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Risks and benefits of functional foods: an overview

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Abstract: A direct relationship between foods and health has led to various scientific studies to find out the significance of foods or food components on specific functions in the body. Studies have identified nutrition as a major modifiable determinant playing a role in health promotion and chronic diseases prevention. The term functional food refers to food with specific beneficial functions over their basic nutritional value. We reviewed the factors that have driven the functional food development, various definitions proposed by different authors and their classification. Moreover, we provided an an overview on various functional ingredients in different food sources along with their potential health benefits and risks of adverse effects associated with these products. Lots of research is required to substantiate the potential health benefits of those foods for which the diet–health relationships are not sufficiently validated, and create a strong scientific knowledge base for proper application of naturally present foods in combating various diseases and disorders.

Keywords: functional food, adverse effect, health benefits

1 Introduction

Food is a term which is basically related to the component necessary for several life sustaining functions like production of energy, supply of nutrients, support of various metabolic activities besides growth and maintenance of the body (Kaur and Das 2011). In the early 20th century, nutrition science was engrossed with preventing deficiencies and supporting body growth. In the last decade, studies have identified nutrition as a major modifiable determinant playing a role in maintenance of body and chronic diseases prevention (Yahfoufi et al. 2018). Nutrition concepts today are moving away from prevention to promotion of health and wellness, and due to increased education and awareness to consumers the link between diet and health (Sohaimy 2012). As such, this trend has created a demand for foods are called as functional foods which are traditional foods modified in such a way that they have health benefits compared to the non-modified products. They are prepared by manipulating the formulations or engineered genetically or by other conventional means to provide the desired function (Doyon and Labrecque 2008).
Functional foods are used to improve certain physiological functions, leading to the prevention of disease, reduction of risk factors, and to complement therapies. They provide additional benefits over their basic nutritional value, contributing to the prevention and reduction of risk factors for different diseases or boosting multiple physiological functions (Yahfoufi et al. 2018).

2 Definition of terms

According to Functional Food Center, functional food may be defined as natural or processed foods that contains known or unknown biologically active compounds; the foods, in defined, effective and non-toxic amounts, provide a clinically proven and documented health benefit for the prevention, management or treatment of chronic disease (Martirosyan and Singh 2015).
Thus, there is no statutory definition of functional foods, because foods consumed perform some functions in one way or the other. Though, a number of definitions have been given, the general opinion is that functional food is any healthy food similar in appearance to conventional foods, consumed as part of a usual diet, and claimed to have a physiological benefits like health-promoting or disease-preventing properties beyond the basic function of supplying nutrients (Gul et al. 2016). Common characteristics of functional food as follows: consumed as part of a normal food pattern, a capsule or any form of dietary supplement and a food that beneficially affects one or more target functions in the body beyond adequate nutritional effects in a way that is relevant to either an improved state of health and well-being and/or reduction of risk of disease (Howlett et al. 2008). Besides the above definitions, a number of different terms (Table 1) have come into perspective which sometimes are linked or interchanged with functional foods.
Thus, natural traditional products containing components influencing the health positively are strictly not functional foods, e.g., cranberry juice that influences the urinary tract infections positively is not a functional food when consumed as such. However, if the juice or its health contributing

ingredient in isolated form is added to another food to enhance health positively, the developed one is a functional food (Kaur and Das 2011).

There is a growing overlap between conventional food and food supplements, including energy bars and teas or liquids. This overlap becomes even wider when we consider functional foods and nutraceuticals. What could be considered a functional food under a given set of circumstances may be named a dietary supplement, medical food, food for special dietary use or nutraceutical under different circumstances, depending on its ingredients (active components) and claims (Santini et. al. 2018).

3.Health benefits

Functional foods and nutraceuticals are prepared by manipulating the formulations or engineered genetically or by other conventional means to provide the desired function. Understanding the requirement of food characteristics in tackling specific health problem(s), and contribution of specific food ingredients towards such benefit will definitely help in development of functional foods (Shadidi 2009). Table 2 categorizes such relationship between various functional ingredients with their beneficial role. Consequently, functional components have health-promoting roles at various stages of disease control that are associated with multiple progressive steps, from initiation to development. Thus, in a time when the role of a healthy diet in preventing non-communicable diseases is well accepted, the borderline between food and medicine is becoming very thin (Pravst 2012). As a result, they are claimed to provide a means to reduce the increasing cost on the health care system by a continuous preventive mechanism.

