17 Human Nutrition, Phytonutrients, Nutraceuticals and Horticulture

Plants are good for you. They contribute immensely to our mental well-being. Simply looking at a plant or a well-groomed landscape brings pleasure to anyone. The beauty surrounding us that is supplied by plants is amazing and is something we often take for granted. For those who are less than confident about their abilities or usefulness in this world, self-contentment from accomplishments derived from growing even a single plant from seed empowers individuals to believe in themselves again.

Plants keep us alive. Whether it is corn growing in Iowa or algae growing in the Sargasso Sea, plants generate the oxygen we breathe. Not only do they generate the oxygen we breathe, they provide us with all of our basic nutritional requirements for protein, fat, carbohydrate, fiber, vitamins, and minerals. Vegetarians and carnivores alike ultimately derive their nutrition from the same basic source: plants.

Over the last several decades, the study of nutraceuticals and phytonutrients has exploded as patients and doctors worldwide focus on the major key to good health: you are only as healthy as the food you eat. Many substances are found in plants that are important for protecting our bodies from stress, ageing, and disease. While many cultures have embraced this idea for centuries, much of the world is just beginning to grasp the concept.

This chapter will explore the contributions that plants make to our basic health and nutrition. A review of basic nutrition will be followed by a review of some of the latest work in the areas of phytonutrients and nutraceuticals. They are becoming increasingly importance as both preventive and therapeutic options in addressing human health.

All information presented in this chapter is for educational purposes only. No recommendations are endorsed or implied by the material presented herein. Please discuss your situation and any planned changes to your diet with a health care provider before embarking on any new diet plan.

Basic Nutrition

Basic human nutrition centers on a well-balanced diet that provides carbohydrates, protein, fat, fiber, vitamins, and minerals at levels that promote optimum health (Fig. 17.1). There is an overwhelming amount of literature available on the subject and just what balance of these key nutrients is appropriate remains a subject of great controversy. Even the recent guidelines jointly published by the USDA and US Department of Health and Human Services (2010) are subject to intense scrutiny (Hite *et al.*, 2010). Even though there are many opinions as to what constitutes an appropriate balance of nutrients for a particular definition of optimum health, some source must be used as a base reference. To that end, the 2010 recommendations of the USDA and US Department of Health and Human Services will serve as the basis for this discussion. What follows is a presentation of the most recent opinions of experts in the fields of nutrition and human health. What is best for you is your decision.

Their general recommendations can be summarized as follows:

1. Maintain an age and gender appropriate weight by balancing caloric intake and physical activity.
2. Reduce obesity by reducing caloric intake and increasing physical activity.
3. Limit sodium intake to 1500 mg/day.
4. Limit total daily caloric intake from saturated fatty acids to less than 10%/day.
5. Limit cholesterol consumption to less than 300 mg/day.
6. Avoid *trans* fats.
7. Avoid refined and processed foods.
8. Eat nutrient-dense foods such as dark-green, red and orange vegetables, whole grains, beans and peas, fruit, unsalted nuts and seeds, with small amounts of low or no fat dairy products, lean meat, poultry, and seafood.

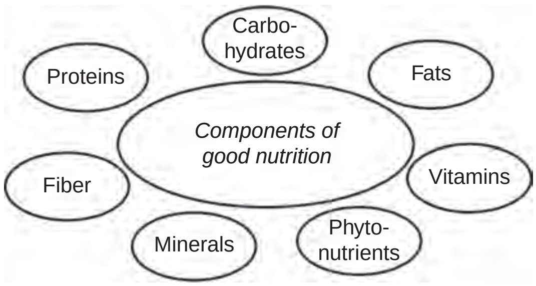

Fig. 17.1. The major components of good nutrition.

A major area of debate in nutrition literature surrounds the balance of carbohydrates, fats, and proteins in the diet that should be maintained for good health. The reader is left to investigate this aspect of nutrition and human health on their own.

Carbohydrates

The first major product of photosynthesis is a carbohydrate, glyceraldehyde 3-phosphate. From this compound, plants are able to synthesize a vast array of molecules in which the solar energy captured during photosynthesis can be stored for later use by the plant or used by another organism when it eats the plant. When humans consume plant-based foods, a major percentage of the energy derived from that food comes from carbohydrates. There are some exceptions where much of the stored energy is in the form of fat (avocado) or protein (soybeans).

Plant-based diets contain a myriad of distinct carbohydrates that impact human health differently (Englyst and Hudson, 1996). Categorization of carbohydrates occurs on three levels. The first is based on atomic composition and chemical bonds which distinguishes carbohydrates from fats, proteins, etc. The second level takes into account molecular configurations, chemical bonds, and physical properties. A third level addresses the nutritional properties and physiological responses to each species (Englyst and Hudson, 1996). The main nutritional properties of carbohydrates include whether or not they are hydrolyzed and absorbed in the small intestine and the relative glycemic response humans have to it. The glycemic index (GI) is a numeric scale from 1 to 100 that indicates how particular food impacts blood glucose levels (Porter, 2010). Foods with a low GI cause a slight to moderate rise in blood glucose soon after consumption while foods with a high GI cause a large and rapid rise in blood glucose levels that may be harmful for certain individuals, especially those with diabetes. A diet containing a large portion of carbohydrates with high GIs is generally considered unhealthy. Another aspect of carbohydrate impact on health is the negative effect high carbohydrate diets can have on blood triglyceride profiles and cardiovascular health risks (Acheson, 2010). There is increasing evidence that reducing caloric intake and reducing the amount of carbohydrates in the diet, replacing them with high quality proteins and unsaturated fats, leads to sustained weight loss and better blood lipid profiles from a cardiovascular disease risk standpoint (Acheson, 2010).

Carbohydrates are most often categorized to include simple sugars, sugar alcohols, starch, and non-starch polysaccharides (Fig. 17.2). Simple sugars include both monosaccharides and disaccharides. Monosaccharides are the true simple sugars, existing as single molecules that do not need to by broken down in the body before being absorbed into the bloodstream. The main monosaccharide consumed by humans is glucose (dextrose). It provides a quick source of energy, however, that energy is not sustained and once the ingested sugar is metabolized, a rapid drop in blood sugar occurs. In addition, glucose is converted to fatty acids and cholesterol in the liver then transported for deposition in adipose tissue (Vanderhoof, 1998). Other monosaccharides include among others, fructose (levulose), galactose, xylose, and ribose.

Disaccharides are sugars consisting of two molecules of the same or different monosaccharides joined together. Some common disaccharides include lactose (glucose + galactose), the only non-plant sugar in the human diet, sucrose (glucose + fructose), and maltose (glucose + glucose). Disaccharides must be broken down into their component monosaccharides before they can be absorbed into the bloodstream. This occurs fairly quickly after ingestion, particularly with sucrose and maltose, thus disaccharides also provide quick energy and may be followed by a large drop in blood sugar levels relatively soon after eating. Some individuals lack sufficient levels of the enzyme required for metabolizing lactose into glucose and galactose and suffer from lactose intolerance. In lactose-intolerant individuals, bacteria, rather than an enzyme, metabolize the lactose, producing uncomfortable amounts of gas and stomach acid in the small intestine.

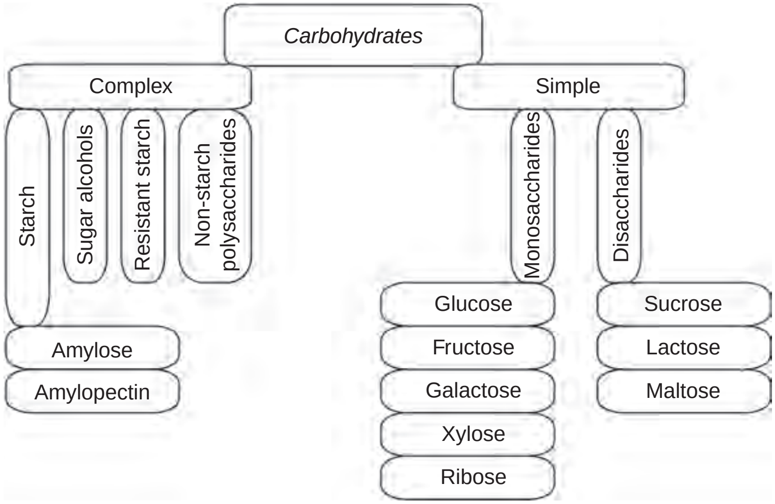

Fig. 17.2. The classes of carbohydrates found in a typical diet.

This can be prevented by avoiding foods high in lactose (dairy products) or by taking lactase (the enzyme that is lacking) supplements prior to consuming lactose-rich foods.

A sugar alcohol is a form of carbohydrate where the carbonyl group of a sugar has been hydrogenated forming a hydroxyl group, thus the classification as an alcohol. The simplest sugar alcohols, ethylene glycol and methanol are sweet tasting but toxic. The other sugar alcohols are generally sweet and non-toxic. Most sugar alcohols are consumed as food additives, not from ingestion of plant products containing sugar alcohols. Some of the more common sugar alcohols used as food additives include glycerol, erythritol, xylitol, mannitol, sorbitol, inositol, isomalt, and maltitol. They are not absorbed well and may be excreted in the urine (Englyst and Hudson, 1996). Sugar alcohols are not metabolized by oral bacteria, thus they do not promote tooth decay. When cooked, they do not caramelize. Many plants in the family *Rosaceae* produce significant amounts of sorbitol, celery (*Apium graveolens*) produces significant amounts of mannitol, and many seaweeds are rich in galactitol.

Polysaccharides are carbohydrates composed of a chain of many monosaccharide units. Starch (many molecules of glucose) is a very common polysaccharide. In many plants, glucose that is produced as a product of photosynthesis is often converted into starch for long-term storage in seeds, roots, stems, and fruit. When needed for energy or other metabolic processes, the starch is broken down into glucose. Since starch must be broken down before the glucose molecules can be used for energy production, starchy foods provide a longer, slower release of energy than either monosaccharides or disaccharides. Blood sugar levels are less likely to fluctuate wildly when a starch is consumed compared with simple sugars, thus consuming carbohydrates as starch is considered healthier than consuming monosaccharides or disaccharides.

The two main types of digestible starch in food are amylose and amylopectin. Amylopectin is more easily broken down than amylose, thus food containing high levels of amylopectin provides energy more rapidly than food containing high levels of amylose. The rate of digestion and energy release from starch also depends on how the starch is combined with other nutrients in the consumed food. For example, starch in whole foods such as whole grains are ingested with large amounts of fiber, thus the starch is more slowly digested compared with processed and refined foods where the fiber has been removed prior to consumption. The physical form of the starch also influences how digestible it is. Starch in a banana or a raw potato is present as granules that are resistant to degradation and digestion. When granular starch is cooked, it gelatinizes and is then readily digested.

Resistant starch is a polysaccharide that is resistant to digestion in the small intestine, and behaves more like fiber in the gastrointestinal tract. It may be fermented in the large intestine by beneficial bacteria producing small-chain fatty acids and associated health benefits. Sources of resistant starch include brown rice (*Oryza sativa*), barley (*Hordeum vulgare*), whole wheat (*Triticum aestivum*), and buckwheat (*Fagopyrum esculentum*).

Dietary fiber

Dietary fiber has become an increasingly important component of good health. Nearly all of the dietary fibers we consume are plant-based carbohydrates (lignin is a polyphenol) that resist digestion in the small intestine. The characteristic of a carbohydrate that renders it digestible or non-digestible by humans is the nature of the bonds connecting adjacent sugar molecules. Amylose (starch) is a polymer of glucose molecules connected via alpha-1,4 glycosidic bonds and is digestible by humans. Change the bond between glucose molecules to beta-1,4 glycosidic bonds and we have cellulose which we cannot digest.

In order to have a comprehensive discussion concerning dietary fiber, a panel of experts gathered in 2001 to establish definitions for fiber that naturally occurs in plants (dietary fiber) and isolated fiber that might be used as a food additive or supplement (functional fiber) (Fig. 17.3). Total fiber is the sum of dietary and functional fiber and most adults need between 25 and 50 g fiber/day, depending on age and gender. While other classification systems for starch exist, this text will discuss fiber using the 2001 Institute of Medicine definitions and classification scheme (Institute of Medicine, 2002).

