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NON-NUTRIENTS IN FOOD AND OPPORTUNITIES FOR PREVENTION

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Biological importance of non-nutrients in food

It has been customary to think of food from a nutritional point of view as a source of essential nutrients: the macronutrients, protein, fat, carbohydrate, alcohol and dietary fibre, and the micronutrients, vitamins and minerals or elements. The basis for this thinking is that, in the short to medium term, human life is not supportable without these compounds. However, the appreciation of dietary fibre or, more correctly, a class of chemicals which are principally non-digestible carbohydrates, as nutrients led to a revision of this view in several ways. One was that the absence of a particular chemical from the diet might alter the quality of life or might shorten life span without the deficiency having a more immediate effect on life.

There are several ways in which non-nutrient components of food may be biologically important. These relate to food physico-chemistry to flavour and smell, to physiological functions, and to the pharmacology and toxicology of food.

Food physico-chemistry

Food physico-chemistry derives from several factors such as viscosity and particle size. These characteristics of food may be deliberately changed through innovative food technology on account of consumer preference for particular textures or for explicitly health reasons. There is often an assumption that, if the chemistry is unchanged, the physico-chemistry is of no health consequence. This is not the case and there are now many examples of how this is not so. For example, glycaemia and related insulin status are affected by particle size of apples[1] and of ground rice[2-5]. If the viscosity of food is altered with fibre sources like that from guar[6,7], then, glycaemic response to food can also change.

Physico-chemistry can affect digestibility. Digestibility affected by particle size or cooking method, can affect the extent of protein absorption[8-11] and the presentation of undigested carbohydrate to the large intestine.[12] With traditional methods of cooking starch foods, like pasta, noodles, and rice, starch can first undergo gelatinization and, on cooling, crystallization, with consequent indigestibility. Such starch behaves as does much of dietary fibre and is fermented in the large intestine by its microflora.[13] Because this resistant starch yields a relatively greater butyrate production than does the fermentation of soluble dietary fibre, it is potentially of greater benefit in the differentiation of the colonocyte and its reduced propensity to neoplastic change. Thus, well-meaning changes in food physico-chemistry could have profound consequences for human biology and health.

Flavour, taste and smell

Taste and smell depend on a myriad of compounds in food for which there are many different receptors.[14-16] There are certainly more than for the principal taste modalities, as work in recent years on non-nutritive sweeteners has shown[14-16]. Even the taste of salt, which may be thought to relate principally to the operation of sodium channels, can be modulated by a number of other factors, including caffeine[14-16]. In some food cultures, there is a greater awareness of taste dimensions, like 'umani' amongst Japanese, not ordinarily articulated by those of Anglo-Celtic culinary tradition.[17,18] The interesting question is, whether these many compounds and their receptor relationships have biological relevance beyond their portal of entry into the human body. For some, like glutamate, this likely to be the case[19]. These compounds are ones that can encourage or discourage food use and may have their own distinctive effects on biological processes. Therefore they must be considered in any approach to preventive health.

Contribution of non-nutrient components

If one were to examine almost any physiologically or anatomically based system in the body, one could find ways in which non-nutrient components of food might affect it.

In the case of the *special senses*, references have already been made to the importance of the compounds which confer organoleptic properties on food. The visual attractiveness of food is dependent on its colour, shape and presentation. As far as colour is concerned, it is dependent on classes of compounds including carotenoids,[20] flavonoids,[21] anthocyanins,[22] phycocyanins and phycoerythrins,[23] the chlorophylls, tannins,[24] hemes and bilins, melanoidins and caramel.[25] Several of these are antioxidant (carotenoids and flavonoids), others lower serum cholesterol[74-76] whilst others alter bioavailability of essential nutrients (tannin decreases iron bioavailability and may interfere with protein metabolism)[77].

When one considers *gastrointestinal physiology*, motility may be affected by the menthol in peppermint oil[26] and peptides[27]; gut integrity, at least in states of metabolic stress, by glutamine which is not ordinarily essential[28]; digestion by enzyme inhibitors[29] like the lectins[30,31] and absorption, as for example with the interaction between cholesterol and phytosterols.[32,33]

Certain foods may have *endocrine* effects. These factors may be regarded as exo hormones.[27,34] Exorphins, peptides derive from food proteins like casein and gluten, can possess opioid activity,[35,36] modulate mineral metabolism and the immune response.[34,37,38] Food also contains compounds which can have mineralo-corticoid activity[39]. There are compounds which process oestrogenic activity belonging to the isoflavins, coumestans and lignans.[40] Some peptides affect pituitary function.[41-43]

Opioid-like activity can be found amongst certain compounds in instant coffee;