Table 1. Definition for food derived products
Functional Food (Diplock et al. 1999)
Product which is shown in a satisfactory manner that, in addition to adequate nutritional effects, induces beneficial effects on one or more target functions of the organism, significantly improving the health status and welfare or reducing the risk of disease.
Food Supplement (Novellino 2018)
Food product whose purpose is to supplement the normal diet and which consists of a concentrated source of nutrients or other substances with nutritional effects or physiological, single or in combination, marketed in dosed formulations, such as capsules, tablets, tablets or pills, designed to be taken in small individual quantities measured.
Medical food (Hardy 2000)
a food which is formulated to be consumed or administered etternally under the supervision of a physician and which is intended for the specific dietary management of a disease or condition for which distinctive nutritional requirements, based on recognized scientific principles, are established by medical evaluation.
Nutrecauticals (De Felice 1995)
Food or part of food that provides medical or health benefits, including the prevention and/or treatment of a disease.
Functional Ingredient (Kauer and Das 2011)
Functional ingredients are the standardized and characterized preparations, fractions or extracts containing bioactive compounds of varying purity, that are used as ingredients by manufacturers in the food.
FOSHU (Martirosyan and Singh 2015)
whole, fortified, enriched or enhanced that should be consumed regularly and at effective amounts in order to derive health benefits.
Prebiotic (Lockyer and Stanner 2019)
a substrate that is selectively utilized by host microorganisms conferring a health benefit.
Probiotic (Kang and Im 2015)
live microorganisms that when administered in adequate amounts provide health benefits to the host.
Colic food (Nocerino et al. 2015)
non-digestible carbohydrate, which provides nutrients for the microflora in the intestines and reaches the column in undigested form.
Phytochemicals (Murano 2003)
plant-derived, non-nutritive and biologically active chemicals that function in the body to prevent the onset of certain noncommunicable diseases.

Table 2 Some functional ingredients of food, their sources and potential benefits

Bioactive components	Source	Potential benefits
Carotenoids		
Alpha-carotene/beta-carotene	Carrots, Fruits, Vegetables	Neutralize free radicals which may cause damage to cells.
Lutein	Green vegetables	Reduce the risk of muscular degeneration.
Lycopene	Tomato products (ketchup, sauces)	Reduce the risk of prostate cancer.
Non-starchy polysaccharide		
Fucoidan (fucose)	Mushrooms (maitake and reshi),brown seaweeds	Immune modulation; apoptosis of cancer cells; stimulates brain development; anti-clotting effect; lower blood cholesterol levels; decrease high blood pressure, stabilize blood sugar.
Insoluble dietary fibre	Wheat bran	Reduces risk of breast or colon cancer.
Soluble dietary fibre (β-Glucans)	Oats, barley	Reduces risk of cardiovascular disease; protects against heart disease and some cancers; lower LDL and total cholesterol.
Soluble Fibre	Psyllium	Reduces risk of cardiovascular disease; protects against heart disease and some cancers; lower LDL and total cholesterol.
Fatty Acids		
Long chain omega-3 Fatty Acids-DHA/EPA	Salmon and other fish oils	Reduce risk of cardiovascular disease; improve mental and visual functions.
Conjugated Linoleic Acid (CLA)	Cheese, meat products	Improve body composition; decrease risk of certain cancers
Phenolics		
Anthocyanidins	Fruits	Neutralize free radicals; reduce risk of cancer.
Catechins	Tea	Neutralize free radicals; reduce risk of cancer.
Flavonones	Citrus	Neutralize free radicals; reduce risk of cancer.
Flavones	Fruits/vegetables	Neutralize free radicals; reduce risk of cancer.
Lignans	Flax, rye, vegetables	Prevention of cancer; renal failure.
Tannins (proanthocyanidines)	Cranberries, cranberry products, cocoa, chocolate	Improve urinary tract health; Reduce risk of cardiovascular disease.
Plant Sterols	Corn, soy, wheat, wood oils	Lower blood cholesterol levels by inhibiting cholesterol absorption.
Stanol ester		
Prebiotics and Probiotics		
Fructo-oligosaccharides (FOS);	Jerusalem artichokes, shallots, onion powder,	Improve quality of intestinal microflora; gastrointestinal health
Lactobacillus;		
Biofidobacterium	Yogurt, other dairy products	Improve quality of intestinal microflora; gastrointestinal health.
Soy Phytoestrogens		
Isoflavones: Daidzein, Genistein	Soybeans and soy-based foods	Menopause symptoms such as hot flashes; protection against heart disease and some cancers; lowering of LDL and total cholesterol.