Dietary fiber includes lignin, cellulose, beta-glucans, hemicelluloses, pectins, gums, inulin and oligofructose, and resistant starch. Lignin is a complex polyphenol found in plant cell walls and seeds. Cellulose is a non-digestible (by humans) polymer of glucose found in plant cell walls. Beta-glucans are mixed glucose polymers with beta-1,4 and beta-1,3 glycosidic bonds. Oats and barley are particularly rich in beta-glucans. Hemicellusoses are polysaccharides with five- and six-carbon sugars, found especially in plant cell walls. Pectins and gums are viscous polysaccharides found primarily in fruits and seeds, respectively. Inulin is a mixture of fructose polymer chains that often terminate in a glucose molecule. Oligofructose is similar, except that its polymers are shorter and may terminate in either fructose or glucose. Plants that store inulin do not store starch. Some plants that have high levels of inulin include agave (*Agave* spp.), banana (*Musa* spp.), chicory (*Cichorium intybus*), dandelion (*Taraxacum officinale*), garlic (*Allium sativum*), Jerusalem artichoke (*Helianthus tuberosus*), jicama (*Pachyrhizus erosus*), and onion (*Allium cepa*). Inulins contain only 25–35% of the calories of starch and have a minimal effect on blood sugar levels, thus are potentially helpful in managing blood sugar-related illnesses. Resistant starch is starch that is isolated within plant cells and is inaccessible to digestive enzymes. Bananas and many legumes contain significant resistant starch.

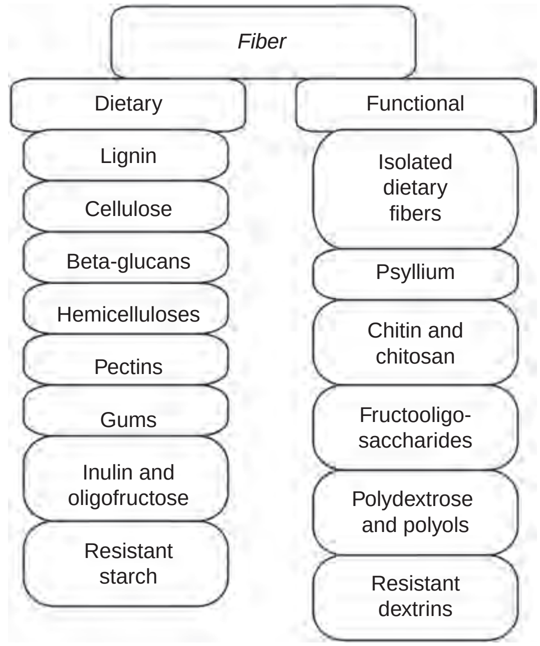

Fig. 17.3. Dietary and functional fibers in the typical human diet.

Functional fiber is isolated, non-digestible carbohydrates that have either been extracted from plant material or manufactured. They benefit human physiology and are added to food or taken as a supplement (Institute of Medicine, 2002). Functional fiber includes isolated forms of dietary fiber, psyllium, chitin or chitosan, fructooligosaccharides, polydextrose and polyols, and reistant dextrins (Niness, 1999; Institute of Medicine, 2002; Hendler and Rorvik, 2008). Psyllium is a viscous mucilage extracted from the husks of psyllium (*Plantago ovata*) seeds. Chitin is a non-digestible carbohydrate isolated from the shells of crustaceans such as crabs and lobsters. Chitin is a long polymer of acetylated glucosamine units. When chitin is deacetylated it becomes chitosan. Fructooligosaccharides are food additives composed of synthetic fructose polymers terminating in a glucose molecule. Polydextrose and polyols are synthetic polysaccharides added to processed foods for bulk or as a sugar substitute. Resistant dextrins (also called resistant maltodextrins) are indigestible polysaccharides synthesized by heating starch with certain enzymes. They are used as food additives.

Other descriptions of fibers include: (i) viscous versus non-viscous; (ii) fermentable versus non-fermentable; and (iii) soluble versus insoluble. Viscous fiber is one that will form a viscous solution or gel with water to produce bulk which tends to delay emptying of the stomach (Lupton and Turner, 2000; Gallaher and Schneeman, 2001). Viscous fibers include pectins, beta-glucans, some gums, and mucilages (psyllium). Fibers may also be categorized as fermentable or non-fermentable by bacteria in the gut. Fermentation products often include gas and short-chain fatty acids, which can be used as an energy source and may help prevent cardiovascular disease. Many fruits and vegetables are high in fermentable fiber. Fiber rich in cellulose is not fermentable. Terms describing the solubility of fiber in water (soluble versus insoluble) were originally used to simply describe this chemical property. Over time, soluble fiber was used as a term describing the potential for bacterial fermentation and thus health benefits, even though the association is somewhat misleading (Marlett, 1992). Other fibers beside soluble fibers have health benefits. When considering fiber as beneficial to health, specific fibers should be discussed.

Increasing viscous fiber intake can significantly lower total serum and low-density lipoprotein (LDL) cholesterol (Brown *et al.*, 1999) and improve blood sugar control (Wolever and Jenkins, 2001) preventing postprandial spikes in blood glucose levels. Both of these factors appear to play a role in the reduced risk of cardiovascular disease associated with increased fiber intake (Liu and Willett, 2002). Increasing any form of dietary fiber improves intestinal flow and relieves constipation by softening the stool and increasing the rate of passage through the intestine. Enhanced regularity may contribute to the reduced risk for colon cancer associated with increased fiber consumption (Bingham *et al.*, 2003) by quickly eliminating potential carcinogens from the body. While increased fiber intake has long been associated with a reduced risk of colorectal cancer, a number of controlled studies have failed to establish causality between the two (Alberts *et al.*, 2000; Bonithon-Kopp *et al.*, 2000; Schatzkin *et al.*, 2000; Ishikawa *et al.*, 2005). The reasons for such a discrepancy are unknown. High fiber intake coupled with a low fat diet seems to reduce the risk of breast cancer (Dong *et al.*, 2011). Increased fiber consumption extends satiety after a meal, thus those with higher fiber intake tend to weigh less than those consuming less fiber (Wanders *et al.*, 2011).

Some of the best sources of dietary fiber include legumes, oats, wheat and rice bran, and most fruits and vegetables. Sources for functional fibers vary depending on fiber type. Beta-glucans are generally extracted from oats, barley, mushrooms, yeast, and algae (Hendler and Rorvik, 2001). Pectin is derived from citrus rinds and apple pulp. Inulins and oligofructans are synthesized from sucrose or extracted from chicory root and are often called prebiotics since they have the capacity to stimulate the growth of beneficial bacteria (*Bifidobacteria*) in the intestine (Gibson *et al.*, 1995). Guar gum is taken from the Indian cluster bean and psyllium is isolated from psyllium husks. Chitosan is derived from chitin obtained from shells of crustaceans.

Protein

Proteins constitute the main structural components of the human body. Besides their structural importance, enzymes are proteins, and enzymes are responsible for orchestrating nearly all metabolic activity in any living organisms. They are also important for regulation of cellular import and export as they form channels in cell membranes through which entry into and exit from the cell is carefully controlled.

The human body is constantly synthesizing new proteins to replace those lost to injury or senescence, or those needed for maintenance and growth. In order to manufacture needed proteins, the human body requires amino acids, basic building blocks that are connected to form proteins. There are 20 amino acids available from which to construct proteins. The number, species and arrangement of the amino acids in a protein give that protein its unique structure and function. Proteins in general can be from 51 (the hormone insulin) to 3000 (the ATPase complex in the mitochondria) amino acids in length.

When we eat proteins they are digested and broken down into amino acids before being absorbed into the bloodstream to be transported to cells throughout the body. In general, protein molecules are larger than carbohydrate molecules and thus take longer to digest. As such, proteins provide a longer, slower source of energy compared with carbohydrates. In general, humans require between 40 and 65 g of protein/day to survive, about 0.8 g/kg of body weight (Porter, 2010). If this amount of protein is not ingested, the body will begin to attack and break down its own muscles. If too much protein is ingested, it will be broken down by the body and stored as fat.

While there are 20 amino acids needed by the human body for survival, only 11 of them can be synthesized from molecules in our bodies. The other nine amino acids, called essential amino acids, must come from the food we eat. We all need eight of the essential amino acids: (i) isoleucine; (ii) leucine; (iii) lysine; (iv) methionine; (v) phenylalanine; (vi) threonine; (vii) tryptophan; and (viii) valine (Fig. 17.4). Infants need the ninth one, histidine (Porter, 2010). While nearly all of the protein we eat has most of the 20 amino acids in them, the proportion of specific amino acids is important for good health. Additionally, protein from different sources varies in terms of how well our bodies can utilize the amino acids in them. Protein derived from animals has a balance of the different amino acids very similar to our own tissues, thus animal-derived protein is often called complete. Many plant-derived proteins lack or are low in one or more of the essential amino acids, thus many consider plant proteins incomplete or of lower quality. However, different plant-based foods have different amino acid profiles, so if the plant-based proteins from various sources are correctly combined, the protein profile is complete.

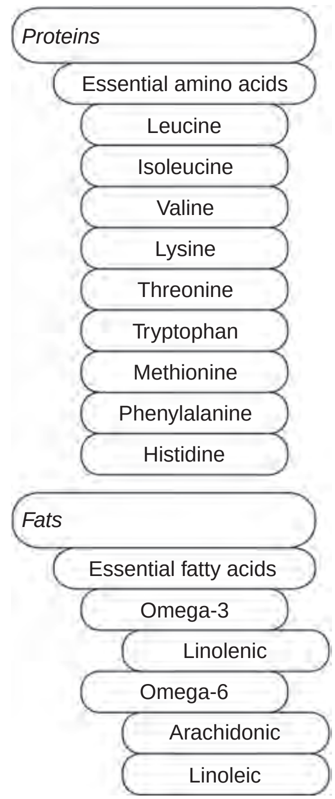

Fig. 17.4. The essential amino acids and fatty acids we cannot synthesize. They must be obtained from the foods we eat.

Fat

Fats are energy-dense molecules composed of glycerol with attached fatty acids. Our bodies can synthesize many of the fatty acids it needs. Others, however, cannot be synthesized and must be obtained from the food we eat. They are called essential fatty acids (Fig. 17.4). In general, essential fatty acids are about 7% of the fat consumed each day (Porter, 2010). The essential fatty acids are: (i) alpha-linolenic acid (an omega-3 fatty acid); and (ii) linoleic acid (an omega-6 fatty acid). Good sources of omega-3 fatty acids include flaxseed, lake trout, mackerel, salmon, herring, tuna, green leafy vegetables, and walnuts. Omega-6 fatty acids can be found in vegetable oils such as sunflower, safflower, corn, cottonseed, and soybean oils, fish oils and egg yolks (Porter, 2010). Omega-3 fatty acids may reduce the risk of coronary artery disease.

While fats are often perceived very negatively, they are required for growth, energy, and overall good health. The type(s) of fatty acid attached to the glycerol molecule determines whether the fat is considered a ‘good’ fat or a ‘bad’ fat from a nutrition point of view. The double bonds within a fatty acid may be saturated with hydrogen atoms, and are hence called saturated fatty acids. If available double bonds are not saturated, the fatty acids are called unsaturated fatty acids. The degree of fatty acid saturation is important in determining the health benefits or lack thereof for the fats we consume. Much of the fat from animal sources is saturated while most plant sources contain unsaturated fats.

The exceptions are palm and coconut oil, both are highly saturated. *Trans* fats are completely man-made by hydrogenating unsaturated fats, often vegetable oils. Saturated and *trans* fats are associated with increased blood cholesterol levels and increased risk of heart disease, thus we are encouraged to minimize the amount of saturated and *trans* fat we consume each day.

A general recommendation for fat consumption is to limit it to less than 30% of the daily caloric needs (less than about 90 g of fat/day) and limiting the amount of saturated fat to less than 10% (less than 30 g/day). In order to get our essential fatty acids, foods rich in both omega-3 and omega-6 fatty acids should replace saturated and *trans* fats in our diets.

Vitamins

Vitamins are organic compounds required by humans in small amounts that are essential for metabolism. They cannot be synthesized by humans, thus they must be obtained in the diet. In order for an organic substance to be considered a vitamin, a lack of it in the diet must produce clear and unmistakable symptoms of deficiency.

