Functional foods from animal sources and their physiologically active components

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SUMMARY

Functional foods are foods that, by virtue of their physiologically active components, provide health benefits beyond basic nutrition. Although the vast number of naturally occurring health-enhancing substances are of plant origin, there are also a number of physiologically active components in animal products that deserve attention for their potential role in health promotion. The aim of this paper was to review the literature for those animal food components that have been linked with human physiological benefits, in order to contribute for the dissemination of this new topic among veterinarians and other animal and food scientists. These components, which potential health benefits and their scientific evidence are described, include: calcium, probiotics, whey proteins and whey peptides, from dairy products; n-3 fatty acids, from fish products; conjugated linoleic acid, from beef and lamb meat; sphingolipids, from eggs; and, the conditionally-essential nutrients L-carnitine, coenzyme Q10, α-lipoic acid, choline and taurine, widely diffused in animal products. In spite of the infancy of functional foods field, increasing evidence supports the observation that functional foods from animal sources may enhance human health.


RÉSUMÉ

Les aliments fonctionnels d’origine animale et leurs composants ayant une activité physiologique. Par J.A. MESTRE PRATES et CRISTINA M.R.P. MATEUS.

Les aliments fonctionnels sont des aliments qui, par leurs composants physiologiquement actifs, ont des effets sur la santé, au-delà de leur simple rôle nutritionnel de base. Bien que la plupart des substances présentant cette activité sur l’homme soit d’origine végétale, il y a aussi un certain nombre de composants d’origine animale qui méritent qu’on leur prête attention à cause de leur activité bénéfique sur la santé. L’objet de ce travail est une revue de la littérature existante sur ce sujet, afin de le divulguer parmi les vétérinaires et d’autres scientifiques des animaux et des aliments. Les composants, dont une éventuelle activité positive sur la santé a été montrée scientifiquement, sont: le calcium, les probiotiques, des protéines et peptides du lactoserum, des produits laitiers; les acides gras n-3, composants des matières grasses du poisson; l’acide linoléique conjugué, de la viande de bœuf et de mouton; les sphingolipides des œufs; et, les nutriments essentiels sous certaines conditions, L-carnitine, coenzyme Q10, α-acide lipoïque, choline et taurine, très répandus parmi les produits d’origine animale. Bien qu’on commence à peine à parler des aliments fonctionnels, ils deviennent un sujet de plus en plus important, compte tenu de la démonstration scientifique de leur action sur la santé humaine.


Introduction

There has been recently an explosion of consumer interest in the health enhancing role of specific foods, containing physiologically/biologically active components in addition to the nutrients, so-called functional foods, designer foods or nutraceuticals [25]. Clearly, all foods are functional, as they provide taste, aroma, or nutritive value. Within the last two decades, however, the term functional as it applies to food has adopted a different connotation: that of providing an additional physiological benefit beyond that of meeting basic nutritional needs [26].

As the food industry has responded to consumer demand for a more healthful food supply, the variety of functional foods that are currently available to consumers has grown tremendously, and functional foods are becoming an increasing percentage of all new products [3, 10]. These functional products should have pre-approved health claims (e.g. in USA, by Food and Drug Administration (FDA)), which are based on scientific evidence and agreement among scientists in the field of food and nutrition, and appear in the market with labels providing a reliable source of applicable nutrition information for consumers.

Health professionals, based on the increasing scientific evidence, are gradually recognising the role of biologically active food components in health enhancement [1, 29]. The scientific evidence for functional foods and their physiologically active components can be categorised into four distinct
areas: a) clinical trials; b) animal studies; c) experimental *in vitro* laboratory studies; d) and epidemiological studies. Much of the current evidence for functional foods lacks well-designed clinical trials; however, the foundational evidence provided through the other types of scientific investigation is substantial for several of the functional foods and their health-promoting components. The potential of functional foods to mitigate disease, promote health, and reduce healthcare costs, can be even more significant than the market value of functional foods [25].

The position of the American Dietetic Association (ADA) is that functional foods, including whole foods and fortified, enriched, or enhanced foods, have a potentially beneficial effect on health when consumed as part of a varied diet on a regular basis, at effective levels [2]. ADA [2] refers also that the knowledge of the role of physiologically active food components, both from plant and animal sources, has changed the role of diet in health. Functional foods have evolved as food and nutrition science has advanced beyond the treatment of deficiency syndromes to reduction of disease risk. However, each functional food should be evaluated on the basis of scientific evidence to ensure appropriate integration into a varied diet.

