to which flavourings and other food ingredients with flavouring properties have been added. The limits in the Directive are based on a list of maximum limits proposed by the Committee of experts on flavouring substances of the Council of Europe. They cover food and beverages in general with exceptions for certain food categories. The Commission wants to protect against too high intake of such substances. The limits proposed continue to allow habitual use of these herbs and spices, the main aim is to avoid exaggerated use.

In the proposal for a new regulation on flavourings, maximum levels are maintained for the food categories which contribute most to the intake. In addition restrictions are proposed for certain source materials for production of flavourings³ and food ingredients with flavouring properties. The maximum levels and the restriction are based on the scientific opinions adopted by the SCF or EFSA.

¹ Regulation No. (EC) 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety (OJ L 31, 1.2.2002, p. 1)

² Council Directive of 22 June 1988 on the approximation of the laws of the Member States relating to flavourings for use in foodstuffs and to source materials for their production (OJ L 184, 15.7.1988, p. 61)

³ Proposal for a Regulation of the European Parliament and of the Council on flavourings and certain food ingredients with flavouring properties for use in and on foods and amending Council Regulation (EEC) No 1576/89, Council Regulation (EEC) No 1601/91, Regulation (EC) No 2232/96 and Directive 2000/13/EC (COM(2006) 427 final, 2006/0147 (COD))

In addition, Council Regulation (EEC) No 315/93⁴ lays down Community procedures for contaminants in food and provides that food containing a contaminant in an amount which is unacceptable from the public health point of view shall not be placed on the market. Where necessary to protect public health, maximum levels for specific contaminants shall be established. The definition of a contaminant implicitly includes inherent naturally occurring toxicants. For the time being, no specific provisions have been established yet for inherent naturally occurring toxicants in the frame of Regulation (EEC) 315/93.

Another legislative approach is to provide the necessary information so that consumers who might be at risk from specific substances in foods can make informed dietary choices. Usually consumers are informed through the labelling of foods. The general food labelling Directive 2000/13/EC⁵ requires all ingredients to be indicated on the label and establishes a list of ingredients liable to cause allergies or intolerances. The presence of ingredients that contain substances that may cause allergies or intolerances must be mentioned on the label, including on alcoholic beverages. In addition, there specific rules may be adopted regarding the labelling of certain substances or ingredients an example is certain labelling statements must be included on the label of foods containing glycyrrhizinic acid or its ammonium salt.

Other legislation that might be relevant to substances in plants is:

Regulation (EC) No 258/97⁶ on **novel foods and novel food ingredients** defines novel foods as those which have not been consumed to a significant degree in the Community prior to 1997 and which belong to one of the categories laid down in the Regulation. These include foods which result from technological innovation (such as cholesterol lowering margarine containing phytosterols) and foods which originate from third countries and have never been imported in the Community (such as exotic fruits and nuts). In order to ensure the highest level of protection of human health, novel foods must undergo a safety assessment before being placed on the EU market. Only those products considered to be safe for human consumption are authorised for marketing.

The European Commission has adopted a proposal to revise Regulation (EC) No 258/97 with a view to improving the access of new and innovative foods to the EU market, while maintaining a high level of consumer protection and ensuring food safety. Under the draft Regulation, novel foods would be subject to a centralised authorisation procedure following the scientific assessment on the product by the EFSA. A notification procedure is introduced for foods which have not been traditionally sold in the EU but which have a safe history of use in third countries.

⁴ Council Regulation (EEC) No 315/93 of 8 February 1993 laying down Community procedures for contaminants in food (OJ L 37, 13.2.1993)

⁵ Directive 2000/13/EC of the European Parliament and of the Council of 20 March 2000 on the approximation of the laws of the Member States relating to the labelling, presentation and advertising of foodstuffs (OJ L 109, 6.5.2000, p. 29)

⁶ Regulation (EC) No 258/97 the European Parliament and the Council of 27 January 1997 concerning novel foods and novel food ingredients (OJ L 43, 14.2.1997, p.1)

Regulation EC 1925/2006⁷ on the addition of vitamins and minerals and of certain other substances to foods provides the basis for scrutinising and, where necessary, regulating the addition of substances with nutritional or physiological effect, other than vitamins and minerals, to foods. The Regulation introduces a procedure that would allow to restrict or even forbid, after consultation of the European Food Safety Authority, the use of substances other than vitamins and minerals that are used in or added to foods (including food supplements), under conditions that would result in the ingestion of amounts of these substances greatly exceeding those reasonably expected to be ingested under normal conditions of consumption of a balanced and varied diet and/or would otherwise represent a potential risk to consumers. In case of scientific uncertainty the concerned substances could be inserted in a "scrutiny list" where they can remain up to 4 years. During this period those substances will remain subject to national legislation and manufacturers will be invited to provide data on their safety to EFSA. Within the 4 years a decision must be taken on whether the substances will be restricted, forbidden or generally allowed.