Vitamins are either water soluble (vitamin C and the vitamin B complex, which includes biotin, folate (folic acid), niacin, pantothenic acid, riboflavin (vitamin B2), thiamine (vitamin B1), vitamins B6 (pyridoxine) and B12 (cobalamins)) or fat soluble (vitamins A, D, E, and K) (Porter, 2010) (Fig. 17.5). All fat-soluble vitamins and the water-soluble vitamin B12 are stored in the liver and fatty tissue. Low fat diets might lead to a deficiency of these vitamins, and health disorders that interfere with fat absorption such as Crohn's disease, cystic fibrosis, and pancreatitis may also lead to a deficiency. Water-soluble vitamins are not stored in the body and are often eliminated in urine.

Many factors determine whether or not vitamins are lost during cooking. In general, brief to moderate cooking does not destroy fat-soluble vitamins (A, D, E, and K) and cooking foods with water-soluble vitamins tends to leach the vitamins into the cooking liquid. If the liquid is discarded rather than consumed, vitamins are discarded as well. Factors such as cooking temperature, length of cooking, light exposure, and pH all affect the stability of vitamins, thus making a blanket statement about the stability of most vitamins during cooking is impossible. There are a few observations about stability that can be made for some vitamins.

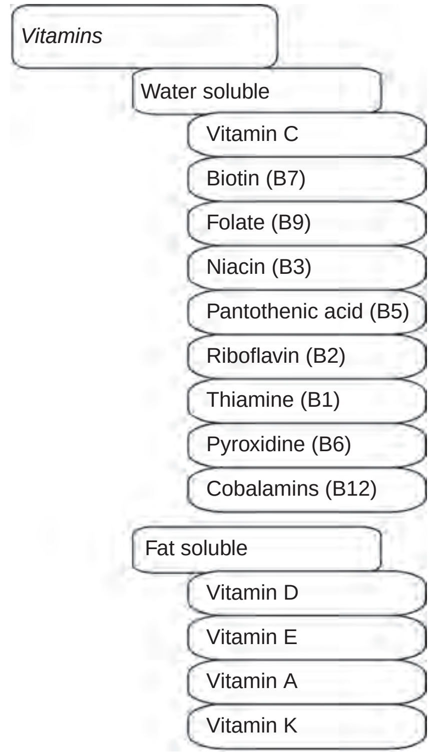

Fig. 17.5. Vitamins required for good human health.

Vitamin C is easily destroyed by heat, but is more heat stable under acidic conditions, such as in the heat pasteurization of orange juice (Morris *et al.*, 2004a). Loss of vitamin C due to oxidation is accelerated by copper or iron, thus using cast-iron or copper cookware may accelerate vitamin C loss. Riboflavin is moderately heat stable under neutral pH; however, it is easily destroyed under alkaline conditions (Morris *et al.*, 2004a). Riboflavin is also destroyed by light at neutral and alkaline pHs. Niacin is relatively heat stable while thiamine is destroyed by heat (Morris *et al.*, 2004a). Folate is destroyed by prolonged heating or by food preparation with copper utensils. Vitamin B6 is fairly heat stabile under alkaline or acidic conditions, however, the pyridoxal form of the vitamin is heat labile (Morris *et al.*, 2004a). Vitamins A and D are destroyed by heat.

Biotin (B7)

Biotin is a non-toxic, heat-stable, water-soluble vitamin that is attached to the active site of carboxylase enzymes (Higdon *et al.*, 2012). Carboxylase enzymes are particularly important in fatty acid metabolism, gluconeogenesis (the production of glucose from protein or fat), and leucine catabolism. Biotin also plays a role in DNA replication and transcription.

Biotin deficiency is rare but may occur in patients that have been fed intravenously without biotin supplementation. Deficiency may also occur in individuals who have consumed raw egg whites for a prolonged period, as biotin binds to a protein in raw egg whites called avidin which prevents biotin absorption.

Since there is not enough scientific data available to establish a recommended dietary allowance (RDA) for biotin, an adequate intake (AI) has been established (Higdon *et al.*, 2012). It ranges from 5 μg/day for infants to 8–20 μg/day for children, the amount increasing with age, 25 μg/day for adolescents, and 30 μg/day for adults. Women who are breastfeeding have an AI of 35 μg/day.

Good sources of biotin include yeast, egg yolks, and liver. The best plant-based source of biotin is Swiss chard (*Beta vulgaris* subsp. *cicla*), containing about 10 μg biotin per one cup serving. Intestinal bacteria synthesize biotin and this biotin may be absorbed by the body providing another source of the vitamin.

Folic acid (B9)

Folic acid, a water-soluble B vitamin, rarely occurs in the human body or in foods (Higdon *et al.*, 2012) but is the form of this B vitamin normally found in supplements. Folates are the forms found in food or the human body and they come in many chemical configurations. Folates are non-toxic, however, ingestion of large doses of folic acid may mask a B12 deficiency which may cause serious neurologic damage. Folates are critical enzyme cofactors important in nucleic acid and amino acid metabolism. DNA synthesis depends on folate coenzymes and the synthesis of methionine also depends on folates. Methionine is need for the production of *S*-adenosyl-L-methionine (SAM) which is important in many methylation reactions, including methylation of DNA. Methylation of DNA may help prevent cancer. Folates are also important in the synthesis of methionine from homocysteine and a deficiency of folate may lead to a build up of homocysteine which has been implicated as a risk factor for heart disease.

Folate may be deficient due to a dietary insufficiency or it may be induced by alcohol consumption, pregnancy, cancer, or when large amounts of non-steroidal anti-inflammatory drugs (NSAIDs), such as aspirin or ibuprofen, are taken in large therapeutic dosages. Folates are particularly important in the development of the nervous system of a fetus, and deficiency can lead to neural tube birth defects. Nervous system development occurs during the first month of pregnancy. Since many women do not know they are pregnant during the first month, folate nutrition is particularly important in women of child-bearing age.

The RDA for folate is most often reported as micrograms of dietary folate equivalents (DFE), which reflects greater availability of synthetic folic acid found in dietary supplements and fortified foods compared with naturally occurring folates in food. One microgram of folate from food provides 1 μg of DFE, while 1 μg folic acid taken with food provides 1.7 μg DFE, and when taken on an empty stomach, provides 2.0 μg DFE (Higdon *et al.*, 2012). Infants require 65–80 μg folate (actual folate, not as DFE), the requirement increasing with time. Children require 150–300 μg DFE, increasing with time, adolescents and adults 400 μg DFE. Women who are pregnant or might become pregnant have an RDA of 600 μg DFE and those breastfeeding, 500 μg DFE (Higdon *et al.*, 2012).

Green leafy vegetables are an excellent source of folates (hence the name, folate). Other plant-based foods rich in folate include lentils, garbanzo beans, lima beans, pinto beans, black beans, kidney beans, orange juice, and asparagus. Prolonged cooking can reduce the folate content of foods significantly.

Niacin (B3)

Niacin, also known as vitamin B3 or nicotinic acid, is a water-soluble vitamin important in forming the coenzymes nicotinamide adenine dinucleotide (NAD) and nicotinamide adenine dinucleotide phosphate (NADP), both extremely important in energy metabolism (Higdon *et al.*, 2012). Both NAD and NADP are important in cellular oxidation–reduction reactions, processes involving electron transfer during metabolism. NAD and NADP function as electron donors or acceptors in many cellular reactions. NAD is normally involved in catabolism of compounds while NADP is usually involved in anabolic reactions (biosynthesis of compounds). NAD is also very important in cell signaling, transcription, apoptosis, DNA repair, and stress responses. Considering these roles of NAD, niacin may be important for cancer prevention.

Niacin deficiency caused the problem known as pellagra in Europe in the 1700s and in the southern USA in the 1900s. The common theme of both locations and times was the widespread consumption of corn and its products as the main dietary staple, especially among the less advantaged. While corn contains significant amounts of niacin, it is relatively unavailable. Cooking corn in an alkaline solution releases the niacin making it available. Even though a considerable amount of corn is consumed as the main dietary staple in Mexico, pellagra is rare. This is because the corn is soaked in a calcium oxide solution prior to cooking, greatly increasing niacin's bioavailability.

Niacin is either consumed in food or formed in the liver from the amino acid tryptophan. Approximately 60 mg of tryptophan are required to synthesize 1 mg niacin. Dietary niacin is reported as niacin equivalents (NE) which represents the ingestion of either 1 mg niacin or 60 mg tryptophan. The RDA for niacin is 2–4 mg NE/day for infants, 6–12 mg/day for children, and 14–16 mg/day for adults. Women who are pregnant should consume 18 mg NE/day (Higdon *et al.*, 2012).

Good sources of niacin include yeast, meat, poultry, and red fishes. Good plant sources of niacin include legumes and seeds, and to a lesser degree green leafy vegetables, coffee, and tea. In some plant products the niacin is bound to a carbohydrate, greatly reducing its bioavailability. Niacin is not easily destroyed by heat, however, it is water soluble, thus when foods are cooked in a liquid, the liquid and the food should both be consumed.

Pantothenic acid (B5)

Pantothenic acid (vitamin B5) is found in all cells as a component of coenzyme A (CoA), vital for all life (Higdon *et al.*, 2012). CoA is important in energy metabolism, in the synthesis of essential fats, cholesterol, steroid hormones, acetylcholine, hemoglobin, and melatonin. Much of the metabolism occurring in the liver requires CoA.

Pantothenic acid deficiency is very rare. There is no RDA for pantothenic acid, however, the AI often recommended ranges from 2 mg/day in infants to 5 mg/day in adults, 6 mg/day for women who are pregnant and 7 mg/day for women who are breastfeeding.

Good sources of pantothenic acid are yeast, egg yolks, yogurt, milk, liver, and kidney. Good plant sources include broccoli, legumes, mushrooms, avocado, sweet potatoes, and non-processed whole grains. Processing, freezing or canning of food products may result in a 35–75% loss of pantothenic acid (Food and Nutrition Board, Institute of Medicine, 1998).

Riboflavin (B2)

Riboflavin, also known as vitamin B2, is a water-soluble vitamin important as part of the coenzymes flavin adenine dinucleotide (FAD) and flavin mononucleotide (FMN) (Food and Nutrition Board, Institute of Medicine, 1998). These coenzymes are important in energy metabolism and the metabolism of drugs and toxins. FAD is an integral component of the electron transport chain in mitochondria. Both coenzymes are also important in the function of a number of antioxidant enzymes such as glutathione reductase and glutathione peroxidase. The production of uric acid, a potent antioxidant in the blood, requires FAD. Riboflavin is also important in the metabolism of many of the other B vitamins and iron absorption (Higdon *et al.*, 2012).

Riboflavin deficiency by itself is rare. However, it may occur concomitantly with deficiencies of other water-soluble vitamins. The RDA is around 1 mg/day, slightly less for infants and children and slightly more for adult males, and women who are pregnant or breastfeeding. Nearly all food contains some riboflavin. Some plant sources particularly rich in riboflavin are almonds, broccoli, asparagus, and spinach. Riboflavin is particularly sensitive to light degradation.

Thiamine (B1)

Thiamine (thiamin) is a water-soluble vitamin also known as B1. It was one of the first substances identified as a vitamin (Higdon *et al.*, 2012). It occurs in humans either as free thiamine or in its phosphorylated form. Thiamine pyrophosphate (thiamine with two phosphate groups attached) is an important coenzyme for several life-essential enzyme systems, particularly enzyme systems involved in energy generation from food and in the synthesis of nucleic acids.

Severe thiamine deficiency leads to beriberi which affects the nervous, muscular, gastrointestinal, and cardiovascular systems. Dry beriberi is characterized by peripheral neuropathy, a tingling, burning or numb sensation in the feet or hands. Muscle pain and seizures may also occur. Wet beriberi leads to rapid heart rate, an enlarged heart, severe edema and eventually congestive heart failure. Cerebral beriberi leads to abnormal eye movements, an odd gait, and confused memory.

Thiamine deficiency may be the result of inadequate intake, alcoholism, an increased thiamine requirement brought on by strenuous physical activity, pregnancy or growth spurts during adolescence, excessive loss from the body due to excessive urination, or consumption of anti-thiamine factors in food (Higdon *et al.*, 2012). Anti-thiamine factors are substances present in some foods (coffee, tea) that create an oxidized, inactive form of thiamine. Thiaminases are enzymes, normally destroyed during cooking, that are present in certain raw foods (freshwater fish, shellfish, and ferns) that break down thiamine. Individuals who consume large quantities of these raw thiaminase-containing foods could suffer a thiamine deficiency.

The RDA for thiamine ranges from 0.2 mg/day for infants to just over 1 mg/day for adults. Pregnant women or women who are breastfeeding require around 1.4 mg/day. Good plant sources of thiamine include whole grains, beans and lentils, nuts, spinach, orange, and cantaloupe. Much of the thiamine is lost during processing of white flour and polished rice, and products made with these products.