Foods can no longer be evaluated only in terms of macronutrient and micronutrient intake, but the analysis of other physiologically active components will be necessary [2]. In addition, research into the emerging area of functional foods should be more widely and effectively communicated to the scientific community and consumers in order to advance public health [18]. Although the majority of physiologically active food components are of plant origin (for review, see e.g. [37]), animal products also have several substances with a potential role in health promotion. This paper reviews the literature concerning animal food components that have been linked with human physiological benefits. The spread of this new topic is very important among veterinarians and other animal and food scientists, in order to optimise public health, through healthier food products, by improving animal nutrition and food processing.

### 1. Definition of functional foods

The designation of functional foods was first introduced in Japan, in the 1980s, and refers to processed foods containing ingredients that aid specific bodily functions in addition to being nutritious. To date, Japan is the only country that has formulated a specific regulatory approval process for functional foods [6]. In the USA and Europe, the functional foods category is not yet recognised legally. Irrespective of this, many organisations have proposed definitions for this new and emerging area of the food and nutrition sciences. The International Food Information Council (IFIC) defines functional foods as "foods that provide health benefits beyond basic nutrition" [30]. This definition is similar to that of the International Life Sciences Institute of North America (ILSI), which has defined functional foods as "foods that, by virtue of physiologically active components, provide health benefits beyond basic nutrition" [13]. The Institute of Medicine of the National Academy of Sciences of USA (IMNAS) limits functional foods to "those in which the concentrations of one or more ingredients have been manipulated or modified to enhance their contribution to a healthful diet" [31].

According to the wide definitions, unmodified whole foods such as fish and beef represent the simplest example of a functional food, since they are rich in such physiologically active components as n-3 fatty acids and conjugated linoleic acid, respectively. Modified foods, namely those that have been enhanced with physiologically active components, from plant (phytochemicals) or animal (zoochemicals) sources, also fall within the realm of functional foods. In addition, food biotechnology will continue to provide new venues for functional food development.

Although the term functional foods may not be the ideal descriptor for this emerging food category, recent focus-group research conducted by IFIC showed that this term was recognised more readily and was also preferred by consumers over other commonly used terms such as nutraceuticals or designer foods [50]. Recent broad use and acceptance of the term functional foods by media, scientists, and consumers makes convenient to work within this framework rather than introduce a new, more descriptive term, because of concern that new terminology could lead to further confusion among consumers [2].

### 2. Dairy products

There is no doubt that dairy products are functional foods. They are one of the best sources of calcium, an essential nutrient which can prevent osteoporosis and possibly colon cancer. In view of the former, the National Academy of Sciences of USA recently increased recommendations for this nutrient for most human age groups. In addition to calcium, however, recent research has focused specifically on other components in dairy products, particularly fermented dairy products, known as probiotics. Probiotics are defined as "live microbial feed supplements which beneficially affect the host animal by improving its intestinal microbial balance" [19].

It is estimated that over 400 species of bacteria, separated into two broad categories, inhabit the human gastrointestinal tract. The categories are: those considered to be beneficial (e.g. *Bifidobacterium* and *Lactobacillus*) and those considered detrimental (e.g. *Enterobacteriaceae* and *Clostridium* spp.). Of the beneficial micro-organisms traditionally used in food fermentation, lactic acid bacteria have attracted the most attention [49]. Although a variety of health benefits have been attributed to probiotics, their anticarcinogenic, hypocholesterolemic and antagonistic actions against enteric pathogens and other intestinal organisms have received the most attention [44].

The hypocholesterolemic effect of fermented milk was discovered more than 30 years ago during studies conducted in Maasai tribesmen in Africa [40]. The Maasai have low levels of serum cholesterol and clinical coronary heart disease despite a high meat diet. However, they consume daily 4 to 5 L of fermented whole milk. Although a number of human clinical studies have assessed the cholesterol-lowering effects of
fermented milk products [49], results are equivocal. Study outcomes have been complicated by inadequate sample sizes, failure to control nutrient intake and energy expenditure, and variations in baseline blood lipids.

More evidence supports the role of probiotics in cancer risk reduction, particularly colon cancer [44]. This observation may be due to the fact that lactic acid cultures can decrease the activity of faecal enzymes (e.g. β-glucuronidase, azoreductase, nitroreductase) that are thought to play a role in the development of colon cancer. Relatively less attention has been focused on the consumption of fermented milk products and breast cancer risk, although an inverse relationship has been observed in some studies [53, 55].