In conclusion, the General Food Law requires that food that is placed on the market is safe and the primary responsibility for ensuring the safety of the food is the food business. In addition there are specific legislative measures that are relevant to the management of potential risks associated with harmful substances in foods.

⁷ Regulation EC 1925/2006 of the European Parliament and of the Council of 20 December 2006 on the addition of vitamins and minerals and of certain other substances to foods (OJ L 404, 30.12.2006, p. 26)

5. New developments in industrial food processing

By Dietrich Knorr

Introduction:

New process developments such as high hydrostatic pressure and pulsed electric field treatment of raw materials and foods are low energy, low process intensity and mainly waste free technologies applicable for preservation and modification of foods with the goal to replace or to support existing thermal processes. This consumer driven development for safe, high quality and high functionality food processed via sustainable technologies is also aimed to retain or enhance the nutritional quality of products and to overcome some of the disadvantages of conventional thermal processing such as destruction or loss of nutrients, induction of unwanted substances, creation of waste products and high energy and water consumption. Figures 1 and 2 illustrate the key differences between thermal processing and the new technologies.

Fig 1: Limitation and advantages of thermal and non-thermal processes.

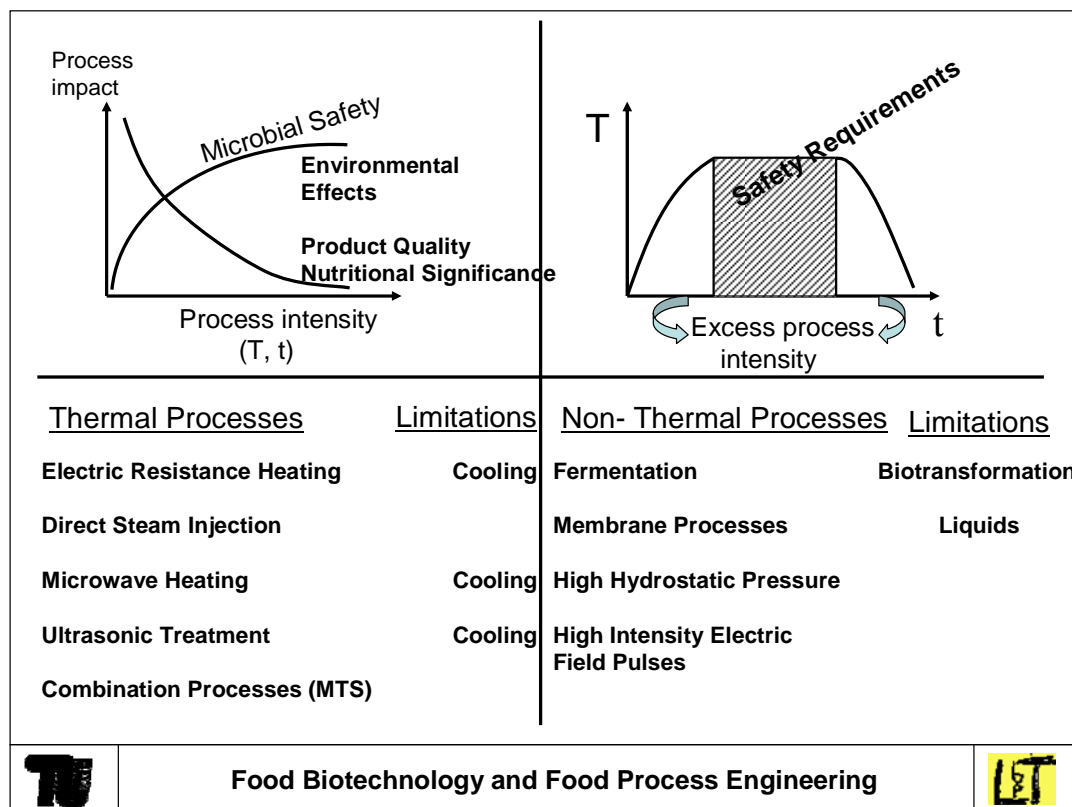




Fig 2: Principle advantages and process application of key advanced technologies.