These have been identified as isomeric (iso) feruloyl quinic acid lactones.[44,45] Salsolinol found in dried bananas, the chocolate-milk-solids-based hot beverage Milo, soya sauce, chocolate and coco-based products mimic the action of dopamine on its *brain* receptor.[46] Duncan has also found that Milo contains the alkaloid tetrahydropapaveraline, a percursor of morphine in the opium poppy.[3]

Whilst it is usually presumed that, as far as food intake is concerned, metabolic balance is determined by the energy value of the food alone, there is a growing awareness that there are factors in food that affect *metabolic regulation*.[38,47,48] Exorphins may have effects on peripheral blood insulin and glucagon levels.[38] Capsaicin derived from chillis may alter the thermic response to a meal.[47,48]

Those peptides which have gonadotrophin releasing hormone activity may well alter *reproductive function*.[41] In a study of postmenopausal women who were given putative sources of oestrogenic compounds, soya flour, red clover sprouts and linseed (flax seed), vaginal maturation indices improved and FSH secretion decreased by 2 weeks.[40] This was achieved where only about 10% of energy intake would have contained such compounds. There is considerable interest in the possible effects of those compounds, especially in Asia, where the order of 50% of energy intake, in both men and women, may contain them. It is conceivable that phyto-oestrogens may modulate the expression of the menopause. Since the compounds are rather weekly oestrogenic, they may be competitive with endogenous oestrogenic hormones as well. The knowledge that tamoxifen can have similar effects on vaginal cytology in postmenopausal women, whilst being antioestrogenic at the breast and useful in the management of breast cancer, raise the possibility that these compounds may also reduced the risk of breast cancer. Indeed, recent work by Lee *et al.* amongst Singaporean Chinese women supports the view that soya products can indeed have such protective properties[49].

The *nervous system* may also be influenced by compounds in food not ordinarily regarded as nutrients. The presence of compounds with opioid-like activity in foods has already be mentioned. There are various foods, notably fava bean (broad beans), which are natural sources of L-dopa[50-52]. Recent work by Bogetic *et al.*[53] indicates that blended broad bean pods may be an effective delivery system for L-dopa, comparable, if not superior to, commercial preparations with decarboxylase inhibitors.

There is increasing evidence that *bone density* may be affected by compounds not ordinarily regarded as nutrients. For example, boron, not a recognised trace element, but present in certain plant foods can increase endogenous oestrogen levels and alter urinary calcium excretion[54]. The findings on weakly oestrogenic compounds in foods may also have relevance for bone density[40]. There is evidence that caffeine may adversely affect bone density[78-80]. Again, compounds like oxalates[55,56] and phytates[57] can adversely affect calcium bioavailability. The *cardiovascular system* may be influenced in various ways. The effects of caffeine on heart rate, and those of the mineralocorticoid-like compounds in licorice and ginseng are well-known[58].

Serum *lipoproteins* can be changed quantitatively and qualitatively by compounds in food which are not nutrients[59,60]. There is a factor in boiled coffee which is lipid-soluble and which adversely affects low and high density lipoproteins (LDL) (HDL)[61]. Allicin in garlic has slight serum cholesterol-lowering properties[62]. At the same time, about a clove of garlic can significantly decrease platelet aggregation and LDL cholesterol-lowering properties[62,63,81]. Colours in foods such as carotenoids, including lycopene from tomato, which may have no pro-vitamin A activity, can protect LDL cholesterol from oxidation, in an heirarchical fashion with different time-lags, so that a spectrum of carotenoids, and therefore a variety of foods, must be required[59,60]. Isoflavones, which have oestrogenic properties, can affect lipoprotein status.

Some food components are anticarcinogenetic, like curcumin in turmeric or increase cellular differentiation, like butyrate from the fermentation of resistant starch in the colon.

There is growing understanding of the way that various factors in food can affect the immune system. These include via glutamine[28] and glutathione[64].

Food pharmacology and 'medical foods'

With advances in food technology it will be increasingly possible to enrich foods with compounds which are natural to those foods and of potential pharmacological value. Alternatively, compounds which are medically unfavourable could be excluded or reduced in concentration; traditional cooking methods have often allowed this in any case as with the use by Aboriginal Australians of the cycad plant, or by various communities of cassava, where the cyanogenetic glycosides have been reduced by washing, soaking or cooking. Perhaps the most contemporary example of food enrichment with substances once not considered nutrients would be the addition of dietary fibre of various kinds, depending on the function or action required. These might be from cereal, wheats or oats, or from vegetables or legumes.

