Functional Foods, Nutraceuticals, and Degenerative Disease Prevention
1.1 CHRONIC DEGENERATIVE DISEASES IN MODERN SOCIETY: IMPLICATIONS ON LIFE QUALITY, PRODUCTIVITY, ECONOMIC BURDEN

The diet of early humans was quite varied and reflected an omnivorous food habit. Being hunter-gatherers, humans used the fruits, vegetables, and tubers that grew wild. It has been proposed that Paleolithic humans used fruits and vegetables as a major source of food (Eaton et al., 1997). A transition from food gathering into organized agriculture may have further diversified the diet. Recognition of the healing properties of foods and plants may have been discovered accidentally; it has been transferred from generation to generation. In the literature of many ancient cultures, there is recognition of the healthy aspects of fruit and vegetable consumption. The ancient texts of the Ayurveda refer to the medicinal and healing properties of several fruits, vegetables, herbs, and spices, which were also used for food purposes. Fruits such as apples, dates, pomegranates, and grapes, prevalent in the Mediterranean, were frequently mentioned in the Biblical literature. These fruits were associated with eternal life in ancient Egyptian and Sumerian culture.

1.1.1 Diet and lifestyle changes: the missing foods

We have observed tremendous changes in the food habits of humans in the past few hundred years; changes that have been even more dramatic in the post-World War II era. The search for a sea route to the spice-growing areas of the East and the subsequent discovery of continents and new forms of edible fruits and vegetables not only enhanced the food variety but also led to the transoceanic migration of several food crops (e.g., the introduction of tomato and potato to Europe and other parts of the world where these were traditionally not grown). However, geopolitical diversities, modern science, and economic changes all resulted in the development of new social food habits. Continued changes in the processing technologies to meet consumer preferences and lifestyle changes have caused the present state of increased caloric intake, sedentary habits, overconsumption of high energy foods...
due to increased portion sizes, and low intake of functional foods, resulting in a significant increase in the prevalence of several chronic degenerative diseases, such as type 2 diabetes, cardiovascular diseases, neurodegenerative diseases, and inflammatory diseases.

1.1.2 Social and economic burden of chronic degenerative diseases

“Metabolic syndrome” refers to an aggregate of several physiological conditions that are indicators of the potential for future development of type 2 diabetes, cardiovascular diseases, and associated health problems. In general, obesity is an initial indication of the development of several other abnormalities such as hypertension and insulin resistance, further magnifying the complications. Thus, coronary heart disease (CHD), obesity, and type 2 diabetes have reached epidemic proportions around the world, and are the leading causes of the loss of living quality and productivity, as well as the high mortality rate in developed and developing countries (Bisbal et al., 2010). Recent estimations indicate that cardiovascular diseases, diabetes, obesity, cancer, and respiratory conditions account for 59% of the 56.5 million deaths annually (Jaganath, 2008).

Across the world, more than 220 million people have been estimated to be affected by diabetes (WHO Fact Sheet, 2011), and among these, type 2 diabetic incidences exceed 90% of the diagnosed cases. A recent report suggests that diabetic cases in the North American and Caribbean region have reached 37.4 million (International Diabetes Federation, 2010). Additionally, type 2 diabetes has been increasing among children in epidemic proportions (Kaufman, 2002). In North America, the occurrence of type 2 diabetes is more prevalent in African-American, Mexican-American, Native-American, and Asian-American children and young adults. However, the increase in obesity-linked diabetes is not limited to North America; it also occurs in affluent regions of other parts of the world, especially in economically emerging regions of Asia. Across the world, cases of type 2 diabetes are increasing rapidly, and such a rapid increase in a short period of time suggests the influence of environment, diet, and lifestyle risk factors in increases of type 2 diabetes. Genetic changes are unlikely to be predominant causative factors for a rapid increase in diabetes, but inherent genetic susceptibility can enhance the chances of its development. Type 2 diabetes is associated with obesity, and the number of people suffering from type 2 diabetes is predicted to rise to more than 350 million by 2030 (WHO/FAO, 2003).

Chronic degenerative diseases in general result in significant losses to society and the economy, in terms of lost productivity, increase in human suffering, and loss of living quality. In addition, the cumulative effects of the diseases create a heavy burden on the health-care system. The health-care costs and economic burden due to various types of cancer in the United States have been estimated to be in billions of dollars (Yabroff et al., 2007; healthservices.cancer.gov). Annual estimates of new cancer cases in the United States are estimated at over 1.5 million, with mortality close to half a million. According to the National Cancer Institute (“The Cost of Cancer”), the direct cost of cancer care was estimated at $104 billion and the indirect cost in terms of lost productivity and economic loss was estimated at $134 billion in 2006.