Vitamin A

Vitamin A is not a single substance, but rather a general term for a large number of related compounds. Major compounds in this class include: (i) retinol (an alcohol); (ii) retinal (an aldehyde); and (iii) retinoic acid, an irreversibly oxidized form of retinol. All are known as retinoids (Higdon *et al.*, 2012). Dietary recommendations are based on the amount of retinol or the retinol equivalents from other forms that are available from foods. Beta-carotene is a provitamin A carotenoid which can be converted into retinol. Plants produce many different carotenoids, however, only a limited number can be converted into retinol.

Retinol is very important for night vision as it is part of the pigment rhodopsin located in the rod cells of the retina. Rod cells are capable of detecting extremely low levels of light. When rhodopsin is stimulated by a photon of light, a series of biochemical reactions occurs leading to the generation of an electrical impulse which ultimately is converted by the brain into vision. Different forms of retinoic acid act as hormones that affect the expression of genes responsible for cellular differentiation and many of the responses to retinol that are observed are results of this regulation. Vitamin A is also important for proper immune system function, specifically by maintaining the integrity and function of mucosal and skin cells (Higdon *et al.*, 2012). Retinol and retinoic acid are crucial for proper differentiation and development of white blood cells important in immune responses. Differentiation of red blood cells and the release of iron from cellular storage sites for incorporation into hemoglobin are both regulated by retinoids. Vitamin A is also important for normal heart, eye and ear development in the fetus.

The RDA for vitamin A is reported as micrograms of retinol activity equivalents (RAE)/day. Different forms of vitamin A and provitamin A carotenoids have different potencies when expressed as equivalents to retinol, thus the dietary value of foods and daily requirements for vitamin A are often expressed as RAEs. For example, 12 μg of beta-carotene from food provide the equivalent dietary benefit to 1 μg retinol, thus 1 μg of beta-carotene from food has the potency of 0.0833 RAE. (Beta-carotene in oil as a supplement has an RAE of 0.5.) The older vitamin A standard, the international unit (IU) provides 0.3 μg RAE. Daily RAE requirements range from 400 to 900 μg RAE/day depending on age. Women who are pregnant or breastfeeding require significantly more vitamin A, 1200 and 1300 μg RAE/day, respectively. It is important to note that therapeutic doses of retinol have been shown to cause birth defects, thus great care must be taken when using any vitamin A supplement or product containing vitamin A.

Retinol in its free form is not normally found in foods. A storage form of retinol, retinyl palmitate, is often found in animal-derived foods. Plant-based foods contain many carotenoids but only four (beta-carotene, alpha-carotene, gamma-carotene, and the xanthophyll beta-cryptoxanthin) can be converted into vitamin A by the body. Cod liver oil is particularly rich in retinol (1350 μg RAE per teaspoon). Good plant sources of ‘vitamin A’ include carrots, sweet potato, pumpkin, cantaloupe, mango, spinach, kale, collards, and butternut squash. Since vitamin A and its precursors are fat soluble, maximum nutritional benefit is obtained by consuming cooked vegetables with a little bit of fat or oil.

Vitamin B6

Vitamin B6 is a water-soluble vitamin that exists in three forms: (i) pyridoxal (PL); (ii) pyridoxine (PN); and (iii) pyridoxamine (PM) (Higdon *et al*., 2012). The most nutritionally important form of vitamin B6 is the coenzyme pyridoxal 5′-phosphate (PLP). Humans cannot synthesize vitamin B6. PLP is particularly important in the release of glucose from glycogen in muscle tissue and for the synthesis of glucose from amino acids (gluconeogenesis). In the nervous system, synthesis of neurotransmitters such as serotonin, dopamine, norepinephrine, and gamma-aminobutyric acid requires PLP. PLP is also required for: (i) the production of the iron-containing portion of hemoglobin; (ii) the conversion of tryptophan into niacin; and (iii) the synthesis of nucleic acids. PLP regulates the function of steroid hormones such as testosterone and estrogen by binding to receptor cites, thus decreasing their effect.

Daily vitamin B6 requirement increases with protein intake. The RDA for vitamin B6 ranges from 0.1 mg to 2.0 mg/day, depending on age and sex. Salmon, chicken, and turkey are fairly high in vitamin B6. Plant-based foods particularly high in vitamin B6 include bananas, baked russet potato, spinach, and hazelnuts.

Vitamin B12

Vitamin B12 has the most complex structure and is the largest in size of the vitamins (Higdon *et al*., 2012). It is unique in that it contains the metal cobalt, and the term ‘cobalamin’ is used to describe compounds having vitamin B12 activity. Methylcobalamin and 5-deoxyadenosyl cobalamin are two forms of vitamin B12 used by the human body. Methylcobalamin is important for the proper functioning of the folate-requiring enzyme that converts homocysteine into methionine, which is converted into SAM which donates a methyl group during methylation of DNA. Methylation of DNA has been associated with cancer prevention. Homocysteine accumulation, which would occur if vitamin B12 or folate were deficient, has been linked to increased risk for heart disease. Vitamin B12 is also needed for energy production from fats and proteins and for hemoglobin synthesis.

Uptake of vitamin B12 is somewhat complicated. After being released from foods by acids and enzymes in the stomach, vitamin B12 binds to proteins called ‘R’ proteins. After passing into the small intestine, vitamin B12 is released from the R proteins and binds to a protein called the ‘intrinsic factor’ (IF). If calcium supplied by the pancreas is present, the IF–B12 complex is absorbed by the small intestine. If the stomach, pancreas or small intestines are not functioning well, vitamin B12 must be absorbed passively, a very inefficient process.

The RDA for vitamin B12 ranges from 0.4 μg to 2.4 μg/day, depending on age, with pregnant or nursing mothers requiring slightly more. Older individuals are encouraged to get their vitamin B12 from fortified foods or supplements since they may suffer from a reduced digestive capacity and vitamin B12 may remain unavailable for absorption. Vitamin B12 is generally not present in plant-based foods, thus all dietary requirements must be met through animal-based foods such as fish, seafood, meat, or dairy, or from supplements.

Vitamin C

Vitamin C (ascorbic acid) is a water-soluble vitamin that cannot be synthesized by humans (Higdon *et al*., 2012). Vitamin C is required for: (i) synthesis of the structural component collagen; (ii) the neurotransmitter norepinephrine; and (iii) the synthesis of carnitine, a molecule essential for transporting fat into mitochondria for energy production. Vitamin C is also a powerful antioxidant. The sometimes fatal disease known as scurvy is due to a vitamin C deficiency and is characterized by bruising, bleeding, tooth and hair loss as well as lack of energy. In most cultures, scurvy is rare since only 10 mg of vitamin C daily will prevent it and most humans generally consume significantly more than that each day.

The RDA for vitamin C ranges from 40 to 90 mg/day for infants and adults, respectively. Smokers are encouraged to consume an additional 35 mg/day to combat the oxidative stress from smoking toxins. Woman who are pregnant or who are breastfeeding require around 120 mg/day. Many plant-based foods are high in vitamin C including: citrus fruits, strawberries, sweet red pepper, and broccoli.

Vitamin D

Vitamin D, a fat-soluble vitamin, is needed for normal calcium metabolism (Higdon *et al*., 2012). Upon skin exposure to UV B radiation in sunlight, humans can synthesize vitamin D3 (cholecalciferol).

Yeasts, higher fungi, and some higher plants can synthesize ergosterol which can be converted to vitamin D2 (ergocalciferol) by UV light (Holick *et al.*, 2002). The generic term 'vitamin D' normally refers to either or both vitamin D3 and D2. In order to be metabolically useful, vitamin D must be converted to 25-hydroxyvitamin D (calcidiol) in the liver followed by conversion to 1,25-dihydroxyvitamin D (the most potent form of vitamin D) in the kidney. The physiological activity of vitamin D is due to its regulation of nuclear gene transcription.

Vitamin D has a number or roles including: (i) being integral in balancing calcium levels in the blood; (ii) reducing cell proliferation while inducing differentiation; (iii) it may enhance the immune system; (iv) it helps regulate insulin secretion by the pancreas especially in type 2 diabetics; and (v) it may help decrease the risk of hypertension. A deficiency of vitamin D may lead to rickets, bowing of weight-bearing limbs, especially in infants and children. It may also lead to bone weakness and softening in older individuals as well as muscle weakness and pain. The RDA for vitamin D increases from 10 μg/day in infants to 15 μg/day in adults and 20 μg/day in older adults (>70 years). Most people can get their vitamin D requirement from 5–10 min of sun exposure each day. Dark-skinned individuals and those who use copious sunscreen may require dietary vitamin D. Additionally individuals living above latitudes 40°N or 40°S may require vitamin D supplementation during the winter as insufficient UV radiation occurs during these months. Most foods contain very little vitamin D unless they are fortified, thus supplements may be required if adequate sun exposure is not available.

Vitamin E

While there are eight antioxidants that belong to the vitamin E family, only alpha-tocopherol is maintained at appreciable levels in the human body (Higdon *et al.*, 2012). Blood serum gamma-tocopherol levels are much lower than alpha-tocopherol levels, even though much of our food contains gamma-tocopherol. The main function of vitamin E is to remove free radicals from the human body, especially protecting fat molecules in membranes and LDLs from oxidation. Oxidized membrane lipids lead to loss of membrane integrity while oxidized LDLs are implicated in cardiovascular disease. Even though the antioxidant capacity of an alpha-tocopherol molecule is lost once it has been oxidized by a free radical, the antioxidant capacity can be regenerated by other antioxidants such as vitamin C. Vitamin E is also important in cell signaling, immune system function, blood platelet aggregation, and vasodilation.

RDA levels for vitamin E range from 4 mg/day in infants to 15 mg/day in adults and are generally expressed as milligrams of alpha-tocopherol. Women who are breastfeeding need around 19 mg/day. Good sources of vitamin E include olive, corn, canola, soy, safflower, and sunflower oils, almonds, hazelnuts, and peanuts.

Vitamin K

Vitamin K is a fat-soluble vitamin vital for blood coagulation (Higdon *et al.*, 2012). The two forms of vitamin K are K1 (phylloquinone), the predominant form in our diet, produced by plants and vitamin K2 (many forms of menaquinones) which is produced by bacteria in the intestines of animals. Vitamin K is also important in the production and activity of 'Gas6', a protein that seems to be involved in cell signaling, proliferation, and adhesion, and also appears to have anti-apoptosis properties.

There is no RDA for vitamin K. However, there is a recommended AI which is around 2 μg/day for infants, 30 μg/day for children 1–3 years, 55 μg for children 4–8 years, 60 μg for children 9–13 years, 75 μg/day for adolescents, and 120 μg/day for adult males and 90 μg/day for adult females. Pregnant or breastfeeding women who are 18 years of age or younger should reduce their vitamin K intake to 75 μg/day. Vitamin K1 is the predominant form of dietary vitamin K and foods rich in vitamin K include kale, broccoli, Swiss chard, and parsley.

Minerals

Minerals are elements that living organisms cannot synthesize. They are obtained from the earth mostly by bacteria, fungi, or plants. Most minerals in our diet are derived from plants. We either eat the plant directly, or consume animals (or their products) that have eaten the plants. Some minerals are also obtained through the water we drink. Since soils and water sources vary around the world, so do the levels of minerals in plants, animals, and water.

There are two classes of minerals: (i) macrominerals; and (ii) microminerals (Fig. 17.6). Macrominerals are those minerals we require in relatively large quantities for good health. They include calcium, chloride, magnesium, phosphorus, potassium, and sodium. Microminerals are no less important, however, they are required in much lower amounts. Microminerals include chromium, copper, fluoride, iodine, iron, manganese, molybdenum, selenium, and zinc (Porter, 2010). Trace minerals such as arsenic, cobalt, fluoride, nickel, silicon, and vanadium which seem to be essential in animal nutrition have not been established as essential in human nutrition.

This section reviews the macrominerals and microminerals essential to human health, their general functions in the human body, and good dietary sources of each.