(Shahidi 2009; , Ferrari 2007; Gry et al. 2007; Plaza, Cifuentes and Ibàñez 2008; Patil et al. 2009; Abuajah et al. 2015)

4.Risks of functional foods

The most important factor in the involvement of functional foods in the diet is a lack of studies on possible mechanisms of action and a lack of in vivo research confirming the claimed beneficial health effects on specific pathological conditions (Santini et al. 2018). Another key aspect is related to the data reported in the literature, which mainly comes from in vitro studies focused on single food constituents (micronutrients); these studies are based on the assumption that micronutrients can be considered safe (or generally recognized as so) because they are derived from commonly used food or food components (Pinto da Costa 2017; Gupta 2016). The use of materials as a food additives can be advantageous in several aspects: their natural origin, health protecting properties, possibility for combination of beneficial physiological properties and the recognition and exploitation of synergistic properties can be used in the production of functional food products. Nevertheless, the ingredients themselves may cause health problems, and proper information on possible unwanted side effects should be provided on the label. The development and commercialisation of novel functional compounds must be pursued to improve the functionality and safety of foods. Moreover, much more work have to be done based on clinical studies rather than only in vitro studies and bioavailability of these products (Santini et al. 2018). Thus, the application of this knowledge might eventually be made food processing to enhance for certain components if, and only if, efficacy and lack of harm are already well established.

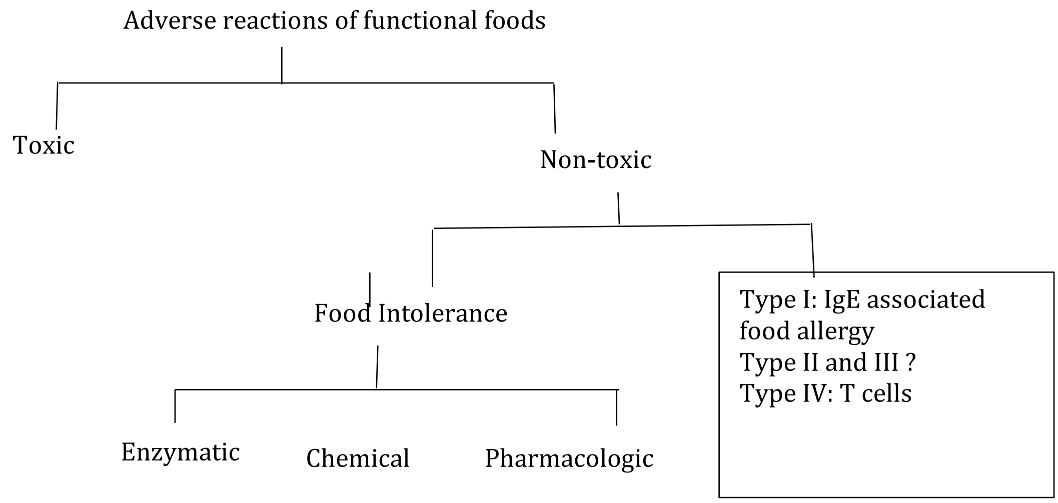
Claims about the nutritional or health benefits of foods can provide information to help consumers adopt a healthy diet (Roberto and Khandpu 2014). Concomitantly, an improved appreciation of the potential beneficial or adverse effects of nutrients and other components in the diet has led to the realization that it is possible to create food items with specific characteristics that are capable of influencing body function over and above meeting the basic nutrition needs. By the way, a direct measurement of the effect a food has on health and well-being and/or reduction of disease risk is often not possible. This may be because the endpoint (the state of health and well-being) does not always lend itself to quantifiable measurement (Keservani et al. 2011). Also, in the case of a disease like cancer, the time frame for development of the disease is very long or it would be unethical to monitor its development under the conditions of a controlled study. Instead, functional food science works from knowledge of the key processes in the attainment of optimal health or in the development of a disease to identify markers that can be used to monitor how those key processes are influenced by foods or food components. Provided that the role of those key processes in the attainment of optimal health or disease development is well established and the markers are chosen accurately to reflect the process, it is possible to study the effect of consuming the food on the final endpoint (the improved state of health or reduction of disease risk) by measurement of the markers (Gallagher et al. 2011). The markers could be chosen to reflect either some key biological function (markers of a target function) or a key stage in development that is unequivocally linked to the endpoint under study, in which case they serve as markers of an intermediate endpoint. Measurements made in the short term on carefully chosen markers of intermediate endpoints can be used to make inferences about effects on final endpoints that would only otherwise be accessible through long-term study. Where the underlying target functions or intermediate endpoints are unequivocally linked to the risk of disease, the markers are also referred to as risk factors for the disease (Howlett et al. 2008).