Diabetes is another disease whose costs weigh heavily on the health-care system. Diabetes can cause both microvascular (retinopathy, nephropathy, and neuropathy) as well as macrovascular (heart attacks, stroke, and peripheral vascular disease) complications.
Type 2 diabetes is the leading cause of blindness and end-stage renal failure in the United States (Klein, 1995). The risk of heart disease and stroke are two to four times more frequent in patients with diabetes; 50% of people with diabetes die due to cardiovascular disease. Diabetes, along with cardiovascular disease, has a significant socioeconomic impact on individuals, families, health systems, and countries. Recent estimates (Dall et al., 2010) suggest that economic burden from prediabetes and diabetes reached $218 billion in the United States in 2007, while the estimates in Canada were close to US$2 billion. The World Health Organization reported that between 2006 and 2015, China will lose US$558 billion in foregone national income due to heart disease, stroke, and diabetes alone. Type 2 diabetes and cardiovascular disease have genetic causes, but other factors such as obesity, physical activity, and food intake have been shown to influence the pathophysiology of both diseases significantly (Fitzgerald and Parekh, 2009). Thus, by adopting healthy living habits and reducing the development of chronic diseases, significant reductions in health-care costs can be achieved, with several indirect social and economic impacts.

1.2 HEALTH REGULATORY PROPERTIES OF FOODS: “PREVENTION IS BETTER THAN CURE”

Dietary patterns vary across the world, according to traditionally based, locally available food. However, increased globalization and changes in lifestyle habits have resulted in variations from traditional patterns, leading to an increased prevalence of chronic degenerative disease (Kris-Etherton et al., 2002). Daily intake of refined processed foods with a high glycemic index has been linked to increased risk of obesity, type 2 diabetes, and cardiovascular disease. Pancreatic β-cell dysfunction, dyslipidemia, and endothelial dysfunction are related to these problem diets (Törönen et al., 2010). Abnormal glucose homeostasis can result in a multi-symptom disorder of energy homeostasis that includes obesity, hyperglycemia, impaired glucose tolerance, hypertension, and dyslipidemia (Burton-Freeman, 2010; Hanhineva et al., 2010).

Several “healthy spots” have been recognized in the world. People living in these areas have characteristic diets and consume foods that may be primarily responsible for their health and longevity. Food habits in the Mediterranean region, Okinawa island (Suzuki et al.), and other regions in Asia lead to some general associations. Overeating, in comparison with eating only what is sufficient, is a factor that tends to promote health abnormalities. Mediterranean food is rich in fiber, fish, and polyphenols (red wine), with a reduced amount of red meat intake compared with the typical North American diet. This has been associated with reduced incidences of cardiovascular diseases (the so-called French paradox). Increased longevity among Okinawan people has been associated with consumption of fish and vegetables such as bitter melon and a range of legumes. Consumption of spices such as turmeric and cumin in the Indian diet has been associated with reduced incidence of cancers. Above all, an active and stress-free life is a key factor that determines the longevity and health of one’s life. The major characteristic of the Mediterranean diet to protect against diabetes includes a high intake of fiber, high intake of vegetable fat (in the form of monounsaturated fatty acids such as in olive oil), a low intake of trans fatty acids, and a moderate intake of alcohol (Martinez-Gonzalez et al., 2008). Details on several dietary patterns are available from several government sources.
1.2.1 Fruit and vegetable consumption and disease prevention

Fruits and vegetables are rich sources of a wide range of vital micronutrients, vitamins (provitamin A carotenoids, vitamin C, and folate), phytochemicals (non-provitamin A carotenoids and polyphenols), and fiber (Amiot and Lairon, 2010; Chapter 2). These components with a wide range of chemical structures and functionality provide different beneficial effects beyond simple nutrition, resulting in improved health. In general, fruits and vegetables are generally low-energy foods because of a high proportion of nondigestible carbohydrate polymers such as cellulose and pectin and lower levels of proteins and lipids. Thus, fruits and vegetables supplement the high-energy foods in diet and can be seen to provide a balance in the transit of food through the gastrointestinal tract (GIT), as well as to aid digestion and subsequent action by the gut microflora in the large intestine. The influence of fruit and vegetable components (prebiotics) in intestinal health, through viscosity modification of foods during their transition through the GIT, immunity modulation, prevention of inflammation, and maintenance of an ideal population of microflora (probiotics) is continuously being unraveled. Thus, secondary plant products such as carotenoids, polyphenols, sulforaphanes, indoles, and essential oils, in conjunction with a milieu of polymeric substances from fruits and vegetables, enhance the healthfulness of foods (Chapter 2). Nutritional recommendations in the majority of developed countries encourage increased consumption of fruits and vegetables (National Academy of Sciences, United States; Health Canada). Extensive campaigns to achieve this target (five-a-day or more) are reported to be successful in many areas, but consumption of fruits and vegetables is still below the recommended level in many countries. The influence of increased fruit and vegetable consumption and decreased incidences of several forms of cancer has been highlighted in several epidemiological studies (e.g., Steinmetz and Potter, 1991; Chapters 5, 6, 8, 11). An intake of fresh fruit and vegetables in an adequate quantity (400–500 g/day) is recommended to reduce the risk of cardiovascular disease, stroke, and high blood pressure (Jaganath, 2008). In the United Kingdom, for optimum health, it is advised to consume five portions of fruit and vegetables (each comprising at least 80 g) on a daily basis (Williams, 1995).