Calcium

The most common mineral in the human body is calcium and most of it is found in teeth and bones (Higdon *et al.*, 2012). While less than 1% of the calcium found in the body is in the blood and extracellular fluid, the levels in these fluids are critical for good health. The major component of our skeletal system and our teeth is calcium and phosphate-rich hydroxyapatite. We usually don't think of it, but our bones are in a constant state of resorption and synthesis throughout our lives. Our bodies resorb bones while specialized cells called osteoblasts regenerate new bone. Calcium is also extremely important in cell signaling for important bodily functions such as vasoconstriction and vasodilation, nerve impulse transmission, muscle contraction, and insulin secretion. Calcium is also an important cofactor for enzyme and protein function. Blood and extracellular fluid calcium levels are highly regulated by the parathyroid glands, kidneys, and osteoclasts, and are crucial for proper calcium-mediated metabolism.

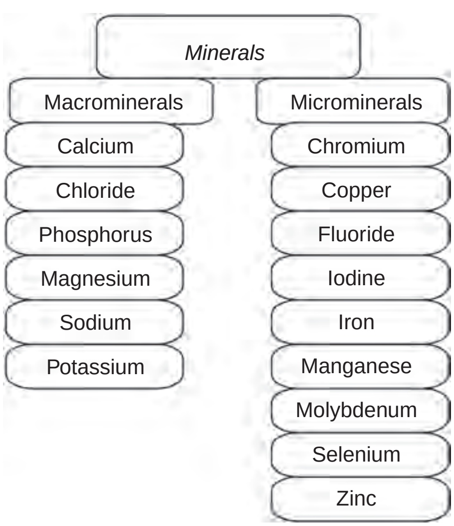

Fig. 17.6. The essential minerals we need to maintain good health.

Calcium deficiency detected in the blood is often a sign of parathyroid or kidney malfunction since the body always has a large reserve of calcium in the skeletal system. Vitamin D or magnesium deficiency or excessive sodium, phosphorus, or protein consumption may also lead to low blood calcium levels. The RDA for calcium ranges from 200 mg/day in newborn infants to 1200 mg/day in adults. Inadequate calcium intake may lead to osteoporosis, especially in older individuals.

While much of our calcium often comes from dairy products, certain plant products have calcium that is as readily absorbed and utilized as dairy-derived calcium. Kale, broccoli, bok choy, cabbage, collards, and mustard greens are rich plant sources of such calcium. Some plants such as spinach and rhubarb, and to a lesser extent sweet potatoes and kidney beans, are rich in oxalic acid, a potent inhibitor of calcium absorption, thus excessive consumption of any of these foods should be avoided to prevent inhibition of calcium absorption. Phytic acid, found in non-fermented grain products and bean products, also inhibits calcium absorption. Fermented grain and bean products are much lower in phytic acid, since yeast used in the fermenting process metabolizes phytic acid.

Chromium

Chromium is considered an essential mineral, however, why it is essential is still unclear (Higdon *et al.*, 2012). Trivalent chromium is the form found in most foods and utilized by the body. Hexavalent chromium at low levels can be reduced to trivalent chromium by acids in some foods and the stomach. However, hexavalent chromium at high levels is a potent carcinogen.

Chromium enhances the effects of insulin on glucose metabolism by enhancing cellular insulin receptors or increasing insulin-stimulated glucose movement into cells. Since chromium has an effect on glucose metabolism, it may also improve blood lipid profiles. There is no RDA for chromium, but rather, an AI which ranges from 0.2 μg/day for newborn infants to 25 μg in adult females and 35 μg/day in adult males. Women who are pregnant require 30 μg/day while women who are breast-feeding require around 45 μg/day. Claims that chromium picolinate supplements enhance weight loss are unfounded (Volpe *et al*., 2001) and may even cause weight gain in some individuals with type 2 diabetes taking sulfonylurea drugs (Martin *et al*., 2006).

Information on the chromium content of foods is limited. Broccoli is particularly high in chromium while green beans, potatoes, grape juice, orange juice, apple, and banana contain moderate amounts. Foods that are high in simple sugars are usually low in chromium and they also are known to promote chromium loss from the body.

Copper

Copper exists as both monvalent and divalent cations in the human body, however, the divalent form is predominant (Higdon *et al*., 2012). Copper easily accepts and donates electrons making it important in oxidation–reduction reactions and free radical scavenging. A number of enzymes called cuproenzymes contain copper and are important in a variety of metabolic activities. One such enzyme, cytochrome c oxidase is important in generating the electrical gradient in mitochondria which makes ATP production possible. Another cuproenzyme, lysyl oxidase, is needed for cross-linking collagen and elastin, important for making strong connective tissue. Copper is also important in iron metabolism, the synthesis and metabolism of neurotransmitters, synthesis and maintenance of the myelin sheath, melatonin synthesis, and regulation of gene expression. Two forms of the powerful antioxidant enzyme superoxide dismutase contain copper.

The RDA for copper is from 200 μg/day in newborn infants to 900 μg/day in adults. Women who are pregnant or breastfeeding require slightly more copper, around 1000 and 1300 μg/day, respectively. Good plant sources for copper include cashews, sunflower seeds, hazelnuts, almonds, peanut butter, lentils, and mushrooms.

Fluoride

Fluoride is a negatively charged molecule of fluorine mostly found in teeth and bones (Higdon *et al*., 2012). It is not considered an essential mineral since it is not required to sustain life, however, it is extremely important in preventing tooth decay. Fluoride interacts with hydroxyapatite in teeth and hardens tooth enamel making teeth less susceptible to decay. No RDA for fluoride exists, however, an AI has been established ranging from 0.01 mg/day for newborn infants to 3 mg/day for adult females and 4 mg/day for adult males. Fluoride is often consumed in fluoridated drinking water, usually between 0.7 and 1.2 mg/l. Excessive consumption of fluoride by infants can lead to dental fluorosis, a whitish speckling of permanent teeth that may lead to staining and pitting in severe cases. Fluoride-containing toothpastes are also a major source of fluoride in children, since they are more likely to swallow the toothpaste rather than spit it out. Tea and grape juice are relatively high in fluoride compared with other plant sources, but even so, both contain very little fluoride (0.6 mg/100 ml serving).

Iodine

Iodine is a non-metallic trace mineral found mostly in ocean water that is required by humans for the synthesis of the thyroid hormones triiodothyrine and thyroxine which are involved in regulating growth, development, metabolism, and reproductive functions (Higdon *et al*., 2012). Iodine deficiency is a worldwide problem, leading to enlarged thyroid (goiter) in children and adults, and when deficient in pregnant women or newborn infants, impaired intellectual development.

The RDA for iodine ranges from 110 μg/day in newborn infants to 150 μg/day in adults. Women who are pregnant or breastfeeding require 220 and 290 μg/day, respectively. Plant-based foods particularly rich in iodine include seaweeds, navy beans, and potatoes. The absolute iodine content of these foods varies widely due to differences in soil and seawater iodine concentrations. In many regions of the world, iodine is supplied through iodized salt. Some foods contain substances called goitrogens that interfere with the uptake of iodine. Cassava, some species of millet, and many cruciferous vegetables contain goitrogens. Several of the soy-based isoflavones including genistein and daidzein inhibit thyroid hormone synthesis. The negative impacts of goitrogens and soy isoflavones are only of concern in areas where iodine deficiency is severe or these products are consumed in excess.

Iron

Iron is a key mineral influencing metabolism in all living organisms as it is a major component of many proteins and enzymes (Higdon, *et al.*, 2012). Iron is a key component of heme compounds, molecules involved in many metabolic functions. Hemoglobin is important in the transport and storage of oxygen in the blood while myoglobin is involved in transport and storage of oxygen in muscles. Cytochromes, molecules containing hemes, are important in mitochondrial electron transport and energy production. Both catalase and peroxidase contain hemes and both are important as antioxidant enzymes, protecting cells from damage by hydrogen peroxide. The immune system also relies on a heme-containing enzyme myeloperoxidase, which is produced by white blood cells which engulf bacteria and kills them by exposing them to ROS. Iron may also be important to physiological adaptations to low oxygen concentrations, such as in high altitude environments, or in patients with chronic lung disease. Iron is also required for DNA synthesis. Since iron can be toxic to cells through generation of free radicals, the human body closely regulates the iron status of our cells, particularly by the enzyme hepcidin which is produced by the liver. Hepcidin inhibits the release of iron from specific cell types that store significant amounts of iron. When iron in the blood is sufficient, hepcidin levels are high, and when iron levels are low, hepcidin levels decrease, allowing iron to be released from storage sites.

Iron deficiency in humans may be one of three types. The first is where storage pools have been depleted, however, there is still enough iron in the blood for normal metabolism. Early functional iron deficiency is the second type. This occurs when the amount of iron in the blood limits the formation of red blood cells, but not low enough to detect anemia. The third level of deficiency, called iron-deficiency anemia, occurs when: (i) blood levels of iron reach a critical level where normal red blood cell formation cannot occur; (ii) red blood cells are smaller than normal; and (iii) their hemoglobin content is lower than normal. At this stage, the oxygen carrying capacity of the blood is compromised and iron-dependent enzyme function is deficient. Symptoms of anemia include those that are concomitant with low blood oxygen levels, such as fatigue, rapid heart rate, and rapid breathing upon exertion.

The RDA for iron varies considerably with age and gender and ranges from 7 to 18 mg/day. Women who are between menarche and menopause generally need 18 mg/day while pregnant women need 27 mg/day. The iron content of food may be of the heme type (hemoglobin and myoglobin, from animal-based foods) and non-heme type (plant sources). The absorption of non-heme iron depends greatly on absorption enhancers and inhibitors consumed with iron-containing food. Non-heme iron absorption is enhanced by vitamin C, organic acids such as citric, malic, tartaric, and lactic acids, and meat, fish, or poultry. Absorption is inhibited by phytic acid (found especially in legumes, grains, and rice), polyphenols, and soy protein. Good plant sources of iron include black-strap molasses, raisins and prunes, potatoes with skin, kidney beans, lentils, tofu, and cashews.

Magnesium

Magnesium is involved with over 300 essential metabolic functions in the human body (Higdon *et al.*, 2012). Magnesium is important in the synthesis of ATP, nucleic acids, carbohydrates, lipids, and the antioxidant glutathione. Magnesium also plays a role in transport of ions across cell membranes, and for the phosphorylation of proteins that is important in cell signaling. Magnesium is also part of structural molecules in bone, cell membranes, and chromosomes.

The RDA for magnesium ranges from 30 to 420 mg/day depending on gender and age and deficiencies are rather rare in generally healthy individuals. Green leafy vegetables are a great source of magnesium owing to their high chlorophyll content. Grains and nuts as well as lima beans, okra, molasses, and bananas are also high in magnesium.

Manganese

Manganese is an essential mineral that is part of some enzymes and an activator of others (Higdon *et al.*, 2012). Manganese is part of an important antioxidant enzyme manganese superoxide dismutase, found in the mitochondria which are particularly susceptible to free radical damage. Manganese-containing enzymes are involved in gluconeogenesis, and liver detoxification of ammonia. Manganese-activated enzymes are important in the metabolism of carbohydrates, collagen (important in wound healing), amino acids, cholesterol, and neurotransmitters. Manganese is a cofactor for enzymes involved in cartilage formation.

Manganese deficiency is extremely rare and no RDA has been established. The AI ranges from 0.003 mg/day for newborn infants to 2.3 mg for adults, and varies with age and gender. Plant-based foods rich in manganese include pineapple, whole grains, nuts, leafy vegetables, and teas. Foods that are high in phytic acid, such as beans, seeds, nuts, whole grains, and soy products, or foods high in oxalic acid, such as cabbage, spinach, and sweet potatoes, may slightly inhibit manganese absorption. The tannins in tea may also reduce the absorption of manganese.

Molybdenum

Molybdenum functions as a cofactor for three important enzymes in the human body: (i) sulfite oxidase; (ii) xanthine oxidase; and (iii) aldehyde oxidase (Higdon *et al.*, 2012). Sulfite oxidase is important in the metabolism of the sulfur-containing amino acids methionine and cysteine. Xanthine oxidase is important in regulating the antioxidant capacity of the blood and aldehyde oxidase is important in the metabolism of drugs and toxins.

The RDA for molybdenum ranges from 17 to 45 μg/day depending on age and gender. Molybdenum deficiency is extremely rare. The best plant sources of molybdenum are legumes (beans, peas, and lentils), grains, and nuts. Most fruits and vegetables are low in molybdenum.

Phosphorus

Most of the phosphorus in the human body occurs as phosphate and is found in the bone in the form of hydroxyapatite (Higdon *et al.*, 2012). Phosphorus is also an important component of membranes, being part of the phospholipid complex producing the membranes' fluid nature. Energy production relies on the phosphorus-rich AMP (adenosine monophosphate), ADP, and ATP family of molecules. Nucleic acids are rich in phosphorus, the buffering system of cells relies on phosphates and many enzymes, hormones, and cell signals rely on phosphorylation for activity.