All foods can cause adverse reactions. The adverse reactions to functional foods are classified in the same way as adverse reactions to conventional foods (Figure 1). By the way, functional foods are biologically active and therefore may cause different effects in the ranges that can vary from the therapeutic effect to the toxic effect depending on the levels. The reactions may occur to the food or to added or enhanced ingredients. Reactions to added ingredients can be toxic or non-toxic. Toxic reactions include carcinogenicity. Non-toxic adverse reactions to foods can be due either to intolerance or allergy (Ameratunga et al. 2016).

Toxic reactions usually occur in products that contain carcinogenic substances or added ingredients at higher doses. Irwin et al. (1996) have observed di acyl glycerol based fatty acids. The response observed in that study was indicative of the carcinogenic potential of glycidol.

Pharmacologically unfavorable reactions may occur when consumed in excess of the recommended amounts for some substances. There is concern that the consumption of large amounts of fish oil may increase the risk of hemorrhage (Komaroff, 2009). Of ore concern have been reports of chronic toxicity to vitamin D supplements. Consumers may be at risk of life threatening hypercalcemia if they consume food supplements with high concentrations of vitamin D (Lowe et al. 2011; Kaptein 2010). It has been seen that many adverse effects such as headache, vomiting, abnormalities in the bones, damage to the liver occur in high doses of vitamin-carotene or vitamin A, which is one of the functional food components with positive effects on health. Moreover, despite its known antioxidant capabilities, ascorbic acid supplements, by themselves, are not consistently associated with decreased oxidative damage. It may be that the water soluble nature of this antioxidant limits its ability to protect against free radicals in lipophilic compartments. Therefore, we may be more likely to observe benefits when this antioxidant is combined with lipid soluble antioxidants such as vitamin E (Wildman and Kelle 2001).

Figure 1. Classification of adverse reaction of functional foods (Valenta et al. 2015)



In the case of functional foods, effects of each component were related to the concentration as well as synergistic or antagonistic effect of some molecules. Many studies have shown that high genistein levels, soy phytoestrogen, were observed to promote certain tumor types in animals. This is contrary to popular opinion on the health benefits of genistein and needs (Marcelo et al. 2019; Nakamura et al. 2011; Kwack et al. 2009). Morever, Xia et al. (2010) has investigated the potential toxicity of some polyphenols from grape, such as epicatechin to the fibroblast, and keratinocyte cell lines. Noticeable DNA damage was observed in mice spleen cells by incubating with higher concentration (150 μmol/L) of catechin.

According to the guidelines of FAO/WHO (2002),"Probiotics are live microorganisms when administered in adequate amounts confer a health benefit to the host such as maintaining bowel mobility, improving the immune system, reducing serum cholesterol levels, and preventing various types of cancers. Nevertheless, patients with suppressed immune systems should avoid them to prevent various infections, although, they have been used safely for years (Suez et al. 2019). Furthermore, prebiotics can potentially serve as functional food ingredients to improve or maintain gut health. They can increase the population of beneficial gut microbiota while suppressing the harmful ones thus help to develop immunologic structures of the intestinal mucos resulting in an improvement in enteric inflammatory disorders and the systemic immune response (Mundi et al. 2017; Johnson et al. 2015). However, inulin, a prebiotic, has been linked to anaphylaxis in at least one reported study (Franck et al. 2005). The safety of probiotics or prebiotics is still among the subjects that science continues to investigate. More information is needed, in particular, on how safe they are for young children, elderly people, and people at risk.