In addition to probiotics, there is growing interest in fermentable carbohydrates that feed the good microflora of the gut. These carbohydrates, called prebiotics, were defined by Gibson and Roberfroid [20] as "nondigestible food ingredients that beneficially affect the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon and thus improves host health". Prebiotics include starches, dietary fibres, other non-absorbable sugars, sugar alcohols and oligosaccharides [21]. Of these, oligosaccharides have received the most attention, and numerous health benefits have been attributed to them [54]. Oligosaccharides consist of short chain polysaccharides composed of three to ten simple sugars linked together. They are found naturally in many fruits and vegetables (including banana, garlic, onions, milk, honey and artichokes). The prebiotic concept has been further extended to encompass the concept of symbiotics, a mixture of pro- and prebiotics [20]. Many symbiotic products are currently on the market in Europe.

Recently, it was found that whey proteins have a putative anti-cancer activity [43]. It was shown that these proteins are efficacious in retardation of colon cancer in young rats, compared with other dietary proteins (meat and soy), which can be a basis for their inclusion as ingredients in functional foods. Additionally, the foods containing whey proteins are generally highly acceptable in taste trials. A recent field of research are biological active peptide sequences of whey, which become effective during digestion and are of importance for secretion of entero hormones as well as for immune enhancing effects [9].

3. Fish

Omega-3 (n-3) fatty acids are an essential class of polyunsaturated fatty acids (PUFA) derived primarily from fish oil. The major PUFA are eicosapentaenoic acid (EPA; C20:5, n-3) and docosahexanoic acid (DHA; C22:6, n-3). Canada has established the Canadian Recommended Nutrient Intake (CRNI) of n-3 PUFA at 0.5 % of energy (e.g. 1.1 g/2000 kcal). It has been suggested that the Western-type diet is currently deficient in n-3 fatty acids, which is reflected in the current estimated n-6 to n-3 dietary ratio of 20:25-1, compared to the estimated 1:1 ratio on which humans evolved [51]. This has prompted researchers to examine the role of n-3 fatty acids in a number of diseases - particularly cancer and cardiovascular diseases (CVD) - and more recently, in early human development.

That n-3 fatty acids may play an important role in CVD was first brought to light in the 1970s when Bang and Dyerberg [8] reported that Eskimos had low rates of this disease despite consuming a diet which was high in fat. The cardioprotective effect of fish consumption has been observed in some prospective investigations [36], but not in others [7]. Negative results could be explained by the fact that although n-3 fatty acids have been shown to lower triglycerides by 25-30 %, they do not lower LDL cholesterol. In fact, a recent review of 72 placebo-controlled human trials, showed that n-3 fatty acids increased LDL cholesterol [24].

Although eating large amounts of fish has not unequivocally been shown to reduce CVD risk in healthy men, consumption of 35 g or more of fish daily has been shown to reduce the risk of death from non-sudden myocardial infarction in the Chicago Western Electric Study [14], and as little as one serving of fish per week was associated with a significantly reduced risk of total cardiovascular mortality after 11 years in more than 20,000 USA male physicians [5].

4. Meat

Beef and lamb meat have been suffered from a negative health image related to the nature of their lipid fraction. Rumen lipid metabolism, through microbial hydrogenation, originates the presence of saturated lipids and trans-fatty acids in ruminant tissues [16]. Actually, scientific evidence has been accumulated that meat itself is not a risk factor for Western lifestyle diseases such as CVD, but rather the risk stems from the excessive fat and particularly saturated fat associated with the meat of modern domesticated animals. In fact, Mann [41] reported that diets high in lean red meat can actually lower plasma cholesterol, contribute significantly to tissue n-3 fatty acids and provide a good source of iron, zinc and vitamin B12. It was concluded that lean meat is a healthy and beneficial component of any well-balanced diet as long as it is fat trimmed and consumed as part of a varied diet.

Additionally, an anti-carcinogenic fatty acid known as conjugated linoleic acid (CLA) was first isolated from grilled beef in 1987 [23]. CLA refers to a mixture of positional and geometric isomers of linoleic acid (C18:2, n-6) in which the double bonds are conjugated instead of existing in the typical methylene interrupted configuration. Nine different isomers of CLA have been reported as occurring naturally in food. CLA is unique in that it is found in highest concentrations in fat from ruminant animals (e.g. beef, dairy and lamb). Beef fat contains 3.1 to 8.5 mg CLA/g with the 9-cis and 11-trans isomers contributing 57-85 % of the total CLA [36]. Interestingly, CLA increases in foods that are cooked and/or otherwise processed. This is significant in view of the fact that many mutagens and carcinogens have been identified in cooked meats.