Phosphorus deficiency is rare but increased consumption of fructose can lead to excessive urinary loss of phosphorus leading to a net daily loss of phosphorus from the body, especially in males (Milne and Nielsen, 2000). This is important since the consumption of high fructose corn syrup has skyrocketed in some areas of the world. The RDA for phosphorus ranges from 460 mg/day in young children, peaking at 1250 mg/day for adolescents lowering to 700 mg/day for adults. Dairy foods, meat, and fish are rich in phosphorus, many food additives contain phosphorus and phosphoric acid is present in soft drinks. The phosphorus in plant-based foods occurs as phytic acid. Only about 50% of the phosphorus in phytic acid is bioavailable to humans since we lack the enzymes required for liberating phosphorus from the phytate. Almonds, peanuts, and lentils are particularly rich in phosphorus.

Potassium

Potassium is important in human nutrition as both an essential mineral and as an electrolyte (Higdon *et al.*, 2012). Electrolytes in the body can conduct electricity. Since many bodily functions rely on electrical impulses traveling throughout the body, extremely precise regulation of electrolyte levels is imperative for good health. Electrical charges throughout the body rely on potassium and sodium ions. Potassium ions are principally intracellular while sodium ions are predominantly extracellular. The general gradients of these two ions are such that there are approximately 30 times the potassium ions inside versus outside the cell and ten times the number of sodium ions outside than inside the cell. These differences create an electrical gradient called the membrane potential. The gradients are maintained by ATP-driven membrane pumps which use between 20 and 40% of the energy consumed by an adult at rest. This gives an idea of how crucial these gradients are. The gradients are particularly important for nerve impulse travel, heart function, and muscle contraction. Potassium is also important in enzyme function, particularly for enzymes involved in carbohydrate metabolism.

Potassium deficiency is usually caused by excessive excretion of potassium in the urine rather than a lack of potassium in the diet. There is no RDA for potassium, but rather an AI which ranges from 400 mg/day in infants to 4700 mg/day in adults. Breastfeeding women require slightly more, around 5100 mg/day. Fruits and vegetables are particularly good sources of dietary potassium, especially bananas, potatoes with the skin, prunes, oranges, tomatoes, raisins, artichoke, lima beans, acorn squash, spinach, sunflower seeds, almonds, and molasses.

Selenium

Selenium is a trace mineral required by humans for specialized enzymes called selenoproteins (Higdon *et al*., 2012). While a number of selenoproteins have been identified, the function of many of them remains unknown. The main identified function for many of the selenoproteins is that of an antioxidant or an antioxidant generator. Selenoprotein P found in plasma helps protect the lining of blood vessels from the damage caused by peroxynitrite, a reactive nitrogen species. The generation of the biologically active thyroid hormone triiodothronine also requires a selenoprotein. Other selenoproteins have roles in spermatogenesis, protein folding as well as inflammatory and immune responses.

Selenium deficiency doesn't appear to cause a specific illness, but rather renders the deficient individual more susceptible to stress-induced illnesses. The RDA for selenium ranges from 20 μg/day in children to 55 μg/day in adults. Women who are pregnant or breastfeeding require 60 and 70 μg/day, respectively. The best sources for selenium are organ meats and seafood. Plants are unreliable for selenium nutrition as they do not have a specific selenium requirement and merely absorb selenium that is in the soil. Levels of selenium in any particular plant-based food are entirely dependent on the soil in which it was grown. Brazil nuts are a good source of plant-based selenium, but their content can vary from 10 to 100 μg per nut depending on where it is grown.

Sodium chloride

Sodium chloride provides sodium and chloride ions, the principal extracellular ions in the human body (Higdon *et al*., 2012). Their concentrations are carefully regulated within the body and an excess of either ion can lead to serious health problems. Both sodium and chloride ions are electrolytes which are critical for generating and maintaining membrane potentials in the body for the transmission of nerve impulses, heart function, and muscle contraction. Sodium is important in the absorption of chloride, amino acids, glucose, and water in the small intestine. Chloride is an important component of hydrochloric acid in the stomach, crucial for proper digestion. Sodium is intricately involved in blood volume and blood pressure, with excess sodium leading to high blood pressure and its negative health consequences.

Sodium chloride is normally not deficient in human diets. On the contrary, the major concern with both nutrients, sodium in particular, is an excess. Rather than an RDA, there is an AI and a maximum limit for sodium consumption. The AI is meant as a guide for the minimum amount of sodium required to replace that lost in sweat each day. This amount ranges from 0.3 g sodium chloride/day for infants to around 4 g/day for adults. The maximum recommended salt consumption by adults is 5.8 g/day (sodium chloride) (Food and Nutrition Board, Institute of Medicine, 2005). Processed foods are particularly high in sodium chloride, and excessive salt intake should be avoided by everyone.

Zinc

Zinc plays a very important role in growth and development, immune responses, neurological function, and sexual reproduction (Higdon *et al*., 2012). Zinc deficiency is an important problem, especially in developing countries. Zinc is an important catalyst for innumerable enzymes. Zinc is also an important structural component in proteins and cell membranes. Proteins containing zinc are important in DNA transcription, cell signalling, and apoptosis.

The RDA for zinc ranges from 3 mg/day for children to 8–11 g/day for adults. Pregnant and breastfeeding women require an additional 3–4 g/day. Shellfish and red meats are good sources of zinc. Nuts and legumes are good plant sources of zinc, however, there is less bioavailable zinc in plant sources due to the presence of phytic acid.

Phytonutrients

Phytonutrients are substances produced by plants that are implicated in maintaining good health or improving poor health (Fig. 17.7). Most phytonutrients are not considered as essential as defined for other nutrients. There are many products with claims of great benefits and the decision of whether or not to use them is daunting to say the least. With the easy

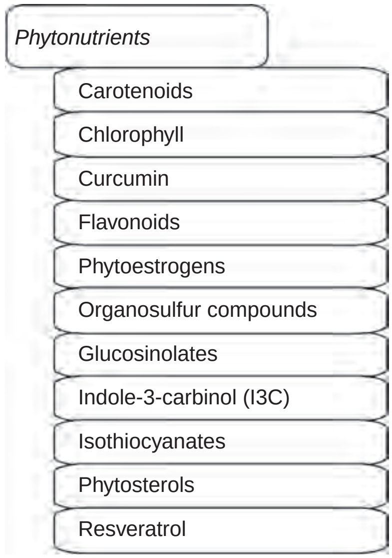

Fig. 17.7. The most commonly studied phytonutrients. Be aware that there are thousands of potential phytonutrients in the foods we eat; they just haven't been discovered yet.

and often immediate availability of information on the Internet, it is relatively easy to research specific claims and determine their validity.

This section explores the major phytonutrients and the latest information available regarding their potential benefits and the risks associated with their use. A wonderful website for information regarding many aspects of nutrition is the Linus Pauling Institute (2013) at Oregon State University (http://lpi.oregonstate.edu/infocenter/). This website and associated references were the sources for much of the material presented in this chapter.

Carotenoids

There are more than 600 naturally occurring pigments produced by bacteria, algae, and plants that are classified as carotenoids (Higdon *et al.*, 2012). These pigments are yellow, orange, and red and are often found in abundance in most fruits and vegetables. Green leaves are often rich sources of carotenoids; they aren't brightly colored because the chlorophyll in them masks the other pigments. The carotenoids most consumed by humans include the carotenes (alpha-carotene, beta-carotene, lycopene) and xanthophylls (beta-cryptoxanthin, lutein, zeaxanthin). Carotenoids are fat soluble, thus they must be consumed with fat to be absorbed by the body.

The most widely documented function of carotenes is as components of provitamin A. Of the six listed carotenoids, only alpha-carotene, beta-carotene, and beta-cryptoxanthin are provitamin A carotenoids than can be converted by the body into retinol (vitamin A) (Food and Nutrition Board, Institute of Medicine, 2000). The vitamin A activity of beta-carotene in food is only 1/12 that of retinol. The vitamin A activity of alpha-carotene and beta-cryptoxanthin are both 1/24 that of retinol (Food and Nutrition Board, Institute of Medicine, 2000).

In plants, all carotenoids function as effective antioxidants, especially lycopene. Whether or not they have the same capacity in humans is not clear. Lutein and zeaxanthin are very effective in absorbing blue light. In our eyes, both pigments absorb blue light before it reaches the rods and cones and may protect them from oxidative damage induced by light (Krinsky *et al.*, 2003).

Carotenoids stimulate the synthesis of a group of proteins called connexins that form pores in membranes that allow intercellular communication via the movement of small molecules between cells (Bertram, 1999) helping cells stay in a differentiated state. Cancer cells often lose the capacity to stay differentiated. While dietary carotenoids might be able to reduce the risk of cancer, in particular, lung cancer (Voorrips *et al.*, 2000; Holick *et al.*, 2002), the benefit is small (Gallicchio *et al.*, 2008) and the best protection against lung cancer is not smoking. Beta-carotene supplements were actually found to increase the risk of lung cancer in high risk individuals, such as smokers and asbestos workers (Anonymous, 1994; Omenn *et al.*, 1996).

While the consumption of tomatoes and cooked tomato products (exceptionally high in lycopene) has been suggested to reduce the risk of prostate cancer in men, the evidence supporting such a claim is limited. In several studies, a significantly decreased risk for prostate cancer was observed in men consuming large amounts of tomatoes and tomato products (Mills *et al.*, 1989; Giovannucci *et al.*, 1995; Gann *et al.*, 1999; Giovannucci, 2002). However, in other studies, high dietary lycopene intake (mostly from tomatoes and tomato products) did not reduce the risk of prostate cancer (Schuurman *et al.*, 2002; Etminan *et al.*, 2004; Key *et al.*, 2007).

Higher blood levels of carotenoids have been associated with lower measures of carotid intima-media thickness, a measure of cardiovascular risk (Iribarren *et al*., 1997; D'Odorico *et al*., 2000; Rissanen *et al*., 2000, 2003; McQuillan *et al*., 2001; Dwyer *et al*., 2004). Studies evaluating decreased risk of cardiovascular disease and plasma carotene content vary, with some suggesting a decreased risk (Street *et al*., 1994; Rissanen *et al*., 2001; Sesso *et al*., 2004; Ito *et al*., 2006; Buijsse *et al*., 2008) while others suggesting no effect (Sahyoun *et al*., 1996; Evans *et al*., 1998; Hak *et al*., 2003; Sesso *et al*., 2005). Consumption of foods rich in carotenoids seems to lead to a decrease risk of cardiovascular disease (Rimm *et al*., 1993; Gaziano *et al*., 1995; Sahyoun *et al*., 1996; Osganian *et al*., 2003). Since consumption of carotenoid-rich foods leads to reduced risk but higher plasma levels of carotenes are not associated with the decreased risk, other factors associated with the consumption of carotenoid-rich food (such as lifestyle, other nutrients) must be involved. Beta-carotene supplements do not offer the same protection as food-derived carotenoids (Voutilainen *et al*., 2006).

Even though many fruits and vegetables are good sources of carotenoids, many of the carotenoids they contain have limited bioavailability due to protein association within the food. Chopping and cooking often release bioavailable carotenoids and bioavailable lycopene from tomatoes is substantially increased if the tomatoes are cooked with a little oil. Pumpkin and carrots are particularly rich in alpha-carotene while pumpkin, spinach, sweet potato, carrots, collards, kale, and turnip greens are rich sources of beta-carotene. Remember alpha- and beta-carotene are both provitamin A carotenoids that can be converted into retinol. Beta-cryptoxanthin, another provitamin A carotenoid, can be found in many orange and red fruits including pumpkin, red peppers, and papayas.

Good sources of lycopene include tomatoes, tomato products, and watermelon. Lutein and zeaxanthin are both xanthophylls and their levels are typically reported combined. Foods rich in lutein and zeaxanthin include spinach, kale, turnip greens, and collards.

Chlorophyll and chlorophyllin

Chlorophyll is the major light-capturing pigment in plants. It closely resembles the hemoglobin in our bodies in that it has in its structure a central porphyrin ring (Higdon *et al*., 2012). In chlorophyll the center of the ring is magnesium while the center in hemoglobin is iron. The two main types of chlorophyll, a and b, are both fat-soluble molecules, situated predominantly in the chloroplast membranes of leaf cells. The difference between chorophyll a and chlorophyll b is that they each absorb light of different wavelengths. Chlorophyllin is a synthetic mixture of chlorophyll and copper salts that is often taken as a supplement.