<u>Key Advanced Technologies</u>		
Process Methods	Principle of Action	
High Pressure (HP)	Pressure Gradient Activation Volume	
High Intensity Electric Field Pulses (HELP)	Potential Difference Membrane Permeabilisation	
Ultrasound	Pressure Gradient p, T Effects	
Process Advantages	Instant Distribution Low Temperature Application Low Energy Requirements Quality Retention/ Improvement Property Engineering Consumer Friendly Waste Free	
Process Applications	Preservation (pasteurisation) Modification (gelatinisation) Process Development (pressure freezing, pressure blanching)	
	Food Biotechnology and Food Process Engineering	

An integrated EC project (www.novelq.org) is currently evaluating critical issues regarding the development of these new technologies including safety, toxicity, allergenicity, quality, chemical, nutritional and consumer aspects. Documents on the safety assessment of high pressure and pulsed electric field processes spearheaded by the German Research Foundation (www.dfg.de) suggest in principle limited amount of existing data for a comprehensive safety assessment and the need for a case-by-case assessment.

High hydrostatic pressure treatment:

High hydrostatic pressure (HP) treatment of foods has been initiated more than 100 years ago and has been put into commercial use for the first time in Japan in 1990. Meanwhile approximately 120 industrial high pressure processing units exist worldwide.

The USA is currently the main user of this technology because inactivation of food pathogens such as salmonella and listeria (especially in meat products) proved to be more effective by high pressure processing than via conventional routes.

Research data accumulated so far indicate that this technology can be used effectively for pasteurisation and sterilization of foods. Proteins and polysaccharides can be modified providing the potential for new product development via a physical process rather than a chemical / biochemical. Further it has been shown that nutrients, flavours, colour, aroma and texture of foods can be well retained by pressure processing and that prions (the most likely cause of BSE) and viruses can also be inactivated effectively.

In summary the safety assessment of HP processing as given by the German Research Foundation (www.dfg.de) states that findings derived from a few already marketed products have not yet revealed any evidence of any microbial, toxicological or allergenic risk as a consequence of high-pressure treatment but do not suffice for a general evaluation. At present an individual case-by-case examination of high-pressure treated foodstuffs is necessary. For any future safety evaluation of high-pressure treated food according to recognised standard criteria the development of product- and process-specific test parameters is desirable.

Pulsed electric field treatment:

The pulsed electric field (PEF) process promotes permeabilization of biological cells (plant, animal, microbial) thus allowing the efficient extraction of cellular contents as well as the inactivation of microorganisms in foods. In addition to this irreversible permeabilization, reversible permeabilization (e.g. the “infusion” of material in biological cells) as well as induction of stress responses with low energy pulses (e.g. increased biosynthesis of antioxidants such as phenols in plants or phytosterols) is possible. The energy input required is much lower than by conventional processes and it can be considered as a waste free technology. Currently one industrial application exists in the USA; Industrial and pilot scale equipment exists in the Netherlands, in Germany and Sweden.

A survey regarding the safety assessment of the PEF process (www.dfg.de) concludes that a consistent evaluation of the PEF process is hindered due to the limited number of studies and the lack of standardisation of process parameters. Development of criteria to assess the process requires, among other things, the characterisation of suitable indicator substances and measuring parameters. According to the assessment criteria given in the document, products treated with the PEF technology require a case-by-case assessment.

Recent data accumulated within a collaborative research project (www.fei-bonn.de) provide evidence that substantial equivalence of PEF treatment vs. conventional treatment for the production of fruit juices is given.

Benefits of PEF include high juice yields from fruits and vegetables (including sugar beets), oils from oilseeds, higher drying and extraction rates and as a result of stress reactions higher concentrations of antioxidants and antimicrobial substances in plant materials as well as the retention of valuable natural antimicrobial components in milk while inactivating pathogenic microorganisms.

Current EC funded research (www.novelq.org) attempts to identify the impact of PEF on allergens and toxins as well as to determine whether stress induction via PEF might lead to the generation of antinutritional or potentially toxic metabolites. The potential of generation of electrochemical reaction products and release of ions from electrodes is being evaluated.

Strategic Research Agenda 2007-2020:

The European Technology Platform (ETP) on Food for Life (<http://etp.ciaa.eu>) which outlines the Strategic Research Agenda within Europe for the 15 years suggests under its key challenge: Developing quality food products the following goals:

- (1) Producing tailor made foods
- (2) Improving process design, process control and packaging
- (3) Improving understanding of process-structure-property relationships
- (4) Understanding consumer behaviour in relation to food quality and manufacturing

Outlook:

As identified in the ETP document the key challenges for future food research and development are:

- (1) Ensuring that the health choice is the easy choice for consumers
- (2) Delivering a healthier diet
- (3) Developing quality food products
- (4) Assuring safe foods that consumers can trust
- (5) Achieving sustainable food production
- (6) Managing the food chain

This clearly indicates that European food RRD is taking a highly responsible role in ensuring highest food quality, sustainability and safety as well as dealing with other key issues such as weight control, consumer trust and optimum integration of the entire food chain. Through implementation of this concept and through the establishment of more targeted EC as well as nationally founded research on key food related issues the EU can become a global role model for responsible food production and processing.