Over the past decade, CLA has been shown to be effective in suppressing forestomach tumors in mice, aberrant colonic crypt foci in rats, and mammary carcinogenesis in rats [32]. In the mammary tumour model, CLA is an effective anti-carcinogen in the range of 0.1-1 % in the diet, which is higher than the estimated consumption of approximately 1 g CLA/person/day in the USA [25]. These results are not due

to displacement of linoleic acid in cells, suggesting that there may be unique mechanisms by which CLA modulates tumor development. Thus, there has been research designed to increase the CLA content in dairy cow milk through dietary modification of the cow regimen [34].

CLA isomers exhibit a protective effect also in atherosclerotic disease at a concentration similar to that found in food [11]. Studies are being carried out to assess the health protective effect of CLA in humans.

More recently, CLA has been investigated for its ability to change body composition, suggesting a role as a weight-reduction agent. Mice fed CLA-supplemented diets (0.5 %) exhibited 60 % lower body fat and 14 % increased lean body mass relative to controls [47], possibly by reducing fat deposition and increasing lipolysis in adipocytes.

5. Eggs

Eggs have not traditionally been regarded as a functional food, primarily due to concerns about their adverse effects on serum cholesterol levels. Furthermore, it is now known that there is little if any connection between dietary cholesterol and blood cholesterol levels and consuming up to one or more eggs per day does not adversely affect blood cholesterol levels [27]. Finally, eggs are an excellent dietary source of many essential (e.g. protein, sphingolipids, choline and n-3 PUFA) and non-essential (e.g. lutein/zeaxanthin) components which may promote optimal health. Thus, the egg will continue to play an important role in the changing face of functional foods [27].

The major food sources of sphingolipids, containing several mmol per kg of edible food, are eggs, dairy products and soybeans [56]. There is no known nutritional requirement for sphingolipids; nonetheless, they are hydrolyzed throughout the gastrointestinal tract to the same categories of metabolites (ceramides and sphingoid bases) that are used by cells to regulate growth, differentiation, apoptosis and other cellular functions. Studies with experimental animals have shown that feeding sphingolipids inhibits colon carcinogenesis, reduces serum LDL cholesterol and elevates HDL, suggesting that sphingolipids represent a functional constituent of food [56].

N-3 PUFA-enriched eggs can be produced by modifying hens diets [39]. Each one of these modified eggs contain about 350 mg of n-3 PUFA, relatively to the standard eggs that contain about 60 mg, and three of the enriched eggs provide approximately the same amount of n-3 PUFA as one meal with fish. When individuals are fed four n-3 PUFA-enriched eggs a day for four weeks, plasma total cholesterol levels and low-density lipoprotein cholesterol (LDL-C) do not increase significantly [52]. Plasma triglycerides are decreased by addition of n-3 PUFA-enriched eggs to the diet. N-3 PUFA may influence LDL particle size, causing a shift toward a less atherogenic particle. Blood platelet aggregation is significantly decreased in participants consuming n-3 PUFA-enriched eggs. Overall results of studies to date demonstrate positive effects and no negative effects from consumption of n-3-enriched eggs.

6. Animal foods

Several compounds widely diffused in animal foods have been suggested as possible physiologically active components. Among them, the conditionally-essential nutrients, also known as vitamin-like substances, L-carnitine, coenzyme Q10, α-lipoic acid, choline and taurine, are deserving an increasing attention.

L-carnitine, a betaine derivative of β-hydroxybutyrate, is synthesised almost exclusively in animal liver and exists in animal derived foods [48]. Skeletal muscles constitute the main reservoir of carnitine in the body and have a carnitine concentration at least 200 times higher than blood plasma. Carnitine has a fundamental biological role as a long-chain fatty acid carrier across the mitochondrial membrane and in ketone body formation. Several considerations suggest that carnitine is a truly essential nutrient in infancy and in other situations where the energy requirement is particularly high, e.g. pregnancy and breast feeding [22].