Both chlrophyll and chlorophyllin form molecular complexes with suspected carcinogens, most notably certain hydrocarbons found in tobacco smoke, compounds found in cooked meat, and aflatoxin-b1, a potent liver carcinogen found in moldy grains and legumes. Combined with chlorophyll or chlorophyllin, these potential carcinogens may be less easily absorbed during digestion, reducing the chances for cancer. Chlorophyllin has been shown to: (i) inhibit the activity of some enzymes involved in the development of cancer (Tachino *et al*., 1994; Yun *et al*., 1995); (ii) neutralize the oxidative capacity of suspected chemical carcinogens and radiation (Park *et al*., 2003; Kumar *et al*., 2004); and (iii) arrest the development of colon cancer cells (Chimploy *et al*., 2009).

Chlorophyllin is often taken as a supplement to act as an internal deodorant for individuals with colostomies, ileostomies, or incontinence to reduce urinary and fecal odor. Clinical trial results are inconclusive as to whether odor is reduced with chlorophyllin supplementation (Higdon *et al*., 2012). A mixture of papain (an enzyme derived from papaya), urea and chlorophyllin seems to enhance wound healing and reduce the odor associated with severe, slow-healing wounds (Smith, 2008).

Leafy greens such as spinach, kale, collards, and herbs such as parsley and basil are the best natural sources of chlorophyll.

Curcumin

The rhizomes of *Curcuma longa*, a relative of ginger, are the raw material from which the spice turmeric is derived (Higdon *et al*., 2012). Turmeric's bright yellow color comes from curcuminoids, fat-soluble polyphenols. Turmeric extracts are often used as food-coloring agents. Curcumin is the most abundant curcuminoid in turmeric.

Detection of cucurmin in the human body after oral ingestion is generally limited to the gastrointestinal tissues where it accumulates. Metabolites of curcumin such as curcumin glucuronides, curcumin sulfates, and hexahydrocurcumin are readily detected in the bloodstream (Lao *et al*, 2006; Baum *et al.*, 2008) but are much less effective than curcumin itself. Only low levels of cucurmin can be detected in the bloodstream after ingestion (Cheng *et al.*, 2001; Sharma *et al.*, 2004). Curcumin is a powerful antioxidant, however, limited translocation may reduce its effectiveness outside the gastrointestinal tract (Garcea *et al.*, 2004). Curcumin also enhances the production of the antioxidant glutathione (Dickinson *et al.*, 2003; Zheng, *et al.*, 2007). Curcumin reduces symptoms of inflammation (Deodhar *et al.*, 1980; Satoskar *et al.*, 1986) by interfering with enzymes responsible for producing the irritants associated with inflammation (Hong *et al.*, 2004). Curcumin has also been shown to arrest cell development in cultured colon cancer cells (Moos *et al.*, 2004; Tsvetkov *et al.*, 2005) and cultured breast cancer cells (Somasundaram *et al.*, 2002). While these responses to curcumin appear promising, it is important to emphasize the very low bioavailability of curcumin outside the gastrointestinal tract. Additionally, the cancer studies were performed using cell cultures, not patients. Curcumin is ingested as the spice turmeric or taken as a supplement.

Flavonoids

Flavonoids are water-soluble polyphenolic pigments synthesized by plants (Higdon *et al.*, 2012). Their many functions in plants include: (i) floral pigmentation to attract pollinators; (ii) stimulating *Rhizobium* bacteria for nitrogen fixation; (iii) promotion of pollen tube growth; (iv) regulation of auxin accumulation; (v) regulation of the resorption of mineral nutrients from senescing leaves; (vi) enhancing tolerance to abiotic stress; (vii) absorbing otherwise damaging UV radiation; (viii) acting as antioxidants; (ix) providing defense against herbivores and pathogens; and (x) promoting allelopathic relationships with other plants.

Flavonoids are often divided into subclasses to include anthocyanidins, flavanols, flavanones, flavonols, flavones, and isoflavones. While flavonoids are ubiquitous in plants, some plants are particularly rich in one or more of the flavonoid classes. Anthocyanidins (cyanidin, delphinidin, malvidin, pelargonidin, peonidin, petunidin) are found in red, blue and purple berries, red and purple grapes, and red wine. Flavanol monomers or catechins (catechin, epicatechin, epigallocatechin epicatechin gallate, epigallocatechin gallate) are found in green and white teas, chocolate, grapes, berries, and apples. The flavonol classes of theaflavins and thearubigins are found in black and oolong teas while the proanthocyanidin flavonols are found in chocolate, apples, berries, red grapes, and red wine. Citrus fruits and juices are particularly rich in flavanones (hesperetin, naringenin, and eriodictyol). Flavonols (quercitin, kaempferol, myricetin, and isorhamnetin) can be found in yellow onions, scallions, kale, broccoli, apples, berries, and teas. Flavones (apigenin and luteolin) are found in parsley, thyme, celery, and hot peppers. Soybeans and soy products as well as other legumes are high in isoflavones (daidzein, genistein, and glycitein).

When flavonoid molecules are attached to one or more sugar molecules they are called flavonoid glycosides. Those that are not attached to sugar molecules are called aglycones. The flavonoids we consume are all of the flavonoid glycoside type except for catechins and proanthocyanidins (Williamson, 2004). Most flavonoid glycosides must be metabolized by intestinal bacteria before being absorbed. Regardless of their form, flavonoids are rapidly eliminated from the body, thus studies linking them to specific health benefits must be considered carefully. In addition, the biological activity of metabolites is often not the same as those of the parent compound from which they were derived.

Contrary to popular belief, flavonoids are probably not very important to human health when it comes to their antioxidant activity (Frei and Higdon, 2003; Williams *et al.*, 2004; Lotito and Frei, 2006). Levels of other antioxidants such as vitamin C, uric acid, and glutathione are often 100–1000 times higher than flavonoids in the bloodstream. Additionally, the little flavonoids found in the blood are usually metabolites rather than the parent flavonoid. Similarly, it is not known whether or not flavonoids are effective as metal chelators in the body (Frei and Higdon, 2003).

Flavonoids are very important in cell signaling pathways (Williams *et al.*, 2004) and may help prevent cancer by: (i) enhancing the excretion of potential carcinogens (Kong *et al.*, 2001; Walle and Walle, 2002); (ii) preserving normal cell cycle regulation, limiting the production of mutations (Chen *et al.*, 2004; Wang *et al.*, 2004); (iii) inducing apoptosis in cancer cells (Kavanagh *et al.*, 2001; Sah *et al.*, 2004; Ramos, 2007); and (iv) inhibiting tumor invasion and the development of tumor blood vessel networks, known as angiogenesis (Kim, 2003; Bagli *et al.*, 2004).

Flavonoids may reduce the susceptibility to cardiovascular disease by: (i) decreasing inflammation (Cho *et al.*, 2003; Sakata *et al.*, 2003; O'Leary *et al.*, 2004); (ii) reducing the expression of adhesion molecules by vascular wall cells, one of the first steps in the development of atherosclerosis (Choi *et al.*, 2004; Ludwig *et al.*, 2004); (iii) maintaining vasodilation (Anter *et al.*, 2004); and (iv) decreasing platelet aggregation and the formation of blood clots (Bucki *et al.*, 2003; Deana *et al.*, 2003).

Soy isoflavones (phytoestrogens)

Soy isoflavones receive a discussion separate from other flavonoids due to their importance as an estrogen mimicking hormone. Since they are plant-derived compounds that exert estrogen-like activity, they are called phytoestrogens (Lampe, 2003). Soybeans are the primary legumes containing phytoestrogens. The phytoestrogens in soybeans are isoflavones attached to sugar molecules, isoflavone glycosides, which include genistin, daidzin, and glycitin. Once fermented or digested, the sugar molecule is removed leaving isoflavone aglycones, genistein, daidzein, and glycitein, respectively.

How the soy isoflavones are metabolized depends on the bacteria in the human intestine (Rowland *et al.*, 2003). For example some individuals metabolize daidzein to equol, a compound with greater estrogenic activity than daidzein, while others metabolize it to other less estrogenic compounds, all depending on intestinal flora (Setchell *et al.*, 2002). An individual gut health and bacterial profile can have great implications for their response to isoflavone ingestion.

Soy isoflavones mimic estrogen, a signaling molecule (hormone) responsible for many aspects of human function, especially heart, liver, bone, brain, and reproductive growth and development. Estrogen works by attaching to estrogen receptors in cells to form an estrogen–receptor complex which then interacts with DNA and alters the expression of estrogen-sensitive genes. Soy isoflavones can bind to estrogen receptors and mimic estrogen effects in some tissues and block estrogen-like effects in others. Soy isoflavones are of interest for their potential for: (i) reducing the risk of certain hormone-related cancers such as breast, uterine and prostate cancers; (ii) enhancing bone density; and (iii) improving blood lipid profiles, particularly cholesterol levels. Soy isoflavones and their metabolites also inhibit the synthesis and activity of some enzymes involved in estrogen metabolism and may alter the biological activity of both estrogens and androgens (Kao *et al.*, 1998; Whitehead *et al.*, 2002; Holzbeierlein *et al.*, 2005). Isoflavones may also inhibit cell proliferation and act as an antioxidant.

Consuming isoflavones may improve cardiovascular health by lowering serum LDL cholesterol (Sacks *et al.*, 2006) and decreasing arterial stiffness (Nestel *et al.*, 1997). While breast, uterine and prostate cancer rates often appear to be lower in populations consuming significant amounts of soy isoflavones (Goodman *et al.*, 1997; de Kleijn *et al.*, 2001; Horn-Ross *et al.*, 2003; Messina, 2003; van Erp-Baart *et al.*, 2003; Xu *et al.*, 2004), there is little direct evidence that consuming soy isoflavones reduces one's risk for these diseases (Murray *et al.*, 2003; Goetzl *et al.*, 2007). Similarly, populations consuming soy foods generally have a lower incidence of hip fracture, suggesting greater bone density in those individuals. However, it is not clear whether or not consumption of soy isoflavones improves one's bone density profile (Setchell and Lydeking-Olsen, 2003). Use of isoflavones rather than estrogen therapy to counter symptoms of menopause, particularly hot flashes, has not been particularly effective (Krebs *et al.*, 2004). However, women who produce equol from ingested isoflavones experienced a significant reduction in the occurrence of hot flashes (Jou *et al.*, 2008).

It is important to note that not all soy products contain isoflavones, therefore it is important when considering the possible benefits associated with soy consumption, that the products include isoflavones. Some soy products rich in isoflavones include soy protein concentrate prepared via an aqueous wash (as opposed to an ethanol wash), miso, tempeh, boiled soybeans, dry roasted soybeans, soymilk, and tofu. Many soy-based infant formulas are high in isoflavones (Setchell *et al.*, 1998). The isoflavone content of soy-based foods can vary considerably even within different lots of a single brand (Setchell *et al.*, 2001). Supplements containing isoflavones are not standardized and quality control is an issue with many available on the market (Setchell *et al.*, 2001; Chua *et al.*, 2004), thus care should be exerted when considering such products.

Garlic (organosulfur compounds)

Garlic (*A. sativum* L.) is an especially rich source of organosulfur compounds. These compounds are responsible for the strong flavor of garlic as well as its possible health benefits (Block, 1985). There are two main classes of organosulfur compounds in garlic: (i) gamma-glutamylcysteines; and (ii) cysteine sulfoxides. The gamma-glutamylcycsteine content is not altered by crushing, chopping or chewing raw garlic. Allylcysteine sulfoxide (alliin) is the predominant cysteine sulfoxide in garlic. When raw garlic is crushed, chopped or chewed the enzyme alliinase is released, converting alliin to allicin in 10–60 s (Block, 1985). Allicin then breaks down over time into a number of organosulfur compounds.

Allicin and allicin-derived compounds are rapidly metabolized by the human body (Lawson, 1998) perhaps into allyl methyl sulfide, which is readily detected in the breath. Gamma-glutamylcysteines are absorbed then hydrolyzed to *S*-allylcysteine and *S*-1-propenylcysteine (Jandke and Spiteller, 1987; de Rooij *et al*., 1996).