Nutrient hypersensitivity refers to any reaction of the organism to any component of the nutrients including allergy and intolerance. Food allergy is a special form of food hypersensitivity that activates the immune system, an exaggerated response (Valenta et al. 2015). Immunological reaction is a reaction against foreign substances entering the body. Allergen is a protein that is usually contained in nutrients, which triggers the immunological reaction of its release in its antibodies (De Silva et al. 2014). There are 4 major types of allergic reactions based on pathogenesis mechanisms. The most common forms of immune-mediated adverse reactions to foods (type I reactions) always are characterized by the development of IgE against food allergens. It can be accompanied by inflammation, induced by cellular components, and mediated by T cells and eosinophils. Patients with IgE-associated food allergy can be identified based on the detection of food allergen–specific IgE in serum and body fluids, and by measuring IgE-mediated cellular and in vivo responses. Milk, eggs, wheat, peanuts, nuts, sesame, fish, fruits, and vegetables are common inducers of IgE-associated food allergy (Longo et al. 2013).

Similarly, the addition of fish proteins to experimental ice creams was described in Iceland (Shaviklo 2011). Persons allergic to fish are at risk of severe reactions to these products. Ice creams have previously not contained fish proteins and fish allergic consumers may be at risk if they inadvertently consume such products. The health promoting effects of kiwifruit have been described (Stonehouse 2013) as causing severe allergic reactions in some consumers. Moreover, there is no solid experimental evidence to support the adverse reactions via type II or type III hypersensitivity reactions to food allergies that develop in patients .

Type IV hypersensitivity, which mainly involves food antigen–specific T-cell responses and can damage the gut mucosa, is associated with disorders such as celiac disease.

Celiac disease is characterized by a hypersensitivity reaction against the wheat gluten fraction comprising alcohol soluble gliadins and acid-, alkali-soluble glutenins, accompanied by an autoimmune component (Schuppan et al. 2009). Type IV hypersensitivity reactions also might be involved in food protein–induced enterocolitis. Studies have shown that certain food proteins can induce inflammation via direct activation of the innate immune system (Junker et al., 2012). For example, wheat amylase trypsin inhibitors and certain milk oligosaccharides can cause intestinal inflammation via activation of Toll-like receptor 4 and certain allergens have been shown to stimulate the innate immune system. Innate immune mechanisms might mediate nonceliac gluten sensitivity (Catassi et al. 2012).

Food intolerance, also known as non-allergic food hypersensitivity, refers to difficulty in digesting certain foods. There are different types of food intolerances, including enzymatic, chemical and pharmacologic reactions (Losurdo et al. 2018). Pharmacological intolerances involve reactions to certain naturally occurring substances in foods such as vaso active amines - of which histamine is one example, salicylates - substances chemically similar to aspirin found in a wide variety of plant foods, and caffeine or theobromine - found in chocolate. Non-coeliac gluten intolerance and fructose intolerance are also recently recognised conditions which can cause symptoms such as abdominal disturbance (usually bloating but sometimes other symptoms as well) and occasionally malaise and tiredness (Akoğlu and Oruç 2018).

The most common type of enzymatic food intolerance is lactose intolerance, which occurs because these individuals have either too little or no lactase – the enzyme which helps to digest milk sugar lactose (Akoğlu and Oruç 2018).

Another rare and important enzymatic food intolerance type is Phenylketonuria (PKU). PKU, is a genetically inherited birth defect that causes an unwanted buildup of the amino acid phenylalanine in the blood. This buildup occurs because the enzyme that routinely converts one amino acid, phenylalanine, to another amino acid, tyrosine, is absent or deficient. Phenylalanine then accumulates in the blood and is toxic to brain tissue (Schuck et al. 2015).