A general point of concern to food regulatory agencies is whether modification of food should be restricted to the restoration of compounds normally expected to be present, or whether it is permissible to fortify purchasable foods. The risk-benefit ratio is less certain where fortification takes place. An example is iron, where fortification of cereals may be advantageous in areas where iron deficiency is prevalent, but disadvantageous for those prone to iron storage diseases.

In occidental and English speaking countries in particular, the strict segregation of food and medicine has been enshrined in legislation[3,19]. However, in the orient, there has always been a grey area between food and medicine, with food being medicine and medicine also being food. What is now happening is that, with the internationalization of food technology from the orient, especially Japan, Western countries are being required to re-examine the demarcation between the two areas. One approach is now at least to legalize health messages, if not health claims, on food labels. Another is to develop an intermediate category of foods which may be regarded as 'medical foods' or 'nutriceuticals'[3,19].

Some notable examples of how foods may be modified or selectively used come from the management of disorders like phenylketonuria, where efforts were made to reduce phenylalanine intake. On the other hand, therapeutic, and preventive approaches to the expression of certain diseases, may simply require a change in food intake patterns. Examples would be the efforts to reduce the expression of impaired glucose tolerance or diabetes through a shift in distribution of food across the day, so that smaller quantities are provided more often; and with atherosclerotic disease, to reduce the intake of saturated fat and to encourage the use of a wide variety of plant food, along with the regular consumption of fish[65].

More specific pharmacological application of the knowledge of non-nutrient components of food would be in an area like the prevention and management of migraine with feverfew[66,82], of nausea and motion sickness with ginger[67] and of extrapyramidal problems in Parkinson's disease with foods containing L-dopa (along with a shift in pattern of protein intake towards the evening)[50-53].

Food toxicity

There is a very large literature on toxicants which occur naturally in food[29,55,57,68,69]. Interesting examples include *estrogens* and *enzyme inhibitors* as a cause of *pulmonary hypertension*, various unusual amino acids which may lead to *neurological disease*[4] and *hypoglycaemia* attributable to hypoglycin from the ackee fruit[70].

There is some evidence that the use of cured meat during pregnancy may increase the risk of *insulin-dependent diabetes* in the child of that pregnancy[83,84], as might certain food additives[85].

Food sensitivity is more than food allergy and is usually attributable to either biogenic amines or salicylates[71-73].

Tannins can reduce the bioavailability of iron.

Individual non-nutrients

The non-nutrients in foods with biological activity can be classified into favourable, unfavourable or both and uncertain categories, as in Table 1.

Table 1. Non-nutrients likely to be favourable or unfavourable to health as part of the diet.

Unfavourable	Favourable	Uncertain
Caffeine	Allicin/ajoene	Peptide hormones
Salicylates	Salicylates	Opioids
Biogenic amines	Lectins	
Tannins	Capsaicin	
Oxalate	Saponins	
Phytate	Oestrogenic compounds	
Lectins (trypsins Inhibitors)	Flavonoids	
	Anthocyanins	
	(enocyanins in grapes)	
	Phenolic compounds	
	(curcumin in turmeric)	
	Carotenoids	
	(non-vitamin A precursors)	
	Menthol (peppermint oil)	
	Glutathione	
	Phytosterols	

Changing food technology

Rapid changes are taking place in food technology, particularly in the creation of new shapes and forms of food. An example is the technique of extrusion, whereby a fine particle size is produced from cereals which are then liquified and presented as liquids or snack foods. This technology could have important effects on colonic microflora which could be desirable or undesirable. In changes such as these we are engaged in substantial human experimentation. There may be opportunities for preventive medicine, and there may be a need to develop additional evaluation and monitoring to avoid the appearance of new types of disease. Food analogues are the new 'smart' technology, ie, foods that look like egg or look like fish. Such developments may be necessary to satisfy world food demand, to increase shelf life, and to make food easier to deliver. There is now a need for people in medical and health care practice to gain an understanding of new food technology and its implications.[19]

Opportunities for prevention

Some non-nutrients of biological importance will be developed to advantage for their unique physiological and pharmacological properties. Others, once understood will be excluded by innovative food preparative methods (as they have been in some traditional food cultures). But the shear complexity of food chemistry and physico-chemistry is most likely to require us to describe food intake in more holistic terms, preferably mathematically, so that food health-relationships can be better understood and taken advantage of.

Food must continue to appeal and, for this reason alone, simple choices of foods for meals and snacks are likely continue to serve the human species best, rather than the creation of more and more formulated food and meals, unless by necessity. However, there are increasingly cogent health reasons to understand the biological significance of the non-nutrient components of foods and to recruit this knowledge in prevention of the major non-communicable diseases affecting the human species.

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