Carnitine and choline are putative ergogenic agents [33]. Choline supplementation reduces urinary carnitine excretion in humans [17]. Carnitine purportedly enhances lipid oxidation, increases VO2max, and decreases plasma lactate accumulation during exercise. Choline supplements have been advocated as a means of preventing the decline in acetylcholine production purported to occur during exercise; this decline may reduce the transmission of contraction-generating impulses across the skeletal muscle, an effect that could impair one’s ability to perform muscular work. Dietary supplementation with carnitine seems to have an immunomodulation effect in chickens [42] and, together with lipoic acid, seems also to delay ageing [4]. Further studies are required to better evaluate possible effects of oral supplementations of carnitine on energy metabolism, cardiac functions and physical performance at rest and during exercise, and to perhaps better characterise the conditions under which carnitine may be beneficial [57].

Coenzyme Q10, or ubiquinone, is a vitamin-like substance which plays a crucial role in the generation of cellular energy and in free radical scavenging in the human body [45, 28]. After the age of 35 to 40, the organism begins to lose its ability to synthesise coenzyme Q10 from food and its deficiency develops. Ageing, poor eating habits, stress and infection - they all affect our ability to provide adequate amounts of coenzyme Q10. Therefore, coenzyme Q10 supplementation may be very helpful for the organism [28]. Favourable cardiovascular effects have been reported with the use of conditionally-essential nutrients, coenzyme Q10, carnitine and taurine [35].

α-Lipoic acid, which plays an essential role in mitochondrial dehydrogenase reactions, has recently gained considerable attention as an antioxidant [46]. Lipopea, or its reduced form, dihydrolipopea, reacts with reactive oxygen species such as superoxide radicals, hydroxyl radicals, hypochlorous acid, peroxyl radicals and singlet oxygen. In addition to its antioxidant activities, dihydrolipopea may exert pro-oxidant actions through reduction of iron. Lipoic acid administration has been shown to be beneficial in a number of oxidative
stress models such as ischemia-reperfusion injury, diabetes, cataract formation, HIV activation, neurodegeneration and radiation injury [46]. Furthermore, lipoate can function as a redox regulator of proteins such as myoglobin, prolactin, thioredoxin and NF-kappa B transcription factor.

Choline is involved in methyl group metabolism and lipid transport and is a component of a number of important biological compounds including the membrane phospholipids lecithin, sphingomyelin and plasmanalog, the neurotransmitter acetylcholine, and the platelet activating factor [12]. Although a required nutrient for several animal species, choline is not currently designated as essential for humans. However, recent clinical studies show it to be essential for normal liver function. Additionally, a large body of evidence from the fields of molecular and cell biology shows that certain phospholipids play a critical role in generating second messengers for cell membrane signal transduction. These recent findings may be appropriate in the consideration of choline as an essential nutrient for humans [12].

7. Safety issues

Although increasing the availability of healthful foods, including functional foods, in the diet is critical to ensuring a healthier population [1], safety is a critical issue. The optimal levels of the majority of the biologically active components currently under investigation have yet to be determined. Thus, Paracelsus’ 15th century doctrine that “all substances are poisons ... the right dose differentiates a poison from a remedy” is even more pertinent today given the proclivity for dietary supplements. The benefits and risks to individuals and populations as a whole must be weighed carefully when considering the widespread use of physiologically active functional foods. Knowledge of toxicity of functional food components is crucial to decrease the risk/benefit ratio.

Table I summarises the putative physiologically active components of foods from animal sources and their suggested benefits for human health. CVD means cardiovascular diseases.

Table II. — Selected functional foods from animal sources with health claim submitted or approved by Food and Drug Administration (FDA), and their key components, potential health benefits and scientific evidence. Adapted from ADA (1999).

Conclusion

Increasing evidence supports the observation that foods from animal sources containing physiologically active components may enhance human health. These biologically active components include: calcium, probiotics, whey proteins and whey peptides, from dairy products; n-3 fatty acids, from fish; conjugated linoleic acid, from beef and lamb meat; sphingolipids, from eggs; and, the conditionally-essential nutrients L-carnitine, coenzyme Q10, α-lipoic acid, choline and taurine, widely diffused in animal products. However, the field of functional foods is in its infancy. Furthermore, a number of factors complicate the establishment of a strong scientific foundation. These factors include the complexity of the food substance, effects on the food, compensatory metabolic changes that may occur with dietary changes, and, lack of surrogate markers of disease development. Additional research is necessary to substantiate the potential health benefits of those foods for which the diet-health relationships are not sufficiently scientifically validated.

References