Chemical intolerances are intolerances to such food additives. The additives most commonly linked to food intolerance are artificial colours, eg tartrazine and preservatives such as sulphites and benzoates. Sulphites have to be declared on all packaged products under the NSW Food Act 2003 (Franck et al. 2005). They are preservatives and are commonly found in wine and dried fruit. Sulphite reactions cause asthma, rashes, irritable bowel syndrome and headaches in sensitive people. Monosodium glutamates (MSG) also occur naturally in such foods as camembert cheese, Parmesan cheese, tomatoes, soy sauce and mushrooms. MSG stimulates nerve endings, perhaps accounting for its function as a flavour enhancer when it is added to food. Many people find digesting certain foods difficult, or that certain foods will make an existing condition – such as irritable bowel syndrome (IBS) - worse. (Losurdo et al. 2018).

There are many other adverse reactions to foods, apart from allergy and intolerance, including: • Feeling unwell after eating from other causes such as heartburn after a fatty or spicy meal or a hangover after too much red wine. • Food aversion is a condition where a person not only dislikes a food, but also experiences unpleasant physical symptoms when they see or smell the food. Symptoms are triggered by emotions associated with food rather than the food itself. This does not usually occur if the food is disguised. • Underlying anxiety can result in unconscious over-breathing or hyperventilation. The symptoms that result (dizziness, tight chest, blurred vision or numbness) can be very distressing, and can sometimes resemble food allergy (Lyra et al. 2013).

5.Conclusion

Global demand for functional foods is expanding dramatically because of technological innovations, development of new products (Granato et al., 2010a) coupled with increasing consumer's consciousness about health (Szakaly et al. 2012) and demand for healthy foods (Bigliardi and Galati 2013). Functional food products resemble conventional food in terms of appearance but are composed of bioactive compounds that may offer physiological health benefits beyond nutritive functions (Arora et al. 2013).

Over the last few decades, tremendous increase in the demand of functional foods have evoked the food processing industries to develop novel methods for maintaining the nutritional quality and functional characteristics of food (Das et al. 2012). Of the various issues being faced by the mankind, diet linked diseases are among the most significant one and need serious efforts to pull up the danger of these physiological maladies. Keeping in view the present conditions, novel health strategies have been devised aimed at highlighting the positive aspects of such healthy diet (Ahmed and Rashid 2019).

This concept has been proposed as a modern approach to food science, and the area of possible use has been defined as beyond the diet, but before the drugs. The potential functions of nutraceutical/functional food ingredients are so often related to the maintenance or improvement of health that it is necessary to distinguish between a food ingredient that has function and a drug. However, because of the complex matrices, the lack of validated analytical methods and the limited availability of reference compounds, the analysis of raw material and finished products may pose a challenge. Thus, current information in this regard is insufficient and hazy. Consequently, there is a need to provide consumers with more information to effectively guide them in making wider choices of diets that contain optimal levels of health-promoting functional food components (Sohaimy 2012).

Success of functional food is influenced by a number of factors like 1) focus on general wellbeing, 2) health benefit for common complaint, 3) mass distribution and market positioning, 4) effective communication of health benefit, 5) extension of existing brand/food company, and 6) focus on taste, convenience, and appropriate pricing. A successful functional food along with its health benefits must be competitive in all these arenas (Martirosyan & Singh, 2015). The consumers need to be better informed with active ingredient in food products and its health benefits addressing general wellbeing issues (Kaur and das, 2011).). Thus, this exercise may require: (i) appropriate target identification; (ii) safety assessment; (iii) a clear understanding of the mechanism of action; (iv) efficacy assessment substantiated by clinical studies; (v) an evaluation of possible unwanted side effects; and (vi) an evaluation of possible interactions with other products (e.g. food, food supplements and drugs (Santini et. al. 2018).

As a result, one of the most important issues is the lack of deceiving consumers by presenting functional foods as miraculous foods. Due to the a wealth of information in the field of functional foods and their impact on human health, additional efforts of governments and diverse organisms related with human health are necessary in order to highlight the benefits and risks of these food types. Likewise, further investigation is required to understand the mechanisms associated with several biochemical and physiological processes induced by functional foods. Manufacturers and regulatory authorities will need to agree on optimal methods for assessing the quantity and quality of health promoting ingredients in functional foods.

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