Garlic may be good for cardiovascular health. The consumption of garlic and derived organosulfur compounds appears to decrease the synthesis of cholesterol by liver cells (Gebhardt and Beck, 1996) by inhibiting enzymes responsible for its production (Liu and Yeh, 2002; Ferri *et al*., 2003). Organosulfur compounds from garlic also inhibit platelet aggregation in lab tests (Chan *et al*., 2002). Cardiovascular disease is at least in part caused by inflammation and garlic has been shown to inhibit two enzymes in the inflammatory response pathway (Ali *et al*., 2000), and to decrease the production of inflammatory signaling molecules *in vitro* (Keiss *et al*., 2003; Chang *et al*., 2005). Hydrogen sulfide may act as a vasodilator, thereby protecting heart health (Pryor *et al*., 2006; Lefer, 2007).

Organosulfur compounds may help the body prevent activation of the carcinogenic capacity of some toxins as well as rid itself of potentially carcinogenic toxins (Loizou and Cocker, 2001; Gurley *et al*., 2002; Chen *et al*., 2004; Fisher *et al*., 2007). They may also act as antioxidants and stimulate the production of the antioxidant glutathione (Banerjee *et al*., 2003). Organosulfur compounds also induce cell cycle arrest in cancer cell cultures (Knowles and Milner, 2001; Herman-Antosiewicz and Singh, 2004; Arunkumar *et al*., 2006) thereby preventing further unregulated cell division. These compounds also induce apoptosis in pre-cancerous and cancerous cells (Balasenthil *et al*., 2002) which are normally resistant to apoptosis (Wu *et al*., 2005). Sulfur compounds are also antibacterial and antimicrobial (Fenwick and Hanley, 1985; Harris *et al*., 2001).

The most potent source of these organosulfur compounds is chopped, crushed or chewed raw garlic. Cooking garlic inactivates the alliinase enzyme, thus if garlic must be cooked for consumption, allow it to stand for 10 min after chopping to allow the alliinase enzyme to convert alliin to allicin (Song and Milner, 2001).

Glucosinolates

Cruciferous vegetables are rich sources of sulfur-containing compounds called glucosinolates. Diets rich in cruciferous vegetables seen to reduce the risk of several types of cancer (Verhoeven *et al*., 1997).

INDOLE-3-CARBINOL Many cruciferous vegetables are rich sources of glucobrassicin (Kim and Milner, 2005). When these vegetables are chewed or chopped, indole-3-carbinol (I3C) is enzymatically produced from glucobrassicin by myrosinase, an enzyme that is normally isolated from glucobrassicin in the plant cell. When I3C hits the acidic environment of the stomach, a number of acid condensation products are formed including the dimer 3,3-diindolylmethane (DIM) and a cyclic trimer (CT) which are the substances responsible for biological reactions attributed to the consumption of cruciferous products. These acid condensation products are less likely to form if the vegetables are cooked since myrosinase is inactivated by heat and any I3C formed by intestinal bacteria is not likely to form condensates in the alkaline environment of the intestine.

The active components of I3C condensation seem to interfere with the transformation many potential carcinogens (pro-carcinogens) must undergo in the body before they become carcinogenic (Wallig *et al*., 1998; Bonnesen *et al*., 2001; Nho and Jeffery, 2001). In addition, I3C and DIM have been shown to induce apoptosis in cultured prostate (Chinni *et al*., 2001), breast (Hong *et al*., 2002; Howells *et al*., 2002; Rahman and Sarkar, 2005), pancreatic (Abdelrahim *et al*., 2006), and cervical cancer cells (Chen *et al*., 2004). They may also inhibit angiogenesis (Chang *et al*., 2005; Wu *et al*., 2005), required for tumor growth.

Rich sources of glucobrassicin include broccoli, Brussels sprouts, cabbage, cauliflower, collard greens, kale, mustard greens, radish, rutabaga, and turnips. Glucobrassicin is water soluble and myrosinase is inactivated by cooking. Both of these factors should be considered in the preparation of any cruciferous vegetable for consumption.

ISOTHIOCYANATES Isothiocyanates are hydrolysis breakdown products of glucosinolates, catalyzed by the enzyme myrosinase. Each glucosinolate has a different breakdown product and specific foods are often rich in one particular glucosinolate. For example broccoli is rich in glucoraphanin and sinigrin, precursors to the isothiocyanates sulforaphane and allyl isothiocyanate, respectively. Watercress is rich in gluconasturtiin which is converted to phenethyl isothiocyanate while garden cress is rich in glucotropaeolin, which yields benzyl isothiocyante. All of the isothiocyanates seem to have possible anti-carcinogenic properties.

Isothiocyanates appear to interfere with the transformation of pro-carcinogens into carcinogens (Hecht *et al*., 1995; Hecht, 2000; Conaway *et al*., 2002). Many isothiocyanates protect DNA from damage caused by carcinogens and ROS (Kensler and Talaway, 2004; Zhang, 2004; Fimognari and Hrelia, 2007). They also induce cell cycle arrest in cultured cells (Zhang, 2004) and induce apoptosis in cultured cancer cells (Hecht, 2004). Cell cycle arrest is an important stage of the normal cell cycle required for normal cell development. Isothiocyanates may also decrease the secretion of inflammatory signaling molecules (Heiss *et al*., 2001; Gerhauser *et al*., 2003). They are also fairly effective as an antibacterial agent towards *Helicobacter pylori*, a bacterial strain associated with an increased risk of gastric cancer (Fahey *et al*., 2002; Normark *et al*., 2003).

Nearly all of the cruciferous vegetables including bok choy, broccoli, broccoli sprouts, Brussels sprouts, cabbage, cauliflower, horseradish, kale, kohlrabi, mustard, radish, rutabaga, turnip, and watercress, are rich sources of the glucosinolate precursors of isothiocyanates (Fenwick *et al*., 1983). The amount of active isothiocyanates derived from each food depends on preparation and cooking methods.

Lignans (phytoestrogens)

Lignans are polyphenolic compounds found in many plants. Lignan precursors are found in many of the plant-based foods we eat and are converted by bacteria in the intestines into enterodiol and enterolactone (Lampe, 2003) where they are then absorbed into the bloodstream. The quantity of enterodiol and enterolactone derived from lignan precursors depends on the microflora in the gut. Both enterodiol and enterolactone mimic estrogen in the human body, thus their precursors are called phytoestrogens. Even though phytoestrogens from soy seem to have received the most attention as phytoestrogens, especially in the popular press, lignan precursor phytoestrogens are equally important, especially in Western diets. The lignan precursors identified in the average human diet include pinoresinol, lariciresinol, secoisolariciresinol, and matairesinol.

Enterodiol and enterolactone both have weak estrogenic activity in the human body including effects on bone, liver, heart, brain, and reproductive health similar to those of soy isoflavones. Lignans may alter endogenous estrogen activity (Brooks and Thompson, 2005) and can act as antioxidants. Diets that are rich in lignans are associated with a reduced risk of cardiovascular disease. Many of the foods containing significant lignans are also rich in other nutrients and phytonutrients which may also contribute to their cardioprotective status. There is little evidence of reduced risk of breast, uterine and prostate cancer with increased consumption of lignan-rich foods. This is not to convey that lignan-rich foods may not reduce the risk of these cancers, just that there is not sufficient evidence yet to make such a statement.

The best source of lignans is ground flax seed. Flaxseed oil is not a rich source of lignans; crushed whole seeds are the source for flax lignans. Other good sources include: (i) pumpkin, sunflower, poppy, and sesame seeds; (ii) rye, oats, and barley; (iii) bran from wheat, oat, and rye; (iv) beans; (v) berries; and (vi) vegetables.

Phytosterols

Phytosterols are plant-derived substances that mimic the structure and function of cholesterol. Plants produce many different sterols. Two main classes of phytosterols are recognized: (i) sterols which have a double bond in the sterol ring; and (ii) stanols which lack the double bond. The most abundant sterols in the human diet are sitosterol and campesterol. Stanols are also present in plants but at much lower levels.

Phytosterols inhibit the absorption of cholesterol in the intestines and reduce both total and LDL serum cholesterol, reducing the risk of cardiovascular disease (Katan *et al.*, 2003; Berger *et al.*, 2004). In addition, sitosterol has been shown to induce apoptosis in cultures of human prostate (von Holtz *et al.*, 1998), breast (Awad *et al.*, 2003), and colon (Choi *et al.*, 2003) cancer cells.

All plant-based foods contain phytosterols with the highest levels in unrefined plant oils including corn, soy, peanut, canola, nut, rice bran, and olive oils (Ostlund, 2002). Wheat germ, nuts, seeds, whole grains, and legumes are also very good sources of phytosterols (de Jong *et al.*, 2003). Many plant-based margarine spreads are enriched with plant sterols and stanols, providing a convenient way to supplement normal phytosterol intake.

Resveratrol

Resveratrol (3,4′,5-trihydroxystilbene) is a polyphenolic, fat-soluble molecule that occurs in two configurations, *cis* and *trans*, or as glucosides, often produced by some plants in response to stress (Aggarwal *et al.*, 2004). *Trans*-resveratrol is readily absorbed by humans when ingested, but it is rapidly metabolized and eliminated from the body (Walle *et al.*, 2004; Wenzel and Somoza, 2005). It is important to keep in mind that many of the studies touting the benefits of resveratrol have been performed with resveratrol at 10–100 times the level observed in human plasma immediately after consumption. Human tissues are exposed primarily to metabolites of resveratrol and not resveratrol itself. Very little is known about the metabolic activity of resveratrol metabolites.

While there are some claims that resveratrol is a powerful antioxidant, there is not much evidence that resveratrol is an important *in vivo* antioxidant (Bradamante *et al.*, 2004). Resveratrol may or may not influence estrogen metabolism (Tangkeangsirisin and Serrero, 2005) and may have anti-inflammatory properties (Pinto *et al.*, 1999; Donnelly *et al.*, 2004).

Resveratrol may help prevent cancer since it has been shown to: (i) increase the transformation of potentially carcinogenic chemicals to excretable forms in cultured cells (Jang *et al.*, 1997; Yang *et al.*, 2003); (ii) induce cell cycle arrest in cancer cell culture (Joe *et al.*, 2002); and (iii) inhibit proliferation of cancer cells in culture and induce apoptosis in them (Aggarwal *et al.*, 2004). Resveratrol has also been observed to inhibit angiogenesis *in vitro* (Igura *et al.*, 2001; Lin *et al.*, 2003; Chen and Tseng, 2007). Again, whether or not these observations can be made *in vivo* remains to be seen, especially considering the fact that resveratrol is quickly metabolized and many human tissues are never likely to be exposed to resveratrol levels used in many studies.

Resveratrol may reduce cardiovascular risk by: (i) reducing vascular cell adhesion (Ferrero *et al.*, 1998; Carluccio *et al.*, 2003), one of the earliest events in atherosclerosis; (ii) inhibiting the proliferation of vascular smooth muscle cells (Haider *et al.*, 2003; Mnjoyan and Fujise, 2003), another component of atherosclerosis; (iii) stimulating arterial relaxation (Wallerath *et al.*, 2002; Klinge *et al.*, 2005); and (iv) inhibiting platelet aggregation (Pace-Asciak *et al.*, 1995; Kirk *et al.*, 2000). Resveratrol is the component in red wine that many have suggested explain the "French paradox" of low coronary heart disease despite the consumption of high levels of saturated fat and extensive cigarette smoking. While some component of red wine or lifestyle associated with red-wine drinkers may account for at least some of the paradox, there is still much work that needs to be done to establish even limited causality.

Some studies with yeast, worms (*Caenorhabditis elegans*), fruit flies (*Drosophila melanogaster*) and fish (*Nothobranchius furzeri*) have indicated that resveratrol seems to extend the lifespan by a mechanism similar to caloric restriction (Wood *et al.*, 2004; Valenzano *et al.*, 2006).

Resveratrol is found in grapes (skins only), peanuts, blueberries, and cranberries (Sanders *et al.*, 2000; Rimando *et al.*, 2004).

Summary

The information available these days regarding what we should and should not eat to achieve and maintain our best health is staggering. All plant-based products that have been implicated in human health concerns could simply not be covered in a text such as this. Rather, a general summary of the most up-to-date information on the major nutrients, minerals, and phytonutrients was presented to stimulate interest in this exciting area of research. The takeaway message from this chapter is be careful what you eat, eat the freshest food you can possibly find (or better still, grow your own), and prepare it in such a way as to minimize the loss of nutrients from it. Eat the whole food, not just a part of it, it'll do you good.