Plant-based foods have been utilized for therapeutic purposes since ancient times and are still being extensively used today. The Ayurvedic system in India has used medicinal plants, herbs, and foods for preventing the development of diseases and also as a means of healing (nccam.nih.gov/health/ayurveda/D287_BKG.pdf; www.ayurvedahealth.org/symposium09.pdf). Ayurveda has approached disease prevention and cure in a holistic manner, and when the root causes of many diseases involve abnormal functioning of the body at multiple levels, targeting these with various types of ingredients is only logical. The mechanistic aspects of the action of several components of fruits and vegetables have been revealed through several studies, and new aspects are still being discovered. A fundamental property of several functional food ingredients, specifically those from fruits and vegetables, is that they are very strong antioxidants, and are sometimes as efficient as vitamins C and E. The conjugated structures of these components can accept unpaired electrons and form a stable structure and gradually detoxify these through the enzymatic antioxidant system. Although the beneficial properties of functional food components have been joined to their antioxidant properties, this is only partly true. Apart from being strong antioxidants, these components are able to modulate biochemical pathways within the cell, especially when some of these pathways are overactive, such as in the case of cancer. Inhibition of calcium-calmodulin-mediated biochemical reactions by polyphenols and inhibition of cyclooxygenase by curcumin (active ingredient in turmeric) are examples of
specific inhibition of enzymes. Still at another level, functional food ingredients can influence gene expression. Several genes that are upregulated during inflammation and cancer development, such as tumor necrosis factor alpha, interleukins, protein kinase C, cyclins, and cyclin-dependent kinases, are downregulated by functional food ingredients. Phenolic compounds are also strong inhibitors of carbohydrate-digesting enzymes such as α-amylase and α-glucosidase and can function in hyperglycemia management linked to type 2 diabetes (Chapters 13 and 14). Therefore, natural forms of α-amylase and α-glucosidase inhibitors from plant-based foods provide dietary strategies to control postprandial hyperglycemia, and could be used in therapies with minimal side effects (Da Silva et al., 2010). Thus, several functional food components are able to provide multilevel protection to the body from abnormalities.

In addition to understanding the mechanisms behind the health beneficial properties of functional food components, there are several aspects that need to be understood. Most of the studies demonstrating health beneficial properties of these components were conducted using in vitro systems, and the observations were generally extended to whole body situations. In most of these studies, unusually high levels of components were tested, which appear to be unrealistic when the bioavailability of these components is taken into consideration. The absorption of polyphenols is very low, in the range of 0.1% to less than 1%, leading to plasma levels of around 1 μM or less. Therefore, even if one consumes large amounts of polyphenol-containing foods, the plasma level of the ingredients could be low. At present, it is not clear if this is a defense mechanism to prevent excessive absorption of these compounds. Considering the evolutionary significance of this mechanism, this may be protective. The interesting aspect is that even at the low levels absorbed, these components are active as antioxidants, modulate second messenger systems and biochemical pathways and, above all, modulate gene expression. In several in vitro studies, polyphenols were selectively able to kill cancer cells without affecting the growth and proliferation of normal cells at 1–2 μM levels, at which concentration these show antioxidant activity and modulation of biochemical pathways. Thus, it is likely that through constant consumption of adequate amounts of functional foods, a threshold concentration of functional food components could be built up within the body at a protective level. If cancer cells originate through mutation, these cells are likely to be killed at the level of functional food components present within the body through consistent consumption within a balanced diet. And this may be the protective mechanism that gets translated into disease prevention. Consumption of functional foods that can contain several grams of polyphenols does not appear to cause any problems as seen in many culture-specific food systems, and achieving a few micromolar levels of these ingredients appears achievable.

Another important aspect of consuming functional foods is that, whether all the ingredients are absorbed or not, the foods containing these ingredients are in contact with the inside cell layers of the GIT, which is a primary site of immune response and initiation of several abnormalities, including inflammation. Protecting these cells is as important as protecting the internal cells of the body. The internal cell layers of the GIT are the primary site of exposure to several food and nonfood chemicals, some of which may even be harmful. In some way, functional food components may have a protective role during the transition of foods through the GIT. In addition, once these reach the intestine, a beneficial microflora can digest and positively modulate the food matrix, releasing several bound functional food components that can get absorbed and enter into the circulation. The large intestine is thus a site with an increased potential to develop several abnormalities, and adequate levels of functional food consumption may have a role in preventing these
abnormalities (e.g., inflammation, ulcerative colitis). Future research will provide answers to these questions.

This book provides a consolidated approach to provide evidence for the importance of functional foods in the diet. At present, there is much debate regarding the relation of diet and health. Even though the importance of functional foods is highlighted in the media, the public is exposed to conflicting messages on food consumption. It is interesting to note that several multinational food companies are using functional food ingredients at increasing levels in some popular foods. It is likely that certain types of food will be classified as potential threats to health, as even legislative bodies are moving forward to deter the consumption of foods with high levels of sugar and fat among children as a measure to prevent childhood obesity. Such pressures will increase as the cost of health care increases, and are even projected to reach 50% of the government budget, leaving little for other areas of necessity. Thus, the importance of functional foods and healthy living habits will come to the forefront of a positive social change across the world.

REFERENCES


